UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

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ILLUMINA, INC.,

Petitioner,

vs.

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

Patent Owner.

----------x

IPR2018-00291 IPR2018-00318

IPR2018-00322 IPR2018-00385

IPR2018-00797

VIDEOTAPE DEPOSITION

STEVEN M. MENCHEN, PH.D.

New York, New York

January 14, 2019

9:21 a.m.

Reported by:

ERICA L. RUGGIERI, RPR

Illumina Ex. 1112
Illumina v. Columbia
IPR2018-00291, -00318, -00322, -00385, and -00797

January 14, 2019

9:21 a.m.

Videotape Deposition of STEVEN M. MENCHEN, PH.D., held at the offices of Venable Fitzpatrick, 1290 Avenue of the Americas, New York, New York, pursuant to Notice, before Erica L. Ruggieri, Registered Professional Reporter and Notary Public of the State of New York.

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FLOYD ROMESBERG, Scripts Research Institute
DEVERELL WHITE, Videographer

THE VIDEOGRAPHER: We are going on the record at 9:21 a.m. on January 14, 2019. Please note that the microphones are sensitive and may pick up whispering and private conversations.

Please place all cellphones away from the microphones as they can interfere with deposition audio.

Audio and video recording will continue to take place unless all parties agree to go off the record.

This is media unit one of the video recorded deposition of Dr. Steven Menchen taken by counsel for the petitioner in the matter of Illumina, Incorporated versus The Trustees of Columbia University in the City of New York, IPR 2018-00291, 318, 322, 385, 797. This is filed in the U.S. Patent and Trademark Office.

We are at the offices of

Venable Fitzpatrick located at 1290 Avenue of the Americas, New York, New York.

My name is Deverell White representing Veritext Legal Solutions.

At this time will counsel please state their appearances.

MR. REINES: Edward Reines on behalf of the petitioner.

MR. LUMAN: Nate Luman on behalf of petitioner.

MR. BIRCH: Marcus Birch, Illumina.

MR. ROMESBERG: Floyd Romesberg, Scripts Research Institute.

MR. SCHWARTZ: And Robert Schwartz from Venable Fitzpatrick for Columbia University and the witness. And with me is John Murnane and Zachary Garrett from Venable Fitzpatrick. Also John White from Cooper & Dunham and Jeff

DR. STEVEN MENCHEN, Ph.D.
Kestler, Karyn Hui and Teresa Chen from Columbia University.
S T E V E N M. M E N C H E N,
called as a witness, having been duly sworn by a Notary Public, was examined and testified as follows:
EXAMINATION BY
MR. REINES:
Q. Please state your name and address for the record.
A. Steve Menchen.
Q. What's your address, please?
A. 768 Vanda Way, Freemont, California.
MR. REINES: We have -- I have entered into an agreement with opposing counsel that, at least for present purposes, we will keep your current employer confidential, but I just wanted to put on the record that we have an agreement that counsel for petitioners will be informed of that under -- under the

DR. STEVEN MENCHEN, Ph.D.

protective order. And the parties are reserving rights to discuss it further beyond that if need be.

Q. You've had your deposition taken before?

A. Yes, I have.

Q. And one time was in the Beckman Coulter case; is that correct?

A. I think so.

Q. And another time was in the Bio-Rad case; is that correct?

A. Yeah, I think -- I think that's correct.

Q. And you've had your deposition taken at other times when you were at Applied Biosystems, isn't that true?

A. That's right.

Q. And all in how many times would you estimate you've had your deposition taken?

A. Around five.

Q. Have you ever served as an

DR. STEVEN MENCHEN, Ph.D.

expert before?

A. No.

Q. When did you receive your assignment in this matter?

A. I don't remember.

Q. To the best of your recollection what's your estimate as to when?

A. It was probably around a year ago.

Q. I'd like to show you what has been marked as Columbia Exhibit 2114, which probably looks familiar to you.

MR. REINES: I'm sorry, but we are going to be a little short on exhibits. I'll just give you a couple and we have got a distance here so I'll be throwing them.

Q. And would you confirm that this is a declaration that you signed on October 25th, 2018, please?

A. Yes.

DR. STEVEN MENCHEN, Ph.D.

Q. And how much time did you spend working on this project through to October 25th, 2018?

MR. SCHWARTZ: Objection, form.

A. In days or?

Q. The best way you can quantify it.

A. Probably about 20 days.

Q. By the way, when you are using the term "days," what approximately is a day for approximately in the terms of hours expended?

A. Yeah, eight to ten-hour days.

Q. What was that?

A. Eight to ten-hour days.

Q. Did you do any independent reviews of the literature for -- in the course of preparing your opinions that are set forth in Exhibit 2114?

A. I did some background

DR. STEVEN MENCHEN, Ph.D.
searches for the references that were supplied by Illumina.
Q. References supplied by Illumina?
A. That's right.
Q. When you say background searches, what did you mean by that?
A. Some of the references cited, other things and, yeah, just generally that kind of thing.
Q. So where there was a citation in a publication that you were reviewing you might have gone and looked at what that -- what was actually --
A. That's right.
Q. -- contained. Okay.
Prior to your work on this project were you familiar with the Ju patents?
MR. SCHWARTZ: Objection, form.
A. Actually not that familiar. I knew about them.

DR. STEVEN MENCHEN, Ph.D.

Q. Because your deposition has been taken before I'll assume you have a basic understanding of the deposition process. But let me go through some of the particulars.

One thing is that if your counsel objects, that doesn't affect your obligation to respond to me. Those objections are for the record.

Do you understand that?

A. Yes.

Q. And during the course of the deposition if you'd like to take a walk to stretch your legs or whatever, let me know and at an appropriate time we will do that.

Do you understand that?

A. Yes.

Q. During the course of the deposition I'll be asking questions obviously. If you don't understand any question or aspect of the question, let me know, otherwise I will assume you understood the

DR. STEVEN MENCHEN, Ph.D.

question. Is that fair?

A. That's fair, yeah.

Q. Is there any reason why you can't give your best, most accurate testimony today?

A. No reason.

Q. How much time did you spend preparing for the deposition?

A. In terms of days?

Q. That's fine.

A. Probably eight days, nine days.

Q. And are we talking about eight to ten hours?

A. Probably eight. Six to eight hours per day.

Q. When were those days, like what was the time frame within which you were preparing for the deposition?

A. They were probably all within the last two months.

Q. What did you do to prepare for the deposition?

DR. STEVEN MENCHEN, Ph.D.

A. We went over the declaration.

Q. And how many people were present for that, numerically?

A. Two to four.

Q. Did you reread the materials cited in your deposition -- I mean -- excuse me. Did you reread the materials cited in your declaration in preparation for the deposition?

A. I read some of it.

Q. In the time you spent preparing for the deposition did you find any errors or mistakes in your declaration?

A. No.

Q. Did you see anything that you felt required or warranted clarification?

A. No.

Q. I'd like to show you what's been marked as Columbia Exhibit 2108, which is a list of

DR. STEVEN MENCHEN, Ph.D.

documents considered by you, that's how it's termed.

And did you come up with this list of materials considered?

A. Some of it.

Q. Can you describe how this was created?

A. What do you mean exactly?

Q. How did you decide what materials you would consider, let me ask that question?

A. It was anything that was in the report.

Q. You selected the materials before you wrote the report, right?

A. The report was generated from this material.

Q. Right. So the documents you considered -- you considered the documents before you prepared the report, right?

A. That's right.

Q. Okay.

A. Some of them.

DR. STEVEN MENCHEN, Ph.D.

Q. First thing first. Some of the materials you didn't consider until after the declaration?

A. Actually that's all of them.

Q. Right. That makes sense. So first you considered the materials --

A. Yeah, yeah. Sorry, yeah. Yeah.

Q. Okay. One of the rules of the deposition is that we need to speak one at a time. So I'll do my best to allow you to complete your answer before I ask my next question and if you can try to accord the same protocol for me, I would appreciate that.

A. Sure.

Q. It's not the easiest thing to do because it's not normal human intercourse but I thought it would be useful. Okay, good.

In terms of the excerpts from

DR. STEVEN MENCHEN, Ph.D.

the prosecution history, which is 1,009, how did you decide what part of the prosecution history you would look at?

A. That was decided by the legal -- legal team.

Q. What was your purpose in looking at the prosecution history?

A. The -- the purpose was to look at the prosecution history of -- well, I need to look at the -- show you the structure but it was -- it had to do with the chemical link or the Y that connects the base with the tag.

Q. Can you describe what the specific purpose you had was for looking at the prosecution history in this case?

A. To look at Ju's declaration on that.

Q. Anything else?

A. No.

Q. In evaluating the

DR. STEVEN MENCHEN, Ph.D.

prosecution history for the Ju patent did you evaluate an independent understanding of why the Patent Office granted it?

A. No.

MR. SCHWARTZ: Objection. Mischaracterizes the witness's testimony.

Q. In terms of the Ju patent you said that you were aware of it but not particularly familiar with it prior to this project; is that correct?

A. That's correct.

Q. What was the context in which you were generally aware?

A. We were -- when I was at Applied Biosystems, we were working on -- on sequencing by synthesis. So we were aware that there were patents out there.

Q. What other sequencing by synthesis patents were you aware of when you were at ABI working

DR. STEVEN MENCHEN, Ph.D.

sequencing by synthesis space?

A. I don't really remember.

Q. The only ones you can remember is Ju?

A. Well, I do remember that we looked at Ju.

Q. But you can't remember any others?

A. I don't remember any others.

Q. And when you looked at the Ju patents while you were at Applied Biosystems, what conclusions did you have about it?

A. We didn't have any conclusions.

MR. SCHWARTZ: Outside the scope. Objection.

Q. Did you continue to do your sequencing by synthesis research even after the Ju patents came to your attention?

MR. SCHWARTZ: Same objection.

A. The research we were doing

DR. STEVEN MENCHEN, Ph.D.

didn't overlap with anything in the Ju patent.

Q. Did your work at Applied Biosystems sequencing by synthesis, did it result in any product?

A. Yes, it did.

Q. What was the product?

A. It was called SOLiD. And then we had another product when I worked with Ion Torrent, which was purchased by Life Technologies, which was Applied Biosystems. That was a different product.

Q. Both SOLiD and Ion Torrent are sequencing by synthesis systems; is that correct?

A. That's correct.

Q. Were you aware of the Solexa product line when it came out?

MR. SCHWARTZ: Objection, form.

A. I don't remember if I was aware of Solexa.

DR. STEVEN MENCHEN, Ph.D.

Q. Were you aware of the Solexa -- that Illumina purchased Solexa, is that something that came to your attention when you were working in the field?

A. Yes, I was aware of that.

Q. When did you first understand the sequencing by synthesis process used in the Illumina systems that were formally Solexa?

A. When we were -- so we knew about Illumina but it was when I was working on SOLiD, which would have been probably 2006, something like that.

Q. When you understood how the Illumina sequencers worked, did you recognize them as having the same technology as you had seen in the Ju patent?

A. I don't remember that.

Q. You don't remember ever reaching that conclusion or thinking

DR. STEVEN MENCHEN, Ph.D.

about that?

A. We -- we weren't concerned with that.

Q. Is that something -- whether you were concerned about it or not, did you observe that the technology described in the Illumina products were related at all to what was disclosed in Ju?

MR. SCHWARTZ: I'm going to object to this whole line of questioning under scope.

A. We -- we just -- like I say, we -- we just didn't -- we were working on our own projects. We knew about Illumina. We didn't really consider the other things.

Q. Did you evaluate the Solexa technology for potential acquisition by Applied Biosystems?

A. I didn't.

MR. SCHWARTZ: Objection, scope.

Dr. Menchen, just give me a

DR. STEVEN MENCHEN, Ph.D.

moment to object before you answer, please.

Q. When you learned of the -- of the Ju patent and patent disclosures in connection with your sequencing by synthesis work with the SOLiD system and the Ion Torrent system, did you conclude that the Ju -- that Ju was significant intellectual property?

MR. SCHWARTZ: Objection, scope. Objection, form.

A. Yeah, I don't quite understand your question.

Q. Did the Ju patented technology have any kind of reputation in the field that you were aware of when you learned about it in connection with your work on the SOLiD and Ion Torrent sequencing by synthesis systems?

MR. SCHWARTZ: Objection, scope. Objection, form.

A. I -- I don't remember,

DR. STEVEN MENCHEN, Ph.D.

yeah.

Q. You don't remember any significance being put on that by anybody?

MR. SCHWARTZ: Mischaracterizes the witness's statement.

A. Yeah, I -- I don't remember what our thinking was back then. It was around 2006.

Q. And after 2006 you never evaluated the Ju patent in connection with the sequencing by synthesis work you were doing?

MR. SCHWARTZ: Same objections.

MR. REINES: Let me -- first of all, your last objection was mischaracterizing the testimony. I want to state for the record that if I'm not characterizing testimony, I view a mischaracterizing testimony objection as coaching and so I'd

DR. STEVEN MENCHEN, Ph.D.

ask you not to do that.

In terms of scope I'm asking about the reputation of the Ju patents. I don't know -- and whether he's evaluated -- you know, whether he looked at the patents. I don't know how that could be more within the scope. That's just my take.

MR. SCHWARTZ: Objection to the scope of those questions.

Q. Did you review the Ju patent after 2006 in connection with your sequencing by synthesis work?

MR. SCHWARTZ: Same objection.

A. I don't remember reviewing the Ju patent, but we did speak with IBS.

Q. When was that?

A. I don't remember the -- the time frame.

Q. What's your best estimate as to the time frame?

A. Around probably 2006-2007.

DR. STEVEN MENCHEN, Ph.D.

Were they a company then? I don't even remember.

Q. I mean if you talked to them, then I assume they were.

A. Well, I just -- yeah. I don't remember when they formed but it was probably shortly after that.

Q. And what was your purpose in talking to the IBS team?

MR. SCHWARTZ: Same objection, scope.

A. Actually that's confidential. That's Life Technologies, confidential.

Q. Why did you bring up your discussions with IBS when I asked you about your awareness of the Ju patent?

A. Because that's what -- that's what we did.

Q. In connection with the Ju patent?

A. Well, it was -- I was of the -- I think their technology was

DR. STEVEN MENCHEN, Ph.D.

based on the Ju patent.

MR. SCHWARTZ: Dr. Menchen, to the extent that you have any confidentiality agreements, please keep those in mind.

THE WITNESS: Okay.

Q. Prior to your involvement in this project did you ever reach the conclusion that the Ju patents were significant patents in the field of sequencing by synthesis?

MR. SCHWARTZ: Requires legal conclusion, objection. Scope objection.

A. I don't remember.

Q. When Ju published his literature related to the patents, were you aware of that literature being published?

A. We -- we were aware of the literature but I don't remember what the time frame was.

Q. At some point in time you reviewed Ju's literature that

DR. STEVEN MENCHEN, Ph.D.
relates to the technology disclosed in his patents that are at issue here; is that correct?
A. I'm sorry?
Q. I said at some point in time you reviewed Ju's literature that relates to the technology disclosed in the patents; is that correct?
A. Yeah, we have read his -- we read some of his articles, yeah.
Q. What was your purpose in doing so?
MR. SCHWARTZ: Objection, scope. Objection, confidential. Objection, legal conclusion.
A. I suppose that would be confidential.
Q. Why you read the Ju literature is confidential?
A. Could you repeat the question?
Q. So at some point you read Ju's literature; is that correct?

DR. STEVEN MENCHEN, Ph.D.

A. That's correct.

Q. And you are saying that the reason why you read Ju's literature is confidential?

A. May be trade secret.

Q. Trade secret. Okay.

A. Yeah.

Q. What did you learn from the Ju literature when you read it?

A. Also trade secret.

Q. Okay. We may be getting to a problem area here. So you are saying what you learned about the Ju literature when you read it is so confidential that you can't mention in this deposition; is that correct? That's your position?

A. So what -- what time frame are you talking about?

Q. Prior to your work on this project.

A. So I would have read that literature while I was working at Life Technologies. Yeah, that would

DR. STEVEN MENCHEN, Ph.D.

be trade secret what my conclusions were.

Q. So in terms of your evaluation of the literature and your awareness of the state of the art of sequencing by synthesis while you were at Life Technologies, you consider that to be trade secret; is that correct?

MR. SCHWARTZ: Also to the extent -- actually all -- Dr. Menchen --

Q. Why don't you answer that question?

MR. SCHWARTZ: Dr. Menchen, to the extent that you have to divulge information that was -- when you were asked by lawyers to do anything, please be careful about divulging that information.

Q. In terms of your evaluation of literature and your awareness of sequencing by synthesis during the time that you were at Applied

DR. STEVEN MENCHEN, Ph.D.

Biosystems, Life Technology you considered that to be trade secret, correct?

