

**UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS**

AMGEN, INC.,)	
)	
Plaintiff,)	
)	
v.)	Civil Action No. 05 CV 12237 WGY
)	
F. HOFFMANN-LAROCHE LTD.,)	
a Swiss Company, ROCHE DIAGNOSTICS)	
GMBH, a German Company, and)	
HOFFMANN LAROCHE INC., a New)	
Jersey Corporation,)	
)	
Defendants.)	

**BRIEF IN SUPPORT OF PLAINTIFF AMGEN’S MOTION *IN LIMINE* NO. 9:
EXCLUDE THE TESTIMONY OF ROCHE’S EXPERTS KADESCH AND LOWE
REGARDING PROTEIN SEQUENCING DUE TO THEIR LACK OF EXPERTISE**

I. INTRODUCTION

Amgen moves to exclude the testimony of Roche's proposed protein experts, Dr. Thomas Kadesch and Dr. John Lowe, regarding the obviousness of obtaining the entire protein sequence of erythropoietin ("EPO") or the sequence of fragments of EPO. Neither Dr. Kadesch nor Dr. Lowe has the expertise required by FRE 702 to explain the protein sequencing art. Drs. Kadesch and Lowe are both scientists, but neither admittedly has enough familiarity or understanding with the complicated subject of protein sequencing to help the jury understand the process and its nuances. Due to their lack of expertise, neither should be allowed to testify about protein sequencing. Any testimony concerning protein sequencing provided by Drs. Kadesch and Lowe is mere speculation that could serve to mislead the jury, and certainly is not helpful to the jury.

II. FACTUAL BACKGROUND

A. **Drs. Kadesch and Lowe did not offer their own opinions on protein sequencing but merely incorporated and adopted opinions of Dr. Fromm**

On April 6, 2007, Dr. Michael Fromm submitted an expert report opining on the alleged obviousness of the asserted claims using certain complex protein sequencing and gene synthesis techniques. He opined, erroneously relying in part upon a later-published 1986 publication by Dr. Lai,¹ that a person of ordinary skill in the art with access to human urinary EPO prior to October of 1983 could have purified the urinary EPO for sequencing, obtained the EPO protein sequence, synthesized the gene, and obtain a biologically active EPO by expressing the gene in mammalian cells. On June 13, 2007, Dr. Kadesch submitted a second supplemental expert report in which he agreed with Dr. Fromm's opinions, and in a conclusory fashion, stated that one of

¹ Amgen has separately moved to exclude Roche's reliance on the 1986 Lai publication since it is not prior art for purposes of this case. *See* Amgen's Motion *In Limine* No. 11: Exclude the 1986 Lai et al. Paper [Roche Trial Exh. 501] Because it is Not Prior Art.

ordinary skill in the art could have obtained the complete and accurate sequence of EPO by October of 1983 if one had sufficient quantities of human urinary EPO.

Like Dr. Kadesch, Dr. Lowe also submitted a supplemental expert report on June 13, 2007 in which he incorporated and agreed with Dr. Fromm's opinions on protein sequencing. During his deposition, Dr. Lowe did not even remember that he agreed with Dr. Fromm's opinion and admitted that he was not prepared to opine on the topic.

Q: You're not planning on offering any opinion that it would have been obvious to produce recombinant EPO by sequencing the entire amino acid sequence of urinary EPO synthesizing a DNA encoding that amino acid sequence, attaching a synthetic leader sequence or signaling sequence to that DNA and then expressing that combination of inter-recombinant cell, are you?

A: I think that this report, and again, I'd have to read it in its entirety to make sure I haven't proposed that opinion, but my recollection is that that's not something that I'm going to offer an opinion on.²

B. Drs. Kadesch and Lowe have no expertise in protein sequencing

Drs. Kadesch and Lowe have no specialized knowledge, skill, experience, training or education in protein sequencing. While Dr. Lowe published two papers with protein sequencing information, he does not remember doing any sequencing work himself.

1. Dr. Kadesch has no knowledge, skill, education, training or experience in protein sequencing

None of the publications in Dr. Kadesch's CV show evidence of any protein sequencing work. Dr. Kadesch admits to his lack of skill and experience with protein sequencing in his deposition. According to Dr. Kadesch, his knowledge of the art was obtained from reading the literature:

Q: Dr. Kadesch, in 1983 you were not –you were not skilled in the art of protein sequencing, were you?

A: That's correct.

² Dr. Lowe Depo. Tr. (6/25/2007) at 204.

Q: And today, you're not a recognized expert in the art of protein sequencing, correct?

A: That's correct.

Q: You've never attempted to determine the complete sequence of a protein, have you?

A: That's correct.

Q: And you've never used a spinning cup type sequencer, correct?

A: That's correct.

Q: And you've not used a gas phase sequencer, correct?

A: That's correct.

Q: You haven't performed solid phase protein sequencing, correct?

A: That's correct.

Q: And you haven't performed normal Edman degradation protein-type sequencing?

A: That's correct.

Q: And the knowledge you have of protein sequencing is derived from reading the literature?

