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IN THE UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

- - -

IN RE: FACTOR VIII OR IX CONCENTRATE BLOOD PRODUCTS LITIGATION : MDL - 986 : NO. 93 C 7452

- - -

IN THE CIRCUIT COURT
FOR THE ELEVENTH JUDICIAL CIRCUIT
IN AND FOR DADE COUNTY, FLORIDA

- - -

GRO-A
Plaintiff,
vs.
BAYER CORPORATION, et al.,
Defendants.
NO. GRO-A

- - -

GRO-A
Plaintiffs,
vs.
BAYER CORPORATION, et al.,
Defendants.
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- - -

VIDEOTAPE DEPOSITION OF FRANK W. PUTNAM, Ph.D.
Taken on Tuesday, April 15, 1997, 9:30 a.m.

- - -

LOCKLEAR REPORTING SERVICE, INC.
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humans?

A. Well, of course, one has to keep in mind --

MR. GOODELL: Just a minute.

Object to form and foundation.

Go ahead.

THE WITNESS: One has to keep in mind that the hepatitis virus is associated with liver cancer in humans because, as a chronic disease, facilitates the development of cancer.

BY MR. SPIVEY:

Q. Are you speaking to hepatitis generally or to some form of hepatitis?

A. Well, I'm speaking both of hepatitis B and hepatitis C.

Q. I'd like to pause here for a minute in terms of discussing your background and qualifications and ask you whether say current to the year 1970, in terms of the treatment of hemophilia, whether it was known that the use of factor VIII and factor IX caused virus transmission in humans.

A. It was well known.

Q. And specifically in 1970 -- let's use that as a frame of reference -- what viruses were known to be

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transmissible through factor VIII and factor IX products then on the market?

MR. BERKMAN: Objection.

MR. GOODELL: Object to form and foundation.

You may answer.

THE WITNESS: Certainly, the hepatitis B virus was known to be transmissible. It was known that there was at least one additional form of hepatitis, later called hepatitis C, that was transmissible by such products. Parvovirus, human parvovirus, was known to be transmissible. There's a -- a suggestion that the Burkitt's lymphoma, the Epstein-Barr virus, was transmissible and cytomegalovirus was transmissible.

BY MR. SPIVEY:

Q. So -- by the way, Dr. Putnam, were you personally aware in the year 1970 that the viruses that you've identified were transmissible through factor VIII and factor IX products?

A. Oh, of course.

Q. If -- I'd like to ask you a bit of a hypothetical question, I guess.

If I was a manufacturer of a factor VIII or a factor IX product in the year 1970, what would I need to be concerned about in terms of the transmissibility of viruses in my factor VIII or factor IX products, based on the state of knowledge at that time?

MR. GOODELL: Again, object to the form, foundation and qualifications.

THE WITNESS: You would need to be concerned about the -- the source of the plasma that you use as to whether it had came from areas where there was a high incidence of hepatitis and related viruses, you would need to be concerned even for the protection of your personnel who worked with such potentially contaminated blood plasma, and you would need to be concerned with the potential transmission of such viruses through your product and how you could prevent such transmission.

BY MR. SPIVEY:

Q. As a scientist in 1970 who, as you've said, was familiar with the field of virology, as we've discussed so far, what concern, if any, would you

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have about the possible transmission of viruses not yet identified in factor VIII and factor IX products?

MR. BERKMAN: Objection.

MR. GOODELL: I'm going to object for the same reasons. I'm also going to object to this being beyond the scope of the designation --

MR. BERKMAN: Right.

MR. GOODELL: -- which has been before us for the entire time Dr. Putnam has been offered as a witness.

He has not been designated to testify about unknown or unforeseen or potentially foreseeable viruses but only the hepatitis virus. So it's outside the scope of his designation, and I object to it for that reason, in addition to which I object on the basis of form, foundation and lack of qualifications.

BY MR. SPIVEY:

Q. Dr. Putnam, do you have the question in mind or would you like to have the court reporter read it back?

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A. Would you read it back, please.

(Whereupon the court reporter read back the requested portion of the record.)

BY MR. SPIVEY:

Q. Now, what I mean by that, Dr. Putnam, just so we're clear, is viruses not yet identified in the field of virology but potentially transmissible in factor VIII and factor IX products.

MR. BERKMAN: Objection.

MR. BECK: I object for the same reasons Mr. Goodell said, plus it's leading.

MR. BERKMAN: Right.

BY MR. SPIVEY:

Q. What concern, if any --

MR. SPIVEY: And your objections are all noted.

BY MR. SPIVEY:

Q. -- would you have had in 1970 about the transmission of viruses not yet identified in factor VIII and factor IX products?

MR. BECK: Same objections.

THE WITNESS: At that time many viruses had not or did -- many diseases which were suspected to be caused by viruses, the

etiological agent, the virus or bacteria or whatever was the cause of the disease, had not yet been identified, and there was always a continuing concern that there might be viruses present in blood products and in other sources as well which had not yet been identified. They could be called emerging viruses.

BY MR. SPIVEY:

Q. I'd like you to assume for purposes of this question that in the year 19 -- or by the year 1970 there was at least one factor VIII concentrated product on the market and at least one factor IX concentrated product on the market.

Did you know at that time that those two products, factor VIII and factor IX, were capable of transmitting hepatitis virus to the recipients of that product?

MR. BECK: Could I please have the question re-read?

The first half you asked him to assume something and then the second half you asked him --

MR. SPIVEY: I asked him --

THE WITNESS: I was looking for literature that dealt with stabilization against heat because of the fact that heat was the best-known way of inactivating viruses.

BY MR. SPIVEY:

Q. And --

MR. BECK: Mr. Spivey, can I make a foundational objection? And perhaps you can clear it up for me.

Early in the examination the witness said many articles he found but some had been provided by the lawyers, and as you're going through the literature search, I have a general concern about foundation of whether these articles were articles that -- that he found or whether articles were presented to him by the lawyers.

BY MR. SPIVEY:

Q. Dr. Putnam, can you tell the jury what is at Tab 29, please.

A. At Tab 29 is a paper by Beilinsson in the "Biochemica Zeitschrift" which I provided to Dr. Laufman and which I had read in reference earlier in

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some of my own publications.
Q. And when you say "Dr. Laufman," just so the record is clear --
A. Yes.
Q. -- Dr. Laufman is one of the plaintiffs' attorneys; correct?
A. That is correct, yes.
Q. And why did you believe the Beilinsson article located at Tab 29 of your binder was relevant on the issues that you've described?
A. Because it showed that rabbit serum in saturated sucrose, that is, cane sugar, can be heated at 62 degrees for one hour without any denaturation or precipitation.
Q. For what purpose was the cane sugar and glycerine being used, as described by Beilinsson?
A. To stabilize the serum, which is equivalent to plasma, to stabilize the serum against the heat coagulation or precipitation.
Q. Did this article which appeared in 1929, was it -- did it appear in the prestigious medical and scientific literature?
A. Yes. At that time --
MR. BECK: Object to leading.

