Amgen Inc. v. F. Hoffmann-LaRoche LTD et al Doc. 57 Att. 2

EXHIBIT B

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UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

VOLUME VII

THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK,

Plaintiff

v.

ROCHE DIAGNOSTICS GmbH, formerly known as BOEHRINGER MANNHEIM GmbH,

Defendant

Civil No. 93-11512-NG

Boston, Massachusetts
July 16, 2001

TRANSCRIPT OF TRIAL DAY 7
BEFORE HON. NANCY GERTNER,
UNITED STATES DISTRICT JUDGE

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(Continued)

Reissue of U.S. Patent No. 6,455,275 B1
Issued: September 24, 2002
REISSUE filed June 17, 2004
Exhibit 28

(Continued)
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Proceedings recorded by stenotype with computer-aided transcription.

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VOLUME VII

WITNESSES FOR THE PLAINTIFF

EXHIBITS

(All agreed upon exhibits were admitted in evidence.)

PROCEEDINGS
SEVENTH DAY OF TRIAL

(The following proceedings were held in open court before the Honorable Nancy Gertner, United States District Judge, United States District Court, District of Massachusetts, at the United States Courthouse, 1 Courthouse Way, Boston, Massachusetts, on July 16, 2001, at 9:28 a.m.)

THE COURT: Good morning, everyone. You can be seated.

Dr. Fritsch?

THE COURT: Okay, go on.

EDWARD FRANCIS FRITSCH, RESUMED
CROSS-EXAMINATION, CONTINUED

BY MR. BAUER:

Q. Good morning, Dr. Fritsch. How are you today?

A. Fine, thank you.

MR. BAUER: Your Honor, if I may, I just want to let you know exactly where we're going this morning. Counsel has read the transcript extremely carefully and would like to basically have Dr. Fritsch present an overview of what GI did, when they did it, when the cell line made, when it was shipped to BMG, so that -- when the stuff was bailed, so that you could see everything, and we'll go right through that in fairly quick fashion.

THE COURT: But you'll do it in the narrative form so

that Mr. Zivin will be able to -- not in narrative form, that is to say, in question and answer form.

MR. BAUER: Correct.

THE COURT: Okay.

MR. BAUER: But I just wanted to tell your Honor where we were headed this morning.

THE COURT: Head away.

MR. BAUER: Excuse me?

THE COURT: Go. Head away.

MR. BAUER: Okay. Thank you, your Honor.

BY MR. BAUER:

Q. Dr. Fritsch, if you could, could you stand up to the board, because I'd like for you to prepare a flow chart for The Court, probably in a somewhat vertical fashion, starting with the isolation of the gene and ending up with the product -- with the EPO product being shipped overseas.

So, when did you first isolate the EPO gene, and you can put that on the board.

A. So, in the June to August time frame of 1984, we isolated the EPO gene, the genomic clone and the cDNA clone.

Q. And then, with respect to the production clone, did you then put the EPO gene into a plasmid?

A. Yes.

Q. And could you then draw with a vertical arrow down the next step in the process?

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the production process efficient enough and that the quality of the EPO that is produced is appropriate.
Q. In layman's terms, does it mean it spits out enough EPO per unit of time to make it worthwhile?
A. Yeah, enough good EPO per unit of time to make it worthwhile. That would be the simplest way to describe it, yes.
Q. Dr. Fritsch, if you would, I would also like you to look at Plaintiff's Exhibit 152 and Plaintiff's Exhibit 112.
A. Okay.
Q. What are those two documents, Dr. Fritsch?
A. Well, the Plaintiff's Exhibit 152 is a telefax to Chugai from GI indicating that we will be shipping them the master cell bank and master working cell bank files from the DN2-3alpha3 cell line.
And --
Q. And what's the date on that?
A. I'm sorry?
Q. What's the date on that?
A. February 24, 1986.
Q. And why did GI ship to Chugai on February 24, 1986, an EPO production clone DN2-3alpha3, 10 micromolar?
A. Our agreement with Chugai was that they would be able to carry out the manufacturing of EPO and that, in order to accomplish that, we needed to send them the production cell

