UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, v. F. HOFFMANN-LA ROCHE LTD, ROCHE DIAGNOSTICS GmbH, and HOFFMANN-LA ROCHE INC. Defendants.	CIVIL ACTION No.: 05-CV-12237WGY **[REDACTED VERSION]**

APPENDIX B, EXHIBIT 3 TO DEFENDANTS' MEMORANDUM IN SUPPORT OF ITS MOTION TO COMPEL PRODUCTION OF DOCUMENTS IMPROPERLY WITHHELD ON GROUNDS OF PRIVILEGE

The filing of this confidential exhibit has been deferred pursuant to the provisions of the Court's Order entered on 2/7/07 [274].

Dated: March 27, 2007
Boston, Massachusetts

Respectfully submitted,
F. HOFFMANN-LA ROCHE LTD,
ROCHE DIAGNOSTICS GMBH, and
HOFFMANN-LA ROCHE INC.

By their attorneys,
/s/ Robert L. Kann

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UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, v. F. HOFFMANN-LA ROCHE LTD, ROCHE DIAGNOSTICS GmbH, and HOFFMANN-LA ROCHE INC. Defendants.	CIVIL ACTION No.: 05-CV-12237WGY

APPENDIX B, EXHIBIT 4 TO DEFENDANTS' MEMORANDUM IN SUPPORT OF ITS MOTION TO COMPEL PRODUCTION OF DOCUMENTS IMPROPERLY WITHHELD ON GROUNDS OF PRIVILEGE

Dated: March 27, 2007
Boston, Massachusetts

Respectfully submitted,
F. HOFFMANN-LA ROCHE LTD,
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EXHIBIT 4

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IN THE HIGH COURT OF JUSTICE
CHANCERY DIVISION
PATENTS COURT

HC 1999 Nos. 02916/02917
HC 1999 No. 03241

Royal Courts of Justice
Tuesday, 5th February 2002

Before:

MR. JUSTICE NEUBERGER

- - - - - - -

HOECHST MARION ROUSSEL
Claimants/Petitioners

v.

KIRIN-AMGEN INC. & OTHERS
Defendants/Patentees

- - - - - - -

(Computer-aided transcript of the Stenograph Notes of Marten Walsh Cherer Limited, Midway House 27/29 Cursitor Street, London EC4A 1LT Telephone Number 0207 405 5010. Fax Number 0207 405 5026)

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MR. ANTONY WATSON QC and MR. ANDREW WAUGH QC and MR. TOM HINCHLIFFE (instructed by Messrs. Taylor Joynson Garrett) appeared on behalf of Kirin-Amgen.

MR. DAVID KITCHIN QC and MR. RICHARD MEADE and MISS LINDSAY LANE (instructed by Messrs. Bird & Bird) appeared on behalf of the TKT parties.

- - - - - - -

PROCEEDINGS
DAY 2

- - - - - - -

MR. WATSON: May I call Mr. Borun.

MR. MICHAEL FRANCIS BORUN, AFFIRMED

EXAMINED BY MR. WATSON

Q. If you can find, or more likely it will be given to you, core bundle 1. If you would go to tab 7, there is a witness statement signed by you. Do you see that?

A. Yes, I do.

Q. I understand you have two corrections and they are non-controversial, so I am going to lead. You would like to change the name of your firm in paragraph 1. Is that correct?

A. Yes, that is correct.

Q. What is the change"?

A. The deletion of "O'Toole and Murray", so that the composite firm name now is "Marthall, Gerstein & Borun".

Q. And in paragraph 29 there is an erroneous date.

A. That is correct.

MR. JUSTICE NEUBERGER: Paragraph?

MR. WATSON: 29.

A. In the second line, the date of the second EPO appeal hearing is set at 1996 and that is clearly 1998.

Q. With those corrections, and now you are on oath, do you confirm the accuracy of that statement?

A. Yes.

Q. With my Lord's leave, I have three very short supplementary topics.

MR. JUSTICE NEUBERGER: Go ahead.

MR. WATSON: I am obliged to my friend. First of all, and this is very formal, if you would take bundle E10, tab 10, and again I think I can lead, is this the declaration signed by Dr. Lin in relation to the applications that we are talking about in this case.

A. Yes, I believe it is.

Q. From your experience, what is the practical significance of having made a misstatement in a US patent application?

A. I think it was foreshadowed by Mr. Waugh's comments that an inaccurate statement could prejudice the validity of the patent and an inaccurate statement countenanced by counsel could prejudice the right of counsel to continue to practise not only before the US Patent Office but to practise law in the United States.

Q. I am obliged. That can go away. In the skeleton put forward by TKT, as you know, they are challenging your account of how the wording in example 10 was derived. With relation to information that you may have received from Dr. Lin about the SDS-PAGE experiment, they say -- and I am quoting: you do not need to get it out but it is in paragraph 48 of their skeleton -- that it is unlikely that Dr. Lin had a grasp of

the SDS-PAGE comparisons sufficient to have passed it on to Mr. Borun. Would you like to comment on that?

A. When I read the skeleton, I was taken aback significantly, my Lord, because they seem to imply that Dr. Lin was less than skilled in the review of technology that must have been part of his lifetime in science. He had had a PhD for twelve years at this point in time. He had taught in Taiwan. The PhD was from the University of Indiana in the United States. It is inconceivable that someone would suggest that Dr. Lin was not competent to analyze SDS-PAGE gels.

Q. Finally, elsewhere in the skeleton, there is a suggestion that Dr. Lin obviously had not checked the drafts very carefully. You cannot speak for him, but can you help my Lord as to what your impression was as to the care with which he treated the drafts that you submitted to him.

A. I can speak for myself in relating directly that each and every draft, and there were four iterations of this patent application, was the subject of very thorough joint analysis involving Dr. Lin and me. In each instance, any new material added, any changes that were made in original material, were gone over very carefully personally with Dr. Lin. I got the impression that Dr. Lin appreciated that as the sole inventor and then as the leader of the research and development project at Amgen, having to do with erythropoietin, he bore a

significant responsibility for the accuracy of material in the patent application. That may not have been the same view he had with respect to publications where everyone was anxious to pitch his name in at the end or at the beginning. It certainly was my experience with him with regard to the patent applications. He was aware of the significance of patents. That is my position in response to the suggestion that he was less than careful in reviewing the application.

MR. WATSON: Thank you.

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A. The purpose for my calling for something would be that, yes.
Q. And it would be very surprising if in the case of any invention, again particularly in the context of this invention an important invention, you did not follow that course?
A. If the materials were what I had called for, that would be the case. More often than not those manila files were actually bits and pieces that Dr. Lin or someone else provided me that were involved in the process of actually drafting in Dr. Lin's presence or in the presence of another person what was to go in. I remember that to be the case with respect to Dr. Browne and Dr. Smalling, and his assistant.
Q. Again, it would be appropriate for you to consider the documents in the file during the course of that process?
A. Yes. If there were documents in the file at that time, I would consider them.
Q. I am grateful. Could I please consider with you the material which was added into the fourth priority document in this case.
A. Certainly.
Q. For that purpose, we have a marked-up document which certainly Amgen's representatives have seen and I hope you have, in bundle E10 at tab 5. This document is a US patent,

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number 5547933 and it is one of the patents which was asserted against TKT in America; is that right?
A. That is my recollection, yes.
Q. What has been done here is to mark it up to show the material added by the successive priority documents, and that has been done in colours which you will see in the left-hand margin on the first page. Do you have that?
A. Yes.
Q. Have you seen this document before, marked-up as it is?
A. I may well have done.
Q. You think you have?
A. I think I have, yes.
Q. What I would like to consider with you is the material added in the fourth priority document, that is to say the 30th November 1984 which is in the colour yellow. Could you please go to column 10 and I would like to draw your attention, please, to the paragraph under the heading "Brief Summary" beginning at line 34.
A. OK.
Q. Through to line 41. It is right to say, is it not, that in this document you were now specifically describing what you wrote as being novel glycoprotein products of the invention?
A. That is certainly what I wrote, yes.
Q. And you describe them as having a primary structural

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conformation sufficiently duplicative — (Reads to the words) — which differs from that of naturally occurring human erythropoietin."
A. That is a correct reading, sir.
Q. So you were specifically directing your attention in this document, this fourth filing, to glycoproteins, polypeptides; that is right, is it not?
A. Yes.
Q. In the next paragraph you have written that vertebrate e.g. COS and CHO cells provided by the present invention comprised the first cells ever available which can be propagated and feature — (Reads to the words) — per million cells in 48 hours as determined by radioimmunoassay." Consequently is it right to say that you yourself were conscious when you drafted this document that you were teaching the reader that both COS and CHO cells would produce substantial quantities of erythropoietin to meet that commercial goal which we have seen described in the 605 patent?
A. Those numbers are numbers that are large enough to distinguish over any type of prior art suggestion of rates of production of erythropoietin. The two cells that had succeeded in overcoming those prior art suggestions of mammalian cell production, of erythropoietin, were both the COS cells and the CHO cells.

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Q. You were drawing attention to the importance of both COS and CHO cells, were you not?
A. Both COS and CHO cells did do this. Those were the only vertebrate cells that had been tested to that date. There were bacterial cells that made this many units when measured by radioimmunoassay. They were yeast cells but the only vertebrate cells that made this amount of material were the COS and CHO cells. Of course no bacteria or yeast cell in the prior art needed to be compared away. It was only vertebrate cells that needed to be compared away.
MR. KITCHIN: Is that a convenient moment, my Lord?
MR. JUSTICE NEUBERGER: Yes. I ought to explain to you -- it is probably the same in the United States -- because you are under cross-examination you must not talk about the case to anybody over the adjournment.
A. I will not.
MR. JUSTICE NEUBERGER: Five-past two. I have to rise at five-to four, as I indicated. Tomorrow I am told I have a judgment to hand down. I will give you a time estimate before we rise this afternoon.
(Adjourned for a short time)
MR. JUSTICE NEUBERGER: Two points before we start. First, the good news for me, but possibly not for you: my dentist appointment has been cancelled so I can sit a little later

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than 4 o'clock, but if anyone has made arrangements, of course I will not sit later. I do not think we should go beyond 4.30.

Secondly, I have had an application, which I have lost, faxed to me asking (I think at Eversheds) asking to see the skeleton arguments in the case.

MR. WATSON: My Lord, we have written to say that we will hope to get them to Eversheds tomorrow morning.

MR. JUSTICE NEUBERGER: I had understood there was an objection.

MR. WATSON: We are going to give them redacted copies within 48 hours. That is what we have offered to them.

MR. JUSTICE NEUBERGER: Right.

MR. WATSON: Obviously we will do one first and then the next.

MR. JUSTICE NEUBERGER: Do redacted copies. If they ask for something else, then I may have to decide something. I am not sure what the rights and wrongs are. I do not want to take up unnecessary time with this, but I thought —

MR. WATSON: My Lord, we have written back saying that is what we are going to do and there is no application. There is nobody here to address my Lord.

MR. KITCHIN: My Lord, I would simply indicate through you, if I may, to my learned friend that in so far as they are proposing to redact our skeleton, we would certainly welcome the opportunity to see what they are going to leave.

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MR. WAUGH: The title!

MR. JUSTICE NEUBERGER: That must be right.

MR. KITCHIN: It is their documents, that is where the worry comes.

