

UNITED STATES DISTRICT COURT  
FOR THE DISTRICT OF MASSACHUSETTS

Civil Action  
No. 05-12237-WGY

\* \* \* \* \*  
\*  
AMGEN, INC., \*  
\*  
Plaintiff, \*  
\*  
v. \* MARKMAN HEARING  
\*  
F. HOFFMANN-LA ROCHE LTD, \*  
ROCHE DIAGNOSTICS GmbH and \*  
HOFFMANN-LA ROCHE, INC., \*  
\*  
Defendants. \*  
\*  
\* \* \* \* \*

BEFORE: The Honorable William G. Young,  
District Judge

APPEARANCES:

DUANE MORRIS LLP (By Michael R. Gottfried,  
Esq.), 470 Atlantic Avenue, Suite 500, Boston,  
Massachusetts 02210

- and -

DAY CASEBEER MADRID & BATCHELDER, LLP (By  
Lloyd R. Day, Jr., Esq., Linda A. Sasaki-Baxley,  
Esq. and Jonathan Loeb, Ph.D.) 20300 Stevens Creek  
Boulevard, Suite 400, Cupertino, California 95014

- and -

McDERMOTT WILL & EMERY (By William G.  
Gaede, III, Esq.), 3150 Porter Drive, Palo Alto,  
California 94304

- and -

WENDY A. WHITEFORD, ESQ., Of Counsel,  
Amgen, Inc., One Amgen Center Drive, Thousand  
Oaks, California 91320-1789, on behalf of the  
Plaintiff

1 Courthouse Way  
Boston, Massachusetts

April 17, 2007

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1 MR. DAY: That's correct. She will, she will  
 2 disagree. It has been many, many years since this invention  
 3 was made and nobody has yet found another way to do what Lin  
 4 did. So, in the case of a pioneering patent, then in a  
 5 pioneering patent claims are ordinarily entitled to a  
 6 broader scope. Amgen's claims are both broad and they are  
 7 narrow. They are not uniformly broad. The impulse to claim  
 8 broad is not unchecked. There is also a reason to claim  
 9 narrowly, and Amgen claims narrowly as well.  
 10 THE COURT: To, to avoid anticipation.  
 11 MR. DAY: Not to avoid anticipation. By claiming  
 12 narrowly, you can delimit what it is that an accused  
 13 embodiment must have in order to infringe. If you claim a  
 14 lot then the accused embodiment has to have all of those  
 15 things. And that, of course, is what's going on here.  
 16 Roche is trying to blow this claim out to include more and  
 17 more things in the meaning of human EPO in order to argue we  
 18 don't have this, we don't have that, we don't have that.  
 19 So you can claim both broadly and you can claim  
 20 narrowly. So the question is in the context of this claim,  
 21 '422, claim 1, where you have to look at the entire claim  
 22 language, in the context of this claim what does the claim  
 23 term human erythropoietin mean. That's the issue for the  
 24 Court.  
 25 I have some binders, too, that I would like to hand

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1 up to the Court, if I may. Could you give them some to  
 2 opposing counsel.  
 3 Okay. And these are simply the slides that I will  
 4 be talking about.  
 5 The first thing that I want to illustrate for the  
 6 Court is the difference in the claim construction that Roche  
 7 proposes and Amgen proposes.  
 8 Amgen's construction is a protein having the amino  
 9 acid sequence of human EPO, such as the amino acid sequence  
 10 of EPO isolated from human urine.  
 11 Now, the question for the Court in considering  
 12 that, is that consistent with the other claim language, is  
 13 that consistent with the specification, is that consistent  
 14 with the prosecution history, as to what that term human  
 15 erythropoietin means in the context of the entire claim,  
 16 '422, claim 1.  
 17 Roche's construction differs. And I've highlighted  
 18 on the right what is importantly different about Roche's  
 19 construction. First of all, they say it's not a protein.  
 20 They say it's a glycoprotein. That means that it must have  
 21 glycosylation. It has the amino acid sequence of  
 22 erythropoietin isolated from human urine. So they agree  
 23 with us about the amino acid sequence. This argument you  
 24 just heard from Ms. Ben-Ami, which was not in their papers,  
 25 was made for the first time this morning on oral argument,