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line.
Q. And this agreement was made prior to the initiation of any collaboration with Boehringer Mannheim; is that correct?
A. That's correct, yes.
Q. And the next document, Dr. Fritsch?
A. Well, the next document, the first three pages relate to a shipment of --
THE COURT: I'm sorry, the next document you're referring to is --
MR. BAUER: Plaintiff's Exhibit 112, your Honor.
THE WITNESS: Plaintiff's Exhibit 112, yes.
THE COURT: Okay. Thank you.
A. The first three pages refer to a shipment of some non-GMP EPO to Boehringer Mannheim, additional shipment of it, and this is in March of 1984.
Q. And what was the non-GMP EPO made from?
A. Yeah, this is, again, additional EPO from the DN2-3alpha3 production line.
THE COURT: And the reason why you had to send the bulk EPO to both Boehringer Mannheim and to Chugai was for their applications for the new drug IND?
THE WITNESS: Right, as part of that process. In order for them to begin to understand how they should formulate the drug and put it into vials for actual injection -- that part of the process was theirs, their responsibility -- they

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needed to have some of the protein to actually work with to do that technical work. So, we were shipping them the protein, they would do the technical work, and then they figured out how to formulate it and put it in the vials. And they needed it for that purpose.
A. The latter pages, I guess, of this exhibit -- again, it's Exhibit Number 112 -- PX-112, referred to our shipment to them of vials of the master cell bank and the master working cell bank.
Q. Now, I think in the transcript you said this was transferred March of '84. Is that what you meant, Dr. Fritsch?
A. That the production clone -- the production clones, the cell bank vials, were sent in March of 19 -- oh, I'm sorry, March of 1986.
Q. Thank you, Dr. Fritsch.
Now, did Chugai -- did GI supply Chugai with bulk EPO for commercial sale in Japan?
A. I believe we never supplied them the bulk EPO for commercial sale. We supplied them bulk EPO that they used for clinical development, for preclinical development. All of the bulk EPO that they actually sold commercially was manufactured by Chugai. And our contract with Chugai allowed that they could be the sole manufacturer, if necessary.
Q. So, regardless of the relationship between GI and Boehringer, GI was making bulk EPO -- would make bulk EPO; is

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that correct?
A. Yes. We needed to make the bulk EPO in order to help Chugai move the process along of its registration quickly, because they still had to build a production facility before they were able to commercially manufacture it.
Q. Now, if you take a look at -- I think it's the fourth page in, it's bearing Bates number 100793?
A. Yes, I have it.
Q. What is that describing, Dr. Fritsch?
A. This is a telefax that accompanied the transfer of the EPO production clone master cell bank and master working cell bank from DN2-3alpha3 to Boehringer Mannheim.
Q. And is these -- the vials which are designated on document 100793, is that the vials from the master cell bank and the master working cell bank that you drew this morning on that chart?
A. Yes.
Q. And could you just make a notation on the chart saying "shipped to Boehringer," "shipped to Chugai," and the dates?
A. (Complying.)
Q. And in these vials is just a gazillion of the DN2-3alpha3 cells that are from box number 7; is that correct?
A. Yes. Each vial contains approximately a million cells. Not a gazillion, but a million, yes.
Q. Now, Dr. Fritsch, I'm going to read something to you. You

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tell me if it's true.
On March 4, 1986, GI transferred to Roche the EPO production clone DN2-3alpha3. DN2-3alpha3 is the only production clone used by Roche to make EPO for sale.
Do you agree with that?
A. Yes.
Q. Now, the next sentence, which refers back to that quote, states, the cited production clone, however, is not the production clone actually used by Roche, but a predecessor cell line which had not been amplified.
Is that statement true, Dr. Fritsch?
A. No. Could you read it again, please?
Q. Sure. The cited production clone, namely the clone that was transfered on March 4, 1986, however, is not the production clone actually used by Roche, but a predecessor cell line which had not been amplified.
A. No, that's not true! It is the production --
Q. And why isn't that true?
A. Well, it is the production clone used by Roche, and it had been amplified at the time that it was shipped.
THE COURT: Because that statement is inconsistent with your characterization of how number 7 came about?
THE WITNESS: That's correct, because number 7 came about after the amplification steps had happened, and it is the production clone that's used by Roche.

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MR. BAUER: I'd like to say that that statement came right out of plaintiff's brief in the motion for support of -- or in its opposition motion to Roche's motion for summary judgment, on page 10.
BY MR. BAUER:
Q. Now, do you remember your first contact with BMG -- I'm sorry, Boehringer Mannheim, Dr. Fritsch?
A. Yes.
Q. When would that be?
A. I believe it was sometime around November of 1985, maybe December.
Q. Well, let me show you Plaintiff's Exhibit Number 149.
A. Okay.
Q. Does that refresh your recollection as to when you first met with Boehringer Mannheim?
A. Well, it -- the -- I mean, what this refers to is a telefax to Boehringer from Katherine Smith, who's our project director, introducing both myself and Dr. Shoemaker as the project leaders of the EPO project. This was at the end of October in 1985, and this was prior to the actual first meeting we had with Boehringer Mannheim in which Dr. Shoemaker and led an EPO discussion. That was --
Q. And prior -- and prior to that date had Boehringer been given knowledge of any of the details of GI's cloning and expression of the EPO gene?