A: That's correct.³

2. Dr. Lowe has no knowledge, skill, education, training or experience in protein sequencing

Dr. Lowe's CV shows no specialized education or training in protein sequencing. While he has two papers that include information obtained through protein sequencing by Edman degradation,⁴ he admits that he did not do the sequencing work himself.

Q: What did you do to characterize the proteins?

A: I isolated them, I purified them, I ran them on gels. In one case, I sequenced them.

Q: What machine did you use?

A: My recollection is that it was a Beckman spinning cup sequenator.

³ Dr. Kadesch Depo. Tr. (6/21/2007) at 195-197.

⁴ Lowe et al., "Expression of a Mammalian Fatty Acid-binding Protein in Escherichia coli," *J. Biol. Chem.* (1984) 259(20):12696-12704; Lowe et al., "Expression of Rat Intestinal Fatty Acid-binding Protein in Escherichia coli," *J. Biol. Chem.* (1987) 262(12): 5931-5937.

Q: Is that the first time you had used a spinning cup sequenator?

A: Yes.

Q: Who taught you how to use it?

A: I didn't use it.

Q: Pardon?

A: I did not use the sequenator myself.⁵

III. LEGAL STANDARD

The Supreme Court's decision in *Daubert* interprets FRE 702 and "establishes the duty of a trial judge to play the role of a gatekeeper" when it comes to expert testimony.⁶ The proponent of expert testimony has the burden of showing by a preponderance of the evidence that its expert's testimony satisfies the requirements of admissibility.⁷ To be qualified to testify as an expert, "a witness needs to have 'knowledge, skill, experience, training, or education,' Fed. R. Evid. 702, 'in the specific subject for which his testimony is offered.'"⁸ In other words, the admission of expert testimony "is premised on an assumption that the expert's opinion will have a reliable basis in the knowledge and experience of his discipline."⁹

The *Whiting* decision explains the difference between general and specific knowledge. "[J]ust as a lawyer is not by general education and experience qualified to give an expert opinion

⁵ Dr. Lowe Depo. Tr. (6/25/2007)at 19-20.

⁶ See *Whiting v. Boston Edison Co.*, 891 F.Supp. 12, 24 (D. Mass. 1995); *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993).

⁷ *Daubert*, 509 U.S. at 592 n.10.

⁸ *Sutera v. Perrier Grp. of Amer. Inc.*, 986 F. Supp. 655, 661 (D. Mass. 1997), citing *Whiting*, 891 F.Supp. at 24.

⁹ *Daubert*, 509 U.S. at 592.

on every subject of the law, so too a scientist or medical doctor is not presumed to have expert knowledge about every conceivable scientific principle or disease.”¹⁰

IV. ARGUMENT

Due to their lack of expertise, Drs. Kadesch and Lowe cannot assist the jury in understanding any of the nuances of the protein sequencing art. An expert testifying about the art of protein sequencing must have adequate expertise in the art to explain something to the jury beyond what the jury can understand from a review of the available materials. Neither Drs. Kadesch nor Lowe has familiarity with the art to establish such expertise, thus both of them should be excluded as experts under FRE 702.

Dr. Kadesch admitted in his deposition that he has no experience with sequencing proteins.¹¹ As he admitted during his deposition, his only familiarity with protein sequencing comes from reading scientific literature.¹² He cannot offer any competent opinion regarding the relatively ease or difficulty of protein sequencing at the time of Dr. Lin’s inventions. His unqualified, inexperienced opinions will serve to confuse the jury about the actual state of the art at that time.

Dr. Lowe admitted in his deposition that the theory of obviousness that he lifted from Dr. Fromm’s report was not his own and that he was not prepared to offer an opinion on the topic. His opinion on the topic was clearly assigned to him, and was the result of neither his deliberation and independent consideration nor his expertise. Since Dr. Lowe is not prepared to

¹⁰ *Whiting*, 891 F. Supp. at 24.

¹¹ Dr. Kadesch Depo. Tr. (6/21/2007) at 195-197.

¹² *Id.*

opine on protein sequencing, this Court should prohibit Roche from presenting testimony from Dr. Lowe on the subject at trial.

Like Dr. Kadesch, Dr. Lowe is not qualified to opine about protein sequencing. Dr. Lowe's CV shows no specialized education or training in protein sequencing. Although Dr. Lowe did publish two papers that discuss protein sequencing, he admitted that he did not actually do any of the protein sequencing work himself. Any testimony Dr. Lowe may offer on protein sequencing will mislead and/or confuse the jury about the actual facts of the art.

Drs. Kadesch and Lowe are not competent to offer expert testimony with regard to protein sequencing and should not be allowed to parrot the opinions of Dr. Fromm at trial. Their testimony about protein sequencing would be entirely based on their own interpretation of the literature, or even just a recitation of the literature, so any testimony they offer on the subject would be of no help to the jury.

V. CONCLUSION

For the foregoing reasons, Amgen requests that this Court exclude any protein sequencing testimony of Roche's experts Drs. Kadesch and Lowe.

Respectfully Submitted,

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CERTIFICATE OF SERVICE

I hereby certify that this document, filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of electronic filing and paper copies will be sent to those indicated as non-registered participants on August 20, 2007.

/s/ Michael R. Gottfried
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