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1 is predicated on an expert report not before the Court, is  
 2 inconsistent with what they acknowledge. This --  
 3 THE COURT: Well, we're trying to get at the best  
 4 construction.  
 5 MR. DAY: I understand.  
 6 THE COURT: You do have, you do have a problem with  
 7 that position 166. I mean, her argument does resonate.  
 8 MR. DAY: No, we don't have a problem with that.  
 9 THE COURT: All right, tell me why.  
 10 MR. DAY: And the reason we don't have -- because  
 11 these are -- this is human erythropoietin purified from  
 12 mammalian cells grown in culture. And the cells cleave off  
 13 the 166 amino acids. And Lin produced and made and had in  
 14 his possession an EPO that was produced by mammalian cells  
 15 grown in culture. So he possessed a 165 species of human  
 16 erythropoietin when he filed his application.  
 17 THE COURT: But he didn't know it.  
 18 MR. DAY: Oh, did he, did he know it?  
 19 THE COURT: Well --  
 20 MR. DAY: He possessed it.  
 21 THE COURT: Well, let's just go back.  
 22 MR. DAY: But, no, your Honor, this is an  
 23 important point.  
 24 THE COURT: Go ahead.  
 25 MR. DAY: You asked a very good question and it's

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1 an important point. But it's irrelevant. It's irrelevant  
 2 whether he knew it. What is relevant is whether he  
 3 possessed it and he taught others how to get the same thing.  
 4 That it was later discovered to be 165 and not 166, not what  
 5 he had deduced it to be, is irrelevant.  
 6 THE COURT: Well, I understand that's your  
 7 position.  
 8 MR. DAY: Okay. The second thing is, that Roche  
 9 seeks to add to this claim is having the structure that  
 10 would be produced in mammalian cells as of the invention  
 11 date.  
 12 Now, let me ask you to turn the page and I'll  
 13 illustrate for you what the difference is first of all  
 14 between these two constructions.  
 15 On the left you have a picture of Amgen's  
 16 construction. Amgen construes human erythropoietin as  
 17 referring to the amino acid sequence of human erythropoietin  
 18 as isolated from urine. Roche construes human  
 19 erythropoietin as referring not only to the amino acid  
 20 sequence but also to all of the glycosylation that's  
 21 attached to that sequence by the cells. And they say there  
 22 is one structure. They call it the structure. And so  
 23 there's only one such structure.  
 24 Now, what's wrong with Roche's construction? Why  
 25 is it inconsistent with the other claims, with the

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1 specification, with the prosecution history?  
 2 Okay, the first thing is they would require that  
 3 the human erythropoietin be glycosylated. That, that  
 4 structure is not provided by the term human erythropoietin  
 5 as the Court will see. That structure is provided by the  
 6 fact that it's produced in mammalian cells. And that's why  
 7 the source limitation in this claim is so important. As  
 8 Roche's own expert, Dr. Kadesh, in the declaration that  
 9 Roche submitted in support of their claim construction,  
 10 describes in detail glycosylation is a cell by cell  
 11 dependent function. The cell determines what glycosylation  
 12 goes on a protein. The glycosylation that will be put on a  
 13 protein varies by cell species. Different species of cells  
 14 will glycosylate proteins differently. That's all laid out  
 15 very clearly by Dr. Kadesh. This was well understood by  
 16 those of ordinary skill in the art. It's the fact that the  
 17 protein is produced in a mammalian cell that gives it  
 18 certain types of glycosylation. A certain structure beyond  
 19 the amino acid sequence.  
 20 Roche then says it must have the identical  
 21 glycosylation as originally attached by the cell. So, in  
 22 other words, there can't be any post-expression changes in  
 23 the molecule. That's the other thing they're trying to do.  
 24 They're trying to narrow the scope of this claim so that  
 25 human erythropoietin, that amino acid sequence, which is