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A. No, they hadn't been given any knowledge of the details. They were, in general, aware of the fact that we had cloned the gene, that we were working on expression; but they had not been given any details.
Q. Now, are you aware that in 1987 GI bailed EPO-produced cells to Boehringer?
A. Yes.
Q. And could you explain to the Court your knowledge?
A. Prior to the issuance of the Amgen patent in the United States, our legal counsel had --
MS. SHANAHAN: Objection. Your Honor, I'd ask and instruct Dr. Fritsch not to divulge internal privileged communications that he had with GI's legal counsel.
THE COURT: Can you ask the question in a way that doesn't require privileged information?
MR. BAUER: Yes.
BY MR. BAUER:
Q. Yes Dr. Fritsch, were you aware that cells were bailed from GI to Boehringer in 1987?
A. Yes, I was aware.
Q. And what was Boehringer's role with respect to keeping those cells?
A. Boehringer was to store the cells for GI's purposes under appropriate conditions, and could return them to GI at our request, or would return them to GI at our request.

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Q. Who initiated the decision to bail cells to Boehringer? Was it Boehringer or was it Genetics Institute?
A. Genetics Institute.
Q. And whose decision was it to have those bailed cells returned?
A. Genetics Institute's.
Q. And whose property were those cells?
A. Genetics Institute.
Q. And Boehringer never used those cells in Germany, did they?
A. No.
Q. Now, if you could, Dr. Fritsch, I'd like to -- if you could, please pull out Plaintiff's Exhibit Number 117.
A. Okay.
Q. There's a -- the fifth paragraph down on the first page, 1407, there is a paragraph referring to the QA conditions?
A. That's correct, yes.
Q. What does that mean?
A. QA stands for quality assurance. So that, essentially, it's part of the sort of GMP principles or ways of conducting business; that there is an appropriate documentation and evaluation of all the various steps that are involved. In this case, it relates to the steps for the storage of cell bank files.
Q. And what would the purpose have been for having these QA

conditions in place?
A. Well, if GI would want to have the cell bank cells returned back to GI and ever use them for manufacturing, then we would need to have all the documentation to show that they had been received and stored in the appropriate conditions.
Q. Now, if we go to the second page, we see a number of descriptions. And I'd like to contrast that with the document that we looked at earlier which described what was transferred to Boehringer in March of -- March 4, 1986. That is Plaintiff's Exhibit Number 112.
If we take a look at Plaintiff's Exhibit 112, the page bearing Bates number 100793, there are also descriptions of vials.
A. Yes. That's correct.
Q. Excuse me?
A. That's correct. Yes.
Q. Could you explain to the Court what the relationship between these two sets of vials is?
A. Well, the set of vials shown in Exhibit 112 on page 100793, there are two sets shown there. One set is DN2-3alpha3, and it goes on, and the date of 12/4/85. These are the master cell bank files. Then, below it, is a similar description with a date of 12/18/85. These are the master working cell bank files.
Those two sets of vials that are described there are

the same as the vials shown in Exhibit 117, on the second page, where it is labeled number 1 and number 2. Number 1 refers to the master cell bank files, number 2 to the master working cell bank files.
I should point out that the date at the end of number 1 is 12/4/87. That's a typographical error. It should have been 12/4/85.
THE COURT: It should be 12/4/85.
A. But other than that, those are the same cells.
Q. Now, the cells that are referenced as being bailed to Roche, do those cells -- are those the same -- are those the same cells as the DN2-3alpha3 clone which is referred to in box number 7?
A. Yes.
Q. And with respect to category number 3 in the bailed cells on page 1408, is that also the same cell as the EPO production clone, DN2-3alpha3?
A. Right. These are basically DN2-3alpha3 cells that have been adapted to grow with no fetal bovine serum.
Q. So, these are not cells that were made after the cells that were made in box number 7; is that correct?
A. No, they all came from the same -- they all came from box number 7. No additional genetic manipulations took place. They were simply allowed to grow under different conditions.
Q. So, would it be fair to say that box number 7 in document