MR. WATSON: That is obvious sense. They will see D Kitchin.

MR. JUSTICE NEUBERGER: Thank you very much.

THE WITNESS: Might I complete the response to the question that you posed to me immediately before the break concerning the paragraph about invertebrate cell.

MR. KITCHIN: I thought you had, but if there is something else you would like to add —

A. I would. Turning back to page 60 in E 10, tab 5.

Q. Which page?

A. Page 60 at the bottom, the previous page.

MR. JUSTICE NEUBERGER: Columns 7 and 8.

MR. KITCHIN: I do not have page numbers at the bottom.

MR. JUSTICE NEUBERGER: Columns 7 and 8.

A. Yes. You will see also in the yellow section in column 7 is a reference to a piece of art that I had determined the existence of during the time period between the September '84 iteration and the November '84 iteration of this application. This referred to cells that were proposed to be able to grow in culture, although not continuously, without the assistance of a mammalian host and produced large quantities of what was

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alleged to be erythropoietin. It is that piece that fits together with the piece in the summary that indicates that through Dr. Lin's inventions we too had cells that produced large quantities of EPO and, in fact, much larger quantities than were producible in mammalian hosts. The pieces go together.

Q. That applied to COS and CHO?

A. My belief at the time was that COS and CHO were both able to grow continuously in culture and produce an excess of 500 units of erythropoietin per 10 to the 6 cells in 48 hours as determined by radioimmunoassay. The Sugimoto reference was a principal reference in the US prosecution. It turned out that it appears to have been fictitious and one, with a number of other Sugimoto references, which proposed to make GCSF and TPA and every other high quality protein known to man by lymphoblastoid fusion. It was just smoke.

Q. I do not think we need worry too much about that for this hearing. Could you please turn to column 25 where you will see example 10. It goes through to column 29. The passage to which I would like to draw your attention appears in column 28 where you have inserted the passage which has been the subject of submissions from Mr. Waugh which you can see at line 33 running through to line 50, first of all?

A. Yes.

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Q. Then there is a second passage beginning at line 51 running through to the bottom of the page. Do you have that?

A. That and the yellow that was added in column 29.

Q. You drafted this passage?

A. Yes, I did.

Q. The passage beginning at line 51 details the carbohydrate analysis?

A. That is correct.

Q. And you drafted that passage, too?

A. Yes, I did.

Q. On the basis of the two paragraphs, the first one I am referring to beginning at line 33 and the second one beginning at line 51, is it fair to say you were able to introduce the paragraph in column 29 beginning "Glycoprotein products" and continuing "provided by the present invention are thus comprehensive of products ... (Reads to the words) ... differs from that of naturally occurring erythropoietin?

A. Those were not the sole basis, but they certainly were the basis for that remark and again I hate to be sounding like I am Mr. Law Student or vice versa, there are other proteins that were first mentioned here in this application such as analogs that also would fit that determination.

Q. These passages would be of importance to you, would they not, and also to a reader because they provided a potential basis

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to introduce claims to the recombinant polypeptide and so to distinguish such a polypeptide from the natural urinary erythropoietin of the prior art?
A. I think that is a fair statement, that and other things in the specification.
Q. Could I please ask you to look at your statement at paragraph 5(c) and just refresh your memory about what you wrote there? (Pause) You point out, is it fair to say, that at the time of the earliest events in this case the application of existing laws to inventions and molecular biology was far from settled in the United States and indeed worldwide? That is fair, is it not?
A. Not in all respects, but certainly with respect to recombinant proteins.
Q. That remained so in 1994 did, it not?
A. No.
Q. In 1994, is it not fair to say that you were concerned about the risk that the European Patent Office would not grant claims based on DNA?
A. In 1994?
Q. Yes.
A. Claims based on DNA?
Q. Yes.
A. I have no recollection of having any concern about that in

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1994.
Q. We will come back to it then. At any rate, back at this time it was clearly important that you try and secure claims to recombinant proteins if you could? That was important to you, was it not?
A. Securing claims to the DNA to Dr. Lin's contribution in DNAs that encoded human erythropoietin was my job.
Q. Because of the uncertainty in the law, you appreciated it was also important that you try and secure claims to recombinant proteins?
A. The uncertainty was with respect to the recombinant proteins. The uncertainty was not with respect to claims to DNA.
Q. Very well. Whatever the uncertainty, you perceived that it was important to try and secure claims to the recombinant proteins, if you could?
A. And as well to every other aspect of Dr. Lin's inventions, including host cells, pharmaceutical compositions, a wide variety of antibodies, a wide variety of things that flowed naturally from the contribution Dr. Lin had made.
Q. You were aware, were you not, that such claims would require support in the specification?
A. They would require written descriptive support, that is an indication under US law that the inventor perceived the subject-matter to be his invention. There is no direct, in

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my understanding, analogous provision in European law or in British law.
Q. Did you perceive there to be an importance in having a textual description of how such recombinant proteins might be distinguished from the prior art?
A. If that was available, yes.
Q. I would like to explore with you where the information we have been looking at in column 28 of the 547933 patent came from. That is the topic I would like to look at with you?
A. That is fine.
Q. First of all, I would like to explore with you who it was you understood was doing the work at Amgen. My question for you is this. The only person that we know who was doing work on SDS gels in 1984 at Amgen was Dr. Egrie; is that not so?
A. I am not sure that that is the case. She certainly was doing work on SDS-PAGE gels. There were other persons at Amgen sharing laboratory space with her doing SDS-PAGE gels, immunologists doing SDS-PAGE gels on other proteins that were the subject of research and development by Amgen. Dr. Nicholson comes to mind and – I apologize – it is either Dr. Cherie Lane or Ms. Cherie Lane who was definitely working with Dr. Egrie at that time.
Q. So Dr. Egrie had an assistant who was Dr. Cherie Lane?
A. I believe so, yes.

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Q. It was Dr. Egrie, with the assistance of Cherie Lane, who was to your knowledge working on SDS gels on erythropoietin; is that not right?
A. I knew she was. I do not know if that exhausts the list.
MR. JUSTICE NEUBERGER: But Dr. Nicholson you mentioned.
A. Yes, Marj Nicholson.
Q. You knew she was working on SDS gels?
A. Yes.
MR. KITCHIN: But on another protein.
A. I did not know that she was not working on erythropoietin, but I had gotten SDS-PAGE relative mobility information from her in prior instances.
Q. Let us put it the other way round. The only person that you knew of at Amgen who was working on SDS gels in relation to erythropoietin was Dr. Egrie assisted by Dr. Lane?
A. That is what I knew for certain at the time.
Q. Thank you. You say in your statement in paragraph 9 that you recall being referred to Dr. Egrie by Dr. Lin?
A. That is my recollection. I had enquired of Dr. Lin, as I usually did every time the application was to be revised basically what is new, what new information you have and are you sure you are providing the best mode known for practising the invention. That is also very important under US law and has no counterpart, as I understand it, in Europe.

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time there were a number of enzymes with multiple activities. This is a specific identifier for endoglycosidase and endoglycosidase as specific endoglycosidase enzyme of some source or another. I am not sure, even as I sit here today, what catalogue you would go into to find that enzyme listed under that number.

Q. You have referred in your statement to the fact that this parallel in results of experiments between what we see in the Egrie input file and what we see in the 605 B1 specification ----

A. There is a parallel ----

Q. It was drawn to your attention by TKT's counsel in the United States.

A. Yes. They drew to my attention in an attempt to suggest that it was more likely than not that I had seen all of the Egrie input file, the fact that there were certain parallels in the language on page 26 at the bottom and of course correspondingly with the graphic representations on page 27, which is also in bundle K1, tab 5, 27A.

Q. Seeing what you have suggested in your statement, in fact your firm drew the parallel itself, did it not, as we can see from bundle E10 at tab 1. Would you have a look at that.

A. I think I understand what you are referring to. This was a document that I did not draft. It was drafted by my firm,

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executed by Edward O'Toole. I am not sure what date it was submitted.

Q. The document we have here is a document submitted by your firm. Is that right?

A. I would say it was executed by Edward O'Toole, submitted by the three different firms.

Q. Including your firm?

A. Including mine, yes.

Q. At page 2 of the document, could I draw your attention to the second paragraph?

A. Right.

Q. Your firms have collectively written: "On page 22 of the Egrie input document, results of SDS-PAGE gels are summarized in a way that parallels the description in the 933 patent, column 28, lines 33-50."

A. That is the page we have been referring to as page 26, which has a 22 at the top right.

MR. JUSTICE NEUBERGER: That is right.

Q. You continue thereby importing the results of the experiments and, in particular, the results of the digestion with neuraminidase and ENDO F?

A. Yes, no. The ENDO F .... You see, this is where there is a bit of slippage. It is explained by the fact that I was not around to have any input on the construction of this

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document. The suggestion is that the ENDO F portion of the text in example 10 is to be found somewhere in this document - and it is not. There is nothing in here that corresponds to it. There is a reference on this last page to CHO and standard EPO digested with ENDO F, same size digestion products, but then the cross-reference is to data and Westerns on section 3, page 9. It does not fit.

Q. Could you go back, please, to page 12 of the Egrie input file, looking again at the bottom.

A. 12, at the bottom?

MR. JUSTICE NEUBERGER: 8 at the top, 12 at the bottom.

MR. KITCHIN: It is in section 3, as you will see from page 9 at the bottom.

A. I will accept that.

Q. Page 9 at the bottom, it indicates that this is from section 3. On page 12, at the top, is written: "ENDO F digestion patterns .... (Reads to the words) .... Chinese Hamster ovary EPO." Do you see that?

A. I see that, yes.

Q. I would suggest to you that there is indeed a parallel between what we see in the Egrie input file and what you have written in the specification which became 605, bundle A2, tab 2, page 146.

A. I can see that there is a parallel with the text on page 28

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in the bottom and page 24 at the top, where it said CHO and standard EPO digested with ENDO F same size digestion products. This does not correspond to the experiment described on page 12 at the bottom, nor the gel, and conclusions at page 13 at the bottom. In that gel and those conclusions, there is an indication that the results of endoglycosidase F digestion, and indeed heterogeneous, and they give a number of bands, so that there is a statement that CHO and Lot 82 and ENDO F gives only one band and a faint lower molecular weight band on ENDO F Lot 82, whereas CHO gives three bands with one higher intensity than another, darker .... This is simply not what appears in the patent.

Q. I would suggest to you that is not the conclusion that Dr. Egrie has expressed, and that the conclusion Dr. Egrie has expressed is indeed what occurs and we see reproduced in the patent.

A. No. The patent does not say anything about multiple bands. The patent makes specific note of the fact that the heterogeneity of the product is resolved by ENDO F glycocosylation, which means that the bands get narrower and they are co-linear, not that there are multiple bands. You do not .... Heterogeneity is the result of this sort of spread on page T1, tab 5, 27. It was page 27 in the Egrie input at the bottom. You see, the bands are very wide. I am

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sure this was the subject of discussion quite frequently during trial and the subject of discussion about leading edge and trailing edge and across the middle and all this business. What this says is that things get resolved very much like the case here where Gene's standard, after treatment with neuraminidase, the assumption is the loading is the same and you have a narrower band than a narrower band and a wider band. You have lost carbohydrate and things tend to tighten up.