A. Well, confidential.

Q. Right. And that's -- and, therefore, you won't disclose that in the course of these proceedings; is that correct?

A. Not anything that -- what I'm bound by confidentiality.

Q. Right. And I'm asking you, do you consider yourself bound by confidentiality such that you can't provide information about your review of the literature and understanding of the state of the art of sequencing by synthesis while you were at Applied Biosystems and Life Tech?

A. That's right.

Q. And what are the years that are covered by that confidentiality obligation of yours?

A. Until 2015.

DR. STEVEN MENCHEN, Ph.D.

Q. And when did it start?

A. I mean it started when I first worked at -- started working at Applied Biosystems.

Q. When was that?

A. 1985.

Q. While you were at Applied Biosystems did you consider Dr. Ju's work to be significant work?

MR. SCHWARTZ: Objection, scope.

A. I -- I don't remember.

Q. And you reviewed his literature and patents; is that correct?

MR. SCHWARTZ: Objection, scope.

Q. I'm not asking you about that, I know you won't provide any information about that, but in terms of whether you did it. You did review his patents and literature when you were at Applied Biosystems; is that correct?

DR. STEVEN MENCHEN, Ph.D.

A. So what do you mean by review?

Q. Read.

A. Yeah, read. Certainly reread some of his publications.

Q. And also his patents; is that correct?

A. I -- I don't remember reading his patents.

Q. Okay. So before your project -- before your involvement with this project you may never have read Dr. Ju's patents; is that correct?

A. Yeah, I -- I don't remember reading them.

Q. Before this project did anyone ever tell you Dr. Ju's were significant?

MR. SCHWARTZ: Objection, scope.

A. I don't -- I don't remember.

MR. SCHWARTZ: I'm also going

DR. STEVEN MENCHEN, Ph.D.

to add objection to form to that question.

Q. Exhibit -- back to your list of materials considered, Exhibit 120 -- 1021, is the Pelletier articles from Science.

Do you recall it? Do you see that?

A. Yes, I see that.

Q. Was that a well-known publication when it came out?

A. I don't know.

Q. Were you aware of that publication prior to your work on this project?

A. I wasn't.

Q. Were you aware of Tsien's work prior to your work on this project?

MR. SCHWARTZ: Objection, form.

A. So what -- the time frame means any time before I started working on this project?

DR. STEVEN MENCHEN, Ph.D.

Q. Yes.

A. I remember hearing about Shen.

Q. What was the context?

A. I just remember hearing about it as prior art.

Q. Prior to anything in particular?

A. I'm sorry, could you repeat that?

Q. You said prior art. Usually prior art is in reference to something else. Prior art in reference to anything in particular?

A. Just as -- for sequencing by synthesis, reversible terminators.

Q. And what was your understanding -- before this project of Shen in terms of its significance in sequencing by synthesis reference?

A. I had no understanding.

Q. Prior to your work on this

DR. STEVEN MENCHEN, Ph.D.

project were you aware of the Dower patent?

A. I was not aware of the Dower patent.

Q. Prior to your work on this matter were you aware of the Metzker 1994 article?

A. Yes, I was.

Q. What was the context?

A. I believe that's also confidential.

Q. Just to be perfectly clear, what you thought about the Metzker article, 1994 article, prior to your work on this project you consider to be confidential and that you are obligated not to discuss it at these proceedings; is that correct?

A. Could you repeat the -- the question before?

Q. Let me just ask this question. Can you discuss what you thought about the Metzker 1994 article prior to your involvement in

DR. STEVEN MENCHEN, Ph.D.

this project?

A. I think I can't discuss that, but I can discuss anything, you know, moving forward into this -- into this project.

Q. Is that -- is it generally true that in terms of the prior art and literature you can discuss what you thought about those things once you started working on this project but not before; is that correct?

A. No, I don't think that's generally true.

Q. Were you familiar with Prober before you began work on this project?

A. Yes.

Q. Were you familiar with the Prober patents?

A. Yes, I was.

Q. Did you know Applied Biosystems had a license to them?

A. I was involved in that.

Q. When you say you were

DR. STEVEN MENCHEN, Ph.D.

involved in that, can you describe what you mean by that?

A. I was developing the technology that -- when -- when we -- when we licensed it, I was kind of one of the technical people.

Q. Did you work on the project to develop terminators for Sanger sequencing?

A. Yes, I did.

Q. Did you ever discuss the Metzger 1994 paper with Dr. Metzker?

A. Yes, I did.

Q. When was that?

A. It would have been around 2006-2007.

Q. What was your purpose in doing that?

A. I think that might be confidential.

Q. Do you have a reasonable basis to believe it's confidential?

A. Yes, there is.

Q. Did Dr. Metzker discuss

DR. STEVEN MENCHEN, Ph.D.

with you the results in his 1994 paper?

A. I believe he did.

Q. And the content of what Dr. Metzker discussed with you about what was in his 1994 paper, you can't provide that because you believe you are under confidentiality; is that correct?

A. I can't disclose our conversations.

Q. Can you disclose your conclusions about the 1994 article while you studied it when you were at Applied Biosystems and Life?

MR. SCHWARTZ: Objection, form.

A. Could you repeat that question?

Q. Yes.

A. Okay.

Q. Are you -- do you believe you are free to discuss your conclusions about the Metzker

DR. STEVEN MENCHEN, Ph.D.

article that you reached before you started this project?

A. So our -- our discussions didn't really involve -- we -- we discussed very little about that particular article. It was more about Metzker's work.

Q. My question to you is, you reviewed the 1994 article to Metzker prior to your work on this project; is that correct?

A. I discussed it with -- yes, I did review it.

Q. But did you review it individually?

A. Yeah, I read it.

Q. Okay. And if I understand you correctly, the conclusions you had about that is trade secret information you can't provide, correct?

A. Yes, I think it is.

Q. Prior to your involvement in this project had you read the

DR. STEVEN MENCHEN, Ph.D.

Kamal publication that's in tetrahedron letters from 1989?

A. No.

Q. If you turn to paragraph 6 on page 2 of your declaration, please. In here you state that you considered and reviewed the documents listed in Exhibit 2108.

Do you see that?

A. I see that.

Q. And that was a correct statement when you made it?

A. Yes.

Q. And did you also consider and review the documents listed in Exhibit 2108 in preparation for the deposition?

A. What is 2108?

Q. I think that's another version of what -- of twenty -- not another version. That is the list that's in front of you.

A. Oh, I'm sorry. Yeah. So could you repeat the question,

DR. STEVEN MENCHEN, Ph.D.

again?

Q. In preparation for your deposition did you review and consider the documents listed in Exhibit 2108?

A. Yes, I did.

Q. And you understood that for this deposition you needed to be prepared to discuss the questions about your declaration and the documents you relied on?

A. Yes.

Q. And you did your best to do that; is that correct?

A. Yes.

Q. In your declaration you state you studied the patent at issue. Do you see that, in paragraph 7?

A. Yes.

Q. And, in fact, you studied the -- each of the Ju patents that's at issue in this proceed- -- in these proceedings; is that correct?

DR. STEVEN MENCHEN, Ph.D.

A. I studied them within the context of whether the propenyl group was cleavable and whether the propenyl group would be a substrate for DNA polymerase.

Q. Did you review the Ju patents that are issue in these proceedings for any other purpose?

A. No.

Q. Are you sure about that?

A. Yes.

Q. Have you ever read the Ju patents from beginning to end?

A. Yes, I have.

Q. Did you understand them?

A. Yes, I did.

Q. Do you also understand how a person of ordinary skill in the art in 2000 would have understood the Ju patent disclosures?

A. Yes.

MR. REINES: Why don't we take a quick break if that's all right with the folks here.

DR. STEVEN MENCHEN, Ph.D.

THE VIDEOGRAPHER: The time on the video monitor is 10:04 a.m. We off the record.

(Whereupon, there is a recess in the proceedings.)

THE VIDEOGRAPHER: We are back on the record. The time on the video monitor is 10:21 a.m. This is the start of media two.

Q. Have you ever heard of the term allyloxy?

A. Yes, I have.

MR. SCHWARTZ: Objection, form.

Q. And what is that?

A. Within what context?

Q. Chemistry.

A. Chemistry? It describes an olefin with a carbon atom next to the olefin, an R group. And then there's -- there's an oxygen in that -- on that, we call it the three position if it's a longer olefin.

DR. STEVEN MENCHEN, Ph.D.

Q. What is the context in which you -- well, did you ever work with allyloxy?

A. I never have.

Q. Is allyloxy different from what people call allyl?

MR. SCHWARTZ: Objection, form.

A. It would be a derivative of allyl.

Q. Is allyloxy a member of the propenyl group?

MR. SCHWARTZ: Objection to form.

A. Allyloxy would be a member of a whole genus of groups.

Q. Is one of them propenyl?

A. One of them could be propenyl.

Q. It might not be a propenyl -- in the propenyl group; is that correct?

A. Well, it's a whole genus. You would have to draw the

DR. STEVEN MENCHEN, Ph.D.

structure.

Q. Which is the whole genus?

A. The allyl is a whole genus of compounds so the allyloxy would be a whole genus of compounds.

Q. Is a propenyl group a whole genus of compounds?

MR. SCHWARTZ: Objection, form.

A. A propenyl group would be an element.

Q. An element? Is that different than a genus of group -- a genus of compounds?

A. Well, it would be one of, yeah, one of the elements of the - of the genus.

Q. Is allyloxy a member of the propenyl group?

MR. SCHWARTZ: Objection, form.

A. So allyloxy is a genus so it's not a member of the propenyl group.

DR. STEVEN MENCHEN, Ph.D.

Q. How about the other way around. Is a propenyl a member of the allyloxy group?

A. If it's a -- a 2-propenyl, yeah, it would be a member.

Q. Is the allyl disclosed in the Ju patent, is that an allyloxy?

MR. SCHWARTZ: Objection, form.

A. Could I look at the --

Q. Of course. Let me show you what's been marked as Exhibit 1075, which is the '985 patent.

A. So could you repeat that question?

Q. Is the allyl disclosed in the Ju patent an allyloxy?

MR. SCHWARTZ: Objection, form.

A. The allyl disclosed in the Ju patent is a propene.

Q. Okay. That sounds like a different question. Please do your best to answer my question if you

DR. STEVEN MENCHEN, Ph.D.

don't mind.

Is the allyl disclosed in the Ju patent an allyloxy?

A. I don't see allyloxy in here.

Q. So it's not a member of that group?

A. So could you -- the -- you asked if the allyl disclosed in the Ju patent is an allyloxy.

Q. Yes. And is it?

A. And he just -- he disclosed as an allyl group.

Q. Do you know whether it's an allyloxy or not? Let me put it this way. Can you tell whether the allyl disclosed by Ju for his processes whether that's an allyloxy?

A. It's a propenyl oxy which is an element of that group.

Q. Is it an allyloxy?

MR. SCHWARTZ: Objection to form.

A. It's a propenyl oxy which

DR. STEVEN MENCHEN, Ph.D.
is an element of that group.
MR. SCHWARTZ: Objection to form to that question.
Q. I don't know what you mean by that group. Is there -- is there a reason why you can't directly answer whether the allyl disclosed in the Ju patent is an allyloxy?
A. Well, I'm trying to be precise. So the allyloxy disclosed in the Ju patent is a propenyl oxy.
Q. And you are confident about that?
A. He doesn't call it allyloxy.
Q. Understood. But as a person of ordinary skill in the art in 2000 reading the Ju patent would recognize the allyl, there is an allyloxy; is that correct?
MR. SCHWARTZ: Mischaracterized the witness's statements.
MR. REINES: I'm not

DR. STEVEN MENCHEN, Ph.D.

characterizing the witness's testimony. That's coaching, please don't do it.

A. So I don't see the term "allyloxy" in this patent.

Q. Do you see the word "propenyl" in the Ju patent?

A. I see the structure for propenyl.

Q. I'm saying do you see the word "propenyl"?

A. No, I don't.

Q. Okay. Are you comfortable calling the allyl in the Ju patent a propenyl even though the word is not there?

A. Propenyl is a form -- yeah, I'm comfortable with calling it propenyl.

Q. Okay. And that's based on your technical expertise; is that correct?

A. Yes.

Q. Employing that same

DR. STEVEN MENCHEN, Ph.D.

technical expertise, is the allyl disclosed in the Ju patent an allyloxy?

A. It becomes an allyloxy. It becomes a propenyl oxy.

Q. Please describe why the allyl disclosed by Ju in his patent becomes an allyloxy as part of his process.

A. I don't understand that question. Could you be --

Q. Yes. The Ju patent discloses an allyl, correct?

A. It discloses a propenyl.

Q. Okay. Maybe this is the way to do it. Can you turn to page 25, Figure 7?

A. 25?

Q. Page 25 in the lower right-hand corner.

A. Of -- of this?

Q. Yeah. Of the patent.

A. Column 25.

Q. No, I see there's a page

DR. STEVEN MENCHEN, Ph.D.

number at the bottom.

A. Oh, I'm sorry. I didn't see that page --

Q. And I'm asking for a figure so there's no column system.

A. Okay.

Q. Do you have Figure 7 of the Ju patent in front of you?

A. Yes, I do.

Q. And do you recognize the disclosure of an allyl there?

A. Yes, I do.

Q. So Ju definitely discloses an allyl, correct?

A. He discloses a propenyl element of the allyl.

Q. Right. He calls it an allyl, right?

A. But he draws propenyl.

Q. I'm not debating with you. I'm asking you do you see that he calls it an allyl?

A. He does call it an allyl.

Q. Why do you -- based on your

DR. STEVEN MENCHEN, Ph.D.

expertise and all the work you've done in this case why do you believe Ju has described his allyl as an allyl rather than using the term "propenyl" like you've been using?

A. I don't know why.

Q. Do you have any idea at all?

A. It's a short -- short way of -- it's a way of describing a genus of groups and then he draws a structure to further identify which allyl he's talking about.

Q. Do you have any understanding at all why Ju would use the term "allyl" instead of propenyl when you keep using the term "propenyl"?

A. Well, because it's one of the allyl genus of groups.

Q. And just to be clear, there's nowhere in his patent that he terms it a propenyl, correct?

A. I would have to reread the

DR. STEVEN MENCHEN, Ph.D.

patent.

Q. Do you have any memory of that based on all the work that you've done in this case in the eight, nine days of preparation for this deposition?

A. I would have to reread it to see if he ever uses the term "propenyl."

Q. Do you have any recollection sitting here prepared for your deposition, prepared to answer questions on the Ju patent of him using the term "propenyl"?

A. I don't remember it.

Q. Now, this allyl disclosed by Ju, that's also an allyloxy, correct?

A. It's a propenyl oxy.

Q. Is it an -- it's important for me that you answer the question. If you don't think you can answer it, or you want to qualify it or, you know, we want fair questioning

DR. STEVEN MENCHEN, Ph.D.

so I'm not trying to straight jacket you into something that's inappropriate, but answering a different question doesn't -- isn't the right spirit for this process in my mind.

So the question is, earlier you testified that Ju's allyl becomes an allyloxy. Do you recall that?

MR. SCHWARTZ: Mischaracterizes statements.

A. Did I say that?

Q. Yes.

THE WITNESS: Could -- could you verify that?

Q. I don't think it's worth the time to do that because I think you'll admit it anyway. So let me just continue that way if we have to go through it because both the words "allyloxy" I have used in a lot of questions so a word search won't be an efficient way to do it, otherwise

DR. STEVEN MENCHEN, Ph.D.

I would do it.

Does the Ju allyl become an allyloxy as part of his processes?

A. The propenyl element of the allyl genus becomes a propenyl element of an allyloxy genus.

Q. So you mean it's a member of the allyloxy genus, is that your argument?

A. That's right.

Q. Okay. Now, you are familiar with analogs that have nucleotides with allyloxys on them?

A. Is propenyloxys.

Q. I'm -- allyloxys is the term I'm using.

A. I'm familiar with the propenyl oxy element of the allyloxy group.

Q. And why do you not want to use the term allyloxy?

A. I'm trying to be precise.

Q. Okay. And when you -- you've been involved in obtaining

DR. STEVEN MENCHEN, Ph.D.

your own patents through patent prosecution, correct?

A. Yes, I have.

Q. And you've got many, many patents; is that right?

A. A few, yes.

Q. When you say a few, how many?

A. Around a hundred.

Q. Okay. That's more than a few, isn't it?

A. Depends on how you define a few.

Q. So you think a hundred could be a few?

A. Some people have many hundreds.

Q. I'm saying in the context of -- of being a patent -- an inventor you think a hundred could fairly be described as a few patents; is that correct?

A. Sure.

Q. And with respect to the

DR. STEVEN MENCHEN, Ph.D.

patenting process would you say you are generally familiar with the patenting process from your experience with a hundred different patents?

A. I wouldn't say I'm familiar with the patenting process but I am familiar with getting patents.

Q. Are you familiar enough with the patent process to understand that inventors need to sign an inventorship oath stating that they read and understand their patent application?