number 06387 is the source of cells from essentially all of the cells originated and which were shipped to Boehringer?
A. That's correct. Yes.
Q. You didn't have the DNA, and then remake the cells, and then ship those to Boehringer after box number 7 was made; is that correct?
A. Right. We did not additional DNA modifications.
I should just point out that there was, in addition to box number 7 --
Q. Uh-huh.
A. -- the right arm of that chart refers to an additional amplification that had already taken place, and cloning of cells from that. And some of those cells are also shown here that were shipped to Boehringer Mannheim.
Q. Now, in terms of the overview, at Genetics Institute cells from the master working cell bank were used to make bulk EPO; is that correct?
A. That's correct, yes.
Q. And that bulk EPO was shipped to BMG in Germany, where it was formulated and then either used for clinical trials or sold; is that correct?
A. That's correct, yes.
Q. The master cell bank that was -- the vials of the master cell bank that were shipped to Boehringer in March of 1986 were eventually used by Boehringer to make its own EPO products; is

that correct?
A. That's correct.
Q. And when Boehringer made it's own EPO product, Boehringer formulated that and then sold that; is that correct?
A. Yes.
Q. What is the relationship, if any, between the bulk EPO that GI shipped to Boehringer and BMG's use of this EPO production clone to make its own EPO? In other words, does Boehringer need GI's bulk EPO in order to make EPO from its own production clone?
A. No. Once Boehringer had the production clone and followed the same steps that Genetics Institute had used to make bulk EPO, it made bulk EPO on its own and no longer required GI to make bulk EPO for Boehringer.
Q. Now, when the bulk EPO goes over to Boehringer, it's formulated and then moved to the end of its life span, so to speak?
A. Right.
Q. Goes into a human?
A. It's formulated and sent to pharmacies and --
Q. The bulk EPO does not replicate itself? It's not like the cell line that keeps spitting out the EPO; is that correct?
A. That's correct. The bulk EPO is the end product of the expression and purification.
THE COURT: When you said BMG had the production

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clone in October and in December, when you sent the master cell bank and the master working cell bank to -- you were actually sending the production clone or the bulk EPO, or both?

THE WITNESS: Well, if you recall, we ended up sending two things, I believe, in October -- or November.

THE COURT: Yes.

THE WITNESS: In November we sent them bulk EPO, non-GMP EPO.

THE COURT: Um-hmm.

THE WITNESS: And in --

MR. BAUER: And what was that made from?

THE WITNESS: That was made from the production clone, DN2-3alpha3. That was material that Genetics Institute made, prepared, purified and sent to Boehringer Mannheim.

In addition, between October and December of 1985, we created the master cell bank and the master working cell bank, the production clone, itself, and that was shipped to Boehringer --

THE COURT: I see.

THE WITNESS: -- in March of 1986.

THE COURT: So, there are essentially two vectors. From the production clone, BMG can, itself, create bulk EPO for its own production. And then the bulk EPO that GI sent, they can likewise process for its own production?

THE WITNESS: They can process. It doesn't

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replicate. It doesn't make more. That's all they have. What they needed ultimately was the production clones, so that then they could make as much of their own EPO as they wanted to.

THE COURT: Why did GI send bulk EPO at all? Why not just send the production clone?

THE WITNESS: Well, because at the time, back of 1985, Boehringer didn't have any of the technology in place to make the EPO from the production clone itself. But GI had already had access to the production clone, was growing it up, and purified EPO. So that we could get them bulk EPO to work with --

THE COURT: I see.

THE WITNESS: -- before they could make it themselves.

THE COURT: Would GI have made bulk EPO in the fall of 1985, were it not for the BMG deal?

THE WITNESS: No. I think, as you'll see -- saw in some of the other documents, we shipped the same bulk EPO to Chugai. Chugai similarly -- we had a contract with them to supply bulk EPO, and even GMP EPO, but they also had the right to do all the manufacturing themselves if they wanted to.

THE COURT: And that was already in place, then, by the fall of '85, when the bulk EPO was shipped to BMG? Is that --

THE WITNESS: That's correct. That had been --

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THE COURT: That is to say, the arrangement with Chugai was already in place?

THE WITNESS: Yes. That had been in 1984, that arrangement.

THE COURT: Okay.

BY MR. BAUER:

Q. Your Honor Dr. Fritsch has a unique characteristic in that sometimes he says yes, and doesn't mean yes, in terms of following the question. And we'll have to clean it up a little bit later. But my counsel has told me that he said no, when I don't think he meant no. So, if we could --

THE COURT: I have a child like that. I don't know what to make of the information. Do you have to clean it up or not?

MR. BAUER: This is the court: At the start, would GI have made bulk EPO in the fall of 1985, were it not for THE BMG deal?