Q. Mr. Borun, do you accept that in this bundle of materials in this Egrie input file, there is data from page 8 through to page 28 relating to the behaviour of urinary and recombinant EPO on SDS?

A. Page appears to relate to urinary erythropoietin. Page 10 would appear to relate to urinary erythropoietin. I cannot tell you what page 11 relates to. Page 12 relates to urinary erythropoietin and a protein from Chinese Hamster ovary cells, but I am not sure for human protein. It might be the monkey protein. Page 13 relates to recombinant and urinary protein. Page 14 appears to relate to two urinary protein. Page 15 relates to two urinary protein, at least. How far did you want - 18?

Q. They all relate, do they not, to the behaviour of urinary and recombinant proteins on SDS is my question to you?

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A. They all relate to urinary and/or recombinant proteins and involved SDS-PAGE in Western blot?

Q. That is right, is it not?

A. I do not know. I do not think so. 17 to —

Q. Are you able —

A. Autoradiogram on 17. That would not necessarily involve a Western blot technology. If there is a reference to antibody, I would give you that one. Most of the time she defines what antibody was being used, either a polyclonal or a monoclonal.

Q. Do you accept that the overwhelming majority of them, with the possible exception of page 17?

A. I certainly accept that they are in here, but I do not know if I would characterize it as an overwhelming majority.

Q. Now, Mr. Borun, let me summarize our position for you. First of all, you accept, do you not, that this was a very important specification to Amgen, this fourth filing?

A. No more than the first second or third, but I accept that it was important to have it right, as was the case with all patent applications filed by Amgen. Every piece of intellectual property at the time was as valuable as every other piece.

Q. And it contained crucial information relating to the characteristics of recombinant EPO, did it not?

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A. I think the most important information concerning recombinant EPO was the information concerning the immense amount of biologically active human erythropoietin that was coming out of CHO cells. This was a marvel to behold.

Q. It also included important information relating to the distinction of recombinant EPO over urinary EPO, did it not, as we can see on page 146 at bundle A2?

A. It contained the information that was available to us at the time, yes.

Q. You were sent experimental data by the scientist you knew conducted the experiments with the assistance of Dr. Lane.

A. That is not true. Let me not say it is not true. I cannot confirm that. My recollection is not .... I do not remember when I first saw the material in the Egrie input file, except for the in the interference, I think, or in the litigation in Boston, Chugai litigation in Boston.

Q. It is overwhelmingly likely, is it not, Mr. Borun, that you knew that this material had been produced by Dr. Egrie, who was the scientist conducting the experiments with the assistance of Dr. Lane?

A. I cannot accept that. You have not qualified that as to when I knew. I know, in the context of the interference, that this was material put together by Dr. Egrie or Dr. Lane. As I said repeatedly, I have no recollection of seeing the

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Egrie input file before drafting the specification. I have no recollection of seeing it ever again, or ever, until the Chugai litigation. The material that we just went over leads me to believe that it is unlikely that I saw it. It is unlikely that I saw it because the results of the neuraminidase digestion are at odds with what is written here, and so it leaves unexplained what was being referred to, what I had been told and what I had put into the application. There are little things, like the neuraminidase enzyme number. I got that somewhere. I did not make it up — Excuse me, the endoglycosidase F? That does not appear anywhere in these materials. There are also other things in here that certainly had I seen them would have given me a heads up. Had I seen the page 24 at the bottom, which purports to indicate that the COS material vibrates identically with Dr. Goldwasser, this in fact is what is in that 1984 poster in the 1985 Egrie application. Had I seen that, I almost certainly would have asked what is the difference between .... It would not put me off. What is the difference between COS cell material behaviour when, you know, before and after neuraminidase and COS cell behaviour in this other experiment that did not involve neuraminidase digestion?

Q. You have not point indeed your witness statement or indeed in

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said anything to you which was inconsistent with the experiments which we see in the Egrie input file. Would you like to comment upon that suggestion?
A. Let me see if I have got the question. You are suggesting to me that Dr. Lin did not say anything inconsistent with these experiments.
Q. Let me put it to you again. I would suggest to you that it is extremely unlikely that Dr. Egrie said to you ----
A. Dr. Egrie?
Q. Start with Dr. Lin. It is most unlikely that Dr. Lin said anything to you that was inconsistent with the contents of the Egrie input file and the experiments included in it?
A. I would certainly embrace that statement with respect to the subject-matter in the specification, but I cannot embrace it with respect to all of the subject-matter in the Egrie input file.
Q. I would also suggest to you that it is most unlikely that Dr. Egrie said anything to you which was inconsistent with the experiments in conclusions she had expressed in the Egrie input file?
A. Again, I would accept that if the focus was what is in the specification. I certainly would not have put in anything that Joan Egrie did not tell me, but as for all of the material in the Egrie input file I cannot endorse that she

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vouched for every bit of information in the context of describing this one experiment that had significance in terms of things that Amgen was interested in, how much sialic difference was there between the urinary and recombinant products, what explains the difference in biological activity of the CHO cell products and the COS cell products. Is the sialic acid content? Things like that were answered by this experiment. I do not know what is being answered by the other experiments in the Egrie input file.
Q. Could you please just have a look at paragraph 10 of your statement, at the top of page 6 of the statement?
MR. JUSTICE NEUBERGER: Is E 10 still wanted?
MR. KITCHIN: No. It is K1 that we want. E 10 can go away.
MR. JUSTICE NEUBERGER: I am sorry, it is just that ----
MR. KITCHIN: Absolutely right, my Lord.
MR. JUSTICE NEUBERGER: You are looking at what paragraph?
MR. KITCHIN: Paragraph 10 of the witness's statement.
MR. JUSTICE NEUBERGER: Pages 5 and 6, yes.
MR. KITCHIN: At the top of page 6 you write "It seemed intuitive to me that urinary Epo would have a lower molecular weight by SDS-PAGE than glycosylated recombinant Epo made in CHO and COS cells, since I thought uEpo lost sialic acid end-caps and might be fragmented during its passage through the body, its retention in the urine, and then its purification therefrom."

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Do you see that?
A. Yes.
Q. What you have written in the patent is that CHO-produced EPO had a somewhat higher molecular weight than the COS-1 expression product which in turn was slightly larger than the pooled source human urinary extract.
A. Mm-mh.
Q. May I suggest to you that you cannot account for the words in the patent on the basis of your intuition?
A. I certainly can; but there is a bit of information missing. You will recall I just said that CHO cell material had a higher specific activity, that is activity in red blood cell formation per unit of protein, whatever that is, in absorbant unit or microgram, than COS cells. It is strange you should ask. As I just mentioned, the urinary EPO had the least biological activity per unit of protein. This suggested that these would differ in terms of the sialic acid end caps. It was known to me as a result of reading up Dr. Goldwasser's papers and conversations with Dr. Lin that biological activity of erythropoietin was a function of sialic acid and that the in vivo biological activity could be diminished by removing sialic acid with, for example, an enzyme like neuraminidase. I am sorry there is a little extra bit of information here missing, but it is in page 26 at the bottom

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the CHO material was more biologically active than the COS material which was more biologically active than the urinary. Maybe I was seeing things, but if I looked at that gel with this kind of understanding in mind ----
Q. Which gel?
A. 27 at the bottom and 27A. If I had seen that gel, as you suggested that I did in the course of discussions with Dr. Egrie, my intuition that is based on information on page 26 at the bottom that CHO was more biologically active than COS than urinary would make me believe or conclude that CHO had the most sialic acid, COS the intermediate amount and urinary the least, and that these differences would be reflected in the molecular weight approximations of (inaudible) and a gel and that once you treat it with neuraminidase these would disappear.
Q. Are you saying you did look at the gel?
A. No. You suggested to me that I did. I am saying that this is consistent with this. I have no specific recollection of looking at that gel.
MR. JUSTICE NEUBERGER: As I understand it, you are saying (a) you have no recollection of looking at that gel and (b) you think if you had looked at that gel you would not have sanctioned what went into the patent in the passages we are talking about. Is that right?

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A. The second passage, the endoglycosidase F I would not have sanctioned.
Q. That last sentence.
A. Moreover, I would certainly have enquired with respect to that COS, the two Genc's crude EPO, which is the publication of Egrie in 1985. Had I seen that -- Joan Egrie was not back from Japan in November -- I certainly would have called her and said what is the deal, Joan?
Q. Let us have a look at page 21 of the Egrie lapsit file and the conclusion which Dr. Egrie has there expressed about COS?
MR. JUSTICE NEUBERGER: 21 at the bottom?
MR. KITCHIN: 21 at the bottom.
Q. We have got Dr. Egrie's conclusion there on page 21. Have you read it?
A. Yes, at the bottom.
Q. Recombinant monkey and human EPO produced by COS cells have the same molecular weight as native urinary EPO Goldwasser's EPO." The result indicates that the recombinant EPO's .... (Reads to the words) .... same extent as the native protein. You see her conclusion there about the molecular weight?
A. I see that, yes.
Q. You understand that. You also have evidently in mind the passage on 26 where in the light of one of her experiments she wrote as a note "Size of Gene's standard is approximately

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equal to the size of COS."
A. That is in relation to the experiment that is shown in the patent. These experiments are not shown in the patent. The monkey is the same as human is the same as Gene's are not in the patent.
Q. Do you recall seeing any molecular weight SDS gels?
A. I do not.
Q. Do you accept that the conclusions which Dr. Egrie has arrived at and are reflected in her input file are inconsistent with the statement in the patent that the studies indicated that the CHO-produced EPO material had a somewhat higher molecular weight than the COS-1 expression product which in turn was slightly larger than the pooled source human urinary extract. Do you accept that the two are inconsistent?
A. No, I do not. I accept that the information on 26 at the bottom and 27 is consistent with what is in the patent specification. I do not accept that the other materials are -- consistent. Essentially, anything that you have pointed me to was consistent with what is in the specification.
Q. Leave aside the digestion experiments for a moment. I am asking you about the statement in the patent which you drafted that "CHO produced-EPO material had a somewhat higher molecular weight .... (Reads to the words) .... which in turn

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was slightly larger than the pooled source human urinary extract."
A. Yes.
Q. That is not a digestion experiment, is it?
A. Yes, it is. It is the first part of a neuraminidase digestion.
Q. That part of it is not a digestion experiment, is it?
A. It is all cut of one cloth.
Q. It is not stated to be a digestion experiment, is it?
A. Yes, it is. The top of page 26 says "COS, CHO and native .... (Reads to the words) .... differ in size of neuraminidase digestion products".
Q. At any rate, at this point the products have not been digested. This comparison relates to undigested product, does it not?
A. This comparison relates to digested and undigested product. The way you do this, as I am sure you are aware, is that you make up your products with and without neuraminidase. Then you turn on the current and run them. So it is all of one cloth. There is no such thing as only a digestion study because you do not learn anything only from digestion.
Q. May I suggest to you, Mr. Borun, looking at this patent as we are at page 146 of bundle A2, the reader is taught that as a result of experiments carried out, there is an indication

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that the CHO-produced EPO material had a somewhat higher molecular weight than a COS expression product which in turn was slightly higher than the pooled human urinary extract, and that that is referring to material which has not been digested. That particular part is referring to material which has not been digested?
A. You cannot refer to only one part of the experiment. It is in the context of a neuraminidase digestive study.
Q. You can run the experiment without enzyme digestion at all, can you not?
A. Yes, you could, and I am not aware of any other gel in any other book ever run by Amgen where they run Gene's standard EPO against CHO and COS. This is the only one that I am aware of, notwithstanding 18 years of fly spec hunting.
Q. Mr. Borun, has Dr. Egrie expressed a conclusion anywhere that CHO-produced EPO has a somewhat higher molecular weight than COS expression product which in turn was slightly higher than the pooled source human urinary extract. Has Dr. Egrie expressed that conclusion anywhere?
A. If she were asked about this experiment, I think she would agree with it.
Q. Has she done it in her input file?
A. I believe that is what the input file says at 26 and 27.
Q. Does it say it at page 21?