THE WITNESS: At that time there were only four major journals of biochemistry in the world, and one of these was this German journal, "Biochemica Zeitschrift."

BY MR. SPIVEY:

Q. Just so the jury again understands, you referenced 62 degrees centigrade.

A. Yes.

Q. Can you approximate what that temperature would be in Fahrenheit, please?

A. About 144 or 145 degrees Fahrenheit.

Q. Would you turn, please, to Tab 30 in your binder.

A. (Witness complies.)

Q. Can you tell the jury what this document is, please.

A. This is an article in "Science" that deals with the protective action of glucose in bovine plasma against heat coagulation, again an article which I had read earlier, which I have cited as early as 1953 and which I've provided to the plaintiffs' attorneys.

Q. Did you give a date for this article, Dr. Putnam?

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A. The date is 1943.

Q. And do you know what the glucose was being used for in these experiments --

A. Yes.

Q. -- by Dr. Hardt?

A. The glucose was being used for -- to protect bovine plasma, cow plasma, against coagulation by heat. And the method for ascertaining that it was protected was the use of a -- a method called electrophoresis.

Q. The bovine plasma that was being used, what proteins did that plasma contain? Just give some examples, if you would.

A. Well, it would contain all the proteins, but of the bovine species, which are present in the human plasma: Albumin, factor VIII, gammaglobulin, ceruloplasmin, haptoglobin, hemopexin, et cetera.

Q. Was the --

MR. BERKMAN: May I note for the record a continuing objection to all of these articles that deal long before HIV ever was -- was recognized or -- or in any plasma with other proteins, other types of plasma and are irrelevant to the issues in this case

other than his serendipity argument that if you had figured this out earlier, you could have solved it earlier.

BY MR. SPIVEY:

Q. From your review of the article, Dr. Putnam, which proteins in the plasma was the glucose stabilizing?

A. The glucose was stabilizing all of the proteins in the plasma.

Q. There is a temperature of 65 degrees centigrade. That's approximately the same temperature in Fahrenheit you mentioned before; is that correct?

A. No. 65 would be roughly getting closer to 150 degrees --

Q. Would you turn to Tab --

A. -- Fahrenheit.

Q. -- 31 and then we'll -- after we discuss this article briefly, Doctor, we'll take a break.

A. Okay.

Q. Can you tell the jury what this article is, please.

A. This is an article dated -- I think it appeared in 1943 by Charles Ball and others which is

entitled "The Influence of Sugars on the Formation of Sulfhydryl Groups in Heat Denaturation and Heat Coagulation of Egg Albumin." And what it does is it shows that a variety of sugars prevent the heat denaturation of this and other proteins.

Q. Did this article appear in the prestigious medical and scientific literature?

A. Yes. The "Journal of Biological Chemistry" is probably the preeminent journal in the field of biochemistry.

MR. SPIVEY: Okay, Dr. Putnam. Let's take a break. Thank you.

THE WITNESS: Okay.

THE VIDEO SPECIALIST: We're off the video record at 2:50, and this is the end of Tape Two.

(Recess, 2:50-3:06 p.m.)

THE VIDEO SPECIALIST: We are now on the video record at 3:06, and this is the beginning of Tape Three.

Proceed.

MR. BECK: Before we proceed with questioning, I'd like to lodge an objection to proceeding further until I'm given a copy

of the materials that the witness has listed as items that he's relying on for his testimony here today.

I had an opportunity briefly to look at Tab 18 over the break. Listed in Tab 18 is something called the JKB trial notebook. I was not at the JKB trial. I was told by Mr. Spivey that the documents are somewhere, apparently not collected in a set, in those 12 or so boxes that are in the room today, and I've asked if I could be provided whatever comprised the trial notebook so I'd know what the witness is relying on and I was told no. So I object to further proceeding since I'm not being given the materials that the witness has testified today he's relying on.

MR. SPIVEY: Just so the record is clear, the JKB trial was the trial against Cutter in Indianapolis. And between the box that you were served, Mr. Beck, in preparation for this deposition plus the materials that were provided at the time of Dr. Putnam's discovery deposition were

materials that Jere Fishback put together into a trial notebook. And I do not have a copy of the trial notebook here, but the documents that comprise the trial notebook are here.

MR. BECK: But nobody can point me to them is the problem and you've given -- you've put 12 boxes in here. That doesn't do me any good.

MR. SPIVEY: Well, I haven't ordered -- I haven't -- that's -- what you just said is correct. I don't know what -- I don't know what they are, except that they're here.

MR. SCHOON: Although an objection for one is for all --

MR. SPIVEY: Correct.

MR. SCHOON: -- I specifically join in Mr. Beck's objection --

MR. SPIVEY: Sure.

MR. SCHOON: -- on behalf of Armour and RPR.

MR. BERKMAN: As do I, and will point out that in addition to the trial notebook, in Exhibit 18 it references documents

provided by Mr. Weinberg, one of the plaintiffs' counsel, to Dr. Putnam that were provided after the deposition in 1995 allegedly dealing with my client that are not identified in Mr. Laufman's letter of April 8th, 1997, in which he said this witness would be prepared to testify and rely on just these documents. So that's further using -- he's relying on things outside of the one box that Mr. Laufman sent us, and I object.

MR. SPIVEY: Are we on the video?

DR. LAUFMAN: Why do you say those were supplied --

MR. SPIVEY: Don't --

DR. LAUFMAN: -- after the deposition because they're not?

MR. SPIVEY: Don't waste your time.

Are you on the --

THE VIDEO SPECIALIST: Yes.

MR. SPIVEY: Are we on the video?

Okay.

BY MR. SPIVEY:

Q. Dr. Putnam, would you turn to Tab 32 in your

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notebook, please.

First of all, would you tell the jury what this is.

A. This is an article by Walter H. Seegers entitled "Purified Prothrombin and Thrombin: Stabilization of Aqueous Solutions" that appeared in the "Archives of Biochemistry" in 1994.

Q. Is --

MR. McGUIRE: '94?

THE WITNESS: Excuse me. 1944.

BY MR. SPIVEY:

Q. Is the "Archives of Biochemistry" an authoritative journal?

A. Since I was an editor at a subsequent time, I would have to say yes.

Q. Can you tell the jury, please, the subject matter of this article --

A. The subject --

Q. -- and how you -- and how you believe it is relevant to the topic of whether it was technically feasible to virally inactivate factor VIII in 1970, factor VIII and factor IX in 1970.