Answer: No.

But it's really yes. And then he reads on.

So, let me just ask you again, Doctor.

THE WITNESS: Okay.

THE COURT: He did the same thing in answer to some of -- during the deposition; was that a problem?

MR. BAUER: Yes.

THE COURT: Go on. I'm sorry.

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MR. BAUER: Exactly.

BY MR. BAUER:

Q. Okay, Dr. Fritsch -- well, I don't want to repeat your Honor's -- maybe you could ask the question?

All right.

At the start, would GI have made bulk EPO in the fall of 1985, were it not for the BMG deal?

A. Well, I won't say yes or no. I will say GI was making bulk EPO in 1985, independent of the Boehringer Mannheim deal.

Q. Now, GI did supply bulk EPO to Boehringer from approximately 1988 through 1991; is that correct?

A. Yes.

Q. And what was the source of the cells that were used to make this EPO?

A. It was the same production clone, DN2-3alpha3, 10 micromolar methotrexate, and it was the same master cell bank and working cell bank files.

Q. So, the EPO -- excuse me, the bulk EPO that GI made and shipped to Boehringer was made using the EPO production clone DN2-3alpha3, 10 micromolar that GI made prior to October 8, 1985; is that correct, Dr. Fritsch?

A. Yes.

Q. Now, do you know if the bailed cells ever came back into the United States, Dr. Fritsch?

A. Yes, some of the vials did come back into the United

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clinical trials and for its commercial production and sale, were made by Chugai; correct?
A. All the bulk EPO was made by Chugai, yes. The bulk EPO that we supplied them was used for other purposes prior to approval.
Q. Well, do you recall Judge Gertner asking you a question about whether you were going to make EPO for Chugai and answering, We already were required to make it for Chugai, our other partner? Do you recall that testimony?
A. Yeah, that's correct.
Q. Isn't that testimony incorrect, sir?
A. Ah, no. It's not incorrect. I mean, we were required to make EPO for Chugai. We had made clinical trial material EPO for Chugai, but they later decided that they should -- they would prefer to use EPO from their facility for their clinical trials. So that the material that we made for them, you know, was part of our obligation to them, they decided not to use and they decided to use the material they made.
Q. So -- so it isn't true that if Boehringer Mannheim had wanted commercial product from GI, that GI would have been making it anyway for Chugai; that isn't true, is it?
A. Well, when you say "commercial product," at the time when we, uhm, shipped the vials to Boehringer, at the time we manufactured the first clinical material for Boehringer, we were also doing that for Chugai. That was the material that

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they were going to use in their clinical studies. By the time Boehringer was requiring material for commercial sale, uhm, Chugai, I believe, already had their manufacturing facility in place and was manufacturing what would be their material for commercial sale.
But at the time we're talking about in late 1985, early 1986, uhm, that was not yet in place with Chugai. So we were doing it for both partners.
Q. Well, isn't it true that in October of 1985 that GI already had a contract with Boehringer Mannheim to manufacture EPO which would be commercially sold?
A. Ah, I believe in the original R & D license agreement we've had with them, we did specify that GI had the right to -- or the obligation to manufacture commercial material for Boehringer, most of it in material in the beginning, and then as the years went on, uhm, the proportion of material that was needed, uhm, reduced at GI and increased at Boehringer.
Q. So there was an obligation for GI to supply Boehringer Mannheim with commercial material; correct?
A. Yes, I believe that's correct. Yes.
Q. Now, isn't it true that there was no such obligation to supply Chugai with commercial material?
A. Uhm, I'd have to look in the wording of the -- how the original contract was worded. Initially, we were -- we had the right or the obligation, possibility of supplying Chugai

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commercial material. I think as the years went on, it was clear that Chugai wanted to make their own commercial materia
Q. Well, you --
A. So in order to develop the product, initially GI was to be manufacturing it.
Q. Well, you have there the contracts with Chugai, the June '84 and November '85 contracts; correct?
A. Yeah. Could you tell me which exhibit again?
Q. Let me just find the number for you, sir. 142.
Can you tell me where in the June 1984 contract there's an obligation for GI to manufacture commercial EPO for Chugai?
(Pause in proceedings.)
MR. BAUER: Your Honor, this is, I think, over a hundred-page document. We may need to take a break for Dr. Fritsch to go through the entire document to see if he can find what he's looking for, plus it may be an interpretation of a legal clause, I'm not sure.
MR. WHITE: Dr. Fritsch has been testifying about the obligations they had under the contracts. A moment ago he said he thought they were obligated under these contracts to manufacture the erythropoietin for Chugai. I am asking him if he can point out where in the contracts.
THE COURT: I know, that's true. You have no objection to him having an opportunity to read it?