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Q. On the contrary, Mr. Borun, I am suggesting to you that the Egrie input file reflects Dr. Egrie's conclusions that there was no difference between the behaviour of COS and urinary EPO on SDS-PAGE, but that was her conclusion and that it is most unlikely she would have said anything different to you.
A. Dr. Egrie quite honestly reported the results of experiments to me and I incorporated them in this application. In earlier instances where there were the RIA things where she actually handed me material, in the context of reports of the biological activity proteins, I obtained information from her. I had no reason to believe that she was shading it. I cannot believe that if she spoke to me about this experiment she would have failed to accurately express her opinion that, as a result of this neuraminidase digestion study where three products were compared, there was a difference in molecular weight to begin with, so to speak, without neuraminidase treatment and the reported differences after neuraminidase treatment. I have no reason to believe, notwithstanding that there is no experiment in the Egrie input that supports it, that if you took CHO EPO and Gene's EPO side by side and subjected them to endoglycosidase ENDO F digestion you would get heterogeneous materials moving down into identically equal moving bands. Never did Amgen pull the punch, so to speak, and refused to say that CHO material was different

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from the urinary standard material of Dr. Goldwasser. Not only, to take your point it, it would have been inconsistent for her to say that COS was different; it would also have been inconsistent for her to say that CHO was different. You have no doubt that she told me that CHO moved differently, do you, or someone did? I am sorry, my Lord, I must be very argumentative and I apologize. Mr. Kitchin, I apologize.
Q. There is absolutely no need to apologize to me, but I am grateful. Thank you. Could I also please just invite you to look at the Egrie input file at page 13 at the bottom. As I suggest is overwhelmingly likely, you had read the Egrie input file before the fourth priority filing. You would have seen, would you not, on page 13 of this document the conclusions expressed by Dr. Egrie at the bottom of the page?
A. If I had seen it, I would have seen it, yes.
Q. And you would have seen, would you not, that she reported her conclusion that CHO and Lot 82 appeared to have the same size by which you would understand the same molecular weight, would you not, apparent molecular weight?
A. The same mobility, although she notes that the CHO is very heterogeneous. Again, I have seen this in other forms before. This is actually a paste-in of page 69 of one of her notebooks.

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Q. You would also have seen, would you not, that Alpha Therapeutics had approximately the same size on SDS as CHO and Lot 82?
A. Had I recognized that to be an alpha, I would have seen Alpha Therapeutics - an approximate sign saying the same size as CHO and Lot 82. I see that in the fourth line from the bottom.
Q. Had you seen that, may I suggest to you that would you have appreciated that it was potentially relevant?
A. Yes, I think I might.
Q. To the filing you were about to produce.
A. I think I would have appreciated enough, because we were talking about size in example 10, to have asked about to have about it.
Q. May I suggest to you that the statement that we see in the patent that CHO had a somewhat higher molecular weight than COS, which in turn was slightly higher than the pooled source human urinary extract, would have been regarded by you as an incomplete statement?
A. No.
Q. Having regard to the fact that Dr. Egrie had found that a commercial product Alpha Therapeutics appeared to migrate with approximately the same size as CHO?
A. I do not accept that suggestion.

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Q. Why not?
A. This is a different experiment. This is not that experiment, OK. This is not the experiment that is at page ---
Q. Why does that matter?
A. It is because things are different in different experiments. This is not a neuraminidase digestion experiment. This is a different experiment; this is a different experiment; and this is a different experiment and the experimental results vary from experiment to experiment. I have no idea whether the gel parameters are the same. I have no idea whether the loadings are the same, what was done to isolate the material. I have no idea if the ENDO F is the same ENDO F that was referred to in the specification. I do not know where I got that number from. It must have been from someone - Dr. Lin or Dr. Egrie or Miss Lane. At that time I would not have known what Alpha Therapeutics is or was. I was not aware of the existence of any commercial erythropoietin available.
Q. What justified you putting in the results of one experiment only?
A. Because it was the preliminary information that they had.
Q. This was also preliminary information they had?
A. I did not ask for all the other preliminary information, and if I had I am sure I would have been told this is the only neuraminidase digestion study we have that compares all

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the basis that its average carbohydrate composition differs from that of the urinary EPO. Is that right?
A. Yes.
Q. And in the paragraph underneath the indent, you say:
"Confirmation of these assertions of novelty is found in the attached declaration of Thomas Strickland which provides detailed description and analysis of the differences in carbohydrate structure between FDA clinical lot preparations of recombinant erythropoietin according to the present invention and human urinary erythropoietin isolates as represented by samples actually obtained by Miyake et al. Is the work forming the basis of the publication, as well as urinary erythropoietin samples obtained by means of a specified modification of the Miyake et al procedure."
A. That is right. Just to add to a note my Lord had this morning, in terms of explanation of this section, the material that Dr. Strickland used was actually isolated in 1976 by Dr. Miyake and Goldwasser. It was the subject of the Miyake et al publication, so we are talking right back to first principles, a sample from his freezer of the material that formed the basis of the 1976/77 publication. That was my understanding.
Q. That is part of the story, is it not, Mr. Borun, because the other part is that you are also relying upon urinary

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Q. If we have a look at page 171, over the page, you will see a paragraph beginning: "The work described in the Strickland declaration and that of the publication cited by Strickland, as well as the results set out in the Sasaki et al publication noted by the examiner, stands as testimony to the differences between applicant's products and those of Miyake et al. In sum, applicant's products are indeed novel." That was your submission to the USPTO, was it not?
A. That was part of the submission. You have read it accurately. There was a reference to Miyake, Takezawa, Chiba and Sugimoto and Papayannopoulo. That is referred to on page 166. This distinguishes them all also.
Q. The Strickland declaration is at K3, tab 6. That was made in November 1988, and it had two principal variations from the Miyake procedure, did it not, first of all the buffer and, secondly, the use of wheatgerm agglutinin?
A. I will accept that if you represent that is the case.
Q. Do not accept it from me. If you cannot accept it —
MR. JUSTICE NEUBERGER: You want him to check?
MR. KITCHIN: I would like him to confirm that those are the differences.
A. Those are two differences or that those are two major differences?
Q. In so far as there are differences, those are they. Do you

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erythropoietin samples obtained by means of a specified modification of the Miyake procedure.
A. That is right.
Q. It fell into two parts, did it not?
A. That is what it says.
Q. And you relied on both of them to establish novelty.
A. They were both naturally occurring urinary EPO. If you are saying that one should imply that they both refer to prior art EPO —
Q. What we know is this, is it not, Mr. Borun, and we can look at the Strickland declaration and perhaps we should in a moment, that the Strickland procedure which involved the modified Miyake process resulted in what we have been describing as Lot 82?
A. Yes.
Q. You here are putting forward to the USPTO a submission that material obtained by the modification of that Miyake procedure is material which can properly be considered in comparison to the recombinant product in order to establish novelty.
A. Or in order to respond to not only Miyake but the other primary and secondary references cited which were alleged to anticipate or render the subject-matter obvious. I am usually pretty good at listing what all was involved.

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want to have a look at K3, tab 6? It is also in D, which we will give your Lordship the references for.
A. At page 2 there is a difference —
Q. Let me just take you through it, if I may, Mr. Borun. First of all, at paragraph 4 we see the claim in issue. Is that right?
A. Yes.
Q. At paragraph 5, is it fair to say that Dr. Strickland appreciated and you were putting this forward to establish novelty over Miyake?
A. Yes.
Q. In paragraph 6, comparison is being made with r-HuEPO obtained from CHO cells. Is that right?
A. Let me back up on paragraph 5.
Q. Of course.
A. This says that products of the 178 and naturally occurring human EPO isolated or naturally occurring EPO isolated from urine, so that is not limited to Miyake.
Q. But it includes Miyake.
A. That would include Miyake, but it is not Miyake exclusively.
Q. In paragraph 7 he explains: "The nEPO employed in the procedure for paragraphs 8 and 9 .... (Reads to the words) .... a modification of the procedure of Miyake." He is going to use Miyake with modifications.

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A. The uEPO from paragraphs 8 and 9 are going to be used to establish a distinction between r-HuEPO, with respect to recombinant human EPO. For those procedures in 8 and 9, he will use the modified material of paragraph 7, which A, B, C, D, E, F and G. That 7, I think, changes.

Q. What do you understand to be the differences from Miyake?

A. In that list in there?

Q. In substance.

A. In all? B is the same, ethanol precipitation, the same. C is essentially as described. D, apparently a distinction is made between some procedures that are essentially as described and others that are not essentially as described. E, I cannot figure it out without the Miyake in front of me. I see that there is an application to the wheatgerm agglutinin on the fraction eluting from the sulfopropyl Sephadex column. There is something being referred to, apparently a further extension on the wheatgerm agglutinin procedure.

Q. Anything else catch your eye?

A. The material eluting from the hydroxyl apatite column. 0.75 mM potassium phosphate does not sound like the final steps of Miyake.

Q. In the light of those points, you nevertheless -- I say you, your firm -- thought it proper to present this as a

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representation of what the prior art Miyake would produce?

A. No. This is an attempt to show differences in carbohydrate with naturally-occurring erythropoietin, or urinary erythropoietin, as is the procedure shown in paragraph 10 where Dr. Strickland used the —

Q. The Goldwasser material?

A. The Goldwasser material, actually obtained right out of Dr. Goldwasser's refrigerator.

Q. I am not disputing that with you for one moment. I am concentrating on the front half of this declaration.

A. The front of this declaration says we have two things to say about urinary EPO. We are going to say those things with respect to one common recombinant EPO, and we will say them about these two different urinary EPOs. One is prior art urinary EPO; one is not.

Q. You were seeking to establish novelty, were you not?

A. We were seeking to put in information concerning differences between recombinant products and urinary-derived EPO products irrespective. You see, Dr. Strickland is prior art neutral. He does experiments. He does experiments, and was doing experiments, to get into the Patent Office .... Excuse me, to get things through, apart from scientific curiosity, I have to attribute to him, because is he here, but to get things through the FDA. He does experiments. There is experimental

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data available to us as patent attorneys who are, what .... We are prior art sensitive. I am not going to cut and paste an entire study of isoelectricfocusing based on two different materials, one prior art and one not and fail to put in, now that I am prior art sensitive, the one that is not prior art and then be accused at some later day of saying, "Ha, you put in less than all the experiments on isoelectricfocusing."