A. Yes.

Q. And you've executed those?

A. Yes.

Q. And when you've done so you've been truthful; is that correct?

A. Yes.

Q. And when you prepare your patent product -- patent documents do you try to be precise?

DR. STEVEN MENCHEN, Ph.D.

A. I try to.

Q. To the best of your ability you attempt to be precise when you prepare your patent documents, correct?

A. Try to.

Q. I'm going to show you U.S. Patent No. 6,111,116.

(Exhibit 1091, U.S. Patent No. 6,111,116, marked for identification, as of this date.)

Q. And this is a patent that you obtained with Scott Benson and Joe Lam; is that correct?

A. That's correct.

Q. And if you turn to column 5, please. Let me know when you have that in front of you?

A. Yeah, I have column 5.

Q. And this is the portion of the patent where you define the terms that you are using, correct?

A. Yes.

Q. And if you turn to

DR. STEVEN MENCHEN, Ph.D.

nucleoside, you see the reference to nucleoside at line 25?

A. I see that.

Q. And then below that you referred to analogs in reference to nucleosides. Synthetic analogs and modified based moieties?

A. What -- what line is that?

Q. That's at line 40?

A. Okay. I see that.

Q. And in terms of the analogs, one of the analogs that you identify for that at line 55, do you see where it says exemplary -- exemplary sugar analogs include but not are limited to.

Do you see that?

A. Line 55.

Q. I'm just asking if you see those words?

A. Oh, yeah. I see exemplary base analogs.

Q. This is why I asked you because it's a little dense there

DR. STEVEN MENCHEN, Ph.D.

but at line 55 it says exemplary sugar analogs.

Do you see that?

A. Oh, okay. Exemplary sugar analogs.

Q. Good. And here you are talking about nucleotides with modifications to the 2' or 3' location; is that correct?

A. That's right.

Q. And one of the modifications is the use of allyloxy. Do you see that?

A. I see that.

Q. Which you prepared this patent document in the 1997-1998 time period you were familiar with allyloxys as modifications; is that correct?

A. Yes, I was.

Q. How did you learn about allyloxys as a modification as a capping group on the 3' position?

MR. SCHWARTZ: Objection to

DR. STEVEN MENCHEN, Ph.D.

form.

A. So this is just a -- these are the specifications.

Q. Understood.

A. Right.

Q. How did you learn about the use of allyloxys as synthetic modifications at the 3' location of a nucleotide in, you know, in the context of sequencing?

MR. SCHWARTZ: Objection to form.

A. Yeah, I guess I don't understand the context of the question.

Q. Okay. Let me take another crack at it.

In your patent, you are talking about dyes that are used for nucleic acid science, correct?

A. That's correct.

Q. And that's work that you did with colleagues at the time, correct?

DR. STEVEN MENCHEN, Ph.D.

A. That's correct.

Q. And one of the applications for the dyes was for sequencing; is that correct?

A. That's correct.

Q. And one of the things you are describing is the nucleotides that can be used with those dyes in the sequencing context; is that correct?

A. I'm sorry, what?

Q. You are describing the nucleotides that can be used?

A. That's right.

MR. SCHWARTZ: Objection to form.

Q. And you also note that not only nucleotides can be used but that analogs, synthetic analogs can be used in the sequencing process, correct?

MR. SCHWARTZ: Objection to form.

A. We -- this is a

DR. STEVEN MENCHEN, Ph.D.

specification.

Q. Understood.

A. Yeah.

Q. And one of the things you propose is that there are analogs that can be used with nucleotides, you'll admit that?

A. That's -- that's correct.

Q. Okay. You are telling people of ordinary skill in the art reading your patent that there are analogs of nucleotides that can be used with your dyes, correct?

A. That's correct.

Q. Okay. And you propose synthetic modifications that can be made to the nucleotides, including the use of allyloxy at the 3' position, correct?

A. So when you read this, you see we have methoxy, ethoxy, that's alkoxy. So we suggest two. Then we have allyloxy, which could include many elements just like alkoxy

DR. STEVEN MENCHEN, Ph.D.
included two elements, allyloxy could include many elements. Then we talk about isopropyloxy, butoxy, isobutoxy. So the allyloxy term here doesn't exclude other elements. It can be many elements.
Q. I didn't mean to exclude anything. My question to you is in your '116 patent you proposed allyloxy as a synthetic modification at the 3' location; is that correct?
A. That's correct.
MR. SCHWARTZ: Objection to form.
Q. And how did you know that that was a good candidate to include it in your patent as something?
A. We didn't know it was a good candidate.
Q. Then how come you included it?
A. We included a lot of things here.
Q. So when you disclosed

DR. STEVEN MENCHEN, Ph.D.

different modifications that could be made at the 3' locations of nucleotides in your sequencing chemistry you didn't think they were -- you didn't think they were good candidates?

A. So we were speculating that they might be good candidates. We had no reason to believe that they would be. We were just speculating that they might be.

Q. Would a person of ordinary skill in the art reading your '116 patent in the 1998 -- 1998 time period understand that you were proposing these as candidates?

MR. SCHWARTZ: Objection to form.

A. We were proposing these as just modifications that you could make and try. That's exactly what this is.

Q. And of all the different chemistries, how come for the 3'

DR. STEVEN MENCHEN, Ph.D.

position in your sequencing chemistry you called out allyloxy as one of the candidates?

A. Because it's a special genus.

Q. What's so special about it?

A. It has a double bond at the 2' position compared to the rest of these which have no double bonds.

Q. Why is that superior?

A. We don't know that it's superior.

Q. What's the advantage of two bonds as compared to one?

A. We didn't know if there was an advantage.

Q. Did you put any of those qualifications in your patent application when you disclosed this?

A. I don't remember. I would have to read it. Reread the patent. This patent issued in -- well, the priority date was I guess filed in 1998.

DR. STEVEN MENCHEN, Ph.D.

Q. When is last time you saw this patent disclosure?

A. When was the last time I saw this? I saw this patent disclosure yesterday or the day before yesterday.

Q. Okay. And coming to the deposition did you know you'd be questioned about your disclosure of allyloxy as a candidate, did you understand that was a possibility?

A. Yeah, it was a possibility.

MR. SCHWARTZ: I'm just going to caution you from now on and including in that question if the way you learned of something was through a conversation with a lawyer, I want you to not answer that question.

THE WITNESS: Okay.

Q. Do you remember where you learned that allyloxy may be a good candidate for the 3' position?

MR. SCHWARTZ: Objection,

DR. STEVEN MENCHEN, Ph.D.

form.

A. I don't remember learning that.

Q. Would a person of ordinary skill in the art reading your '116 patent understand that you had no idea whether allyloxy would work at the 3' position?

MR. SCHWARTZ: Objection to form.

A. Yeah, what -- what exactly do you mean by that?

Q. I mean something very pointed by that. Do you think a person of ordinary skill in the art reading your '116 patent and specifically your definition of analog -- let me step back. In your definitions of different terms in the '116 patent you attempted to be very precise in that? You tried to be as precise as you could be?

A. In this patent?

Q. Yeah.

DR. STEVEN MENCHEN, Ph.D.

A. Yeah.

Q. And you used the term allyloxy; is that correct?

A. That's correct.

Q. Okay. And you were comfortable with that?

MR. SCHWARTZ: Objection to form.

Q. Were you comfortable with the specification of the '116 patent when you signed your oath of inventorship?

A. Yes, I was.

Q. And you'll agree that you -- I think you've agreed at least that you've disclosed allyloxy as a candidate for synthetic modification at the 3' location; is that correct?

A. That's correct.

Q. And will you agree that the allyloxy is described as a good candidate for modification at the 3' location in sequencing for a person

DR. STEVEN MENCHEN, Ph.D.
of ordinary skill in the art?
A. Do I --
MR. SCHWARTZ: Objection to form.
Q. Do you think a person of ordinary skill in the art reading your definition of analog would understand that?
MR. SCHWARTZ: Same objection.
A. Would a -- would understand what?
Q. That you believed allyloxy was a good candidate and is a potential modification at the 3' location?
MR. SCHWARTZ: Objection to form.
A. A person skilled in the art would read this and say these are possibilities, not necessarily good candidates but they are possibilities. And that's what this specification says. That's all it is.

DR. STEVEN MENCHEN, Ph.D.

Q. And that's --

A. I don't think I use the word "good" in here or we used the word "good," as a good candidate.

Q. And are you saying that your list of potential modifications at the 3' location was total speculation when you signed your oath of inventorship?

MR. SCHWARTZ: Objection, mischaracterizes.

A. They were possible candidates.

Q. I'm saying did you --

A. Things that we could try.

Q. Did you believe it to be speculation?

A. They were -- yes, it was speculation.

Q. Total speculation?

A. What do you mean total speculation?

Q. Would a person of ordinary skill in the art reviewing your '116

DR. STEVEN MENCHEN, Ph.D.

patent in the 1998 time frame assume that your inclusion of allyloxy as a candidate for modification at the 3' location would be total speculation?

A. What does that mean?

Q. Would a person of ordinary skill in the art in 1998 reading your '116 patent and looking at your candidate list for modifications at the 3' location assume that your inclusion of allyloxy was based on speculation?

A. Well, they would see that there -- in the examples that we didn't -- that we didn't make it. So if we didn't make it, then it has to be speculation.

Q. And explain to me your logic there.

A. Well, if you didn't make it, you haven't tried it.

Q. Do you consider it speculation to include a candidate for chemistry without including data

DR. STEVEN MENCHEN, Ph.D.

showing you actually used it and proved it?

A. Could you clarify?

Q. Do you consider it speculation to include in a patent a candidate chemical design if you don't include the data proving that it would work?

A. I consider it a part of a specification where you are thinking forward, forward thinking, yeah.

Q. But my question to you is do you consider it speculation to include a candidate chemistry in a patent if you don't show data proving that it actually works?

A. I -- I don't really understand that question.

Q. Why not? What about the question don't you understand?

A. Repeat -- so yeah, repeat the question so I --

Q. Do you consider it speculation to include a candidate

DR. STEVEN MENCHEN, Ph.D.

chemistry in a -- in a patent if you don't show data proving that it actually works?

A. It may not be speculation. It could be that you didn't show that example in your text. So I don't think you could say that it's absolutely speculation.

Q. So in terms of your inclusion of allyloxy would a person of ordinary skill in the art know whether or not you were basing that suggestion of it as a candidate as being speculation?

A. I would say that's a correct statement.

Q. They would know whether or not you would --

A. They wouldn't know.

Q. Was your inclusion of allyloxy as a candidate for modification at the 3' position in a sequencing chemistry based on your technical expertise, not just you

DR. STEVEN MENCHEN, Ph.D.

but you and Scott Benson and Joe Lam?

MR. SCHWARTZ: Objection to form.

A. I don't remember why it was included.

Q. Do you know enough sitting here now to know that when you create a list of candidate chemistries for working with your invention that you do so based on your technical expertise as an inventor?

MR. SCHWARTZ: Same objection.

A. So that's a legal issue that I'm not familiar with.

Q. It's not. I'm asking as a factual issue, not a legal issue.

A. I -- I'm not familiar with that -- that -- if that's a rule, I'm not familiar with it.

Q. Would a person of ordinary -- do you believe it would be fair for a person of ordinary

DR. STEVEN MENCHEN, Ph.D.

skill in the art reading the '116 patent to assume that the list of candidates you have, including allyloxy -- let me step back.

Do you believe it's fair for a person of ordinary skill in the art in 1998 reading your '116 patent to assume that your inclusion of allyloxy as a candidate for modification at the 3' location was based on the technical expertise of the inventors?

A. Yeah, I still don't understand what you mean by technical expertise.

Q. Do you know what technical expertise is?

A. I'm not sure how you are using it.

Q. Do you have technical expertise?

A. I have some technical expertise.

Q. When you say some, what do

DR. STEVEN MENCHEN, Ph.D.

you mean by that?

A. Well, organic synthesis.

Q. Do you consider yourself to be qualified as an expert in this -- in this field?

A. In this field?

Q. In the field of the patents at issue.

A. Yes.

Q. Do you consider yourself to be a dye chemist?

A. That's one of the things that I do.

Q. Is that your primary expertise?

A. No.

Q. Do you have technical expertise in the area of analogs for nucleotides and the modifications that can be made to them?

A. I'm sorry, could you repeat that.

Q. Do you have technical expertise in the area of analogs of

DR. STEVEN MENCHEN, Ph.D.

nucleotides and modifications that can be made to them in the context of sequencing?

A. Yes.

MR. SCHWARTZ: Objection to form.

Q. Okay. Would a person -- so you understand what technical expertise is in that context?

A. It's someone who could make something.

Q. You understand generally what the term "technical expertise" means in that context?

A. I think so, yeah.

Q. Okay. Would a person -- is it fair for a person of ordinary skill in the art reading the '116 patent in 1998 to conclude that your inclusion of allyloxy as a candidate for modification at the 3' location was based on your technical expertise, you and the inventorship group?

DR. STEVEN MENCHEN, Ph.D.

A. It would be based on our technical expertise and the ability to make that compound.

Q. In terms of why using your technical expertise you believed allyloxy was a candidate to include in your patent disclosure for modification at the 3' location in your sequencing chemistry, what were the virtues of it?

MR. SCHWARTZ: Objection. Mischaracterizes the testimony.

A. The virtues are that we could make it and test it.

Q. Anything else beyond the mere fact that you could make it and test. Are you saying it's just merely the fact that it was something that could synthetically be accomplished?

A. Yeah. I mean it's -- it's analog chemistry. It's what they do in the pharmaceutical industry. You can't really predict if something is

DR. STEVEN MENCHEN, Ph.D.

going to work but if you can make it, you might want to -- you might want to do it.

Q. In order for it to be a nucleotide analog that worked with sequencing chemistry, it also needs to be such that it doesn't interfere with the DNA processes, correct?

MR. SCHWARTZ: Objection to form.

A. Which DNA processes are you talking about?

Q. I'm just saying if it was some -- the mere fact that you can make something if you knew it would be completely disruptive of DNA sequencing, you wouldn't have listed it here, how about that? Let me ask the easy question.

A. I don't think -- yeah. If we knew it was going to fail you probably wouldn't make it.

Q. Can you think of modifications at the 3' position

DR. STEVEN MENCHEN, Ph.D.

that you could make synthetically that you wouldn't have included here because it would be incompatible with your invention?

A. I can't think of anything right now.

Q. Really, you can't think of anything? You can't think of something that would be so inconsistent with your sequencing chemistry that you could make it but you would never want it to be in there?

A. So these are at the 2' position?

Q. 2' or 3'.

A. 2' or 3'. So this is -- these are your Sanger sequencing. These are not for SBS.

So for Sanger sequencing, yeah, I can't think of anything that -- there are -- I'm sure there are things that have been made that have failed for Sanger sequencing but I

DR. STEVEN MENCHEN, Ph.D.

can't think of anything offhand.

Q. Were you the first person to propose the use of an allyloxy at the 3' position for sequencing reactions?

MR. SCHWARTZ: Objection, form.

A. Yeah, what -- in what context?

Q. Sanger sequencing.

A. I don't know if we were the first people to propose that.

Q. Do you believe your disclosure of allyloxy as a modification at the 3' position for sequencing was inventive?

MR. SCHWARTZ: Objection, form. Objection, requires a legal conclusion.

A. Yeah. What do you mean by inventive? Is that a legal term?

MR. SCHWARTZ: Objection, form.

A. So repeat the question one

DR. STEVEN MENCHEN, Ph.D.

more time.

Q. Did you believe it to be innovative for you to include allyloxy as a candidate for modification at the 3' location in your '116 patent?

MR. SCHWARTZ: Objection, form. Objection, legal conclusion.

A. I can't say what we considered it then. This was -- you know, this was made in 1998. So I don't remember.

Q. Would a person of ordinary skill in the art reading your '116 patent in 1998 understand that your -- your disclosure of allyloxy as a candidate for modification at the 3' position in a sequencing context was an innovation?

MR. SCHWARTZ: Objection, form. Objection, legal conclusion.

A. Yeah, I don't think I can answer that.

Q. Why not?

DR. STEVEN MENCHEN, Ph.D.

A. Because I don't understand the context.

Q. The context of what?

A. Of -- yeah -- so is -- is -- is that a legal issue?

Q. No.

A. Okay.

MR. SCHWARTZ: Objection to form.

Q. Let me try it this way.

A. Yeah.

Q. Would a person of ordinary skill in the art reading your '116 patent in 1998 assume that the use of an allyloxy as a modification at the 3' location in the context of sequencing was part of your invention?

A. I don't know.

MR. SCHWARTZ: Objection to form. Objection, legal conclusion.