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MR. WHITE: Absolutely not, your Honor.
THE COURT: Okay. We will take a short break to give the doctor an opportunity to read the document.
And also while we're -- let me ask about another question. I'm sorry that my questions come up in inopportune times, but I believe in our findings on partial summary judgment, there was a March '88 EPO, bulk EPO -- is that right? -- a March '88 bulk EPO transfer?
MR. BAUER: In January 1989 there was a supply agreement between Boehringer Mannheim and GI.
THE COURT: And was bulk EPO transferred after that?
MR. BAUER: What happened was in the '85 agreement, as Dr. Fritsch testified, GI was to supply the beginning number of years and eventually it phased out. The '88 agreement supplemented that, flushed it out, and that was where the parties agreed that GI would supply 130 grams of bulk EPO. And then that was supplied.
THE COURT: That was supplied in January of '89?
MR. BAUER: I'm not exactly sure when the first shipment, ah, it may have been prior to that. There may have been shipments in late '88. But that's the two agreements.
THE COURT: So did that involve a production process again, in other words, of the taking the master working cell bank, taking a vial out and putting it in the beer vat, as we call it?

and time-consuming; correct?
A. Yes, that's correct.
Q. And it's dependent upon using a certain manufacturing process to make the product; correct?
A. Yes.
Q. And it's dependent, in this case, erythropoietin case, on using these master cells; isn't that correct?
A. For erythropoietin, yes, it's using those master cell bank cells; correct.
Q. That's the basis for approvals by the various governments, that one use these master cell bank cells to make the commercial product; correct?
A. Ah, well, at least within the current products that are approved; yes.
Q. Now, erythropoietin's not a commodity product, is it?
A. By a "commodity," you mean can be made by any of a number of manufacturers?
Q. Correct.
A. That's correct, it is not.
Q. It's not a commodity, is it?
A. Not at this point in time, no.
Q. Now, several times a little while ago you referred to the cells in the master cell bank and the master working cell bank as being genetically identical to the DN2-3alpha3 10 micromolar methotrexate cells that were available in 1985.

Do you recall that testimony?
A. Yes.
Q. And there's a reason they're genetically identical, is because they're all made using the same cotransformation followed by amplification steps?
A. Well, they're genetically identical because the cells that are used for all subsequent uses are derived from the same, uhm, set of cells that had gone through that process. They don't become genetically identical by repeating that process. It is the output of that product that is what becomes the term genetically identical.
Q. Now, I'd like to ask you if you can look at this Plaintiff's Exhibit 267.
A. Okay.
Q. Now, this refers to shipments of bulk EPO from GI to Boehringer Mannheim; correct?
A. Ah, yes.
Q. So were there continuous shipments made of bulk drug from GI to Boehringer beginning in '87 and continuing through 1991?
A. Ah, yes. That's what the document indicates; that's correct.
Q. Well, did Boehringer Mannheim pay GI approximately $40 million for that bulk drug?
MR. BAUER: Objection; lack of foundation.
THE COURT: Are you simply --

MR. WHITE: I'm asking him if he knows whether or not Boehringer Mannheim paid GI.
THE COURT: But are you asking him to tell you the figures on the invoice amount of bulk EPO?
MR. WHITE: The number's been agreed upon. There's no dispute about the number, I'm asking him if he knows whether this number was paid.
THE WITNESS: Uhm, well, yes I'm aware that Boehringer paid GI for the bulk EPO shipments. I can't specify or testify to any of the specifics, but --
BY MR. WHITE:
Q. Right.
THE COURT: But this is an agreed-upon exhibit with a total 39,758,300?
MR. WHITE: Yes, your Honor.
THE COURT: Okay.
BY MR. WHITE:
Q. Now, in addition to what's listed on this exhibit, isn't it true that GI supplied Boehringer Mannheim with erythropoietin made by the DN2-3alpha3 10 micromolar methotrexate in November of 1985?
A. Well, I think in November 1985 we shipped them non-GMP material from that cell line; correct.
Q. Right. And that was a benchmark of the October 1985 Boehringer Mannheim contract to do so, wasn't it?

