

EXHIBIT H

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Exhibits: 1-8

Volume 1, Pages 1-281

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS
Civil Action No. 05 Civ. 12237 WGY

Certified Copy

AMGEN INC.

Plaintiff

vs.

F. HOFFMANN-LA ROCHE LTD.,
ROCHE DIAGNOSTICS GmbH, and
HOFFMANN-LA ROCHE INC.

Defendants

VIDEOTAPED DEPOSITION OF
EDWARD E. HARLOW, JR., Ph.D.

Wednesday, June 20, 2007, 8:52 a.m.

] Duane Morris LLP
470 Atlantic Avenue
Boston, Massachusetts

** TRANSCRIPT DESIGNATED CONFIDENTIAL ***

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1 modified glycoprotein? . . .

2 MR. BROMBERG: Objection.

3 A. Try the question again -- now I've lost
4 the train of thought.

5 Q. Would one of skill in the art as of
6 December 1983 have had a reasonable expectation that
7 with a DNA sequence in hand he or she could produce
8 a properly modified, post-translationally modified
9 secreted glycoprotein?

10 A. It depends.

11 Q. You know I'm going to follow up. What
12 does it depend on?

13 A. I won't be mean. It depends on the
14 protein under study.

15 Q. As of December 1983 is it your opinion
16 that one of skill in the art had a reasonable
17 expectation of success in producing a recombinant
18 erythropoietin that had undergone proper
19 post-translational modification to achieve an in
20 vivo biologically active protein?

21 A. With the available clone, yes.

22 Q. Now, among the post-translational
23 modifications that you've identified, I'd like to
24 focus for a moment on glycosylation. So can you
25 describe briefly what "glycosylation" means?

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1 A. Addition of various sugar moieties to a
2 polypeptide -- in this case, anyway, to a
3 polypeptide.

4 Q. There are a number of different kinds of
5 glycosylation; correct?

6 A. There are.

7 Q. And different types of host cells
8 produce different types of sugars?

9 A. Yes.

10 Q. And different types of host cells
11 produce different sugars with different branch
12 structures?

13 A. Correct.

14 Q. Can small changes in glycosylation
15 produce significant changes in a protein's
16 biological activity?

17 A. I think that is known, yes.

18 Q. Was it known in 1983?

19 A. Yes.

20 Q. Different proteins require different
21 kinds of glycosylation?

22 A. Yes.

23 Q. And some glycoproteins do not require
24 glycosylation in order to be biologically active in
25 vivo; correct?

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1 A. That's my understanding.

2 Q. Was that known in 1983?

3 A. That I don't know.

4 Q. In addition to glycosylation, there are
5 other post-translational modifications that were
6 known in 1983; correct?

7 A. There were. Yes, there were.

8 Q. Do different cells in different cell
9 lines affect post-translational modifications
10 differently?

11 A. Yes.

12 Q. And do different proteins require
13 different post-translational modifications?

14 A. Yes.

15 Q. Can different post-translational
16 modifications lead to different species of any given
17 protein?

18 A. Define "species."

19 Q. Okay. Can different post-translational
20 modifications affect the in vivo biological activity
21 of any given protein?

22 MR. BROMBERG: Objection.

23 A. You've gotten more complicated. Try it
24 a different way, please.

25 Q. Can differences in the

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1 correct?

2 A. That's my understanding, yes.

3 Q. And so the fact that you were able to
4 produce in a particular mammalian host cell another
5 glycoprotein that does not require glycosylation for
6 in vivo activity would not provide one of ordinary
7 skill in the art a reasonable expectation that that
8 particular host cell would have produced functional
9 glycosylation of a human protein, would it?

10 MR. BROMBERG: Objection.

11 A. I don't agree with that logic.

12 Q. Why not?

13 A. You've posed a situation that doesn't
14 lead to an outcome that's required.

15 Q. Well, if a protein does not require
16 glycosylation for in vivo activity, the fact that
17 you see in vivo activity even of a glycosylated
18 protein can't provide you with any certainty that
19 the host employed produces functional or correct
20 glycosylation, can it?

21 A. That part's true, yes.

22 Q. Okay. And so if what had been shown as
23 of 1983, December 1983, is that a protein that did
24 not require glycosylation for in vivo activity was
25 produced using a particular host cell, one of

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1 ordinary skill in the art would not have had a
2 reasonable expectation based on that fact that the
3 particular host cell employed could produce EPO with
4 a functional glycosylation, would they have?

5 A. I think that is true.

6 Q. Okay. So, to put it into simpler terms,
7 by December 1983 you cite to various examples where
8 CHO cells had been used to produce recombinant
9 glycoproteins; correct?

10 A. Correct.

11 Q. And in fact, I think it's at Paragraph
12 25 of your report, you say, "CHO cells were well
13 known by 1983 to express foreign glycoproteins
14 having their known in vivo biological activity."

15 A. What paragraph are we on?

16 Q. It's Page 11, Paragraph 25. Do you see
17 that?

18 A. Yes.

19 Q. So first of all, here you use the term
20 "in vivo biological activity"; correct?

21 A. Yes.

22 Q. What did you mean by it in this
23 sentence?

24 A. The series of different responses that
25 are often referred to as "in vivo." We talked

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1 recombinant glycoprotein has biological activity --

2 A. Okay.

3 Q. -- and it can have biological activity
4 even without glycosylation --

5 A. Yes.

6 Q. -- does the demonstration of biological
7 activity provide any certainty that the
8 glycosylation imparted on that particular
9 glycoprotein is functional?

10 MR. BROMBERG: Objection.

11 A. So the glycoprotein is glycosylated, and
12 the glycosylation isn't needed. Does that mean that
13 the protein --

14 Q. Does that tell you anything about the
15 function of the glycosylation, whether it's
16 functional?

17 A. You know, it depends. It's a
18 meaningless combination of things in the logic.

19 Q. -- Okay, let me give you a specific
20 example. Alpha interferon --

21 A. Okay.

22 Q. -- is a known glycoprotein.

23 A. Good.

24 Q. You produce it in a CHO cell, you get
25 glycosylated alpha interferon.

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1 A. Uh-huh.

2 Q. If you had unglycosylated alpha
3 interferon and you stick unglycosylated alpha
4 interferon into a body, you get in vivo biological
5 activity.

6 A. Okay.

7 Q. If you stick glycosylated CHO-produced
8 recombinant alpha interferon into a body, you get in
9 vivo activity.

10 A. Yep.

11 Q. Does the demonstration of in vivo
12 activity for recombinant alpha interferon tell you
13 anything about whether the CHO cell can impact
14 functional glycosylation on a recombinant human
15 protein?

16 A. It says nothing about glycosylation.

17 Q. It doesn't tell you one way or another
18 whether the host cell employed can make functional
19 glycosylation; correct?

20 A. That's correct.

21 Q. Now, by December of 1983 it was known
22 that EPO was a heavily glycosylated protein; is that
23 correct?

24 A. That's my understanding.

25 Q. In fact, by that date it was known that