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1 then glycosylated by the cell, can't be modified in any way,  
 2 has to be exactly as produced by the cell.  
 3 And then what they're trying to do, then what they  
 4 say is that it must be produced in cells that were available  
 5 as of 1983. In other words, any mammalian cell that was  
 6 adapted for growth in culture after 1983 couldn't be used.  
 7 Couldn't be used to make this product. And if it was, if it  
 8 was it wouldn't infringe according to that.  
 9 And then they say that there has to be no  
 10 alteration in the secreted glycoprotein due to  
 11 post-expression modification. It's a point I made earlier.  
 12 Now, what's wrong with all that? Why is all of  
 13 that not correct as a matter of law and as a matter of claim  
 14 construction? Claim construction. Construing what this  
 15 claim means.  
 16 Well, the first thing is that their construction  
 17 would be inconsistent with Lin's other claims. When Lin  
 18 claimed a human erythropoietin that was a glycoprotein he  
 19 said so expressly. Take a look at '933, claim 4 where he  
 20 refers to human erythropoietin glycoprotein. Roche's  
 21 construction would render the word glycoprotein irrelevant.  
 22 And for that reason it is erroneous as a matter of law.  
 23 Every word in a claim must be given meaning. Where related  
 24 claims from a single application use the same terms they  
 25 should be given consistent meanings. The use of human

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1 erythropoietin glycoprotein shows that when Lin is referring  
 2 to human erythropoietin he is saying nothing about whether  
 3 it's glycosylated or not.  
 4 The second thing is that Lin's specification makes  
 5 clear that the polypeptides of the invention may or may not  
 6 be glycosylated. There's no necessary requirement. The  
 7 only thing that requires in '422, claim 1 the human  
 8 erythropoietin to be glycosylated is the fact that it is  
 9 produced in mammalian cells and purified from mammalian  
 10 cells grown in culture. And that step, that source from  
 11 which the EPO's obtained imparts a structure in addition to  
 12 the amino acid sequence of human erythropoietin.  
 13 The last thing in the specification that is  
 14 critical to understand is that when Lin took his DNA, he did  
 15 not express it only in mammalian cells. As described in  
 16 Examples 11 and 12 of the patent he also expressed it in  
 17 E.coli. E.coli does not glycosylate. There is no  
 18 glycosylation on human erythropoietin. And yet Lin still  
 19 describes that as human erythropoietin. The human  
 20 erythropoietin that Lin is talking about in his patent is  
 21 the amino acid sequence that is produced by the DNA that  
 22 encodes human erythropoietin. And when that DNA is placed  
 23 into a mammalian cell and the cells are produced in  
 24 mammalian cell culture, the cells cleave off the 166 and  
 25 they may or may not glycosylate the cell, the protein.

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1 This was all brought out in the prosecution history  
 2 specifically with reference to the amendment of an allowance  
 3 of '422, claim 1. In Exhibit 8 of Amgen's original claim  
 4 submission, claim brief, we attached the prosecution history  
 5 for this claim. And in that prosecution history Amgen  
 6 explained what human erythropoietin means. It defined the  
 7 term. Human erythropoietin is understood to include any  
 8 polypeptide having amino acid sequence of EPO isolated from  
 9 human urine and may be produced in human cells or other  
 10 mammalian cells.  
 11 And so, what does that necessarily mean? That  
 12 language means that human EPO includes any, any polypeptide  
 13 having the amino acid sequence of EPO. If a polypeptide has  
 14 the amino acid sequence of EPO it is by definition human  
 15 erythropoietin as the claim term reads.  
 16 Having is open-ended. It's a term of art in patent  
 17 law, which means an open-ended construct. It's not limited.  
 18 And so it doesn't exclude additional elements. There's no  
 19 reference to glycosylation in the prosecution history, let  
 20 alone any specific glycosylation, any statement that it must  
 21 have the structure. And there's no limitation on the  
 22 mammalian cells that can be used to produce it.  
 23 THE COURT: All right, I think I have it.  
 24 Brief rebuttal, Ms. Ben-Ami.  
 25 MS. BEN-AMI: Well, I have an extensive rebuttal.