A. Ah, yes.
Q. And there was a payment for that non-GMP erythropoietin of $500,000; correct?
A. Yes.
Q. That's an additional $500,000 not listed on Exhibit 267; correct?
A. Ah, I believe that's correct; yes.
Q. Right. Now, there's another benchmark in the October 1995 contract which was to supply 400 grams of erythropoietin to Boehringer Mannheim; correct?
A. I can't testify to the number, but 400 grams or 400 milligrams, I don't remember which, but --
Q. Actually, I believe you're correct that it was milligrams.
A. Okay.
Q. And that was for the clinical trials that Boehringer Mannheim was going to conduct; correct?
A. That's correct, yes.
Q. And that 400 milligrams of erythropoietin was shipped in 1986; correct?
A. Ah, yeah. I believe it was shipped late 1986. Yes.
Q. And for that material, Boehringer Mannheim paid GI $1 million; correct?
A. If that's what the benchmark called for then, yes.
Q. And again, that number is not included in this exhibit, Plaintiff's Exhibit 267; correct?

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A. Ah, no. I have no idea why this exhibit, in particular, what the question was when it was put together, but that is not included in here; correct.
Q. Now, in addition to the payments that we just were discussing, it's true, is it not, that Boehringer Mannheim also paid Genetics Institute royalties when it resold the erythropoietin; isn't that correct?
A. Yes, that's correct.
Q. In an amount of approximately $120 million; correct?
A. Uhm, I can't testify to the specific amount.
Q. Do you know --
A. Total. I mean, if you're looking at over the total number of years it's been sold, I don't know what the exact total number is.
Q. Do you know whether it was over a hundred million dollars?
A. I believe it's over a hundred million dollars.
Q. And this is dollars in addition to the dollars we've just been discussing, the 49 million, the 1 million, the 500,000; correct?
A. That's correct; yes.
Q. Now, for all of the EPO for which Boehringer Mannheim paid GI, except for that first shipment of non-GMP EPO, all of it was made using the master working cell bank; correct?
A. Well, I -- I do believe that the very first shipment that occurred in 1986 used the master cell bank. We ended up, the

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initial production campaign that we did, we used the master cell bank. And then subsequent campaigns used the master working cell bank.
Q. Okay. So again, let me restate the question: Except for that first shipment of non-GMP material for which there was a payment of $500,000, all of the erythropoietin that was purchased by Boehringer Mannheim, for which Boehringer Mannheim paid GI, was made by either the master cell bank or the master working cell bank; isn't that true?
A. Yeah, I believe that's correct. Yes.
Q. So again, all the -- but in the commercial erythropoietin that was sold by Boehringer Mannheim, that all came from the master working cell bank; correct?
A. Ah, yes.
Q. Right. So if there's a goose that lays a golden egg, it's the master working cell bank, isn't it?
A. Ah, no, not at all. I mean --
Q. Well, isn't that the source of all the erythropoietin that's been sold throughout the world by Boehringer Mannheim?
A. Right. But that's just sort of the convenient way of producing and storing a normal production -- a routine production source as a process. I mean, the clear -- there's no question in my mind that the clear goose that laid the golden egg is the 10 micromolar methotrexate cell line. And the master cell bank, the master working cell bank are simply

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sort of practical manifestations of turning that cell line into a commercial reality.
But the clear goose is the DN2-3alpha3 10 micromolar cell line.
Q. That's the one that doesn't grow in suspension; correct?
A. Yeah. It doesn't grow in suspension, it does grow in suspension, there are -- it is the clear -- the clear source of EPO. And the ability or not to grow in suspension are, again, sort of practical decisions that one makes as far as how one manufactures it.
Q. Well, isn't that either the mother or the grandmother of the cell that was actually used to produce the erythropoietin?
A. Uhm, no. I mean, the cell is the same cell, okay. You haven't changed the cell in going from DN2-3alpha3 10 micromolar methotrexate. You keep the same -- the cell's the same the whole way through. It's simply, you know, under which conditions that cell will grow and how you have stored it that's different.
So I don't -- my terms, okay, I would not say that the 10 micromolar methotrexate is the mother or grandmother or whatever of the production clone. It is the production clone.
Q: Now, the regulatory authorities that regulate the sale of the product, however, they would not permit the product to be made using this cell line, the one that doesn't grow in suspension, they require that it be made using the cells that,