MR. BECK: Object; leading. I also object on foundational grounds. This is the

first one that he hasn't mentioned whether he provided to the lawyers or the lawyers provided to him.

MR. SPIVEY: Well, you haven't --

MR. BECK: It may be an oversight.

MR. SPIVEY: You haven't given him an -- a chance to answer the question yet.

BY MR. SPIVEY:

Q. Dr. Putnam, would you tell the jury how you -- if at all, you believe this article is relevant to the subject we've been discussing.

A. This article, which is one I read in earlier years -- in fact, Dr. Seegers sent me his entire book on prothrombin and endorsed it to me -- this article I have referenced in the past in some of my publications.

And the point of this article, it shows that thrombin, which is the initial enzyme in the coagulation cascade, can be stabilized against heating at 50 degrees centigrade for 48 hours by use of a series of saturated solutions of different sugars and sugar-related alcohols. In particular, the best stabilization of thrombin was obtained using about 66 percent sucrose, a nearly saturated solution

of cane sugar.

The relevance is that it shows that a coagulation factor can be stabilized by use of a neutral sugar against denaturation by heating at 50 degrees for a period of up to 48 hours.

MR. BERKMAN: Objection on relevance.

It is irrelevant whether some factors can be or some coagulation proteins can be stabilized to the relevant question of this case, which is whether back in 1943 or 1944, as he has suggested, it was known how to stabilize factors VIII and IX without -- in a way that would work.

MR. SPIVEY: Mr. Berkman, you and the rest of the defense counsel represented here have a continuing objection to that.

BY MR. SPIVEY:

Q. Dr. Putnam, is -- are prothrombin and thrombin plasma proteins?

A. Yes, they are plasma proteins.

Q. And --

A. I -- I failed to add one additional relevance of this article. It is an article that is cited frequently in the publications of the fractionator

companies, it is an article that is cited regularly in the patents for the stabilization and heat inactivation of factor VIII and factor IX.

Q. What do you mean, cited by?

A. Oh, cited by, that is, referenced. It is referenced as a source, a source of prior art in the patents.

Q. Doctor, do you -- did you at any time, that is, in the 1940s and the 1950s, know who Dr. Seegers was?

A. I knew him personally.

Q. Was he considered by his peers to be an authority on the subject of prothrombin and thrombin?

A. He was --

MR. BECK: Object; leading.

THE WITNESS: He was the authority on prothrombin and thrombin. He literally wrote the book.

BY MR. SPIVEY:

Q. Would you turn, please, to Tab 33 in your notebook.

A. (Witness complies.)

Q. First of all, would you describe the document

for the jury and then tell the jury why you feel this article is relevant to the subject of what I'll refer to shorthand as technical feasibility.

MR. BECK: Object; leading.

THE WITNESS: This is an article by Gerald Ballou and others entitled "The Heat Coagulation of Human Serum Albumin." It is one of a series of articles that this group published that appeared in this case I believe in the "Journal of Biological Chemistry," although it is not clearly referenced here. In the "Journal of Biological Chemistry" in the year of 1944.

The significance of this article, it was the -- it was this set of experiments that established that human serum albumin could be stabilized against heating at temperatures up to and even above 60 degrees centigrade by the addition of certain specific stabilizers, which were long-chain fatty acids or acetyl-dl-tryptophane or mandelic acid.

BY MR. SPIVEY:

Q. In 1944, when this article was published, was

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the structure of albumin known?
A. No, it was not known.
Q. Would you turn to Tab 34 of your book, please. And, again, would you describe the document for the jury.
A. Basically, this is another article in the series by that group, by Dr. Ballou. This appeared in the "Journal of Clinical Investigation" in 1944. And it describes the influence of non-polar anions on the thermal -- that is, the heat -- stability of serum albumin.
It amplifies the experiments described in the preceding article and shows that one can stabilize serum albumin for periods of many, many days at temperatures of 50 degrees and 57 degrees --
Q. Would --
A. -- centigrade.
Q. Would you turn to Tab 35, please, in your notebook.
A. (Witness complies.)
Q. Would you first describe the document and then tell the jury what relevance you have -- you believe it has to the subject of technical feasibility.

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MR. BECK: Object; leading.

THE WITNESS: The article is by Chester R. Hardt and collaborators, and it's in the "Journal of Biological Chemistry" in 1946. The title is "An Electrophoretic Analysis of Changes Produced in Blood Serum and Plasma Proteins by Heat in the Presence of Sugars."

The significance of this article is that it was known that if you heated serum, you developed a -- a component which is really a composite of a number of the plasma proteins that they called the C component and that by adding, by saturating the plasma with glucose, you could heat it for -- at 65 degrees for one hour and prevent that change, the electrophoretic change, that produced -- excuse me -- prevent the change in the molecule that produced the electrophoretic component called component C.

BY MR. SPIVEY:

Q. Did -- did you say that -- I didn't hear you -- that this article was published in 1946?

A. Yes, this was published in 1946.

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Q. And do you know from reviewing the article what purpose the sugar was being used for by Dr. Hardt and his colleagues?

A. The purpose was to prevent the heat -- changes in plasma by heat.

I should also add that this is an article that I had for many years, have the original reprint, I've referenced in my -- in my own review articles and I gave to the plaintiffs' attorneys.

Q. As -- at the time that this article was published, did you consider it and do you still consider it authoritative in the field on which -- in which it's addressing?

A. I consider it authoritative and still consider it authoritative, and I found it extremely interesting because it was an area that was of particular interest to me at the time.

Q. Can you tell the jury, please, what proteins in the plasma that Dr. Hardt was stabilizing with the sugars.

A. Well, he was stabilizing all of the proteins in the plasma.

Q. Including factor VIII and factor IX?

A. Of course. Yes.

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Q. Would you turn, please, to Tab 16 in the binder.

DR. LAUFMAN: 36.

BY MR. SPIVEY:

Q. I mean, I'm sorry, 36.

A. 36, yes.

Q. Would you tell the jury, please, what Tab 36 represents.

A. Tab 36 is a article -- actually a review article or a chapter in "Advances in Protein Chemistry," Volume III, which is authored by John T. Edsall, who was the -- at that time the director of the Physical Chemistry Laboratory at Harvard, which was a laboratory that had previously developed the Cohn fractionation method for plasma.

Q. Did -- were you aware of this publication at the time it came out in 1947?

A. Certainly. It was in -- very much in my area of interest. I have referenced it.

Q. Did -- is this the Dr. Edsall that you referred to previously in connection to your review article?

A. Yes. It's the same Dr. Edsall.

Q. And can you tell the jury, please, why, if at

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all, you believe this article is relevant to the subject of technical feasibility.

MR. BECK: Object; leading.