Q. Do you have any understanding at all what a person of ordinary skill in the art would

DR. STEVEN MENCHEN, Ph.D.
take away from your disclosure of allyloxy as a potential modification at the 3' location in 1998?
MR. SCHWARTZ: Objection to form.
A. This is a person ordinarily skilled in the art in what?
Q. In the -- as you've defined it in your declaration.
A. In -- in Sanger sequencing?
Q. You've got your definition. It's in your declaration. So let's do it --
A. So the person would be -- what would be --
Q. My question is withdrawn.
A. Okay.
Q. Would you turn to Exhibit 2114.
MR. SCHWARTZ: It's your declaration.
THE WITNESS: Okay.
Q. And if you turn to page 2. And do you see Roman numeral three?

DR. STEVEN MENCHEN, Ph.D.

A. Yes, I see it.

Q. And that is your description of a person of ordinary skill in the art, correct?

A. What page are we on?

Q. We are at page 2 of your declaration.

A. Page 2, Roman numeral three. Yeah, I see that.

Q. Okay. And Roman numeral three has your definition of a person of ordinary skill in the art, correct?

A. That's right.

Q. And you did your best to come up with a definition?

A. Yes.

Q. And you understand what your definition is?

A. Yes.

Q. Would a person of ordinary skill in the art as you've defined it in your declaration -- do you under- -- do you know how they would

DR. STEVEN MENCHEN, Ph.D.

understand your disclosure of allyloxy as a candidate for modification at the 3' location in the context of sequencing?

MR. SCHWARTZ: Objection to form.

Q. If you don't know, that's fine. If you do know, acknowledge it.

A. Yeah, I don't know.

Q. Okay. In your list of candidate modifications at the 3' location for sequencing in column 5 of the '116 patent, is the disclosure of hydrogen, is that a group or is that just a single chemical structure?

MR. SCHWARTZ: Where are you in column 5?

MR. REINES: You know, they don't always match up exactly. It's like a half line. But I'm at -- I'm calling it 58.

A. Column 5, 58.

DR. STEVEN MENCHEN, Ph.D.

Q. Yeah. Do you see where it's discloses hydrogen -- where you disclose hydrogen?

A. Hydrogen, yes.

Q. Is that a genus or is that just a single chemical structure?

A. That's a single chemical structure.

Q. And hydroxy, is that a genus or a single chemical structure?

A. That is a single chemical structure.

Q. Alkoxy, is that a genus or a chemical structure?

A. That's a genus.

Q. And two members of it are methoxy and ethoxy; is that correct?

A. That's correct.

Q. And then dropping down to isopropoxy, is that a genus or is that a single structure?

A. That's a single structure.

Q. Butoxy, a genus or a single

DR. STEVEN MENCHEN, Ph.D.

structure?

A. That's a genus.

Q. And that includes isobutoxy or is that is a different genus?

A. In includes sec-butoxy.

Q. Isobutoxy, is that a group or a single element?

A. That is a -- that is a single.

Q. Phenoxy, is that a single chemical structure or is it a genus?

A. That's a genus.

Q. Amino or alkamino, are those genus or are those each structures, single structures?

A. Amino is a group. Alkamino is a genus.

Q. Is propenyl identified anywhere in your list?

A. Well, they call -- isopropoxy is prop- -- would be propenyl.

Q. Anything else?

A. Propanol, I don't see it

DR. STEVEN MENCHEN, Ph.D.

anywhere else.

Q. How come you used the term "allyloxy" rather than propenyl?

A. Well, because it's a genus. We can include many elements of allyl.

Q. In the 1998-1999 time period which was the most natural candidates for 3' modification in the allyloxy genus?

MR. SCHWARTZ: Objection to form.

Q. To a person of ordinary skill in the art.

A. What -- yeah. What's the question?

Q. Yes. In the 1998 to 1999 time period which were the most natural candidates for 3' modifications within the allyloxy group?

MR. SCHWARTZ: Objection to form.

A. I don't know.

DR. STEVEN MENCHEN, Ph.D.

Q. You have no idea whatsoever; is that correct?

A. I mean there's a whole series that you could try.

Q. Based on your technical expertise you have no idea at all which allyloxys were the most natural candidates for 3' modification in the 1998-1999 time period?

A. Yeah, I don't know what you mean by natural candidates.

Q. Best candidates, how about that.

A. Best candidates.

Q. To you based on your technical expertise at the time.

A. So if you read this list they include isopropoxy, butoxy, phenoxy, so obviously what we're -- we could have any of those -- we could have the propene, the butene or we could have a phenyl group on there. So any of those.

DR. STEVEN MENCHEN, Ph.D.

Q. When you say any of those, just if you could -- let me ask that whole question and then you can include what any of those are.

Based on the state of the art at the time in 1998-1999 within the allyloxy group which are the best candidates for 3' modification in the sequencing context?

MR. SCHWARTZ: Objection, form.

A. Yeah. I mean I don't -- I don't know what the best candidates would be.

Q. What's your best judgment on that?

A. What's my best judgment? I'd rather not speculate on that.

Q. You can't identify any, is that what you are saying?

A. There's several.

MR. SCHWARTZ: Objection, mischaracterizes.

Q. Please identify the

DR. STEVEN MENCHEN, Ph.D.

several. This is within the allyloxy group.

A. So if we read on the others that we have here, there's the propenyl, the butenyl, the isobutenyl and then having a phenyl group coming off.

Q. And do you consider that speculation as to which the best candidates are?

A. I don't think you could decide which the best candidates would be.

Q. A person or ordinary skill in art if they wanted to pursue your suggestion of an allyloxy modification at the 3' location for sequencing would need to test different members of the group in order to see which ones actually worked best; is that correct?

A. It's the same chemistry to make all of them.

Q. But they would need to test

DR. STEVEN MENCHEN, Ph.D.

them in order to see which ones worked best in the sequencing context?

A. Yes, they would.

MR. SCHWARTZ: Objection to form.

Q. Is that process within the skill, the competency of a person of ordinary skill in the art?

A. The testing of them?

Q. Yeah.

A. Yes.

Q. And the synthesizing them?

A. Yes.

Q. Okay.

MR. REINES: Why don't we take another break?

THE VIDEOGRAPHER: The time is the video monitor is 11:11 a.m. We are off the record.

(Whereupon, there is a recess in the proceedings.)

THE VIDEOGRAPHER: We are back on the record. The time on the

DR. STEVEN MENCHEN, Ph.D.

video monitor is 11:28 a.m. This is media three.

Q. Do any of your candidate modifications at the 3' location have three bonds?

MR. SCHWARTZ: Are we back to the same exhibit?

MR. REINES: Yeah. I think the witness is there.

A. These are listed -- yeah, a few of them have three -- wait.

Q. It's called triple bonds. Sorry.

A. This is column 5?

Q. Yeah. Between -- between 51 and the end.

A. Yeah, yeah, okay. Yeah. Did you say?

Q. Triple bonds.

A. Triple bonds? I don't see any here.

Q. How come you didn't include any candidates with triple bonds?

A. I don't remember.

DR. STEVEN MENCHEN, Ph.D.

Q. Do you remember anything about the invention -- the inventions of the '116 patent?

MR. SCHWARTZ: Objection, form.

A. What does that mean? Do I remember anything about --

Q. Just take it at face value.

A. Yeah. Yeah. I remember why we made the dye compound molecules.

Q. Why we what?

A. Why we made the dye -- so this is a dye patent.

Q. Right.

A. That's what this is.

Q. Right.

A. So I remember all about that.

Q. So when you say the '116 is a dye patent, you weren't attempting to innovate in the area of modifications at the 3' location; is that right?

DR. STEVEN MENCHEN, Ph.D.

A. Actually that -- that's true, we weren't trying to do that.

Q. The list of candidates for 3' modifications in -- for sequencing in the '116 patent, was it the state of the art at the time in 1998, that wasn't something that you were innovating?

MR. SCHWARTZ: Objection to form.

A. I don't think it was the state of the art. But it wasn't something we were trying to innovate.

Q. When you described what analogs are, your definition of them in column 5 of your '116 patent, that was describing the state of the art for analog chemistry at that time period; is that correct?

A. Where is the analog again? Analogs. So could you repeat the question about analogs?

Q. Okay.

DR. STEVEN MENCHEN, Ph.D.

A. Sorry.

Q. No problem. Your '116 patent was directed to new fluorescent dyes for sequencing, correct?

A. That's right.

Q. And you included a set of definitions in here of what those dyes could work with, such as nucleosides and nucleotides; is that correct?

A. That's right.

Q. And your definition of what analogs are in the context of nucleotides for purposes of your patent was describing what the state of the art was in 1998; is that correct?

MR. SCHWARTZ: Objection, form.

A. Yeah.

Q. It wasn't -- you weren't adding new science to it?

A. I don't think we were

DR. STEVEN MENCHEN, Ph.D.

trying to.

Q. You were trying to capture what the state of the art was; is that correct?

MR. SCHWARTZ: Objection.

A. I -- I -- I don't know that this was state of the art. I don't remember, you know, what -- exactly where this came from.

Q. Do you have any reason to believe that your list of candidate modifications at the 3' position for sequencing in your 1998 patent application was anything but state of the art?

MR. SCHWARTZ: Objection, form.

A. Could you --

Q. Do you have any reason to believe that your list of candidate modifications at the 3' location for sequencing in your '116 patent was anything but a description of what the state of the art was for that?

DR. STEVEN MENCHEN, Ph.D.

A. I don't think I can answer that. I don't know.

Q. Turning back to the '985 patent, do you have that, Exhibit 1075?

A. Yes.

Q. Now, let's start back at page 25, which is that Figure 7 that you looked at before. Do you have that?

A. Page 25. I have that.

Q. And there the reference, do you see the reference to allyl?

A. Down at the bottom?

Q. Yes.

A. Yeah, I see that.

Q. Do you see the specific chemical formula for the allyl that's described there?

A. I do see that.

Q. And is it your belief that allyl there refers to that specific structure or is it a reference to a genus to you?

DR. STEVEN MENCHEN, Ph.D.

A. Allyl is a reference to a genus and then he refines it down to propenyl in the structure.

Q. Let me just confirm. Do you have any rea- -- do you have any understanding why he would refer to the genus in brackets but then the chemical formula would be specific --

MR. SCHWARTZ: Objection to form.

Q. -- if it's really referring to a genus?

A. You know, it's his convention to do that.

Q. All right. If you could turn to -- and you have nothing else beyond that, just convention? Do you have any other basis? That's it?

A. That's right, yeah.

Q. I'm sorry, you need to say that for the record.

A. I'm sorry, yeah.

DR. STEVEN MENCHEN, Ph.D.

Q. Thanks. Turn to column 3, please. And I'd like you to start at line --

A. Wait, there's a lot of figures here.

Q. Sorry.

A. Column 3. I'm there.

Q. You see the reference to MOM on line 41?

A. Yeah, I do.

Q. And it refers to MOM groups can be used to cap. Do you see that?

A. That's right.

Q. When it says MOM groups is that a specific group or is that a genus?

A. I don't know. I don't know about MOM.

Q. Would a person of ordinary skill in the art read the reference to MOM groups understand that to be referring to one chemical structure or a genus?

DR. STEVEN MENCHEN, Ph.D.
MR. SCHWARTZ: Objection to scope.
A. So MOM stands for methoxy methyl. So that would be a single -- that would be like naming the compound.
Q. And then you see the reference to allyl groups right next to it?
A. I see it.
Q. And is allyl groups referring to a single chemical structure or genus, according to you?
MR. SCHWARTZ: Asked and answered.
A. Refers to a genus.
Q. And here Ju refers to the Kamal paper, correct?
MR. SCHWARTZ: Objection, form.
Q. This should be an easy one.
A. It is known -- yes, he does refer to the Kamal paper.

DR. STEVEN MENCHEN, Ph.D.

Q. The Ireland publication supports the disclosure of MOM as a capping group and the Kamal paper supports the disclosure of allyl as a capping group; is that correct?

A. So it is known that MOM and allyl groups can be used to cap an OH group. So -- and high yield. So could you repeat the question. I just want to make sure that I get this right.

Q. The Ireland publication supports the disclosure of MOM as a high-yield capping group?

A. That's right.

Q. And Kamal supports the disclosure of allyl as a high-yield capping group?

MR. SCHWARTZ: Objection, form.

A. It supports propenyl, yes, Kamal does.

Q. When you say propenyl, I'm referring to the sentence, I'm not

DR. STEVEN MENCHEN, Ph.D.

referring to other made up lexicons.

A. I -- I'd have to look at Kamal.

Q. I'm not asking what Kamal actually does, but in terms of how this disclosure discloses things, Ireland supports the disclosure of MOM as a high-yield capping group and Kamal teaches the disclosure of allyl as the capping group; is that correct?

A. So that's --

MR. SCHWARTZ: Objection, form.

Let me get my objections in before you answer, please.

THE WITNESS: I'm sorry.

Q. That's correct, right?

A. That's how they segregate, yeah.

Q. Now, in terms of the teaching in column 3 of Ju, this is describing the state of the art before the invention, correct?

DR. STEVEN MENCHEN, Ph.D.
MR. SCHWARTZ: Objection, form.
A. So Ju uses the present tense, it is known. So that's -- you are going to have to give me a context for that.
Q. Do you see in column 4 there's a reference to the summary of the invention?
A. Yeah. I do see that.
Q. Okay. And you see in column 1 it refers to the background of the invention?
A. Yeah, I see that.
Q. And from your hundred patents you are familiar with that structure of patent application, of a description of the background of the invention?
A. That's right.
Q. And then the summary of the invention?
A. That's right.
Q. And the material in column

DR. STEVEN MENCHEN, Ph.D.

3 between line 20 and -- or 18 and 54, is that describing the state of the art, correct, and not the invention of Ju?

MR. SCHWARTZ: Objection, form.

A. So you are talking 41 to 44 is describing the state of the art. So it's describing the state of the art for an NOH group that a synthetic chemist would do, not necessarily a nucleotide. So it's basically -- so it describes NOH group that is disclosed in Kamal.

Q. Let me just ask the question again. The paragraph starting in column 3 at line 17 through line 54, do you have that -- do you see that paragraph?

A. Yeah, I see it.

Q. Okay. This paragraph is describing a state of the art before Ju's work not Ju's invention, correct?

DR. STEVEN MENCHEN, Ph.D.
MR. SCHWARTZ: Asked and answered.
A. I would say it describes more than just the state of the art.
Q. In this background of the invention section in this paragraph?
A. Let me -- I -- I have to read the whole paragraph. Is that okay?
Q. Yeah. No, please do. I didn't mean to interrupt you.
A. So this is -- I would say this is Ju's view of the state of the art.
Q. Okay. He's not attempting in column 3, lines 18 through 54, to describe his invention there, right, that comes later?
A. I think he is attempting to describe his invention.
Q. In this background of the invention section?
A. Yeah.
Q. Okay. And where do you see

DR. STEVEN MENCHEN, Ph.D.

that?

A. The approach disclosed in the present application is to incorporate nucleotide analogs, which are labeled with cleavable, unique labels such at fluorescent dyes or mass tags and where the 3'-OH is capped with a chemically cleavable moiety such as either MOM, CH2OCH3 and allyl specifically, CH2CH CH2 into the growing chain strand of DNA as terminators.

Q. You acknowledge the prior sentence starting "It is known that," that is describing the state of the prior art and not his invention?

A. Let me go back.

That's the state of the art.

Q. And when he states what he thinks the invention is and -- excuse me. When he states it says the approach disclosed in the present application, do you see that

DR. STEVEN MENCHEN, Ph.D.

sentence?

A. I see that.

Q. When he refers to using a chemical moiety such as an allyl group, do you see that?

A. Yeah, I see that.

Q. Okay. Is that referring to allyl the genus or a specific -- or just the specific chemical formula that's disclosed there?

A. Yeah. He's -- he's defining it as propenyl.

Q. In terms of Ju's disclosure of the invention, other than the MOM group or the propenyl, is there anything else that he discloses as usable for the 3' modification to a person of ordinary skill in the art?

A. Yeah, I don't see anything else.

MR. SCHWARTZ: Objection, scope.

Q. Would a person of ordinary skill in the art reading the Ju

DR. STEVEN MENCHEN, Ph.D.

patent and seeing the disclosure of the MOM group and the allyl disclosure understand that there's any commonality between those two chemical structures?

MR. SCHWARTZ: Objection, form.

A. The commonality that Ju describes is that they -- that they can be used to cap the OH group.

Q. Anything else?

A. And that they can be cleaved chemically in high yield as disclosed in the Kamal reference.

Q. Anything else?

A. That's what he says.

Q. Can you identify anything else?

A. No.

Q. Okay.

A. Actually, I can identify something else.

Q. What else?

A. They both have three atoms

DR. STEVEN MENCHEN, Ph.D.

without the hydrogens.

Q. Without what?

A. Without the hydrogens. They both have three atoms.

Q. Anything else?

A. No.

Q. Referencing column 26, please.

And the paragraph at line 12 through 30. 29, 12 through 29, do you have that in front of you?