Q. So you appreciate you had a duty of candour at this point.

A. I appreciated I had a duty of candour. I did not appreciate this was Lot 82.

Q. Never mind about the words "Lot 82".

A. OK.

Q. I am talking about the procedure. Be kind enough now to go back to E9, tab 136.

A. I appreciate duty of candour, and I also appreciated that you can be charged with disregarding your duty of candour the minute you do not put something in. You make a conscious attempt to leave something out. That is why I generally put everything in, although I did not in fact work with Dr. Strickland on this. I am aware of what it includes.

Q. Would you turn back to bundle E9, tab 136. You have explained you had a duty of candour. Look please with me at page 170, at the paragraph which we examined a moment ago, just below the indent, which sets out the glycoprotein in

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issue.

A. Yes.

Q. You write: "Confirmation of these assertions of novelty is found in the attached declaration of Thomas Strickland."

A. Absolutely.

Q. So for the purposes of dealing with a novelty objection, you are relying upon Dr. Strickland's work both with the actual Miyake method and with the modification of the Miyake method, are you not?

A. I am using Dr. Strickland's data in support of the fact that we have novel glycoproteins. That is certainly supplied, you will agree with me, by the cross-reference to isoelectricfocusing with Dr. Goldwasser's. If in an abundance of caution we put in additional material which went to the FDA .... That is another thing. Send something to the FDA that you do not send to the Patent Office, you are charged with fraud. That is something that the Patent Office said, "You do not send to the FDA, you are charged with fraud." Yes, I am aware of the duty of candour and I am aware how easily it is abused.

Q. Your position before the USPTO was that the differences which Dr. Strickland had introduced into the Miyake procedure made no difference with regard to the final product because it was, despite those differences in procedure, nevertheless

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A. Yes.
Q. You did know about the Egrie publications; you did know about the Egrie declarations in connection with the interference proceedings; and you did know about the brief which you had submitted in connection with those interference proceedings. So by that stage you unquestionably knew that there was a large body of experimentation upon which the Amgen scientists had expressed the view that COS and urinary EPO migrated to the same extent on SDS. That we know. Is that not right?
A. That is not right. There was not a large body of experimentation. As far as I have ever been able to tell, there was a single experiment when the COS material, which was the first significant amount of recombinant material, was produced where the crude material from the COS cell supernatant was compared to Dr. Goldwasser's EPO and Dr. Egrie joyously observed that this material, which was biologically active, also appeared to migrate in the same area as Gene's EPO. That was wonderful to her. I am sure it stuck in her memory forever. That same gel was cut up and republished again and again and again, and that same gel was the subject of Prof. Cummings's opinion that, indeed, they did not necessarily migrate identically.
Q. By 1992 you knew of the Egrie declarations filed in connection with the interference?

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A. Yes, certainly.
Q. Those indicated that as a result of those experiments Dr. Egrie had come to the conclusion that COS and urinary migrated to the same extent on SDS; correct?
A. In certain experiments, yes, I certainly knew that.
Q. You knew that data had been published by Amgen to the same effect in the papers and the Post-its(?) to which we have referred.
A. Based on those same experiments.
Q. You have also submitted that based upon those experiments COS recombinant EPO and pooled human urinary EPO migrated identically on SDS-PAGE?
A. That point was made in the briefs in the interference as a point of distinction with respect to the CHO cell material which did not, and as I submitted to you earlier, had I been involved in the drafting of Dr. Egrie's declaration I would have insisted on finding the underlying experiments that go to the fact that COS cell additionally is larger, moves slower than the urinary EPO.
Q. You say that you did not at this stage in 1992 know about page 27 of the Egrie input file as suggesting a conclusion which you may have come to at some point later that COS was greater than urinary EPO?
A. It is very hard. I have been asked about this before. It is

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very hard to tell from the page of the Egrie input file I kept circulating, but you can see that —
Q. I am just looking at your state of mind now; I am not asking you to interpret the data. I am asking what your state of mind was in 1992, and as I understand you, you say you had not formed the view at that point in 1992 that page 27 showed that COS was greater than urinary EPO.
A. You could not determine it from that page.
Q. Accordingly, you must have known that this statement in the patent in connection with COS and urinary EPO, so far as their relative migration on SDS was concerned, was incorrect?
A. That is wrong. We see it in page 27A that it was correct, and Dr. Matsudaira thought so and that Prof. Cummings states so.
Q. What is more, in connection with the CHO comparison with SDS, you knew that work had been carried out comparing CHO with Lot 82 on SDS?
A. By 1994 - you are talking about the date of the hearing?
Q. No; by 1992 you knew that CHO and urinary EPO had been compared on SDS?
A. Yes.
Q. And you knew in connection with that CHO and urinary EPO work on SDS that it had been published by Dr. Egrie in the 1986 publication and by Dr. Browne and otherwise in 1986, did you

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not?
A. Yes.
Q. And you knew that both of them had described their product as having been produced by the Miyake process?
A. I disagree with that, but I understand how you can find that suggestion. There was one document that you showed me where I was not permitted to look, an FDA document where I was not permitted to look, to see if there was an explanation of any possible differences in the purification of the EPO. There was one publication that you showed me that just had Miyake et al as a site for the urinary EPO, but the questions you posed to me were as to Dr. Egrie's state of mind in making that statement. I specifically asked if you wanted my opinion about whether a person who was skilled in the art would understand that and you did not want my opinion.
Q. You also knew at this stage, because you had read the Egrie input file, about work carried out by Dr. Egrie on Alpha Therapeutics and that the Alpha Therapeutics product migrated to the same extent as CHO on SDS. Is that not right?
A. I knew of that conclusion. I was unaware at that time that there were other gels that showed a difference in migration and I continued to be unaware as to exactly what that Alpha Therapeutics material is. It is certainly not prior art material in any context that I am aware of.

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consider under parameter 1 SDS?
A. Yes.
Q. He points out at the bottom of page 3 that the patentee has published itself through two Egrie papers that COS recombinant EPO migrates identically to human urinary EPO?
A. That is correct. That is a fair comment and you have made that repeatedly.
Q. At page 4 just cast your eyes through that, please. Is it fair to say that in summary it is his evidence that proteins may behave anomalously on SDS?
A. I am sure that is a conclusion. In each instance he is saying that Western blot and all these other things, all these other parameters, are not suitable for distinguishing urinary and recombinant EPO preparations, and our point in response, by Prof. Cummings, was that for any two given urinary and recombinant preparations, that are both glycoproteins, there will always be a distinction to be made, whether or not it is SDS-PAGE.
Q. Could we have a look at the Amgen response, please, which you will find in bundle E3 at tab 67. You will need to keep out E10, if you would be so kind.
A. I have it still, yes.
Q. At E3, tab 67, you respond to the various submissions made by the opponents and annex a series of annexes in connection

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with particular aspects of the objections raised.
A. I will accept that, yes.
Q. That was filed in February of 1994.
A. Yes.
Q. The novelty issue was developed by you in annex A; is that right? If it is a help, please take out E10, tab 12. My Lord may have been looking at it in D2, tab 32.
A. I see, yes, E10, tab 12 is a complete form of what has been extracted ... No.
Q. This is the annex dealing with the arguments on novelty?
A. Yes. There is an annex that deals with the argument on novelty and that is E10 at tab 12.
Q. Very good. Could we have a look at that, please.
A. Yes.
Q. Did have you a chance to review this?
A. For purposes of this hearing?
Q. No. At the time of filing you would have had a chance to review this?
A. I would agree, presumably I did.
MR. KITCHIN: My Lord may have been working off the copy at D2, tab 32.
MR. JUSTICE NEUBERGER: That is the one I have been working off.
MR. KITCHIN: I will work of the page numbers, if I may, of the document. Page 7.

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MR. JUSTICE NEUBERGER: That is page 415. I am just reading that into the transcript for my own note. D2, 32, 415.
MR. KITCHIN: At page 7 of the document you will see a reference at the top to Miyake.
A. Yes. Page 165 at the bottom, yes.
Q. In connection with the Miyake publication you say that the publication reported a seven-step purification procedure developed by Dr. Eugene Goldwasser in 1976 for preparing homogeneous uEPO form the urine of patient with aplastic anaemia. "The procedure includes ethanol precipitation, DEAE-agarose fractionation", and so forth.
A. Yes.
Q. "This purification procedure produced homogenous uEPO as shown by SDS-PAGE in two separate fractions from the final purification step. These two fractions of uEPO were analyzed and shown to be distinctly different from recombinant rEPO in the Strickland declaration (Exhibit B), discussed infra."
A. Yes.
Q. That Strickland declaration is at E 3, tab 67, or the next tab in your Lordship's bundle, I think.
MR. JUSTICE NEUBERGER: E3, 67?
MR. KITCHIN: My Lord, it is there as well. There is duplication, but I just heard from my left that the same document, the Strickland declaration —

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MR. JUSTICE NEUBERGER: Page?
A. My Lord, it has P273 at the top. It is about three-quarters of the way through tab 67.
MR. JUSTICE NEUBERGER: I have it, thank you. It comes after page 27; you are quite right. Thank you very much.
A. I see that, yes. I have that in front of me. It is four pages long, Mr. Kitchin. Is that the one you are referring to?
MR. KITCHIN: I think there may be some confusion because my understanding is that the Strickland declaration exhibited as B is a four-page document, yes.
MR. JUSTICE NEUBERGER: That is right. If you go to E3, 67, you come out at page 27 and then you start with page 1 and that is a four-page document, just four pages, signed by Thomas Strickland.
MR. KITCHIN: It sounds as if we have the same one, my Lord.
MR. JUSTICE NEUBERGER: The last page is just the solemn declaration.
MR. KITCHIN: Dated 5th January 1984.
MR. JUSTICE NEUBERGER: Thank you very much.
MR. KITCHIN: That itself refers in paragraph 2 to the work that he has carried out at Amgen since 1984 and that one of his responsibilities has been the analysis of the carbohydrate portion of recombinant EPO as produced by Amgen. He says.

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"As part of this work, I have studied and compared the carbohydrate portion of recombinant EPO with that of urinary EPO. I attach hereto as Exhibit TWS-2, a copy of a declaration which was filed during the prosecution of Amgen's product claims in the US on rEPO, application Serial Number 113178", and so forth.

A. Yes.

Q. He continues at the end of that paragraph: "In that declaration, I reported on isoelectric focusing experiments which I had conducted and which demonstrated that uEPO exhibits a lower or more acidic isoelectric point as compared to rEPO. This more acidic nature was determined to be due to differences in the carbohydrate composition of the molecules." That is the Strickland 88 declaration which we have looked at before.

A. I am certain that that is what he was referring to.

Q. And that in my bundles is at K3, tab 6. In this brief, annex A, you were relying upon the Strickland declaration which itself relied upon the 1988 work carried out by Dr. Strickland on Lot 82 and Goldwasser?

A. As well as the material obtained apparently later from Goldwasser, two samples of urinary EPO that are designated Alpha and Beta, and that is tied into E10, tab 12, page 7 as the two fractions of uEPO that were analyzed and shown to be

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distinctly different from rEPO in the Strickland declaration.

Q. Specifically here, in connection with the appeal hearing, you are again relying upon Dr. Strickland's work, inter alia, upon Lot 82 to establish novelty?

A. I think it is clear that Dr. Strickland said, "I am the same Strickland that made a declaration in the United States. Here is a copy. It showed that material I got from Gene Goldwasser that was actually purified in July 1976 and was the basis for the paper behaves differently in terms of isoelectricfocusing results from CHO cell EPO." That is correct. There is also a reference there to Lot 82. Is that what you are referring to?