THE WITNESS: Well, I think it's relevant in several respects. First of all, it is relevant because of the fact that it -- it gives review of the procedures for stabilizing albumin against heating so that the albumin no longer transmitted the hepatitis virus. At the same time, it indicated that fibrinogen, which is a component of plasma and which is more labile -- heat labile, I should say -- than factor VIII, that fibrinogen heats -- I'll read the sentences.

"As yet" -- and this is on Page 446. "As yet all attempts to separate the antihemophilic factor," factor VIII, "from fibrinogen by chemical means have proved unsuccessful. The two are clearly distinct; fibrinogen, for instance, is readily heat coagulated in 5 minutes at 53 degrees, whereas the antihemophilic activity of Fraction I is still high after this

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treatment, although it is rapidly lost at 65 to 70 degrees centigrade. Further research on the chemical nature" or the antihemophilic -- "of the antihemophilic factor is clearly necessary."

There's another reference in here which I may not have at hand which reports the fact that actually they were also able to stabilize gammaglobulin with the use of sugars.

BY MR. SPIVEY:

Q. Is gammaglobulin another plasma protein?

A. Oh, yes. It's the protein which basically is the antibody fraction.

Q. Would you explain to the jury, if you can, in lay terms what Dr. Edsall was saying in this article about fibrinogen and heating in relationship to AHF, or factor VIII.

A. Well, he was saying that if you heat a solution, this -- he was heating what's called fraction I. The main components of fraction I are fibrinogen, antihemophilic factor and another protein they call cold, insoluble globulin, now called fibronectin.

And he was showing that if you heated this fraction I, which was known to have antihemophilic activity, that the fibrinogen precipitated at 53 degrees centigrade by very short time heating and thus would -- could be separated from the AHF, that is, the antihemophilic factor, factor VIII, which retained its activity at that temperature.

Q. What retained its activity at that temperature?

A. The -- the factor VIII, the AHF, the antihemophilic factor retained its activity.

Q. You said that the temperature being used was 53 degrees. Can you give the jury an approximation of what temperature that would be in Fahrenheit, please.

A. I would say it would be about 144, 145 degrees.

Q. With respect -- well, strike that.

Would you move to Tab 37, please, in your notebook.

A. Excuse me. I made an error there. 60 degrees, 60 degrees would be 140 degrees Fahrenheit, roughly. We'll multiply the difference by 2,

00273
subtract 14 and we now have 160, minus 14, which is 144.

Q. Okay. Would you turn to Tab 37, please, in the notebook.

MR. GOODELL: I'm sorry. Tab 41?

MR. SPIVEY: 40 -- I'm sorry. 37. I'm sorry.

MR. GOODELL: No. No. I didn't hear you.

MR. SPIVEY: It's Tab 37.

BY MR. SPIVEY:

Q. Would you describe this article, please, for the jury in terms of where it was published.

A. This is an article by Sydney S. Gellis and other individuals from the Harvard Laboratories, and it appeared in the "Journal of Clinical Investigation" in 1948. It is the 36th in the series of articles that were published as a result of the studies -- well, let's see.

It says 36th there and at the bottom it says Paper Number 70 in the series of studies on plasma proteins from this Department of Physical Chemistry, the Cohn Laboratory.

And the significance of this article is

it was the first to establish by use of human volunteers that the plasma which had been -- excuse me -- the albumin which been -- had been pasteurized by heating at 60 degrees for 10 hours did not produce hepatitis, whereas albumin from the same lot which had not been heated produced hepatitis in volunteer individuals.

MR. BERKMAN: Same objection; relevance.

BY MR. SPIVEY:

Q. Were you aware of this article at the time it was published?

A. I certainly was.

Q. And is the "Journal of Clinical Investigation" considered to be a prestigious journal?

MR. BECK: Object; leading.

THE WITNESS: It certainly is in this area.

BY MR. SPIVEY:

Q. Is it considered to be authoritative?

MR. BECK: Object; leading.

THE WITNESS: Absolutely.

BY MR. SPIVEY:

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Q. Would you turn, please, to Tab 38.

Before we leave this area, is the heat methodology that was being applied to the material used by Dr. Gellis, was that pasteurized?

A. That was pasteurization, yes.

Q. The -- can you tell the jury what proteins pasteurization was first applied to.

A. Well, pasteurization, that is, the principle of pasteurization, was first applied by Pasteur to the pasteurization of milk.

Q. And at the time --

A. Well, I should say he actually -- beer was the first one that he applied it to, then milk and other fluids of that sort.

Q. At the time pasteurization was applied to milk, was it known what proteins were constituted in the milk preparation?

A. No. They knew very little about the proteins in milk at that time.

Q. Has pasteurization been applied to other proteins where the full content of the protein activity was not known?

A. Frequently.

MR. GOODELL: Objection to the form and

foundation.

BY MR. SPIVEY:

Q. Can you give another example for the jury, please.

A. Well, I gave you the example of beer.

Q. Okay. Can you turn to Tab 38, please.

First of all, can you describe again what is included in Tab 38.

A. This is an article by Hink and Johnson, who were at the Cutter Laboratories at this time. It appeared in the "Journal of the American Pharmaceutical Association" in 1951. It's studies on the stabilization of human serum albumin, the effect of the pH, the stabilizers and the albumin.

Q. Did you -- were you aware of this article at the time it was published?

A. I believe I was, yes.

Q. And --

A. I -- I supplied this article to the attorneys.

Q. And is the Journal of -- of the American -- did you say Pharmacology Association?

A. No. Pharmaceutical Association.

Q. Is that considered a reputable and

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authoritative journal?

A. Certainly, in the area of pharmacy. That is, in the area of products for medicinal use.

Q. Would you describe for the jury what relevance, if any, you think this article has to the subject matter of technical feasibility.

A. Well --

MR. BECK: Object to the leading.

THE WITNESS: -- the principal contribution of this article was it's the publication which shows the capability of doing systematic experimentation to determine the factors that are needed for the stabilization of a -- of a plasma protein. In this instance it was albumin. And so it showed that, in fact, that the Cutter Laboratories knew about the process of systematic experimentation to study heat stabilization.

BY MR. SPIVEY:

Q. Would you turn to Tab 39, please.

First of all, as we've done before, describe the document for the jury.

A. Yes. This is a chapter, a review chapter, by

Walter Hughes, who had been associated with the Cohn Laboratories, which appeared in 1954. The source is not given but I believe it was in the "Advances in Protein Chemistry." Is that -- oh, I have it at the end. Excuse me. It was in "The Proteins." Sorry. In "The Proteins," Volume II, Part B, edited by Neurath and Bailey.