A. I see that.

Q. And this is describing how one would synthesize the analogs; is that correct?

A. We are on column 26?

Q. Yeah.

A. And line 12?

Q. Actually, let me -- yes. Of Exhibit 1075.

A. So this is written in the present tense so it is Ju's statement on how to make these.

Q. In column 26 at line 12

DR. STEVEN MENCHEN, Ph.D.

through 29, that paragraph, that describes how to synthesize the nucleotide analogs; is that correct?

A. This -- like I said, this is written in the present tense so this is Ju's view of how to synthesize the analogs.

Q. Synthesize, right. And he states that the MOM group and the allyl group can be -- can be synthesized using well established synthetic procedures.

Do you see that?

A. Where does it say that?

Q. I see that at line 20.

A. Line 20. MOM group. So, this -- again, this is written in the present tense so it's his view. It's his statement and then he uses his backup, Fuji and Metzker as backup information.

Q. Ju is disclosing here that the synthetic procedures for developing the analogs are well

DR. STEVEN MENCHEN, Ph.D.
established, correct?
MR. SCHWARTZ: Objection to form.
A. I don't think he says that.
Q. Do you see the words "well established" on line 20.
A. Line 20.
Q. I don't know if we are looking at the same thing. You are at the '985 patent?
A. That's right. That's right.
Q. Column 26?
A. So.
Q. Line 20.
A. So the procedure is well established, referring to Metzker, but...
Q. Okay. And so Ju directs you to Metzker as illustrating that this synthetic procedure for allyl is well established in the art?
A. That they can be made, yeah.

DR. STEVEN MENCHEN, Ph.D.
MR. SCHWARTZ: Objection to form.
Q. Do you agree with Ju that as of 1999 the synthesis of allyl groups as a capping group for the 3' location was well established?
MR. SCHWARTZ: Objection, scope.
A. Yeah, what do you mean by well established?
Q. Do you understand what Ju means by well established in line 20 of column 26? Simple question, do you understand it?
A. Yeah. He's saying it's well established. But do I agree with it?
Q. Let's just start simply. You questioned what that word means so let me follow up on that. Ju uses the term "well established."
Do you see in that column 20 -- column 26, line 20?
A. I see that.

DR. STEVEN MENCHEN, Ph.D.

Q. Do you understand what he means by that?

A. Not necessarily.

Q. So when Ju states that it's well established to synthesize allyl as a capping group at the 3' location, in that context you don't understand what he means -- well, he means, intends, by well established; is that correct?

A. That's correct.

Q. With respect to Metzker in 1994, does Metzker disclose a synthetic procedure for allyl as a capping group at the 3' location?

MR. SCHWARTZ: Outside -- objection, scope.

A. He only makes one compound. That's the 1994.

Q. Does Metzker in 1994 -- let me ask the question. That's the one at a time thing.

Does Metzker 1994 disclose a synthetic procedure for synthesizing

DR. STEVEN MENCHEN, Ph.D.

an allyl group as a cap at the 3' location in -- for sequencing?

A. He discloses it for making one analog, A. He doesn't disclose it for the other three analogs.

Q. Which analog?

A. The A.

Q. Do you agree with Ju that as of 2000 it was well established how to synthesize allyl groups to cap to 3' location for sequencing by synthesis?

MR. SCHWARTZ: Objection, form. Objection, outside the scope.

A. So I don't know what -- I wasn't there when Ju wrote this so I don't know what he means by well established. So I can't tell you whether I agree or disagree with this.

Q. Based on your technical expertise, someone presenting themselves as an expert to the PTAB

DR. STEVEN MENCHEN, Ph.D.

board, do you believe it was well established how to synthesize an allyl group to use it as a capping group at the 3' location for sequencing by synthesis in 2000?

MR. SCHWARTZ: Objection, scope.

A. It was established by Metzker to make the A. That's the only thing that I know about in the -- in the prior art.

Q. So you are limiting it to the one chemical A, right, that's the limitation that you are putting on it?

A. That's the one that was presented.

Q. In terms of using a MOM group as a cap on a 3' location, was that well established in synthetic chemistry by the year 2000 for sequencing by synthesis?

A. To put the MOM group on 3' hydroxyl --

DR. STEVEN MENCHEN, Ph.D.

Q. Yep.

A. -- with a nucleotide?

MR. SCHWARTZ: Objection, scope.

Q. Yeah.

A. I don't know.

Q. You have no idea at all?

A. I wasn't asked to look into that as part of this deposition.

Q. And therefore you have no idea?

A. I wasn't asked to look into it.

Q. Right. And now I'm asking you the question. So whether you were asked to look at it or not, do you have any idea whether it was known to use MOM as the capping group at the 3' location?

A. I don't know.

Q. Ju states in his application that the MOM or allyl group is used to cap the 3' group using well established synthetic

DR. STEVEN MENCHEN, Ph.D.

procedures. Do you have any reason to believe that they were not well established at that time?

MR. SCHWARTZ: Objection, scope.

A. Yeah. I wasn't asked to evaluate that.

Q. Do you have an opinion one way or the other on that?

A. No, I don't.

Q. A person of ordinary skill in the art in the year 2000 would have known as a matter of a preexisting state of the art that a MOM group or allyl group could be removed chemically with high yield from the 3' location; is that correct?

MR. SCHWARTZ: Objection, scope.

A. And what's the context?

Q. Sequencing by synthesis.

A. Sequencing by synthesis. I would say that's not in the state of

DR. STEVEN MENCHEN, Ph.D.

the art.

Q. Kamal discloses that the chemical cleavage of the allyl group is fairly mild and specific so it doesn't degrade the DNA template moiety, right?

A. Are -- are you reading that?

Q. This is what Ju says, but I want your independent acknowledgment if that's true or not.

A. So where does he say it?

Q. He states it at lines 24 through 29.

MR. SCHWARTZ: Objection. Mischaracterizes. Objection, form.

A. So the statement says the chemical cleavage of the MOM and allyl groups is fairly mild and specific so as not to degrade the DNA template and moiety.

So this -- again, this is written in the present tense.

Q. Yeah. Whatever tense it's

DR. STEVEN MENCHEN, Ph.D.

written in.

A. Well, this is Ju's statement and not prior art.

Q. Do you see where it says, for example, the cleavage of the allyl group takes three minutes with more than 93 percent yield? Is that -- is it -- are you taking the position that that's a statement of what Ju did or is that his characterization of Kamal or can't you tell?

MR. SCHWARTZ: Objection, form.

Q. Let me ask -- let me do it this way. Was it part of your assignment to determine whether the sentence the cleavage of the allyl group takes three minutes with more than a 93 percent yield, whether that's characterization of Kamal or whether that's Ju's own work?

MR. SCHWARTZ: Objection, form, and to the extent that in

DR. STEVEN MENCHEN, Ph.D.

order to answer that you have to reveal conversations you had with your lawyer, I instruct you not to answer that question.

A. Actually, I don't even remember the question.

Q. Do you see where Ju states that the cleavage of the allyl group takes three minutes with more than a 93 percent yield?

A. I see that.

Q. Okay. And that's a high yield; is that correct?

MR. SCHWARTZ: Objection, form.

A. 93 percent is a pretty good yield.

Q. Would you call it a high yield?

A. If you was -- if you were doing synthetic chemistry, compound A to compound B, I would call that a high yield. If it was SBS, I wouldn't call it a high yield.

DR. STEVEN MENCHEN, Ph.D.

Q. What's a high yield in SBS according to you?

A. Well, quantitative.

Q. And what is that numerically?

A. 100 percent.

Q. And when it says in the Ju patent the cleavage of the allyl group takes three minutes with more than 93 percent yield, is that describing the yield in the context of sequencing by synthesis?

A. No, it's not. We'd have to look at Kamal. He refers to Kamal.

Q. When Ju says the cleavage of the allyl group takes three minutes with more than 93 percent yield, he's characterizing Kamal there or is that his own work?

A. I think I need to look at Kamal to verify that.

Q. I'm showing you Exhibit 1037, which is the Kamal

DR. STEVEN MENCHEN, Ph.D.

reference.

A. So there's only one compound in Kamal that shows this yield. But Ju doesn't refer to any compound in Kamal. He just refers to Kamal. So I can't tell what -- if this is his work or Kamal's work.

Q. And with respect to the MOM group, Ju reports the MOM group is reported to be cleaved with close to a hundred percent yield.

Do you see that?

A. I see that.

Q. Is that quantitative?

A. 100 percent?

Q. It says close to 100 percent.

A. 100 percent would be quantitative.

Q. Is close to 100 percent quantitative?

A. It depends on how close to 100 percent it is.

Q. And what would be your

DR. STEVEN MENCHEN, Ph.D.

metric?

A. My metric would be anything over 99 percent would be close to 100 percent.

Q. Can you turn to page 33, please.

A. Okay.

Q. And you see the figure there, it's Figure 14?

A. I see it.

Q. Is it your understanding from the Ju patent that this is the disclosure of Ju's work or Ju's actual synthesis or is it theoretical or is it prior art?

MR. SCHWARTZ: Objection, form.

A. So this, could we go back to the summary of Figure 14, the description of the figures?

So could you repeat the question?

Q. Yes. Is -- do you know whether Ju ever performed the

DR. STEVEN MENCHEN, Ph.D.

reactions described in Figure 14?

A. I don't know if he performed it.

Q. Do you know whether Figure 14 is a characterization of prior art?

A. It's not prior art.

Q. Do you know whether Ju performed any experiments with an allyl group before submitting this -- his patent applications?

A. I wasn't asked to -- that wasn't part of my task, to determine that.

Q. Based on your review of the Ju patents have you seen any evidence that he performed actual experiments with allyl groups?

A. I would have to reread the patent to determine that.

Q. Sitting here now based on all the work that you've done to prepare for today you are not aware of any?

DR. STEVEN MENCHEN, Ph.D.

A. I would have to reread the patent to determine that.

Q. Sitting here now are you aware of any evidence that Ju actually performed the experiments with allyl?

A. I don't have any evidence, positive or negative, to that.

Q. And you spent eight or nine days preparing for the deposition; is that correct?

A. I read through a lot of papers and patents.

Q. And one of the most important documents for you to review was the Ju patent, correct?

A. That was one of the important documents.

Q. And sitting here now you can't recall ever seeing any evidence that Ju actually performed experiments with allyl; is that correct?

A. That's not what I said.

DR. STEVEN MENCHEN, Ph.D.

MR. SCHWARTZ: Mischaracterizes. Just let me get my objections in, please.

Q. Sitting here now can you recall ever seeing any evidence that Ju actually performed experiments with allyl?

A. I can't say positive or negative to that.

Q. Sitting here now, can you state -- have you seen any evidence in all the work that you've done that Ju performed experiments with MOM?

A. It's summarized in Figure 14. I don't know -- yeah. I don't know, you know, whether he did or he didn't. That's not -- I certainly, looking at for MOM was not one of the things I was supposed to look for when I was reviewing these patents.

Q. But with respect to the allyl group and MOM you don't know

DR. STEVEN MENCHEN, Ph.D.

whether Ju actually performed experiments, correct, sitting here today?

A. That wasn't something that I was supposed to study.

Q. And you just don't know for that reason; is that right?

A. That's right, I don't know.

Q. Turning back to paragraph -- column 26, please. Do you see at line 22 it says, "These groups can be removed chemically with high yield as shown in Figure 14," and then it cites Ireland and Kamal?

A. I see that.

Q. Do you know why there's the citations to Ireland and Kamal right next to Figure 14?

A. Yeah. It's historical evidence, you know, that -- using, you know, synthetic organic chemist was able to deprotect alcohols.

Q. At high yield?

DR. STEVEN MENCHEN, Ph.D.

A. I would have to look at Ireland and Kamal. So high yield depends on the context of what Ireland and Kamal were doing.

Q. Would a person of ordinary skill in the art reading Ju's disclosure in paragraph -- in column 26 of the synthetic procedures for allyl understand that it might be well established for some of the -- for example, for A but not for T, C or G?

MR. SCHWARTZ: Objection, scope.

A. So what's the context of that?

Q. The sentence at line 20.

A. The sentence at line 20. And what was the question again?

Q. Do you see up at line 15 where Ju says the 3' can be capped in all four nucleotide analogs?

A. So it says the 3'-OH is capped in all -- in all three

DR. STEVEN MENCHEN, Ph.D.

analogs, which is a statement in the spec and not -- doesn't refer to prior art.

Q. And then he states that using allyl to cap that group can be done with using well established synthetic procedures.

Do you see that?

A. I see that.

Q. Does Ju describe any synthetic procedures for synthesizing all four nucleotide analogs with an allyl group?

MR. SCHWARTZ: Objection, scope.

A. Yeah. Again, I wasn't asked to determine that synthesis. I was only asked to determine the cleavage.

Q. Do you know?

A. It's not something that I have looked for in the patent.

Q. Would a person of ordinary skill in the art in 2000 know how to

DR. STEVEN MENCHEN, Ph.D.

synthesize all four nucleotide analogs with an allyl group?

MR. SCHWARTZ: Objection, scope.

Q. Based on -- based -- just based on their basic competency.

A. I -- I don't know. It wasn't something that I was asked to do.

Q. Do you have any idea at all?

A. I know that one was made.

Q. Do you have any idea as to whether a person of ordinary skill in the art just based on their own basic competency would know how to synthesize all four nucleotide analogs with an allyl group at the 3' position?

A. I wasn't asked to review that.

Q. Do you have any idea at all?

A. There's a lot of things

DR. STEVEN MENCHEN, Ph.D.

that you have to do to convert a nucleotide or a nucleoside into a cap nucleoside. So yeah, without reading the literature I'd rather not -- I'd rather not speculate.

Q. In terms of what the state of synthetic chemistry is with allyl groups in the 2000 time period that would be speculation for you because that's not something you looked into; is that correct?

MR. SCHWARTZ: Outside scope, objection.

A. Could you give that context, that statement context?

Q. Yes. In the 2000 time period would it be speculation for you to state what the state of the art is for synthetic chemistry with allyl groups in the context of sequencing?

MR. SCHWARTZ: Objection, form. Objection, scope.

Q. Because you haven't looked

DR. STEVEN MENCHEN, Ph.D.

at it.

A. I haven't studied those.

Q. So that would be speculation?

A. That would be speculation.

MR. REINES: Well, now might be a good time to take lunch if everybody agrees. Does that make sense? All right. Thank you very much.

THE VIDEOGRAPHER: The time on the video monitor is 12:17 p.m. We off the record.

(Luncheon recess taken at 12:17 p.m.)

DR. STEVEN MENCHEN, Ph.D.
AFTERNOON SESSION
(Time noted: 12:59 p.m.)
STEVEN M. MENCHEN,
resumed and testified as follows:
THE VIDEOGRAPHER: We are back on the record. The time on the video monitor is 12:59 p.m. This is start of media four.
EXAMINATION BY (Cont'd.)
MR. REINES:
Q. Please turn to column 21 -- actually column 20 of the '985 patent. You see at the bottom it says the sequencing by synthesis approach?
A. Yes, I see it.
Q. And then the sentence after that says, "Sequencing DNA by synthesis involves the detection of the identity of each nucleotide as it is incorporated into the growing strand of DNA in the polymerase reaction."
Do you see that?

DR. STEVEN MENCHEN, Ph.D.

A. I see that.

Q. And the next sentence says, "The fundamental requirements for such a system to work are," and then it lists four requirements.

Do you see that?

A. One, okay. Yeah. Yeah, I see that. I have read it I mean.

Q. Are the fundamental requirements for SBS listed by Ju, is that your understanding as to what the fundamental requirements were in the 2000 time period?

A. There's, yeah, one missing requirement that I know about.

Q. What's the missing requirement?

A. There has to be aqueous.

Q. Anything else missing?

A. Let me just make sure, please.

The other missing requirement is that the -- wait. Yeah, the other missing requirement is that

DR. STEVEN MENCHEN, Ph.D.

the capping group needs to be removed rapidly.

Q. Anything else?

A. Well, if you substitute high yield for quantitative, but I don't want to, you know. So Tsien teaches quantitative but I assume that high yield will satisfy that.

Q. Anything else?

A. No, that's good.

Q. Do you have any explanation for why Ju omitted the fundamental requirement of an aqueous solution in the capping group being removed rapidly as you described?

MR. SCHWARTZ: Objection. Outside scope.

A. Yeah, I -- I don't know.

Q. Are the fundamental requirements for working sequencing by synthesis system, would those have been known from the prior part to a person of ordinary skill in the art in 2000 before reading the Ju

DR. STEVEN MENCHEN, Ph.D.

patent?

A. Can I read my declaration?

Q. Sure. It's in front of you. Read whatever you --

A. Just take that time, yeah.

Q. -- need to read to answer most accurately.

A. So the only other thing that's taught in the prior art is that it needs to be -- the cleavage of the capping group needs to be mild. That's not really mentioned here.