Q. Yes. He relied on both of them. That is my question to you. Is that not right?

A. You have to go back and look at what the material was being submitted for in the first place in the United States Patent Office. It was submitted for the purposes of supporting a statement that urinary EPO will differ from recombinant EPO in carbohydrate composition. In that declaration, as I explained yesterday, there was a prior art EPO and a non-prior art EPO. If you want to say that only the prior art EPO was valuable for distinguishing difference in urinary EPO, that is fine. You can take that position and we have superfluously put in the Lot 82 material.

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Q. Let us go on together on this particular issue to page 14 of annex A —

A. Yes.

Q. — paragraph 1.4.4, where I would suggest to you that your position was made clear beyond argument.

MR. JUSTICE NEUBERGER: This is page 422 of D2, 32.

MR. KITCHIN: That is right, my Lord.

MR. JUSTICE NEUBERGER: Page 13, 1.4.4, yes.

MR. KITCHIN: Here, paragraph 1.4.4, headed "Strickland declaration", you have written Dr. Strickland's work on isoelectricfocusing sialidase-resistant charges and sulfation analysis are reported in his declaration and represent the best comparison of recombinant EPO made according to the disclosure of 605 and the prior art uEPO of Miyake et al."

A. Right.

Q. "The results of Dr. Strickland he isoelectricfocusing experiments demonstrate that uEPO demonstrates a lower (more acidic) isoelectric point compared to rEPO and are completely consistent with the results reported in Storring et al. The uEPO used in this study was purified according to the seven-step process described in Miyake et al except for slight modifications as noted in exhibit 2 to the Strickland declaration."

My suggestion to you is that this makes it absolutely

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clear that you were saying to the board that Lot 82 was made according to the Miyake process with slight modifications which did not make any material difference.

A. In your premise, you indicated that I wrote this and I am not sure I wrote this; but I certainly accept it as an argument that I reviewed and was put in. If your point is that it should have said "and additional uEPO used" rather than "the uEPO used", I take your point. It does say a comparison to the prior art uEPO of Miyake et al. Anyone reading that declaration attached to Strickland's declaration as TW2 would understand that. Anyone reading Dr. Strickland's declaration, which is the four-page declaration that we are referring to, would understand that those were absolutely the alpha and beta uEPO products that came out as the two homogenous fractions of the hydroxyl apatite-type column. We just went through that on page 7. That is what is referred to on page 7. On page 14, we are saying that Dr. Strickland's work on isoelectricfocusing sialidase resistant charges and sulfation analysis are reported in this declaration. That is the four pager, plus its attachments. There is also attached to that the 1988 declaration that had both. Perhaps it should have said "and the uEPO used in a prior study in his 1988 declaration". I will accept criticism on all those points for having let this go through

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with some degree of ambiguity.
Q. I am not criticizing you in that respect, Mr. Borun. My suggestion to you is that you believed that the modifications made to the Miyake process, and which are referred to here, made absolutely no difference to that process in terms of what it would produce.
A. I think it would make absolutely no difference to the protein in terms of there being differences in isoelectricfocusing results, and that was the case. Both were different from the recombinant EPO in terms of the isoelectricfocusing data - both the prior art EPO and the non-prior art EPO.
Q. You thought that it was appropriate to rely upon a process which had these modifications in it as good and, indeed, best evidence of what EPO made according to Miyake would be, such that you could compare it with your recombinant EPO and seek to show novelty.
A. I reject that position. The document that you are referring me to here talks about the attached study, TWS2. It talks about paragraph 10, and addresses the fact that it was uEPO obtained from Dr. Goldwasser which was prepared in 1976 according to the Miyake procedure. I do not see how this could be taken to indicate my belief that the Lot 82, or the belief of anyone involved in the authorship or review of this, material which was not prior art EPO was prior art EPO.

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Q. I suggest to you that when you wanted to make a specific reference, or thought it appropriate to make a specific reference to, to the different fractions of uEPO, you did so and you so made it clear, as we can see from the beginning of the third paragraph: "For his sulfation studies, Dr. Strickland also used actual samples of the .... prepared according to Miyake."
A. Yes.
Q. Do you have any comment upon that?
A. That is what it says.
Q. Could you go back to page 9 of annex A, please, where again you are addressing the question of novelty, paragraph 1.4.
A. I have it.
Q. You say here in the title: "EP 148 605 and the literature references demonstrate differences between rEPO and uEPO".
A. Mm-mh. Whether isolated to the prior art or not.
Q. In the first sentence you write: "EP 148 605 and the relevant literature references demonstrate a detectable and significant difference between rEPO produced in any number of known recombinant host cells and uEPO, whether isolated according to the prior art Miyake or Sasaki et al references or isolated by procedures published after the relevant priority date." Specifically, Mr. Borun, in so far as you are referring to 605 and any number of known recombinant host

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cells, you can only have there been referring, can you not, to the passage that we see in the 605 specification?
A. I am sorry. There is no reference to host cells in the part that you pointed me to.
Q. At page 29.
A. There is no reference to host cells in what you have pointed me at .... I am sorry. "Any number of known recombinant host cells", so that would be CHO, COS —
MR. JUSTICE NEUBERGER: That is right.
A. — baby hamster, kidney. I do not think anyone was doing anything else in mammalian host cells. That would include yeast cells and, of course, bacterial cells.
MR. KITCHIN: What material in the patent demonstrated a detectable and significant difference between recombinant EPO produced in any number of known recombinant host cells and uEPO?
A. Well —
Q. Let me help you. It is the passage on page 146 of bundle A2, is it not?
A. No. It is not exclusively that.
Q. Importantly, it would include that, at any rate. You would accept that?
A. I would say, as I sit here today, that it importantly includes that experiment as described there that has never

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been contested successfully before us having taken place and as having accurately represented what did take place. Yes. The importance I attach to it is an importance that is keyed to the importance that has been attached to it today and yesterday and in these proceedings - not in any terms of scientific importance. It is an experiment. Various other experiments were performed that do show differences. They have always shown differences between any kind of .... As we state right here, urinary EPO will always be different, that is glycosylated, from any glycosylated recombinant EPO in some way. That is the point that we were arguing. Maybe we undertook too large a task, but certainly the science supported us in this manner.
Q. You intended the reader of this to understand that the 605 patent describes a difference between COS and CHO urinary EPO on the one hand and urinary EPO on the other on SDS, did you not?
A. That does in fact hold up, as is set out in Prof. Cumming's table. Yanagi, he had a difference in molecular weight. Sasaki has a difference in molecular weight on SDS-PAGE. Imai have a difference in the molecular weight on SDS-PAGE, as set out on page 12.
MR. JUSTICE NEUBERGER: That is not quite an answer to the question. Mr. Kitchin, you had better repeat the question.

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A. That is correct.
Q. I have two points, Mr. Borun. First of all, Prof. Cummings did not there say — and you have not suggested here — that the papers show that COS EPO has a higher apparent molecular weight on SDS-PAGE than uEPO. Is that not right?
A. I would have to see precisely what Prof. Cummings said in his declaration to confirm that.
Q. At any rate, your argument here is that they migrate to similar regions but are not identical. There is no support in those papers for the proposition that COS EPO has a higher apparent molecular weight than urinary EPO.
A. I would have to see what Prof. Cummings says about that. He can say similar slower or similar faster.
Q. I am talking about your submission at this stage.
A. Our submission is Dr. Prof. Cummings's submission.
Q. So you rely on nothing other than Prof. Cummings. Is that right?
A. I think it would have been unsafe for me to rely on anything but Prof. Cummings for this section. It was referring to Prof. Cummings. It was his opinion. He is certainly the most significant glycobiologist I have ever met.
Q. We have seen that you have repeatedly relied upon a passage in the specification as support for the fact that there is a difference in the behaviour of recombinant EPO whether

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produced by COS or CHO cells on the one hand and urinary EPO on the other.
A. Yes.
Q. That is right. You have consistently relied upon the passage in the specification.
A. Absolutely, and I rely on it today, as I sit here.
Q. Did you ever disclose to the Board of Appeal that there was nothing underlying that statement other than the Egrie work which we have been looking at?
A. I think it is understandable, from a reading, that that was a preliminary experiment, exactly what it involved, exactly what the results looked like. By saying that there is nothing underlying it rather than the description of it, there is something underlying it and that is the description.
Q. You see, my point, which I am trying to explore with you —
A. If you are suggesting that the work was never done —
Q. What I am trying to explore with you, Mr. Borun, is this, that the patent was published, and you were relying upon the published statement in your patent, in Amgen's patent, that COS and CHO recombinant EPO on the one hand behaved differently from urinary EPO on the other hand on SDS.
A. In an experiment involving the three together, subjected to neuraminidase digestion, yes.
Q. And Conradt here is putting against that proposition some

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Egrie papers.
A. Yes. Prof. Cummings is putting against Dr. Conradt his interpretation of the Egrie papers, that they do not establish that the materials migrate identically. That is what the controversy is about.
Q. But did you ever disclose that there was nothing underlying example 10 other than that Egrie work?
A. I do not understand what you mean by "underlying". Do you mean had it been repeated? No, not to my knowledge, it had not been repeated. Had I known that it was going to be important, I would have said, "Jump into your freezers and see if you have any of that COS cell material left. Let us run that one again."
Q. Did you ever disclose to your opponents or to the Board of Appeal that there was nothing underlying example 10 other than the work carried out by Dr. Egrie?
A. Example 10 is the work carried out by Dr. Egrie. I have no idea what you mean by "nothing underlying it".
Q. Other than the work by Dr. Egrie, because what —
A. There was nothing underlying any of the experimental results in any of these publications other than the work done by the authors of the publications. I do not understand the question.
Q. I will try once more.

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A. We did not tell them there is nothing underlying the Sasaki experiments but the Sasaki experiments.
Q. Did you tell them there was anything underlying example 10 other than work carried out by Dr. Egrie?
A. We never said that there was.
Q. Could you please just look at the last section on page 21 where you observe: "Moreover, comments on the similarities of recombinant EPO and urinary EPO in some of the early publications describing recombinant EPO must be placed in the proper temporal context."
A. I am sorry, I have missed our —
Q. It is page 21 of annex A, at the bottom.
A. Yes.
Q. "At the early states of analysis of rEPO, it was quite surprising (and hence most noteworthy) that rEPO could be as similar to uEPO as it was found to be."
A. I think that is exactly what I said about Dr. Egrie's first work on the COS cell material. She was happy, delighted.
Q. I suggest to you, Mr. Borun, that the impression that you were seeking to give there was that the work reported in the Egrie publications was early work and consequently it was subject to doubt.
A. Yes. It was as preliminary as the work that is reported in the specification.