This was a general review. The particular significance is that among other points that were made, they point out that they're talking about stabilizing concentrated solutions of gammaglobulins, then called fraction II, and they mentioned they are stable for some hours at 50 degrees centigrade. The stability is markedly increased by the addition of various substances of which sugars, for example, lactose, and amino acids, for example, glycine, have proved most effective. And the sugars should not be used for -- should not be reducing sugars. And they also point out that large organic anions, which have proved so effective in albumin stabilization, didn't have effect for gammaglobulins.

So they've pointed out there are two classes of stabilizers, one that may be specific, in

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this case for albumin, and stabilizers which have a more general effect, namely, neutral chemicals such as saturated solutions of cane sugar, sucrose.

Q. Is the protein being worked with and described in this article a plasma protein?

A. Oh, yes. Yes.

MR. BERKMAN: Objection; relevance.

BY MR. SPIVEY:

Q. By the way, Dr. Putnam, would you know -- would you know whether sugar would work on a particular plasma protein without doing the experiment?

A. Well, of course, you couldn't know whether it would work without doing the experiments.

Q. So, for example, if this reported -- this reported stabilization of one plasma protein, how would you know whether sucrose would work to stabilize factor VIII or factor IX?

A. You'd have to do the experiment.

Q. In any of the documents that you've looked at from the various defendants that sit around this table -- and let's talk just about Armour, Baxter and Alpha -- did you ever see any evidence that in the early 1970s any of those companies did the kind of

systematic experimentation that's described in the articles that we've been reviewing?

A. I --

MR. GOODELL: Objection.

MR. BERKMAN: Objection.

MR. BECK: Object to form of the question.

Alpha didn't exist in the early 1970s.

MR. SPIVEY: Yes. Alpha is -- let's modify the question to include Alpha's predecessor, Abbott.

MR. BERKMAN: Objection.

BY MR. SPIVEY:

Q. Did you see -- did you see any evidence of the systematic experimentation that's being reported in these articles --

MR. BECK: Objection.

BY MR. SPIVEY:

Q. -- with reference to factor VIII or factor IX?

MR. BECK: I object for lack of foundation in terms of what documents the plaintiffs' lawyers chose to give him.

MR. BERKMAN: Exactly.

THE WITNESS: In the extensive series of documents that I carefully reviewed, for the three fractionators mentioned, including the predecessor of Alpha, I saw no evidence of any kind of a systematic experimentation to stabilize factor VIII or factor IX for the equivalent of pasteurization and for the purpose of inactivation of viral diseases or prevention of viral diseases.

BY MR. SPIVEY:

Q. Would you turn, please, to Tab 40 in your notebook.

And we'll discuss Cutter a little bit later in the deposition.

MR. GOODELL: No. That's all right.

BY MR. SPIVEY:

Q. First of all, will you, as you have before, tell the jury where this article was published and the title of the article, please.

A. The inclusion here does not give the source. To me, it would appear to be in the "Journal of Clinical Investigation."

It is an article by Dwight Mulford and others entitled the "Preparation of a Stable Human

00282
Plasma Protein Solution." Perhaps the plaintiffs' attorneys' assistant can help me identify the source of publication and the date.

Q. Well, why don't we come back to --

A. Okay.

Q. -- Tab 40 and go to Tab 41. And we'll -- we'll try to look for that, Dr. Putnam.

A. Right. I -- go ahead.

Q. Tab 41.

A. Yes.

Q. Would you describe, please, the document contained at Tab 41.

A. This is an article from the Swiss Red Cross Service which is entitled "A Heat Stable Human Plasma Protein Solution Obtained by Desalting," called PPL, which is by Nitschmann, Kistler and others and appeared in -- I think this is Biochimica Chemica Acta but, again, I don't believe that the -- it is -- sorry. It's Vox Sanguinis, Vox Sanguinis, Volume I, and appeared in 1956.

Q. Would you tell the jury, first of all, what plasma protein solution is.

A. Well, this plasma protein solution, sometimes called by the trade name Plasmanate by other workers,

00283

consisted of a partially purified albumin. The albumin comprised from 83 to 88 percent of the protein and the rest of the proteins were alpha and gammaglobulins.

I could illustrate it in a sense here by pointing out this is the electrophoretic pattern of serum or plasma and each of these peaks represents a particular group of components. This is albumin here. This is albumin (indicating).

Q. Dr. Putnam, would it be easier for you to draw it on the --

A. Right.

Q. -- board there than it would be to -- this is -- you were referring to one of your volumes of "The Plasma Proteins"; is that correct?

A. That's correct. Yes.

This is a rough approximation of the electrophoretic pattern of serum or plasma and --

Q. Meaning what exactly? What do you mean by electrophoretic --

A. Well --

Q. -- pattern?

A. Well, what -- what has been done here is to cause the different fractions or groups of proteins

to separate based upon their electrical charge under a certain condition of pH or acidity. Usually it shows at pH 8.6.

Under those conditions, you get the best separation of the major families or groups of proteins. And this -- and the large one here, this large peak, is albumin.

I should point out that the area under each peak represents the relative amount of the material of protein -- of the protein or the protein family or group of proteins present in the plasma. So you see albumin comprises about half of the total area. Alpha. Beta. Gamma -- sorry. This would be alpha too in this one, and this becomes beta and this is gamma. I'm going to start that over. Well, just label --

Q. That's okay. Just -- just for illustration purposes.

A. All right. And so basically that Plasmanate would comprise approximately this much of the al -- of the total plasma and the beta globulins, many of them, especially the lipid ones, would be excluded. The immunoglobulins, the fibrinogen, which are all down in this region, would be excluded.

00285

Q. Well, in terms of the Nitschmann article that we're looking at at Tab 41, what material was he stabilizing, as described in his experiments?

A. Well, he was -- he was stabilizing this section of plasma, which is to say the albumin, and much of the alpha globulins and the beta globulins. So about 15 -- up to 15 percent of the protein was not albumin.

Q. And so, in other words, there were other proteins that were in that mixture that were --

A. Yes.

Q. -- being stabilized?

A. There's quite a number of different proteins in this alpha group, quite a number of different proteins in the beta group.

Q. Different plasma proteins?

A. Different -- oh, they're all plasma proteins. Yes.

Q. Would you turn to Tab 42, please.

MR. BECK: Just before you leave 41, he failed to mention whether this is one that he was aware of at the time, or are we now on one that the lawyers gave him?

BY MR. SPIVEY:

Q. Were you aware of this article, Dr. Putnam, at the time it appeared in the --

A. The one by Mulford?

Q. The one by Nitschmann.

A. Oh, Nitschmann. Oh, yes. Of course.

I believe that I -- all of these articles I provided to the plaintiff attorneys.

MR. BECK: That cures my problem.

BY MR. SPIVEY:

Q. Dr. Putnam, would you turn to Tab 42, please.

By the way, before we leave 41, was PPL, or Plasmanate, a product that was manufactured by one or more of the defendants represented around this table?