Q. Would a person of ordinary skill in the art before reading the Ju patent as a matter of level skilled in the art know of the four requirements for a working sequencing by synthesis system as described in column 21, line 1 through 13?

A. Do you mean would they think that those are the only four requirements?

DR. STEVEN MENCHEN, Ph.D.

Q. No. Would they know of these requirements?

A. I think they would.

Q. In terms of high yield versus quantitative is there any difference there that you see?

MR. SCHWARTZ: Objection, form.

Q. That's meaningful.

A. Well, quantitative means a hundred percent. High yield is defined by Tsien as being higher than 98 percent. So higher than 98 percent is close to quantitative.

Q. Do you see any meaningful difference between high yield and quantitative?

A. Well, it depends on how he defines high yield, which he doesn't do.

Q. Ju doesn't define high yield?

A. Not in this paragraph.

Q. Does Ju ever define high

DR. STEVEN MENCHEN, Ph.D.

yield?

A. Not that I can remember. That's not something that I checked on in the -- in the patent.

Q. If you turn down to column 21 at line 65, please.

A. I see that.

Q. And there's a list of different enzymes. Do you see that?

A. I see that.

Q. Do you know which ones would work with an allyl group?

MR. SCHWARTZ: Objection, scope.

A. I wasn't asked to evaluate polymerases and their activities as one of my tasks.

Q. Are you an enzymologist?

A. No, I'm not.

Q. Do you know which polymerases would work with allyl just based on your technical expertise in the field?

MR. SCHWARTZ: Objection,

DR. STEVEN MENCHEN, Ph.D.

scope.

A. Yeah. I'm not -- I don't have the background to -- to say that or determine that.

Q. Do you have any idea which enzymes would work with MOM?

MR. SCHWARTZ: Same objection.

A. I -- I have no idea.

Q. Would a person of ordinary skill in the art reading the Ju disclosure know which enzymes would work with allyl group with a reasonable degree of work?

MR. SCHWARTZ: Objection, form. Objection, scope.

A. I can't really comment on that. That wasn't something that I read up on to prepare for this deposition.

Q. Do you have any idea what a person of ordinary skill in the art would know about polymerases in relation to capping groups in the 2000 time period?

DR. STEVEN MENCHEN, Ph.D.
MR. SCHWARTZ: Objection, form. Objection, scope.
A. Yeah. I can't really comment on that.
Q. Why not?
A. Because it's not something that I studied during -- preparing for this deposition.
Q. And do you know based on your own technical expertise? Are you familiar with that subject from your own technical expertise?
A. Polymerases that incorporate allyl groups?
Q. For example.
A. I -- I know of none that incorporate them officially.
Q. Did you -- as part of your assignment in this project did you need to understand the scope of Claim 1 of the '985 patent?
MR. SCHWARTZ: Objection, form.
A. So I don't know what you

DR. STEVEN MENCHEN, Ph.D.

mean by scope.

Q. You don't know what I mean by scope?

A. Yeah. Could you rephrase that?

Q. Was it part of your work in this case to have a good understanding of what Claim 1 covered and what it didn't cover?

A. That was part of my assignment.

Q. And does Claim 1 cover the use of an allyl group as a capping group for the 3' location?

A. Which allyl group?

Q. The one described in the Ju patent.

MR. SCHWARTZ: Objection, scope.

Q. Just if you know.

MR. SCHWARTZ: Objection, requires legal conclusion.

A. Yeah, I don't think I can answer that.

DR. STEVEN MENCHEN, Ph.D.

Q. Why not?

A. Let me --

MR. SCHWARTZ: Same objections.

A. Because --

Q. Let me take a step back.

A. Because that's a legal evaluation and I'm a technical expert.

Q. Do you know of any capping group at the 3' location that would meet the requirements of Claim 1?

MR. SCHWARTZ: Objection, scope.

A. In what time frame?

Q. That you know of now, sitting here now. Well, what did you mean by at which time frame?

A. I mean is this before 2000, is that what you are asking?

Q. I mean it could be at any time. I mean it's just -- it's a scientific fact, right?

Let me ask you, can you

DR. STEVEN MENCHEN, Ph.D.
identify any capping group that you think would meet the requirements of Claim 1?
MR. SCHWARTZ: Objection, scope.
Q. Of the '985 patent.
A. I mean in -- in what time frame?
Q. Any time frame.
A. Any time frame. Well, I mean Ju has a publication that describes the use of these compounds. I don't know, 2006, whenever. I'm not familiar exactly with those.
Q. Can you identify with a reasonable degree of confidence any capping group that meets the requirements of Claim 1 of the Ju patent?
MR. SCHWARTZ: Objection, scope. Objection, form. Objection, legal conclusion.
A. Yeah. I really don't

DR. STEVEN MENCHEN, Ph.D.

understand the context of the question.

Q. The context is just what I'm asking you. I mean it's not really -- the context is Claim 1.

A. And if it -- if it re- -- requires a legal conclusion I can't -- I can't find opinion on that.

Q. In your role as a technical expert can you identify any capping group that meets the requirements of Claim 1 of the '985 patent?

MR. SCHWARTZ: Same objections.

A. I can refer to what Ju has published since 2000.

Q. Okay. And can you -- can you identify, leaving aside referring to other things, can you identify any chemical compound?

A. The -- the compound, the capping group that's in the Ju publication.

DR. STEVEN MENCHEN, Ph.D.

Q. Anything else?

MR. SCHWARTZ: Objection, scope.

A. Yeah. Anything else --

Q. Yes.

A. -- in what -- in what terms?

Q. The question I'm asking you is can you identify any capping group that meets the requirements of Claim 1 of the '985 patent? So far you've identified one from Ju's 2006 publication; is that correct?

Let me say. Do you have a reasonable degree of confidence that you know whether the Ju capping group disclosed in his literature after 2000 actually meets the requirements of Claim 1 of the '985 patent?

MR. SCHWARTZ: Objection, scope. Objection, legal conclusion.

A. Yeah, I -- I don't have an

DR. STEVEN MENCHEN, Ph.D.

opinion on that.

Q. Do you have any opinion as to whether there's any compound that meets the requirements of the capping group of Claim 1 of the '985 patent?

MR. SCHWARTZ: Same objections and asked and answered.

A. Yeah, I can't comment on that. That's -- if it's -- you know, if that's a legal conclusion.

Q. In your role as a technical expert are you aware of any?

A. Any what?

Q. Any -- any compound that meets the requirements of the capping group of the '985 patent in Claim 1.

MR. SCHWARTZ: Same objections.

A. Within the context of the prior art for cleavage?

Q. No, just in general.

A. Well, in general --

DR. STEVEN MENCHEN, Ph.D.
MR. SCHWARTZ: Same objection.
Q. What's that?
A. What do you mean by in general?
Q. All right. I'll withdraw the question.
I'd like to show you what's been marked as 1001, which is the '852 patent, and if you'd open up to Claim 1, please.
A. I'm sorry, can you repeat that? Open up to what?
Q. Claim 1.
A. Claim 1, okay.
Q. It's at column 34. Do you have a -- do you understand what Claim 1 covers of the '852 patent?
A. Yes.
Q. Can you identify any capping group that meets the requirements of Claim 1 of the '852 patent?
MR. SCHWARTZ: Same objections. Legal conclusion.

DR. STEVEN MENCHEN, Ph.D.

Scope.

A. So this is prior to 2000?

Q. At any time.

MR. SCHWARTZ: Same objections.

A. I mean I guess I have the same answers for this as I had with the last one.

Q. And that's that you don't know sitting here now; is that correct?

A. That I don't want to provide an opinion.

Q. And that's because you don't have an answer with a reasonable basis, right?

A. That's right.

Q. And that -- and if I went through each of the four other -- the three other patents that you analyzed, you would have the same answer; is that correct?

A. Yeah. I mean the claims are pretty much the same.

DR. STEVEN MENCHEN, Ph.D.
MR. SCHWARTZ: And I'll just make a note for the record that we are going to object to any new exhibits that are put in front Dr. Menchen that are not part of his report or Dr. Romesberg's reports.
MR. REINES: What's the basis?
MR. SCHWARTZ: It's outside the scope of his patent -- of his declaration.
MR. REINES: Marked as Exhibit 1092 is one of your rhodamine patents. It's the '884 patent.
(Exhibit 1092, '884 patent, marked for identification, as of this date.)
Q. And just to be clear, the patent of yours we went through before you actually prepared for the deposition by looking at that document; is that correct?
A. The patent before?

DR. STEVEN MENCHEN, Ph.D.

Q. Yeah.

A. So --

MR. SCHWARTZ: Before you answer that question, I want to make sure that if the only way you can answer that question is to divulge information that was provided you by your attorneys, I instruct you not to answer.

Q. In preparing for your deposition one of the documents you considered was your dye patent, the '116 patent, correct?

A. Is that on the list of exhibits?

Q. No.

A. So --

Q. It is not. I'm not talking about for your dep. Maybe I need to disconnect. I'm not talking about for your declaration. To prepare for the deposition one of the documents you considered was your dye patent, the '116 patent,

DR. STEVEN MENCHEN, Ph.D.

correct?

A. Yeah, that's privileged information.

Q. I don't think that's privileged. I don't think your counsel interposed an objection.

A. Okay.

Q. Okay. So the answer is yes, isn't it?

A. Yes.

Q. Okay. If you turn to, and this is work that you did with Joe Lam and Scott Benson. This time Joe Lam is the first named inventor.

A. That's correct.

Q. Is this related work to the '116 patent work, your '884 patent?

MR. SCHWARTZ: Objection to form.

A. It is not related.

Q. Let me just go through the same set of questions. Even though the '884 patent, according to you, is not related to the '116 patent it

DR. STEVEN MENCHEN, Ph.D.

is about dyes for use in sequencing chemistry?

A. It's for Sanger sequencing.

Q. Right. The dyes that are proposed in the '884 patent are for use in Sanger sequencing; is that correct?

A. That's correct.

Q. Okay. And let's look at the definitions section. And I'll get you there. First I need to get myself there.

A. I'm there.

Q. You are quicker than me on it. Do you see in column 10 the reference to analogs is the definition? Do you see the paragraph regarding analogs at column 10 at line 16?

A. I see that.

Q. Okay. And there, again, one of the candidates that you identify for 2' to 3' position is allyloxy that's at line 43, maybe

DR. STEVEN MENCHEN, Ph.D.

44?

A. Yeah, I see that.

Q. So -- and this is an application you filed in 1999 so you were still proposing allyloxy as a -- as a candidate for modification at the 3' position in sequencing chemistry, correct?

MR. SCHWARTZ: Objection.

A. For Sanger sequencing, also.

Q. And if you go to your definition of terminators in column 11. Do you see that?

A. I see that.

Q. And at line 24, 25 you refer to the Metzker 1994 article?

A. I see that.

Q. And as you testified earlier, you were familiar with the Metzker article in the 1990s time period?

A. Yes, I was.

Q. And your purpose for citing

DR. STEVEN MENCHEN, Ph.D.

Metzker was to demonstrate that reversible terminators, nucleotide terminators were known in the art; is that correct?

MR. SCHWARTZ: Objection, form.

A. I don't know why we cited this.

Q. Do you see where it says nucleoside terminators also include reversible nucleoside -- excuse me. Do you see where it says nucleotide terminators also include reversible nucleotide terminators?

A. I see that.

Q. And then you cited to Metzker for that proposition?

A. Yeah, we did. Yeah.

Q. And you are not -- you agree that in 1999 people skilled in the art knew that terminators include reversible terminators?

A. Not Sanger -- not for Sanger sequencing.

DR. STEVEN MENCHEN, Ph.D.

Q. People didn't know that?

A. Didn't know what?

Q. What you just agreed to.

A. What --

Q. I'll start again.

A. Okay.

Q. Did people in the field of Sanger, in the I guess subfield, but did people working with Sanger sequencing know that terminators could include reversible terminators?

A. We state that.

Q. Were you stating that as part of your invention or were you stating that as characterizing the art?

A. I don't remember why we stated it.

Q. Do you believe that you and Joe Lam and Scott Benson were -- were the first to recognize that nucleotide terminators could include reversible nucleotide terminators?

DR. STEVEN MENCHEN, Ph.D.

A. I don't know. I have no comment on that.

Q. So maybe you were the first to think of that?

A. I don't know.

Q. Did you invent the concept of using reversible terminators for Sanger sequencing?

MR. SCHWARTZ: Objection. Requires legal conclusion.

A. I -- I can't answer that.

Q. Why not?

A. Because it requires a legal analysis.

Q. Every time you signed an oath of inventorship for your hundred patents did you consider that to be a legal conclusion when you signed that?

A. What do you -- I don't understand.

Q. Yes. Amongst your hundred patents you signed documents stating that you believed you invented what

DR. STEVEN MENCHEN, Ph.D.

was disclosed in the application, right?

A. I suppose I did, yeah.

Q. And when you submitted patent applications at the time that you signed your oath of inventorship did you have an understanding of what it was that you thought you invented?

A. Yes.

Q. Are you capable of understanding what you think you invented?

A. So this was submitted in 1999. And I can't remember if we were -- thought we had invented something or we were citing prior art.

Q. Okay. So --

A. I can't make that judgment.

Q. So it's a matter of just absence of memory, right, that's why you don't know?

A. That's right.

DR. STEVEN MENCHEN, Ph.D.

Q. If you had invented reversible terminators for use in sequencing, is that something you think you would have remembered?

MR. SCHWARTZ: Objection, form.

A. Could you -- could you repeat that question?

Q. Sure. If you had invented the use of reversible terminators for DNA sequencing, do you think that's something that you would have remembered?

MR. SCHWARTZ: Objection, form. Objection, legal conclusion.

A. Yeah, I really don't understand that question.

Q. What is it you don't understand about it?

A. So there's nothing in here that's saying that we thought we invented reversible terminators.

Q. And that's in part because you cite Metzker for the

DR. STEVEN MENCHEN, Ph.D.

proposition; is that correct?

A. Yeah, we -- we refer to Metzker.

Q. And if you are going to rely on Metzker for a proposition like that that's -- well, let me step back. You included allyloxys candidates for 3' modifications even though you had read the Metzker article?

MR. SCHWARTZ: Objection, form.

Q. Let me -- let me -- let me put it this way then. Let me address that.

Was there anything in the Metzker article that dissuaded you from continuing to disclose allyloxy as a suitable candidate for the 3' capping group?

MR. SCHWARTZ: Objection, form.

A. So for Sanger sequencing?

Q. For whatever you disclosed

DR. STEVEN MENCHEN, Ph.D.

it for in column 10 at line --

A. So this is -- yeah, this is for Sanger sequencing.

Q. At line 43.

A. Column 10? So, yeah, these compounds were for Sanger sequencing. We don't describe anything about reversible terminators with respect to -- to this.

Q. Yeah, I'm not asking about that. My question to you is you disclosed allyloxy as a suitable candidate for a modification at the 3' position, correct? That's it in column 10.

A. Do I --

MR. SCHWARTZ: Objection, form.

A. Yeah.

Q. It's line 43 to 44.

A. Okay, could you repeat the question?

Q. In your '884 patent you

DR. STEVEN MENCHEN, Ph.D.
disclose allyloxy as a suitable candidate for 3' modification for incorporation in your sequencing, correct?
MR. SCHWARTZ: Objection to form.
A. For Sanger sequencing.
Q. Right. That's what you say, that's fine. And there was nothing in the Metzker article that dissuaded you from disclosing it for that, correct?
A. I don't -- I don't remember correlating the Metzker article with what we wrote here.
Q. Knowing what you know now, would you still include allyloxy as a suitable candidate for modification at the 3' position given -- given your knowledge of Metzker?
MR. SCHWARTZ: Objection, form. Objection, scope.
A. So Metzker, his 1994 paper

DR. STEVEN MENCHEN, Ph.D.

includes compounds that are not allyloxy that were successful -- successfully incorporated. So I can't discriminate between if we were pointing toward the nitrobenzyl in Metzker and if that correlates with the allyloxy that we describe here, I don't remember. And I can't really comment on that.

Q. Is there anything in Metzker that's inconsistent with your disclosure of allyloxy as a suitable candidate for your 3' modification in your sequencing which you are saying is for Sanger sequencing?

A. For Sanger sequencing?

Q. Let's take that for example.

A. Yeah, we never tried those compounds.

Q. Is there anything in Metzker that you think is inconsistent with disclosing

DR. STEVEN MENCHEN, Ph.D.

allyloxy as a suitable candidate for a 3' modification?

A. For Sanger sequencing?

Q. That's fine. As long as you answer the question after I say that's fine.

MR. SCHWARTZ: Objection, scope.

A. Yeah, that's not the kind of thing that, you know, I prepared for this deposition for, for transferring Sanger sequencing and reversible terminators for SBS. So I would have to study that before I can answer that question.

Q. Metzker discloses the successful use of allyloxy as a capping group at the 3' position, correct?

MR. SCHWARTZ: Objection, form.