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Q. Or that Amgen had changed its mind over those early Egrie publications. That was the impression that you were trying to give, was it not?
A. No. I am saying in reference specifically to Prof. Cummings's comments that .... Again, to the extent that I am talking about this as though I wrote it, I do not recall if I did. I certainly do vouch for every word of it as far as has been brought to my attention so far. This is a comment about terms like "migrates identically".
Q. I suggest to you that this comment at the end of page 21 was positively misleading because you knew that Amgen, as late as 1991, in the context of the interference proceedings, was still of the view that the work carried out by Dr. Egrie and published in those publications was indeed accurate and correct.
A. The 1991 Egrie declaration and interference brief was submitted in the context of the interference as an historical document. That is what you are going after in interference, the issue of priority and who was first. It was an historical document in which Dr. Egrie accurately set forth COS comparisons with urinary and CHO comparisons with urinary, saying that in the enumerated COS comparisons there was a similarity in movement on SDS-PAGE and with CHO there was a significant difference. Yes, those statements were

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A. Prof. Cummings had no evidence on the experiment that gave rise to the text on SDS-PAGE, as far as I know, in the specification.
Q. Then what evidence are you relying upon in support of the statement in the patent that COS had a higher apparent molecular weight on SDS than urinary EPO?
A. I believe the Egrie input document, pages 26 and 27, and 27 and 27A, as it is sometimes referred to, support that. That is hindsight and I freely admit that I told Judge Young that that text supports it, but it was hindsight reconstruction.
Q. Were you relying on that at the time in 1994?
A. I am not sure if I was relying on the text, and I certainly do not believe I had a good clean copy of the gel to personally confirm that they line up -- boom, boom, boom, the way that Prof. Saw them and the way that Prof. Matsudaira saw them.
Q. In that case, then, all the evidence that you had that was persuasive to you pointed in the opposite direction, namely that COS and urinary EPO behaved identically on SDS. Is that not right?
A. No. The evidence I had included my impression that I got that information from Dr. Lin or Dr. Egrie, and that it accurately represented a preliminary experiment that they undertook. No one has ever said, "Mike we made that up." I

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made in 1991. They are completely consistent with this, which says that early times, when it comes to publications, "migrates identically", is a joyful and exuberant position about the remarkable similarity, which Prof. Cummings thought was a bit of an overstatement.
Q. As I understand it, your position before this court today is that you were right and justified in relying upon the statement contained in the patent --
A. Yes.
Q. -- as to the difference between recombinant CHO and COS on the one hand and urinary on the other, in the light of Prof. Cummings's evidence at this point. Is that right?
A. No. Prof. Cummings did not give any evidence about the experiment in the specification. He only gave evidence concerning his opinion, and that was opinion evidence, the experiments such as in the 1985 Egrie paper where the report was that COS and urinary moved identically.
Q. I suggest, Mr. Borun, that, by this time, you knew very well that the statement in the patent could not be supported as a result of the work carried out by Dr. Egrie or anybody else at Amgen.
A. I reject that suggestion.
Q. Are you relying upon the evidence of Prof. Cummings in that regard or not?

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certainly did not make it up, so I rely on the trustworthiness of the Amgen personnel for that purpose.
Q. For the sake of the record, I must make it clear that we do not agree with your characterization of Prof. Matsudaira, but I put that on one side and I am not inviting you to --
A. Then I think you will find citation to that in Mr. Waugh's presentation.
MR. JUSTICE NEUBERGER: Just on the record, you do not have to worry about argument.
MR. KITCHIN: When you say that you were relying upon statement of Dr. Lin or Prof. Cummings --
A. Dr. Lin or Dr. Egrie or perhaps Miss Lane who explained it to me.
Q. What on earth statement can you have had in mind in 1994 to support this statement of the patent in the light of all the scientific data which, by that time, you had seen?
A. I had never seen a similar experiment, Mr. Kitchin. I had never seen a similarly formulated experiment.
Q. You had not seen such an experiment showing that COS migrated with the greater apparent molecular weight at all, had you?
A. I had never seen an experiment that only addressed the issue of COS, CHO and Dr. Goldwasser's EPO run with and without neuraminidase. If there is such a one, and I fail to see it, then shame on me. I do not believe there is one.

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Q. I suggest to you, Mr. Borun, that you had not seen, and indeed you cannot now point, to any experiment showing that COS migrates with a higher apparent molecular weight than urinary EPO on SDS.
A. I can point to the experimental results in the Egrie input now that the gel is clarified and read consistently with the text of approximately equal migration. Approximately equal as you might say, could be up or down. The gel establishes that it is heavier rather than lighter.
Q. I suggest to you that approximately equal cannot be equated on any basis with COS has a higher apparent molecular weight.
A. If you are looking at a gel it can.
Q. At the hearing, you were present. Dr. Strickland was present?
A. Yes, Dr. Egrie was present.
Q. Dr. Odre?
A. Mr. Odre, yes.
Q. Mr. Odre, and Mr. Brown?
A. Yes.
Q. Prof. Cummings and Dr. Browne?
A. Yes. Dr. Egrie was certainly aware of the position taken by Dr. Couple when he disagreed with the way she had read those gels, yes, but they were there to help us, notwithstanding their difference of opinion on that.

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Q. I am going to just try and pin this one down on Prof. Cummings. Could you please have a look at bundle D2, tab 31?
A. I have it.
Q. Where I think you find a paragraph which is cited in your annex at 17.4.2. Do you have that?
A. Yes.
Q. Prof. Cummings wrote, "Dr. Conradt cites two articles by Egrie et al which show several SDS-PAGE and Western blot analysis on rEPO and nEPO. Again, these gels in these articles show that the rEPO and nEPO migrate to similar regions, but they do not precisely co-migrate. The gels would suggest the samples were similar but not identical, and any comments in the articles must be interpreted with the gels in view."
A. Yes.
Q. What I would suggest to you is that looked at at its most favourable for Amgen that provides absolutely no support for the statement in the patent that CHO-produced EPO has a somewhat higher molecular weight than COS expression product which in turn was slightly higher than the pooled source human urinary extract.
MR. JUSTICE NEUBERGER: I was making a note. Which paragraph was it? I apologize.

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A. 17.4.2. May I have your question again?
MR. JUSTICE NEUBERGER: I do apologize.
MR. KITCHIN: I read to you paragraph 17.4.2.
A. Yes, you did; thank you.
Q. My suggestion to you was that reading 17.4.2, even in its most favourable light from Amgen's perspective, it provides no support for the statement in the patent that CHO-produced EPO material had a somewhat higher molecular weight than the COS-1 expression product which in turn was slightly larger than the pooled source human urinary extract?
A. It does in a sense support what is in the patent because, first of all, the two articles that are being referred to in the context of a material that migrates identically are articles addressing COS-produced material. You yourself said that those articles are contrary to the material in the specification. In the sense that Prof. Cummings's opinion was that the "migrates identically" was an overstatement, that does support the experiment set out in example 10.
Q. He does not conclude that COS migrates with a higher apparent molecular weight than urinary, does he?
A. He says "take a look at it with the gels in hand", and I believe there has been that discussion with those gels in hand at this trial, not at this hearing but at the trial in general.

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Q. You have explained that in 1994 you did not have a good copy of the experiment at page 27?
A. I do not believe I had a good copy of the SDS-PAGE results.
Q. Where did the decent copy come from and when?
A. My understanding is that a decent copy came into existence in the context of litigation where gels that were sitting in the back of one of Dr. Egrie's notebooks were for the first time linked up with pages in her notebook.
Q. Was that this year, last year, the year before?
A. I do not know.
Q. When was it? When did you come up with this view based on a better copy of page 27?
A. As soon as I saw a better copy of page 27.
Q. When was that, last year?
A. Certainly within the last two years. Perhaps last year. It is likely to be sometime in the spring of 2001.
Q. Before that time the work of Dr. Egrie had been looked at in minute detail in the proceedings before the US Patent Office, in the proceedings that took place by way of interference and in the Amgen and Chugai litigation. If there was anything in what you are saying, why did this point not come to light during those proceedings and why did Dr. Egrie not say that in her view that experiment provided support for the conclusion that COS migrated with a higher apparent molecular

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weight than urinary EPO?
A. I have great difficulty with the "why did not" parts of your question. I can only tell you what I know. I personally felt gratified that the gels that corresponded to what was in the patent were located and that TKT had them, and that is all I can say. I cannot assess the entirety of your question because it goes to strategy. It goes to the procedures in a number of litigations. Not only do I not know, if I did know I believe that would be privileged information.
Q. I am certainly not going to ask you to waive privilege. Could you please now turn with me to consider the hearing itself before the Board of Appeal and for that purpose take out bundle D2, tab 30 where we have the minutes of the proceedings. Mr. Waugh has pointed out who was present. Could you go to page 335 of the bundle?
MR. JUSTICE NEUBERGER: A blown up version of the first part of the table that Prof. Cummings had.
MR. KITCHIN: Yes.
A. I am sorry; page 235?
MR. JUSTICE NEUBERGER: 335.
MR. KITCHIN: We have a blow-up of Prof. Cummings's table here; is that right?
A. Yes.
Q. By this stage, as I understand it, an indication had been

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given by the board that only prior art uEPO was relevant. Is that your recollection, too?
A. It was my recollection that the board had indicated that with respect to the Strickland 1988 declaration the isoelectric focusing results in the earlier paragraphs, as you say the ones that came first, were not relevant because they did not deal with prior art EPO but that the results that came later were relevant, at least to some extent, because of the use of prior art uEPO.
Q. Look with me at 335, which is the first slide, "SDS-PAGE analysis shows a difference". Yanagi, Sasaki and Imai, none of those are prior art, are they? Do you recall that?
A. I do not recall.
Q. Take it from me. So you were left relying upon the passage in the patent (lines 6 to 16) in relation to SDS; is that right?
A. If that is your submission, I understand what you are saying. You have represented to me that in no instance did Yanagi, Sasaki or Imai show an SDS-PAGE difference with a material purified by the method of Miyake or the method of Yanagawa, so by the process of elimination you have told me that none of these relates to prior art methods, which would be Miyake and Yanagawa, so I will have to admit that there is nothing left if there is a comparison here between the prior art

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urinary EPO and a recombinant product.
Q. As we understand it, Yanagi is '87, Sasaki is a modified Miyake process and Imai, certainly is the submission of Amgen, as we understand it, is not prior art.
A. I will have to take your word on it. I have not analyzed those.
Q. At any rate, you were relying upon the EP patent to show an SDS-PAGE analysis?
A. Absolutely.
Q. A difference?
A. Yes, absolutely, and I rely on it as I sit here today.
Q. In your statement —
MR. JUSTICE NEUBERGER: Core bundle 1, tab 7. Which paragraph?
MR. KITCHIN: Paragraph 24. You start to address the question of amendment to claim 19.
A. In 24?
Q. Paragraph 24?
MR. JUSTICE NEUBERGER: Paragraph 24, page 9.
A. OK.
MR. KITCHIN: As we understand it — and as I say, Mr. Borun, my clients were not present, so correct me if I go wrong, please, again without waiving privilege, which I understand you have claimed — the board appeared to take the view that claim 20 lacked novelty over Miyake. Is that right?

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A. That is my recollection, that the product by process language was not going to be sufficient to confer novelty over Miyake.
Q. You tried to insert the word "recombinant" and see if that was acceptable and the board thought that was not. Is that right?
A. I believe that is an accurate statement. I believe that is exactly what Mr. Waugh said the other day.
Q. You retired overnight and no doubt you considered what might be done; am I correct?
A. You are putting to me that we put in one auxiliary request that changed it to recombinant and then that was not acceptable, and then we retired overnight? I do not recall that.
Q. At any rate, can you help me with this. Is it right to say that at some point before the close of business on one day you appreciated you had a difficulty with novelty and that as a result you had to consider how to present auxiliary requests which might address that problem?
A. We appreciated that there might be a difficulty with novelty and considered a number of auxiliary requests that incorporated prior amendments such as taking out the antibody claims.
Q. We know that you formulated auxiliary request 11, which was ultimately accepted, and which included the SDS limitation?