MR. BERKMAN: Objection; no time frame, no relevance.

THE WITNESS: The same -- that product was manufactured in the period of the 1950s through the 1960s by a number of the fractionators around this table.

BY MR. SPIVEY:

Q. And what --

A. And it was licensed for sale.

00287

Q. And was that product, as it was being sold in the 1950s and 1960s, did it contain a viral inactivation method?

A. Yes. It contained the same viral inactivation method that had been used for albumin.

As a matter of fact, they did not establish that the material was hepatitis-free by injection into volunteers; they did that by analogy -- as they pointed out, they did that by analogy to what had been established for the albumin in the Gellis article.

Q. Current to the time period we're talking about, which is in the 1950s and 1960s, was it generally recognized that Plasmanate was free from the transmission of hepatitis virus?

A. I don't believe that there were any reports about the transmission of hepatitis from Plasmanate.

Q. Would you turn to Tab 42, please.

A. Yes.

Q. Would you tell the jury, first of all, what the article is and briefly, if you can, the relevance to the subject of technical feasibility.

A. This is an article by John Hink and others who were at the Cutter Laboratories. It appeared in

00288
"Vox Sanguinis," which translated from the Latin means the voice of blood, which is a standard journal in the field of blood coagulation. It appeared in 1957.

The title is "Preparation and Properties of a Heat-Treated Human Plasma Protein Fraction." And they describe a procedure for developing what is called stable -- stable plasma protein solution, SPPS, and they describe the relationship, how it's somewhat similar to the Nitschmann method but they had their own proprietary differences. And I believe that these are the authors who made the conclusion that although they had not proven the efficacy of -- of inactivating the viruses by actual volunteer experiments, I believe they -- yes, they say that Gellis, the article we've described previously, "have shown that a 25 percent albumin solution contaminated with known icterogenic," that is, hepatitis transmitting, "plasma is rendered safe for infusion into humans after heating at 60 degrees centigrade for ten hours. Their investigations only suggest that similar heat treatment of the 5 percent solution of human plasma protein fractions described here would

accomplish the same degree of virus inactivation."

Q. Doctor, you're describing what's at Tab 43; is that correct?

A. That is correct, yes.

Q. And is Dr. Hink, as the article --

MR. BERKMAN: 42.

MR. GOODELL: Now we're on 42.

MR. SPIVEY: Well, it's 40 --

BY MR. SPIVEY:

Q. Is it 42 or 43 in your --

A. The article I've just described is at Tab 43, by Hink, et al.

Q. Okay. And is Dr. Hink the Dr. Hink you referred to earlier who was employed by Cutter Laboratories?

A. Yes. All of the authors of this paper were apparently employed by Cutter Laboratories, I conclude from the -- the title of the article.

Q. And is the preparation that Dr. Hink was discussing the Plasmanate that you mentioned before, same -- same material?

A. Yes.

Q. Would you turn to Tab 42 that we skipped over. I apologize. It was inadvertent.

And, again, would you briefly describe the article, where it was published and its relevance, if any, as you see it, to the subject of technical feasibility.

A. The article in Tab 42 is by Dwight Mulford and Edward Mealey. Mulford had formerly been associated with the Cohn fractionation group. The title is "Heat Stability of Protein Solutions Obtained From Human Plasma by Different Ethanol Concentrations and Temperatures."

And what they basically do is again describe the effect of heating at 10 hours for 60 degrees centigrade, that is, pasteurization, on the electrophoretic properties of the plasma protein solutions. And they also made a series of studies by a variety of methods, such as ultracentrifugation, and they concluded that certain of the plasma protein factors were stabilized and others showed a new component in the electrophoresis pattern on the heating.

That's similar to the component that we mentioned previously in the Hardt article which -- the appearance of which was prevented by heating in the presence of saturated sugar, glucose.

00291

Q. Dr. Putnam, I'd like to discuss with you -- and I think the next tabs that we're going to be discussing are some of the other plasma proteins over the years that were stabilized with various stabilizers, but to do that we're going to need to put the second binder in front of you so --

MR. GOODELL: Could we get the date on that particular one?

MR. BERKMAN: '56.

MR. GOODELL: '56?

MR. McGUIRE: '86?

MR. BERKMAN: '56.

THE WITNESS: '56.

BY MR. SPIVEY:

Q. And for the time being, Dr. Putnam, we'll be -- we're finished with Binder 1.

A. Okay.

Q. Would you turn to the first tab, which is Tab 44, in Binder Number 2, please.

A. Yes.

Q. Would you describe for the jury the title of the article and where and when it was published.

A. This article has a title "Clinical Investigations with a Heat-Treated Plasma Protein

Fraction-Plasmanate," which is a registered trademark. It appeared in "Vox Sanguinis" in 1959, a series of authors, including one of the authors from the Cutter Laboratories, because the Plasmanate was the plasma protein fraction prepared by pasteurization as we've described in the articles by Hink and others.

Q. Was "Vox Sanguinis" in 1959 considered to be an authoritative article -- or journal, rather?

A. It's an authoritative journal certainly in the field of blood coagulation.

Q. And can you tell the jury what the Cutter investigators and the other authors are reporting in this article.

A. Basically, they're talking about the use of this Plasmanate as a plasma expander; that is, instead of using albumin, you use this partially purified albumin, and also for the purposes of nutrition because the body can utilize the albumin which has been injected. And they state that it is safe by a variety of -- of procedures, using laboratory procedures and by clinical observations in individuals for -- they made a total of 895 administrations.

00293

Q. Safe in what respect, Dr. Putnam?

A. Well, safe -- here they're primarily describing toxicity. They're -- they don't mention any aspect of anybody getting hepatitis.

Q. Would you turn, please, to Tab 45 in your book.

A. Yes.

Q. And would you tell the jury what this represents.

A. This is the United States patent which was granted on November 1st, 1960, Number 2,958,628, titled "Heat Treatable Plasma Protein Product and Method of Preparation." The patent is in the name of John Hink, whose articles we've referenced previously, and it is assigned to Cutter Laboratories.

It basically is a patent which describes the preparation and the properties of the Plasmanate solution product.

Q. Would you turn to Tab 46, please.

A. Yes.

Q. And would you tell the jury what this represents.

A. This is a article which is a United States

Patent, Number 3,057,781, granted October 9, 1962, titled "Stabilization of Plasma with Invert Sugar," by Robert Mace and others and assigned to the United States Pharmaceutical Company.

Q. Did you review this patent, Dr. Putnam?

A. Yes, I reviewed the patent.

Q. And would you tell the jury what Dr. Mace is describing here in the patent dated October 9, 1962.

A. Yes. Dr. Mace is -- actually, it's also Mehl, who was the one who was the carbohydrate expert here, and Moore. They're all describing an invention by which they were able to stabilize plasma so that it could be pasteurized using what they called invert sugar and levulinic acid.