A. In what context?

Q. 1994 article.

MR. SCHWARTZ: Objection,

DR. STEVEN MENCHEN, Ph.D.

form.

A. Could you repeat that question one more time.

Q. Sure. Metzker in his 1994 article discloses allyloxy as a successful capping group at the 3' position, correct?

MR. SCHWARTZ: Objection, form.

Q. Isn't that true?

A. So are you talking about synthesis or incorporation?

Q. Both.

A. He was successful in synthesizing it. He was not successful in getting efficient incorporation.

Q. All right. And if Metzker was unsuccessful in getting efficient incorporation, isn't efficient incorporation important for Sanger sequencing?

MR. SCHWARTZ: Objection, scope.

DR. STEVEN MENCHEN, Ph.D.

A. I have never studied incorporation rates of these compounds for Sanger sequencing, at least not in the past 20 years.

Q. But efficient incorporation is a requirement for Sanger sequencing, correct?

A. I don't know.

MR. SCHWARTZ: Objection, scope.

Q. Do you know if efficient incorporation is a requirement for sequencing by synthesis?

A. It's a requirement by Tsien.

Q. Do you know if it's generally to a person skilled in the art a requirement?

A. In what time frame?

Q. 2000.

A. It's one of the requirements, efficient incorporation.

Q. Would you have any

DR. STEVEN MENCHEN, Ph.D.

explanation for why efficient incorporation would be a requirement in the context of sequencing by synthesis but not for Sanger sequencing?

MR. SCHWARTZ: Objection, scope.

A. I do have an explanation.

Q. What is your explanation?

A. Because you don't need to have good incorporation because when you do Sanger sequencing you are competing the natural nucleotide with the terminator. So that you can tolerate some inefficiencies in the incorporation during the Sanger sequencing experiment.

Q. Please explain why the presence of natural nucleotides allows for a greater tolerance of the incorporation efficiency for terminated nucleotides?

A. I didn't say that. I said within the context of Sanger

DR. STEVEN MENCHEN, Ph.D.

sequencing.

Q. Why is that true?

A. Because --

MR. SCHWARTZ: Objection, scope.

A. For Sanger sequencing each time you do a -- you do an experiment with Sanger sequencing you are expecting to not terminate all of the ends. You are terminating say 500 ends in one experiment. So you are only using a little bit at -- at each termination. So you can tolerate some inefficiency.

Q. Why does the presence of natural nucleotides make it tolerable to have less efficiency with your terminated nucleotides?

MR. SCHWARTZ: Objection, scope.

A. I didn't prepare anything, you know -- I didn't prepare or read any literature on this to refresh

DR. STEVEN MENCHEN, Ph.D.

myself on Sanger sequencing for this -- for this deposition. So I'm not going to answer that.

Q. For purposes of this deposition are you prepared to answer questions regarding Sanger sequencing?

A. I will answer any questions that I feel that I can answer.

Q. If you turn to the '985 patent. Do you have that in front of you? Do you have it?

A. Yes.

Q. Okay. If you turn to column 35, please. Do you see where it says "Wherein, R" and then "A represents a small chemically cleavable chemical group"?

Do you see that?

A. I see that.

Q. And do you understand what small means there?

MR. SCHWARTZ: Objection, scope.

DR. STEVEN MENCHEN, Ph.D.

A. That wasn't something that -- that I really prepared for this.

Q. Do you have any idea what would qualify as small?

MR. SCHWARTZ: Objection, scope.

A. Yeah, I -- I can't answer that.

Q. Can you identify any compound at all that would satisfy the small requirement?

MR. SCHWARTZ: Same objection.

A. Well, you know, first we have to know what small is.

Q. You did your best to understand the scope of Claim 1 of the '985 patent; is that correct?

A. The scope.

MR. SCHWARTZ: Objection, form.

A. Yeah, could you -- what do you mean by the scope?

Q. Did you do your best to

DR. STEVEN MENCHEN, Ph.D.

understand what Claim 1 meant?

A. Yeah, I understand what Claim 1 means.

Q. And do you have an understanding of what small means?

MR. SCHWARTZ: Objection, scope.

A. Again, I wasn't asked to study that.

Q. You studied the '985 patent, correct?

A. That's correct.

Q. And you know the claims are important?

A. Yeah, they are.

Q. And one of the things you made sure was that you understood Claim 1?

MR. SCHWARTZ: Objection, scope.

Q. I was asking you, did you make sure you understood Claim 1?

A. I made sure I understood Claim 1 in terms of the chemically

DR. STEVEN MENCHEN, Ph.D.

cleavable part of it and in terms of the, acting as a substrate.

Q. Anything else?

A. Those are the two things that I was supposed to focus on.

Q. Did you put in any effort into understanding the rest of the claim?

A. I have read it.

Q. Other than just reading it?

A. Yeah, the why.

Q. Anything else?

A. Yeah, I mean the rest of it is pretty obvious.

Q. Do you consider small to be obvious as to what it means?

MR. SCHWARTZ: Objection, mischaracterizes. Objection, legal conclusion. Objection, form.

A. Could you repeat that question?

Q. Do you think it's obvious what small means in the context of Claim 1 of the '985 patent?

DR. STEVEN MENCHEN, Ph.D.
MR. SCHWARTZ: Same objections.
A. No, I don't think it is obvious.
Q. Would a person of ordinary skill in the art reading Claim 1 of the '985 patent in the context of the patent document -- relevant patent documents understand what it covers?
MR. SCHWARTZ: Objection, scope.
A. A person skilled in the art I think would overall.
Q. And so, therefore, you have an understanding?
MR. SCHWARTZ: Objection, scope.
A. I have an understanding of some of the limitations.
Q. Okay. With respect to the term "small" would a person of ordinary skill in the art reading all the relevant for patent

DR. STEVEN MENCHEN, Ph.D.

documents under what that term means?

MR. SCHWARTZ: Objection, scope.

A. Yeah. I -- I don't know.

Q. Okay. Do you know one way or the other whether MOM is -- qualifies as small as that term is used in the '985 patent in Claim 1?

MR. SCHWARTZ: Objection, scope.

A. I can't comment on that.

Q. Do you know whether a person of ordinary skill in the art would understand that allyl is small as that term is used in Claim 1 of the '985 patent?

MR. SCHWARTZ: Objection, scope.

A. Yeah, I can't -- I can't comment on that either.

Q. And is your testimony regarding that the same for all of the different Ju patents in the use

DR. STEVEN MENCHEN, Ph.D.

of the small in the claims or is it different in different claims?

A. What -- what -- you mean in the other nucleotides?

Q. Other patents?

A. Yeah. Yeah, that would be -- yeah.

Q. The same testimony?

A. Same testimony.

Q. Do you know what it means to not interfere with the recognition of the analog as a substrate by a DNA polymerase?

A. It means that compared to a natural nucleotide it's going to have the same rate or a similar rate of incorporation.

Q. When you say similar, what's the variability that could be tolerated pursuant to the claims of the Ju patents?

A. I think that's open to interpretation.

Q. What's your understanding

DR. STEVEN MENCHEN, Ph.D.

based on all the work that you've done?

A. I don't think I have a -- a fixed view of what that is.

Q. When you say you don't have a fixed view, what do you mean by that?

A. Well, it could be different for different polymerases so.

Q. Do you know any polymerase that would satisfy the polymerase requirement of the Ju patent claims?

A. Of what time frame?

Q. Any.

A. Any time frame? It depends on what the other -- what the other -- how that fits in with the other limitations.

Q. Can you identify any?

A. Any what?

Q. Can you identify any polymerase that fits in -- that meets the requirement of the claims of the Ju patents in any system?

DR. STEVEN MENCHEN, Ph.D.

A. In any system. I wasn't asked to study polymerases.

Q. But based on your work in this case do you know of any?

A. I don't know of any.

Q. And you understand -- you said one of the things you did look at was why, correct?

A. That's correct.

Q. In the Ju claims. And in terms of why in the Ju claims do you know of any linker that would actually satisfy the requirements of the Ju claims?

A. I wasn't asked -- I was only asked to determine what the -- what the scope of why is.

Q. Do you know of any though?

A. I wasn't asked to -- to look into that. I didn't study that.

Q. And, therefore, you don't know of any?

A. I don't know of any right

DR. STEVEN MENCHEN, Ph.D.

now.

Q. When you say right now, you just spent eight or nine days preparing for the deposition. Today you don't know of any, correct?

A. I spent eight or nine days preparing for a deposition that didn't include looking into that.

Q. One of the things you focused on was the claim requirement of why in the Ju claims?

A. That's right.

Q. And today even though you prepared for a deposition for eight or nine days you can't identify any linker that meets the requirement of Claim 1, correct, that's what you just testified to?

A. Well, there are the linkers that are in the Ju patent.

Q. But when I asked you the question sitting here now you don't -- you can't identify any particular linker that would meet

DR. STEVEN MENCHEN, Ph.D.

the requirements of claim Y of the Ju patent claims, correct?

MR. SCHWARTZ: Objection, asked and answered.

Q. Isn't that right?

MR. SCHWARTZ: Same objection.

A. Yeah, the linkers of the Ju patent.

Q. Do you recall before that you testified that you could not identify any linkers that meet the requirements of claim Y of the Ju patent claims, do you remember that?

A. I said that.

Q. And then --

MR. REINES: All right. Why don't we take a short break.

THE VIDEOGRAPHER: The time on the video monitor is 1:54 p.m. We off the record.

(Whereupon, there is a recess in the proceedings.)

THE VIDEOGRAPHER: We are back on the record. The time on the

DR. STEVEN MENCHEN, Ph.D.

video monitor is 2:12 p.m. This is media five.

Q. I'd like to direct your attention back to your declaration, which is Exhibit 2114, and specifically paragraph 76. Let me know when you have that in front of you, please.

A. I'm there.

Q. I want to ask you some questions about the sentence you have in here that the allyl with palladium chloride in water -- well, let me put it this way, that olefin using palladium chloride in water would proceed according to the Whacker process.

Do you see that?

A. I see that.

Q. Before your work on this project did you know what the Whacker process was?

A. In fact, I did, but not within the context of DNA.

DR. STEVEN MENCHEN, Ph.D.

Q. In what context were you familiar with the Whacker process?

A. I worked four years at Atlantic Richfield, which was a petrochemical company.

Q. And I'd like to show you Exhibit 2115. How did you find this piece of literature?

A. I had a book describing this.

Q. This is from your book?

A. Yeah, it's from the book.

Q. And the Whacker process, if we look at Figure 6.1, please.

A. Figure 6.1, yeah.

Q. And you see the reference to CU there in the upper left-hand corner at -- at 11:00?

A. I do see that, yeah.

Q. What is CU referring to there?

A. Copper 2 and copper 1.

Q. What is the purpose of the copper in the Whacker process?

DR. STEVEN MENCHEN, Ph.D.

A. That's to keep the palladium in the plus two state.

Q. And what's the purpose of the H2O?

A. The H2O, that's a solvent. Oh, H2O -- well, yeah, it's a solvent which takes place in the reaction.

Q. If the copper was removed from this process, would you still obtain oxidation?

A. You would except it would only last as long as the -- as you had palladium 1. Once -- once you converted it all to Pd0 it would stop. And that's described in the -- on page 102.

Q. The copper is required to refresh the palladium catalyst?

A. That's right. And the copper. So it's run in an atmosphere of oxygen. You keep the copper in the plus 2 state from the oxygen in the atmosphere -- the copper in the plus 2 state with the

DR. STEVEN MENCHEN, Ph.D.

oxygen from the atmosphere and the copper 2 keeps the palladium in the plus 2 state because that's -- that's the kinetics of the reaction. So as long as there's oxygen and copper, the reaction will happen.

Q. In any of your DNA sequencing research work did you use copper?

A. In fact, we did.

Q. Could you describe that please?

A. It was to -- so this is for Sanger sequencing?

Q. Yes.

A. And we used copper to, in order to make the -- put the linkers, basically the Prober linkers, we followed the chemistry of Prober, and he describes how to couple the acetylenes to the iodo purines of pyrimidines using the copper in palladium.

Q. In that situation is the

DR. STEVEN MENCHEN, Ph.D.

copper being used as a catalyst?

A. I don't know.

Q. Do you know what the role of the copper is in that reaction?

A. I -- I don't think people really understand that copper is required. I don't think they really understand exactly what it does.

Q. If you turn to page 29, please, of your report.

A. Page 29?

Q. Yeah. Paragraph 51.

A. Which paragraph?

Q. The indented paragraph -- well, it's within paragraph 51.

A. Got it. Okay.

Q. Do you see the reference to CircumVent Kit that you quote?

A. Yes, I do.

Q. And you are familiar with the CircumVent Kit; is that right?

A. I know about it.

Q. Do you know enough about the CircumVent Kit to know that it's

DR. STEVEN MENCHEN, Ph.D.

in the context of Sanger sequencing?

A. I -- I believe it's been promoted to use for Sanger sequencing. I don't know anything about CircumVent and Sanger sequencing.

Q. Do you have a good understanding of what the CircumVent Kit is?

A. No, not really.

Q. In the part where you quote Exhibit 2084 in paragraph 51 you state that -- it states there that "Inefficient incorporation leads to different intensities in peak heights."

Do you see that?

A. Yes.

Q. You bolded it?

A. What?

Q. You bolded it. I'm just trying to help you find it.

A. Yeah, yeah, right.

Q. Okay. And you'll agree

DR. STEVEN MENCHEN, Ph.D.

that the -- that inefficient incorporation of terminators is problematic in Sanger sequencing?

A. It can be.

Q. Does Metzker teach that allyl groups are inefficiently incorporated?

A. He teaches that they are inefficiently incorporated with Vent(exo-). He teaches it for dA for one compound.

Q. What would a person of ordinary skill in the art gather from Metzker 1994 as to the incorporation efficiency of allyl groups, do you know?

A. I'm sorry, could you repeat that?

Q. What would a person of ordinary skill in the art in 2000 gather from Metzker 1994 in terms of the incorporation efficiency of allyl groups, do you know?

A. They would look at Metzker

DR. STEVEN MENCHEN, Ph.D.

and see that when the allyl group's on dA that it's inefficiently incorporated with Vent.

Q. How come you still identified allyl groups as a suitable modifier for 3' position in your patents?

A. Because that's what Metzker calls it. But he definitely refers to the structure of propenyl in that paper. He calls it allyl in the paper.

Q. My question is a little different. In your patent you identify allyl groups as suitable modifiers to the 3' position even though you had the Metzker publication in front of you. And you are saying that -- you're saying now that there is inefficient incorporation shown in Metzker in some form.

A. I didn't say that.

MR. SCHWARTZ: Go ahead.

DR. STEVEN MENCHEN, Ph.D.

Mischaracterizes the witness's testimony.

Q. Do you believe that Metzker teaches allyl groups are inefficiently incorporated?

A. With Vent polymerase on dA they are inefficiently incorporated.

Q. Does Metzker teach anything to a person of ordinary skill in the art in 2000 more broadly than just that the incorporation is inefficient for allyl groups in that one context which is on As using that -- the Vent(exo-) polymerase?

A. Can we look at -- at the Metzker...

Q. Sure.

A. Yeah.

Q. I'm showing you Exhibit 1016, which is the Metzker 1994 article.

A. So if you go to page 4263 and Table 2. So he has this screening experiment where he

DR. STEVEN MENCHEN, Ph.D.
screened a bunch of capped nucleotides A and T and he used a bunch of, you know, seven different or, one, two, three, four, five, six, seven -- eight different polymerases. So you can look at the table and see what he teaches.

Q. Do you believe that Metzker 1994 broadly discourages the use of allyl groups for terminator chemistry?

MR. SCHWARTZ: Objection, form.

A. He teaches within this context that if you have a propenyl group on the 3' of A that it's only -- it doesn't incorporate with seven of the polymerases and is inefficiently incorporated with the Vent (exo-). He doesn't teach anything else.

Q. How come you continued to promote allyl groups as a suitable candidate for 3' modification with

DR. STEVEN MENCHEN, Ph.D.

your inventions notwithstanding Table 2 of Metzker?

MR. SCHWARTZ: Mischaracterizes testimony.

A. So all the R structures in the patent is possible candidates were not really -- for Sanger sequencing, that's all that is.

Q. I understand what your argument is, I'm asking how come you still did that, notwithstanding Table 2 and what you are saying is issues with incorporation?

A. Well, for Sanger sequencing you don't have to have efficient incorporation.

Q. Doesn't inefficient incorporation lead to different intensities in peek heights?

A. So are you referring to -- you are referring to the CircumVent Kit.

Q. Yeah.

A. So it does with this

DR. STEVEN MENCHEN, Ph.D.

enzyme. You know, they don't have any results from other enzymes.