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are made in cell suspension; isn't that true?
A. Well, they require it to be made using cells from that master working cell bank. That is true. And that's because that master working cell bank was derived from the DN2-3alpha3 and under conditions in which they feel is the appropriate way, and we feel is the appropriate way to -- to store such valuable production clones.
Q. Now, I'd like to ask, if you would, to look at Plaintiff's Exhibit 141.
A. Okay.
Q. You recall testifying last week that this is a description of the plan to make erythropoietin, and there was a blowup of page 2 of the plan?
A. That's correct; yes.
Q. Right. Do you recall testifying that this plan was given to Chugai and other potential partners?
A. Ah, yes.
Q. Isn't it true that it was given to Boehringer Mannheim?
A. I believe it was given to Boehringer Mannheim; yes.
Q. Right. This is the plan that you testified provides all the information about how to make the erythropoietin-producing cell line; isn't that true?
A. Yeah. The plan described that we were using -- we were planning on using a CHO DHFR-negative cell line as the host, that was transfected with EPO genes, and it would undergo

presumably, says something about after 1987. But the little memo refers to the master working cell bank 1 vials. And there isn't another master working cell bank derived from the same master cell bank. And I think that was the question that was being addressed, as a second master working cell bank.
Q. What's the second master working cell bank? Is that one that's got a designation like -2 or -3, or something else like that?
A. I believe it's called -3. It's made as a replica of the first master working cell bank and it's part of the process that I described earlier.
Q. When was that made, sir?
A. Uhm, specifically, I don't recall when it was made. Sometime, you know, well -- sometime well after the first working cell bank was made, yes.
Q. So sometime well after December of 1985, there was another master working cell bank made by GI; correct?
A. Ah, yeah, I believe so.
Q. And that was designated -3, because the one that was made in December of 1985 was designated -1; correct?
A. That's correct; yes.
Q. When was master -- the master working cell bank -3 transferred to Boehringer Mannheim?
A. Uhm, I don't know if it was ever transferred. I believe GI used it.

Q. So your understanding is that that was used by GI to manufacture bulk EPO for Boehringer Mannheim; correct?
A. That's -- my understanding is, yes, that we had -- we manufactured some bulk EPO from the second master working cell bank.
Q. One that was made well after December of 1985?
A. Well, "well after" meaning a year or two after.
Q. Yeah.
A. Yeah.
Q. Meaning December 1986 or December 1987; correct?
A. It could have been, yes.
MR. WHITE: I have no further questions for this witness, your Honor.

RECROSS-EXAMINATION

BY MR. BAUER:
Q. Dr. Fritsch, you testified that you did not believe that any cells other than the bailed cells came back to GI; is that your testimony?
A. That's correct. I'm not aware that any cells other than the bailed cells have come back to GI.
Q. Could you take a look at Exhibit D1 and see if that refreshes your recollection as to whether or not any cells other than the bailed cells came back to Genetics Institute?
MR. WHITE: Your Honor, there's an objection to this document.

THE COURT: What's the nature of the objection?
MR. BAUER: Your Honor, I'm entitled to, I believe, have the witness look at something in order to refresh his recollection regardless of whether there's an objection.
MR. WHITE: Not if it's not in evidence.
THE COURT: Wait a minute. What's the nature of the objection?
MR. WHITE: It's an affidavit of a party that's not here to give direct testimony. It has on it total numbers of vials ostensibly being shipped, which are inconsistent with testimony -- with other documents and actual testimony of this witness.
THE COURT: Well --
MR. BAUER: Well, that's not true.
THE COURT: The rules permit a witness to refresh his recollection by using anything. In other words, you know, it could be anything. It could be, you know, a napkin cover. The document itself does not then come into evidence, the question is refresh your recollection.
So the question is whether or not Dr. Fritsch, when he testified that he didn't believe any other cells other than bailed cells came back to GI, whether he has -- that is his entire recollection.
Actually, you're right. As I'm spitting this out, it seems clear that this is not refreshing his recollection.

That's his recollection. You're trying to impeach him with another document.
Objection is sustained, go on. Sorry.
MR. WHITE: Thank you, your Honor.
MR. BAUER: Well, I guess it stands, then, that none of the cells came back other than the bailed ones?
THE COURT: That's right. It stands --
MR. WHITE: It stands as testified.
THE COURT: That's right.
BY MR. BAUER:
Q. Dr. Fritsch, counsel mentioned a number of $120 million of royalties going from Boehringer to Genetics Institute; do you remember that?
A. Correct, yes.
Q. Is that based on the bulk EPO that GI supplied to Boehringer, or a combination, or is it based on all the EPO sold by Boehringer in Europe?
A. I believe it's a combination -- it's all the EPO sold by Boehringer in Europe, so it's a combination of whatever GI shipped and what Boehringer Mannheim has manufactured as far as bulk.
Q. So it's not the sales based on solely the GI bulk data that was formulated and then sold in Europe?
A. That's correct; yeah.
Q. Now, if we go back to this -- the sets of figures, there's