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<p>1 What if we modified yours, I'm still working with                  2 Amgen's, but called it a glycoprotein. Is that a problem?                  3 Isn't that -- that's the, that's the most accurate and we're                  4 going to hear a lot about glycosylation. So it would seem                  5 to me that that would be both accurate and fair.                  6 MR. DAY: Your Honor, I think it would be -- I                  7 don't think it's a problem. I think it would be an                  8 erroneous claim construction. And I think it would be                  9 erroneous for the reasons I cited. Because the claims                  10 differentiation -- and your Honor may have noticed when,                  11 when Ms. Ben-Ami flashed that specification up, she                  12 didn't point to the fact that it denominates the EPO as                  13 hEPO. H stands for human.                  14 THE COURT: Well, no, she said it was a different                  15 --                  16 MR. DAY: No. No. H, little h stands for human.                  17 Amgen identified the EPO that's being produced in this                  18 E.coli as human EPO, and then it made a number of                  19 alterations to the amino acid sequence. It made a number of                  20 analogs to that human sequence and said, well, we take this                  21 out, we put this in, we take this out, we put this in.                  22 These are all the changes from the human EPO. It would be                  23 wrong as a matter of claim construction, your Honor, because                  24 you would be reading out of the definition of human EPO                  25 human EPO produced in E.coli cells. It would be wrong as a</p>	<p>1 Roche's contention that the limitation cannot define the                  2 structure of the claim product. And let me --                  3 THE COURT: Well, I'm not, I'm not proposing that.                  4 What I'm proposing is the Court's language.                  5 MR. DAY: That's fine.                  6 THE COURT: Purified from mammalian cells grown in                  7 culture means obtained in substantially homogenous form from                  8 mammalian cells, using the word "from" in the sense that it                  9 originates in mammalian cells, without limitation to,                  10 without limitation to it only taking it directly out of the                  11 interior of the cells which have been grown in the in vitro                  12 culture.                  13 MR. DAY: And that's fine. And we merely offered                  14 an alternative --                  15 THE COURT: All right.                  16 MR. DAY: -- clarifying statement to that.                  17 THE COURT: Then we'll stick with my language for                  18 now. But that's without prejudice to revisiting it if I                  19 think I can explain it to the jury better.                  20 Then, next, a non-naturally occurring glycoprotein                  21 product of the expression, et cetera. Now, here it seems                  22 that Amgen's proposal makes the most sense. And of course                  23 we're bound by the Federal Circuit. Non-naturally occurring                  24 means not occurring in nature, but that makes perfect sense                  25 and we'll follow it. And that's, that's in the Amgen</p>
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<p>1 matter of claim construction because you would be construing                  2 human EPO in a way that renders human erythropoietin                  3 glycoproteins redundant and unnecessary. So as a matter of                  4 claim construction you would be making a mistake. That's                  5 Amgen's position.                  6 THE COURT: Thank you.                  7 Here's what we're going to do. At this stage and                  8 for these purposes we're going to adopt Amgen's proposed                  9 construction. I'll reflect on whether I'll add the                  10 glycoprotein before the word, substitute it for protein.                  11 Turning now to purified from mammalian cells grown                  12 in culture. Now, Roche's proposed construction comes                  13 straight out of this Court's own analysis of this subject.                  14 And why ought I not stick with it? I've analyzed this and I                  15 see -- so I'll hear from you, Mr. Day. What's the matter                  16 with that?                  17 MR. DAY: Okay. First of all, I don't think                  18 Roche's construction comes right out of the Court's                  19 construction. I will certainly grant you that the first                  20 part of their construction is a verbatim recitation and                  21 Amgen offered an alternative, if this is to be a jury trial,                  22 Amgen offered an alternative statement of that which I think                  23 says the same thing.                  24 The difference between the parties in claim                  25 construction here is what I have highlighted. And that is</p>	<p>1 proposal.                  2 What's the matter with that, Ms. Ben-Ami? They're                  3 a glycoprotein product not occurring in nature that is                  4 expressed in a mammalian cell from a DNA sequence that does                  5 not originate in the genome of the host and comprises a DNA                  6 sequence encoding human erythropoietin.                  7 MS. BEN-AMI: Well, first of all, your Honor, I                  8 think non-naturally occurring is a separate element. And so                  9 I do think that's important.                  10 THE COURT: Well, non-naturally occurring, aren't                  11 we bound by the Federal Circuit? It means not occurring in                  12 nature.                  13 MS. BEN-AMI: I agree with that, but that's a                  14 separate element than glycoprotein product of the expression                  15 of a mammalian cell. That's all I'm saying. In other                  16 words, you'd have to break down the claim. And I think                  17 non-naturally occurring is one element. Glycoprotein                  18 product of the expression of mammalian host cell, et cetera,                  19 is a different product. Element. That's my first                  20 fundamental difference.                  21 THE COURT: Well, all right. But in trying to                  22 explain it to the jury I say, I come to this and I say, now,                  23 non-naturally occurring, what that means is it does not                  24 occur in nature. Now --                  25 MS. BEN-AMI: That means --</p>