Now, invert sugar is really sugar which has been changed so that it has -- normal sugar has what we call mirror images, D and L images, and it's been changed from having a single-image optical image to the mirror image form, both forms present, and also levulinic acid, which is a sugar acid. And these were used to prevent the denaturation of the whole plasma.

Q. Can you tell the jury, please, what proteins were in the plasma that Dr. Mace and his colleagues

were working with.

A. I believe all the proteins of plasma were present, with the exception that they removed the plasma -- the proteins which are most sensitive to heat, which are the lipoproteins, and fibrinogen, which is very sensitive to heat.

Q. From your review of this patent, was Dr. Mace working with plasma which included factor VIII and factor IX?

MR. BECK: Objection.

THE WITNESS: Yes, it would have had all of the other components except the fibrinogen.

BY MR. SPIVEY:

Q. And which -- which proteins in the plasma Dr. Mace was working with were stabilized by the sugars that you've described?

A. Well, all of the proteins were stabilized. And, of course, they thought that -- they claim that the resulting stabilized plasma may then be heated at 10 hours, 60 degrees centigrade method to render it hepatitis-free.

Q. Did the stabilizers stabilize factor VIII and factor IX in the preparations Dr. Mace was working

with, as described in this patent?

A. Well, they stabilized all the proteins insofar as at least there was no precipitation of these proteins.

Q. Would you turn to Page -- or excuse me -- to Tab 51 in your notebook.

And tell the jury, if you can, what this represents.

A. This is a patent by Funokashi, et al., United States Patent, it was a prior Japanese patent, here and actually patented in 1973 in Japan. A procedure -- the title of the patent is "Haptoglobin in Aqueous Solution and Process for Preparing the Same."

Actually, I heard a presentation by Funokashi, et al., at that conference on the trace components.

Q. We're going to discuss that next.

A. Right.

Q. Can you tell the jury whether haptoglobin is a plasma protein.

A. Yes, it's a plasma protein.

MR. BERKMAN: Objection.

Can you identify -- I'm sorry. I

missed which -- what's the date of the patent?

THE WITNESS: The date? December 6th, 1977.

BY MR. SPIVEY:

Q. And what did you say the date of the Japanese patent was?

A. There are two Japanese patents referenced here which are dated November 15, 1973.

Q. And would you tell the jury what Dr. Funokashi is describing in this patent.

A. Basically, Dr. Funokashi is describing the pasteurization of a particular plasma protein called haptoglobin by heating it at 10 hours for 60 degrees centigrade and he stabilized this, I believe, in this instance with a solution of glycine but indicated that other materials could be used for this process.

MR. BERKMAN: Same continuing objection; relevance, different proteins.

THE WITNESS: I just would go on to complete my statement saying concrete examples of the stabilizer are neutral amino acids, such as glycine, et cetera; monosaccharides, that is, sugars such as

glucose, et cetera; disaccharides, such as sucrose, et cetera; sugar alcohols, such as mannitol, et cetera.

BY MR. SPIVEY:

Q. Would you turn, please, Dr. Putnam, to Tab -- I -- I think it's 50 in your notebook.

A. (Witness complies.)

Q. Is that?

A. Yes.

Q. Does this describe the -- have we looked at this before in -- in another context, not this particular part of it, but have we talked about the Trace Components of Plasma Conference earlier in your deposition?

A. Yes, we did earlier.

Q. Would you just remind the jury, please, since we're at this particular point again, what that conference was about.

A. That conference was held in May 1975 at the American National Red Cross Laboratories just outside of Washington there in Bethesda, and it dealt with the trace components. This was the one to which I said I gave the keynote lecture.

Q. And can you tell the jury what Dr. Funokashi

reported at this conference, which is described as part of Tab 50?

A. Yes. At this conference Dr. Funokashi described the preparation of haptoglobin in such a way that it could be used clinically and also the pasteurization of haptoglobin. And he says -- here he says, since B type hepatitis infection caused by the infusion of plasma derivatives is a serious problem, it is desirable that the hepatitis antigen which might be contaminating the preparation be inactivated. So far we know the most reliable method is to heat the preparation for 10 hours at 60 degrees; however, haptoglobin is heat labile and loses its hemoglobin binding capacity. The problem was solved by heating haptoglobin in solutions of highly concentrated amino acids and sugars. The possibility of applying this method to other plasma components is being examined.

Q. And did you hear Dr. Funokashi make this presentation at the time?

A. Oh, I certainly did. Yes.

Q. And do you agree with Dr. Funokashi, as stated in this article, that when this paper was presented, the most reliable method to heat plasma

preparations or to kill virus, rather, was pasteurization at 60 degrees centigrade for 10 hours?

MR. GOODELL: Object. Excuse me. I object to the form and foundation. Virus in general.

BY MR. SPIVEY:

Q. Do you -- let me restate the question, Dr. Putnam.

Do you agree that at the time this article was presented, this paper was presented in 1975, that the most reliable method to kill or inactivate the hepatitis virus --

MR. BERKMAN: Objection.

BY MR. SPIVEY:

Q. -- was heat treatment at 10 hours at 60 degrees centigrade in the pasteurized state?

MR. BERKMAN: Objection.

THE WITNESS: Well, I certainly agree, because there are millions of applications that pasteurize albumin which have been -- have been treated in the same manner.

BY MR. SPIVEY:

Q. For how long, Dr. Putnam, would you say that the most reliable method to inactivate hepatitis at

10 hours for 60 degrees centigrade was known to the medical and scientific community?

MR. BERKMAN: Objection.

THE WITNESS: To inactivating plasma.

MR. SPIVEY: To inactivating plasma. Correct.

THE WITNESS: Well, it was known to the scientific and medical community since certainly somewhere in publications, I would say 1944, 1945, '46.

BY MR. SPIVEY:

Q. By the way, before we leave Tab 50, I'd like you to turn back to the front of the article. And can you tell the jury whether Dr. Funokashi was associated with any particular pharmaceutical company?

A. Yes. Dr. Funokashi and one of his associates were associated with the Green Cross Corporation, which several years later I believe bought the blood/plasma product business from Abbott.

Q. Would you turn to Tab 52, please, in your notebook.

To speed things up, would you agree that this is another presentation that was made at

the trace components meeting in 1975?

A. Yes.

Q. The particular presentation we're looking at was made by who, please?

A. It was made by Dr. Schwick, who was the president of Behringwerke.

Q. Was --

A. A fractionator.

Q. Was Dr. Schwick present at the conference in 1975?

A. Yes, he was. He gave this paper.

Q. Do you recall seeing Dr. Schwick and speaking with him at this conference?

A. Oh, I certainly do, because we discussed the trace components and -- and his giving me certain of the proteins I was interested in.