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BORUN - KITCHIN

A. Auxiliary request 11 was formulated and it was accepted.
Q. Who formulated it? Again, I do not want you to waive privilege, save in so far as you are entirely happy to do so.
A. That is good, because I do not recall who formulated it.
Q. Presumably you would have been involved?
A. Presumably I would have been involved.
Q. You say in paragraph 27 of your statement that the scientists were not shielding. What does that mean?
A. There was an implication in one of the papers you filed that the insertion of SDS-PAGE as a limitation was done purposely without the knowledge or consent, to the extent that they could have consented, of Dr. Egrie, for example, and the only point I am making there is that while they were to my recollection involved in the formulation of those 15 sets of auxiliary sets of claims, there was nothing that kept them from having a copy, and in fact they probably did have a copy when they were handed up.
Q. The next day?
A. I know Mr. Brown is very clear on this. I will defer to his recollection. Mine is certainly not inconsistent. I knew the board got them the next day. It might have been the case that they were done right there in the large appeal room and distributed to other parties overnight, but I think it is more likely than that Mr. Brown's recollection is correct

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that the board, as well as the other parties, got those on the morning of the third day. That would make more sense in terms of getting copies made and things like that. I doubt that there were the facilities to do 15 different things and make a couple of sets for each opposing party and have some for ourselves.
Q. Looking at bundle A2, tab 2, page 146, you knew, did you not, that the passage from line 17 to 26 was wrong and could not be relied upon?
A. 17 to 26. Some of it was wrong.
Q. And you knew you could not rely upon that passage.
A. We knew we could not rely on it if you are referring to the carbohydrate data. We knew we could not rely on the hexose value to establish a difference because there was a question about the validity. It just was a bad experiment. There was too much material out rather than came in. We certainly did not want to rely on the data reflecting fucose content. There the data was wrong both with respect to urinary and recombinant EPO. That was completely missed on O-glycosylation. That was not the difference. We would not have relied on it in any event. 0 and 0 are the same; not different. We could not rely on the hexose.
Q. The only other paragraph upon which you could rely was the one immediately above it, the SDS-PAGE comparison.

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A. As well as the generalized statement. 20/20 hindsight tells me that in 1984 I should have gone to Lin or somebody and say, "Well, we are going to say there are differences in every carbohydrate composition. We have got these preliminary tests. Give me some more so I can put them down - linkages, tetraantennary structure and the like. They will probably be supportable." If I had done that, we would have had tetraantennary structure to put into the claim instead of SDS. We would have had linkage differences which even Dr. Cumming (GI's expert glycobiologist) said were entirely different between human and CHO cells. If that is the bad practice I am accusable of, I accept that too.
Q. So in practice then you would have had a claim which was really to CHO cells; is that right?
A. No. We would have had a claim that addressed the difference; for example, some of these differences were with bovine and hamster kidney cells.
Q. I understand. The point you have just made would have been a distinction between human cells on the one hand and CHO or COS cells on the other; is that right?
A. It would have been between urinary EPO and recombinant EPO of whatever strike as long as you got a glycoprotein coming out.
Q. That would have raised, no doubt, its own interesting questions of infringement?

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A. I am at a loss to understand your question.
Q. I will leave it. At any rate, there is no basis in terms of textual description of any such distinction in the patent, is there?
MR. JUSTICE NEUBERGER: Once you have taken out lines 16 onwards.
MR. KITCHIN: Yes. The board had indicated —
A. There are no experiments to describe. I will give you that. There are no experiments to describe.
Q. The board had indicated that relying upon average carbohydrate composition as a whole was not acceptable. We have looked at all those general distinctions sought to be drawn by Dr. Cummings, have we not?
A. I am trying to remember whether or not there was a reference to a difference in molecular weight for the yeast-produced material.
Q. But you were left as a practical matter —
A. In that section certainly.
Q. Relying upon and having to rely upon the paragraph from line 6 through 10, which concerned SDS. Is that not right?
A. I am looking now, that you have invited me to look to, see if there is something that addresses the apparent molecular weight of the yeast-produced material.
MR. JUSTICE NEUBERGER: While he is looking, Mr. Kitchin, how are we doing in terms of time? We are running quite slowly.

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UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, v. F. HOFFMANN-LA ROCHE LTD, ROCHE DIAGNOSTICS GmbH, and HOFFMANN-LA ROCHE INC. Defendants.	CIVIL ACTION No.: 05-CV-12237WGY

APPENDIX B, EXHIBIT 5 TO DEFENDANTS' MEMORANDUM IN SUPPORT OF ITS MOTION TO COMPEL PRODUCTION OF DOCUMENTS IMPROPERLY WITHHELD ON GROUNDS OF PRIVILEGE

Dated: March 27, 2007
Boston, Massachusetts

Respectfully submitted,
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EXHIBIT
5

In the Matter of:

Amgen, Inc. v.
Hoechst Marion Roussel, Inc., et al.

Trial Volume 22
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6c, correct?
A: That's correct.
Q: And Mr. Borun was still attorney of record on this application; isn't that true?
A: I believe that is the case formally. He had the original power of attorney as well as others.
Q: He never withdrew as attorney of record to the best of your knowledge?
A: Not to my knowledge.
Q: And you're also aware that at the time of this April 28th, 1999 amendment he had already prosecuted or was prosecuting to issue the other four patents-in-suit, correct?
A: At the time of this amendment the other four patents-in-suit had already issued, and yes, Mr. Borun was involved in the prosecution of those patents-in-suit.
Q: Each one of them, correct?
A: Yes, each one of them.
Q: Now let's take a look at argument that Amgen made in support of the patentability of claims 64 and 65 submitted here. I would like to ask you to please turn to Page 5 of Exhibit 2215. Five of the amendment.
Now, in the second full paragraph Amgen argued with respect to claim 65 that it had submitted that the two Goldwasser references reviewed at the interview, quote, do

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not disclose a pharmaceutically acceptable preparation, and it goes on. Correct?
A: Yes. As I stated, that was one of the points I had made at the interview.
Q: And you also said that those references involved use of, quote, partially purified EPO preparations obtained from sheep plasma, correct?
A: Yes, that's what's written here.
Q: Okay. And you argued that the subject matter of claim 64 and 65 were novel and nonobvious over the prior art?
A: Yes, the second full paragraph makes that statement, and then there are reasons discussed not only on this page but the following page for that statement.
Q: Okay. And the prior art included the two Goldwasser sheep plasma articles that you had disclosed at the interview, correct?
A: Well, they were prior art in the sense that they were prior published references. I did not consider them to be relevant for novelty or obviousness purposes and that's not why I disclosed them to the Patent Office. But here it is stated that they do not disclose a pharmaceutically acceptable preparation, that's correct.
Q: Okay. So it's your testimony that you did not consider these sheep plasma articles to be relevant prior art?
A: Well, we were claiming pharmaceutical compositions, and

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partially purified sheep plasma is not a pharmaceutical composition as stated here.
Q: But you still gave these two articles to the examiner?
A: Yes, I disclosed them to the examiner because they both contained a suggestion that EPO in solution requires a stabilizer in order to prevent the loss of activity. So that was the point of disclosing them.
Q: I see. And that was important because claim 65 which you had submitted mentioned human serum albumin, correct?
A: Claim 64 does not specify human serum albumin; claim 65 did. So it was important for both purposes —
Q: I see.
A: — that the examiner understood that there was literature that suggested that EPO required a stabilizer.
Q: Let me show you an Exhibit marked 6b which is Information Disclosure Statement in the 197 application leading to the '422.
Mr. Watt, this is the Information Disclosure Statement that you submitted to the Patent Office on the same day as the exhibit we just looked at, Exhibit 2215, correct?
A: Yes, it bears the same date.
Q: Okay. And it lists — and in this Information Disclosure Statement you listed 441 references, correct?
A: Yes, this was the same Information Disclosure Statement

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that was submitted in the other patents-in-suit, and so it was filed of record here as well.
Q: Okay. And it listed about 441 references, correct?
A: I haven't counted them all. There are over 400 references, yes.
Q: Including about a dozen Goldwasser references, correct?
A: I can't say there are a dozen. There are several Goldwasser references cited here. But —
Q: Amgen did not disclose Dr. Goldwasser's human EPO study or the results of that study to the examiner when it made these submissions to the Patent Office, did it?
A: There was no publication of that study or those results.
Q: It didn't disclose the existence of the study or its results when it made this submission in the '422 application, did it?
A: The existence of this study was disclosed previously through —
Q: That's not my question.
A: — documents.
Q: My question is whether Amgen disclosed at the time it was making this amendment to get the claims of the '422 patent, at the time it made this information disclosure disclosing 441 references, it didn't disclose the existence or the results of the Goldwasser human EPO study, did it?

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, v. F. HOFFMANN-LA ROCHE LTD, ROCHE DIAGNOSTICS GmbH, and HOFFMANN-LA ROCHE INC. Defendants.	CIVIL ACTION No.: 05-CV-12237WGY **[REDACTED VERSION]**

APPENDIX B, EXHIBIT 6 TO DEFENDANTS' MEMORANDUM IN SUPPORT OF ITS MOTION TO COMPEL PRODUCTION OF DOCUMENTS IMPROPERLY WITHHELD ON GROUNDS OF PRIVILEGE

The filing of this confidential exhibit has been deferred pursuant to the provisions of the Court's Order entered on 2/7/07 [274].

Dated: March 27, 2007
Boston, Massachusetts

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UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

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Plaintiff,	
v.	
	CIVIL ACTION No.: 05-CV-12237WGY
F. HOFFMANN-LA ROCHE LTD, ROCHE DIAGNOSTICS GmbH, and HOFFMANN-LA ROCHE INC.	**[REDACTED VERSION]**
Defendants.	

APPENDIX B, EXHIBIT 7 TO DEFENDANTS' MEMORANDUM IN SUPPORT OF ITS MOTION TO COMPEL PRODUCTION OF DOCUMENTS IMPROPERLY WITHHELD ON GROUNDS OF PRIVILEGE

The filing of this confidential exhibit has been deferred pursuant to the provisions of the Court's Order entered on 2/7/07 [274].

Dated: March 27, 2007
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UNITED STATES DISTRICT COURT
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Plaintiff,	
v.	
	CIVIL ACTION No.: 05-CV-12237WGY
F. HOFFMANN-LA ROCHE LTD, ROCHE DIAGNOSTICS GmbH, and HOFFMANN-LA ROCHE INC.	**[REDACTED VERSION]**
Defendants.	

APPENDIX B, EXHIBIT 8 TO DEFENDANTS' MEMORANDUM IN SUPPORT OF ITS MOTION TO COMPEL PRODUCTION OF DOCUMENTS IMPROPERLY WITHHELD ON GROUNDS OF PRIVILEGE

The filing of this confidential exhibit has been deferred pursuant to the provisions of the Court's Order entered on 2/7/07 [274].

Dated: March 27, 2007
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