Q. Would you turn to Tab 53, please, in your notebook.

A. Yes.

Q. Would you tell the jury, please, what is at Tab 53.

A. This is an article that appeared in a Japanese journal but is in English, "Chemical Pharmacological Bulletin," I believe, by Higashi and

other individuals, several of whom are associated with the Green Cross Corporation. The title is "Inactivation of Viruses Intentionally Added to Urokinase Samples by Heat-Treatment."

Q. Did you -- if you did, I'm sorry, I didn't hear it.

Did you tell the jury the date of this particular publication?

A. 1977.

Q. Did it appear in a reputable and authoritative scientific and medical journal?

A. Well, it was a reputable journal --

MR. BECK: Objection; leading.

BY MR. SPIVEY:

Q. Go ahead.

A. It was a reputable journal. It -- it didn't have, shall we say, the same circulation that the "New England Journal of Medicine" had.

MR. BERKMAN: Again, I'm assuming we've had this standing objection to all of these articles dealing with other proteins and other viruses.

BY MR. SPIVEY:

Q. Would you tell the jury what urokinase is.

A. Urokinase is an enzyme that has an activity in which it dissolves the fibrin clot and it -- it -- that is, what it really does is it facilitates the action of plasminogen to become an active enzyme, plasmin, and the plasmin dissolves the fibrin clot.

We now use a analogous material for people who have a sudden heart attack. This was isolated from the urine of healthy men but it also appears in the plasma.

Q. Is urokinase a plasma protein?

A. Well, it would appear in the plasma. It usually is harvested from the urine.

Q. Would you turn to Tab 54, please, in the --

MR. BECK: Before you do, Mr. Spivey, the witness indicated earlier that I think in his words were all these articles were articles that he had found and -- and presented to the lawyers, and I haven't asked since then but since this is a translation of a foreign language article, could you please establish whether this is an article that he provided to you or vice versa?

BY MR. SPIVEY:

Q. Dr. Putnam, would you turn to Tab 54, please,

00305
in your binder.

Can you tell the --

A. Well, it's 53.

MR. BECK: I object and move to strike the last series of questions and answers for lack of foundation.

BY MR. SPIVEY:

Q. Would you turn to Tab 54, please.

A. Yes, I will.

May I make one correction? This is not a translation; this is an article published in English.

Q. Thank you.

You were saying that for Mr. Beck's benefit?

A. That is correct. Yes.

Q. It was originally published in English, was it?

A. Yes, the original publication is English.

Q. Would you turn to Tab 54, please.

A. Yes.

MR. BECK: I renew my objection.

If the witness will say whether he provided it to you or you provided it to him,

that would solve the problem I'm having.

BY MR. SPIVEY:

Q. Would you describe, please, for the jury what is contained at Tab 54.

A. Tab 54 contains an abstract which actually was presented as a poster at the Sixth International Congress on Thrombosis and Haemostasis in 1977. It is an article entitled -- the abstract is entitled "Isolation of Human Antithrombin-III by Affinity Chromatography on Heparin-Agarose," and the authors are W. H. Holleman and others who were at the Abbott Laboratories.

Q. And how was the antithrombin III stabilized, as described in this poster?

MR. BECK: I'm going to object and ask that the same foundation be laid that he laid for the articles that he said he provided to the lawyers.

BY MR. SPIVEY:

Q. Do you have my question in mind, Dr. Putnam?

A. Yes, I have your question in mind.

And the answer is that the antithrombin III was found to be stable to heating at 60 degrees for 10 hours, that is, pasteurized. In this case

MR. GOODELL: Same objection.

MR. BECK: Same objections.

THE WITNESS: With the provisions I've already made, namely, the motivation, the financial support, provision of the necessary ancillary services such as the virology and, of course, they already had the methods for doing assay, given the personnel or the, if necessary, hiring additional personnel, that with these provisions, it is my opinion that the stabilization of factor VIII, the pasteurization of factor VIII, could have been accomplished within a three-year period.

BY MR. SPIVEY:

Q. And do you have a similar opinion, that is, do you have an opinion as to whether if work had began in 1970, how long it would have taken the companies represented around this table to stabilize and virally inactivate factor IX?

MR. GOODELL: Same objection.

MR. BECK: Same.

MR. BERKMAN: Same objection.

THE WITNESS: Yes. I have the opinion

asking whether the opinion that you gave on factor IX -- VIII also applies to factor IX.

MR. BECK: Same objections.

MR. SCHOON: Same objection; assumes facts.

THE WITNESS: The opinion I gave previously and the opinion I give now with reference to the dates involved initiates in 1970 through a three-year period afterwards. And my opinion is that beginning in 1970, that it would have taken probably three years to develop a dry heat process that would have inactivated factor VIII and, likewise, to develop a dry heat process that would have inactivated -- excuse me, not inactivated factor VIII, that would have inactivated the hepatitis virus or other viruses present in factor VIII or in factor IX by heating in the dry state for the appropriate time and temperature.

MR. SPIVEY: Dr. Putnam, that's all of the questions I have for today's examination, and we'll see you in the morning.

THE WITNESS: Okay.

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on November 22nd, 1984.

BY MR. SPIVEY:

Q. Dr. Putnam, it -- does it appear to you from your review of the literature that it was Behringwerke that first stabilized and virally inactivated factor concentrate?

MR. BERKMAN: Objection.

MR. BECK: Objection; leading.

BY MR. SPIVEY:

Q. Which of the fractionator companies in the world was the first to virally inactivate factor concentrate?

A. Well --

MR. BECK: Note my objection. Having led him once, it's still leading.

THE WITNESS: Well, Behringwerke was the first company which developed a product that was commercially available, that was clinically tested and that was licensed.

BY MR. SPIVEY:

Q. And when was that, Dr. Putnam?

A. The development process was in the late '70s. The -- according to the article in the "New England Journal of Medicine" by Schimpf, et al., it

was commercially available in 1980.

Q. And in the 1970s, during the time period that you just mentioned, was the structure of factor VIII known?

A. The structure of factor VIII was not known in that time period.

Q. Impediment Number Two on the list, Dr. Putnam -- and I'm quoting again -- "The indirect clotting time assays that were available during this period did not provide an adequate means in which to evaluate the extent to which potential hepatitis inactivation processes would affect the ability of the factor concentrates to perform their function in vivo."

Have you reviewed that particular impediment before?

A. Yes, I have.

Q. We really haven't taken the time to define what an assay is.

Would you tell the jury what a factor VIII assay is, please.

A. Well, an assay is a procedure for determining the activity of a particular biological product. There may be a variety of ways of conducting the