Q. Do you know of any enzymes where inefficient incorporation is fine for Sanger sequencing?

A. That's not something that I -- I looked into.

Q. Do you have any opinion on that subject?

A. No, not really. It's been like 20 years.

Q. Have you personally worked with Vent(exo-) DNA polymerase?

MR. SCHWARTZ: Objection to form.

A. I have never worked with any polymerase myself.

Q. What is the efficiency of incorporation of allyl groups with -- well, actually let me take that back, a step back.

Other than what's shown in Table 2 regarding the incorporation efficiency of capping groups, do you

DR. STEVEN MENCHEN, Ph.D.

have any other knowledge about incorporation efficiency for capping groups?

MR. SCHWARTZ: Objection, form.

A. I was only asked to look into the allyl group for this deposition.

Q. Other than what's shown in Table 2, do you have any other knowledge about the incorporation efficiency of allyl groups?

MR. SCHWARTZ: Objection, form.

A. Any other knowledge?

Q. Anything beyond -- holding aside Table 2, do you have any knowledge of the incorporation efficiency of allyl groups?

MR. SCHWARTZ: Objection, form.

A. I don't.

Q. With respect to the -- if you can turn to -- while we are on

DR. STEVEN MENCHEN, Ph.D.
the subject can you turn to page 17, please, in Figure 1.
MR. SCHWARTZ: Page 17 of what?
A. Of what?
Q. Of your report, sorry. Of your declaration. Sorry about that.
Do you have page 17 of your declaration?
A. Yes.
Q. You see Figure 1?
A. I see Figure 1.
Q. Figure 1, that's not an actual figure from the Metzker 1994, correct?
A. That's a cartoon.
Q. And in terms of the cartoon on page 17 of your report, where is the data that supposedly supports this?
A. That support -- that supports?
Q. Your cartoon.
A. This cartoon? It's in some

DR. STEVEN MENCHEN, Ph.D.

figures -- so it's basically just copying a figure, if you look at Figure 3, 3B. And if you look at lines 12, 13 and 14.

Q. 3?

A. 3B.

Q. B, got it.

A. And the figure legends are really hard to read so this could take a while, but 3B shows lines 12, 13 and 14 and it shows -- it talks about dA that's been capped with propenyl. And dA capped with propenyl has around 1 percent contamination of the dA that's not capped with propenyl. And it shows that you get with -- the enzyme is AMV-RT, which according to the table is, if you look at AMV-RT with O-methyl you see that it passed the screen so it's efficiently incorporated.

So then you go to this figure and you can see that these bands

DR. STEVEN MENCHEN, Ph.D.

that terminate where the T base is, and then there is some, because there's small amount of contamination of the natural nucleotide and the reactivity of the natural nucleotide is obviously quite a bit faster than the methyl capped one, you can see that you can get the bands at the top which are the read through bands.

Q. First of all, in terms of the 1 percent -- for a normal PCR run I mean in your work what's -- is 1 percent a normal, a typical amount that you'd expect to have of residual natural nucleotide?

MR. SCHWARTZ: Outside -- outside the scope.

A. Yeah. If you are doing PCR, the amount of contamination -- are you talking about Sanger sequencing?

Q. I'm talking about in 1994 if one took -- did this experiment

DR. STEVEN MENCHEN, Ph.D.

is this -- is the amount of residual natural an unusually small amount?

MR. SCHWARTZ: Same objection.

Q. Unusually high amount, about what you'd expect?

A. 1 percent, yeah, I don't really know. I haven't really looked into that, what the specifications are for those compounds. I didn't --

Q. Is that something you have expertise in?

A. Expertise in what?

Q. The percent of natural nucleotide that you'd have after a PCR experiment.

A. You are going to have to reframe -- so you're going to have to reframe that question.

Q. Do you understand what Metzker did in terms of coming up with his mixture that he used for this experiment that's reflected in 3B?

DR. STEVEN MENCHEN, Ph.D.

A. Yes. When he made the -- the compound and he purified it, he could not purify away the contaminant by HPLC. He got most of it out. He left around 1 percent.

Q. Was that an unusually high or low amount for an experiment like this or you have no opinion?

MR. SCHWARTZ: Same objection.

A. Yeah. I mean no one had done this experiment before so I -- I don't know.

Q. No one had done any experiment like this?

A. With these compounds.

Q. I'm not saying with these compounds. Okay. All right. I'll figure out a way to do this.

When you saw 1 percent contamination, did you consider that to be a high or low amount or you had no idea?

A. It seems like it would be significant when I saw that, but it

DR. STEVEN MENCHEN, Ph.D.

didn't seem particularly high.

Q. How many micromoles of NTPs are typically used in PCR?

MR. SCHWARTZ: Objection, scope.

A. Yeah. I don't know.

Q. And you don't know because you don't perform PCR experiments or you don't -- you haven't read literature in this area?

A. Yeah. Neither. I have not read the literature carefully enough to understand the nuances of PCR in terms of contamination.

Q. All right. Let's turn to your cartoon on page 18. Do you have that?

A. Yeah, I have it.

Q. And what does this show?

A. This shows what happens when you have inefficient incorporation. And it shows that while you get some -- a termination peak, that you get a peak that fails

DR. STEVEN MENCHEN, Ph.D.

to incorporate the nucleotide. So you get this peak that's one base shorter in the experiment.

Q. Is this based on any experiments?

A. What, this?

Q. Yes.

A. Yes, it is.

Q. And which experiments according to you?

A. If you go to Figure 4. And this is going to be a really bad one. We can pick any -- so I can just give you a description and then we can go into details if you need it. But what these are, are titration experiments where what Metzker did was he used his primer template system and he took different tubes and each tube there was a different concentration of the 3'-O-methyl-dTTP. For example for -- if we look at Figure 4B. And we look at AmpliTaq and lanes 7

DR. STEVEN MENCHEN, Ph.D.

through 9. So 7 through 9 represents a titration of the 3'-O-methyl against the -- the template primer system. And in the first lane he had very little of the 3'-O-methyl-dTTP so the concentration was so low that the incorporation was -- was inefficient.

So you can see that you get very little of the complete termination band and a lot of the failure band. And in the next -- in lane 8 I think he goes from like -- I can actually for AmpliTaq, he goes from 1 micromolar to 5 micromolar to 25 micromolar.

So the first -- lane 7 is 1 micromolar so it's not active enough to get in. Lane 8 is 5 micromolar and you can see you are getting about a 50/50 mixture, you are getting successful incorporation but you still have a lot of failure.

DR. STEVEN MENCHEN, Ph.D.

And at the 25 micromolar you can see that it all went in. You don't see any of the, what we call the efficiency incorporation band or, what do I call it, the efficiency test band, which is this failure peak.

So this is -- this is what he sees when he does the titration. And then if he sees this in his screening assay he can tell that, you know, a 250 micromolar which things work and which ones don't or don't work very well.

Q. So the lane 8 in Figure 4B that shows efficient incorporation of the labeled --

A. It's not efficient. You get some lane 8, yeah.

Q. I may have misspoke. Lane 9.

A. Lane 9, okay.

Q. Excuse me. Let me start again.

DR. STEVEN MENCHEN, Ph.D.

A. It's a terrible legend here so.

Q. Lane 9 is efficient incorporation in Figure 4B; is that correct?

A. That's right.

Q. And does -- this Figure 4B teaches that increasing the concentration increases the efficiency of the incorporation?

A. For this experiment, yeah, it does.

Q. Is that also shown for the -- in 3B?

A. For which, 3B?

Q. Yeah.

A. For 3B the -- at every concentration he got a hundred percent incorporation.

Q. Is it -- is it not getting -- I thought you said before, maybe I'm just seeing it myself, doesn't the line at the T in 3B get darker as the concentration

DR. STEVEN MENCHEN, Ph.D.

increases?

A. Well, it looks that way but I mean these are radio labeled, so. Radio labeled P32, P32 labeled so.

Q. Would you expect the increasing concentration of labeled terminator to increase the efficiency?

A. Sometimes if it's not saturated, yeah.

Q. Did you see any evidence of saturation in the Metzker paper?

A. Well, this -- this 3B it looks like it's saturated because you don't see any change over the different concentrations.

Q. I thought -- I thought you said you thought it might be? Maybe I misunderstood that. Do you think in 3B there's increasing concentration with the -- with the increasing concentration is increasing incorporation or you think it's static?

DR. STEVEN MENCHEN, Ph.D.

A. No, no, I didn't say that.

Q. Okay. All right. In terms of lane 14 in Figure 2 or cartoon 2 as you've put it, where is lane 14, what lane is that referring to?

A. We don't have an example of this.

Q. Is there any experimental -- experimental data that corresponds to lane 14 in your cartoon 2?

A. You are talking about in the Metzker paper?

Q. Yes.

A. No. He doesn't -- he doesn't show that.

Q. Is there any experimental data that you are aware of from any source that corresponds to channel 14 in cartoon 2 on page 18?

A. Yes.

Q. Based on the, your expertise in the Metzker paper, is it your belief that increasing the

DR. STEVEN MENCHEN, Ph.D.

concentration increases efficiency until you are basically a hundred percent efficient?

A. No. I -- I don't think you can assume that.

Q. Would that be your expectation going into your experimental protocol?

A. Excuse me?

Q. Would that be your expectation going into your experimental protocol?

A. Not necessarily.

Q. Why not?

A. Well, because once you get to a certain concentration bad things start to happen between the polymerase and the substrate.

Q. Is that something you've looked into?

A. That's something that I have read about.

Q. Is that something that you looked into for purposes of this

DR. STEVEN MENCHEN, Ph.D.

project?

A. I did see -- I saw a paper that described that.

Q. What paper are you referring to?

A. I can't -- I actually can't -- I can't remember which one it was, but I think it's -- I actually think it's on the -- yeah, I can't remember which one it was.

Q. Do you have any opinions in this matter about what happens if you increase the concentration beyond saturation?

A. Well, you start to get misincorporation.

Q. And what's that based on?

A. I mean there's a lot of -- there's a lot of literature on that.

Q. Have you looked into that for purposes of this matter?

A. For the purpose of this matter?

Q. Yes.

DR. STEVEN MENCHEN, Ph.D.

A. Not really. But I knew about it.

Q. Have you -- did you include any opinions on that subject in your report?

A. No.

Q. And can you identify any paper that or other literature that supports your statement?

A. I can't do it this afternoon. But it is well known in the literature.

Q. Generally speaking, if you haven't looked into it specifically for this project, you are not comfortable testifying on the topic; is that correct?

A. I'm sorry, what?

Q. Generally for topics that you haven't looked into for purposes of your work on this matter, you are not comfortable testifying as to them, is that -- isn't that true?

A. That's true.

DR. STEVEN MENCHEN, Ph.D.

Q. With respect to the lane 10 in your cartoon 2, is there any experimental data anywhere that corresponds to that?

A. Yes. There's a Metzker paper that was published in 1998 that shows this, basically this same -- this same thing.

MR. SCHWARTZ: Feel free to read your declaration, Doctor.

THE WITNESS: Okay.

Q. With respect to column 14, column 14 -- I mean the lane 14 in cartoon 2, that shows a read through band co-existing with an sufficiency test band.

Do you see that?

A. Yeah, I see that.

Q. First of all, efficiency test band, that's a name that you came up with?

A. That's correct.

Q. Does Metzker label that, the band where, you know, what -- I

DR. STEVEN MENCHEN, Ph.D.

guess what you call minus one maybe, the minus one band in his paper?

A. In which paper?

Q. His 1994 paper.

A. He -- he doesn't describe it.

Q. And in your cartoon 2 for lane 14 you have a read through band and an efficiency -- what you call an efficiency test band co-existing. Is there any gel that you have from the Metzker paper that has those two things co-existing?

A. Not in this paper.

Q. Are you saying that's from another paper?

A. That's right.

Q. And that's from a 1998 Metzker paper?

A. That's right.

Q. How come -- do you cite that paper in here?

A. No.

Q. Why not?

DR. STEVEN MENCHEN, Ph.D.

A. It didn't make it into the declaration.

Q. Why not?

A. The declaration got -- well, it didn't make it in under the deadline.

Q. So it was a function of time?

A. Essentially, yeah.

Q. Was there anything else that didn't make it into the declaration because of you ran out of time other than this analysis of the 1998 Metzker paper?

A. Not that I can think of right now.

Q. In Figure 4B, if there was the presence of natural nucleotides, you know, what's called contamination, would you expect to see what you are calling an efficiency test band?

A. Yes.

Q. Doesn't the presence of

DR. STEVEN MENCHEN, Ph.D.

natural nucleotides speed up the experiment?

MR. SCHWARTZ: Objection, form.

A. Yeah, what do you mean by that?

Q. If you have natural nucleotides, they will incorporate and that speeds up the overall process, correct?

MR. SCHWARTZ: Objection, form.

A. Yeah, I wouldn't make that conclusion.

Q. Do you know what a gel would look like if -- do you have idea what the gel looked like for the termination with asterisk, what it, in fact, looked like for Metzker?

A. Metzker doesn't show any data on any -- terminated with with asterisk.

Q. Do you have any idea what

DR. STEVEN MENCHEN, Ph.D.

it would be?

A. So this is --

Q. Without doing experiments.

A. This is just a screening assay, yeah.

Q. But do you have any idea what it would be without doing any experiments?

MR. SCHWARTZ: Objection, form.

A. Yeah. In terms of what?

Q. In terms or the gel for the termination with an asterisk?

MR. SCHWARTZ: Objection, asked and answered.

Q. Do you have any idea what the gel would look like without performing experiments?

A. Yeah, I have an idea of what it might look like.

Q. And let's take the example of the O-methyl with the MuLV-RT. Do you see that?

A. Yeah, I see that.

DR. STEVEN MENCHEN, Ph.D.

Q. Do you have any idea what that -- what do you think the gel would look like for the data that Metzker created for this?

A. I mean he shows it.

Q. Where is that?

A. I think so.

Q. Please show me.

A. I think it's Figure 3B, lanes 12 through 13 and 14. I think.

Q. So Exhibit 3B shows what an asterisk plus would be; is that correct?

A. So I'm sorry.

Q. Excuse me --

A. Which enzyme are you talking about?

Q. MuLV-RT.

A. Yeah. I'm sorry, I made a mistake. No, he doesn't show that.

Q. But do you have any idea what it would be? Do you have any -- do you have any idea in Table

DR. STEVEN MENCHEN, Ph.D.

2 what the termination plus asterisk data looks like for any of them?

A. He didn't show it.

Q. Do you have any idea what it would be?

MR. SCHWARTZ: Objection, asked and answered. Objection, form.

A. Yeah, I mean it probably looked pretty bad because he did the screening assay and whenever he got termination star, at 250 micromolar, which is a very high concentration, he rejected those.

Q. When you say it probably looked very bad, is it speculation?

A. It's speculation, yeah.

Q. And in terms of 250 micromolar that's a relatively low amount, correct?

MR. SCHWARTZ: Objection.

A. That's a relatively high amount based on the teaching of Tsien.

DR. STEVEN MENCHEN, Ph.D.

Q. As a person of ordinary skill in the art in 2000, 250 micromolar is a small amount, right? You know that from your technical work, your own work?

A. My own work?

Q. You don't know that?

A. 250 micromolar?

Q. Yes.

A. That's a very high concentration.

Q. And what are you basing that on?

A. Teachings of Tsien.

Q. Anything else?

A. Well, I mean the only other thing I have to go on is Sanger sequencing but that's not really relevant here.

Q. In terms of what -- in terms of information that's relevant to the question here the only thing that you are relying on to say 250 -- 250 micromolar is a large

DR. STEVEN MENCHEN, Ph.D.

amount is Tsien; is that correct?

A. I'm sorry, is what?

Q. In terms of what's relevant here today the only thing that you have to go on to say that 250 micromolar is a small amount is -- excuse me -- is a large amount, is the Tsien reference; is that correct?

A. Yeah, the teachings of Tsien.

Q. And do you have any personal expertise beyond that that's relevant?

A. I have never worked with reversible terminators that -- that are capped.

Q. Have you worked with reversible terminators at all?

A. Yes.

Q. When was that?

A. 2006-2007.

Q. In the 1990s did you work with any sequencing by -- sequencing

DR. STEVEN MENCHEN, Ph.D.

by synthesis experimentation?

A. Not in the 1990s.

Q. Did you follow the literature?

A. During the 1990s?

Q. Yes.

A. I don't remember being interested in sequencing by synthesis in the 1990s.

MR. REINES: All right. Why don't we take a break.

THE VIDEOGRAPHER: The time on the video monitor is 2:58 p.m. We off the record.

(Whereupon, there is a recess in the proceedings.)

THE VIDEOGRAPHER: We are back on the record. The time on the video monitor is 3:21 p.m. This is media six.

Q. Do you have the Metzker 1994 paper in front of you, please, Exhibit 1016.

A. Got it.

DR. STEVEN MENCHEN, Ph.D.

Q. And if you could put Table 2 in front of you. And compound three, you see where it says O-allyl?

A. Yes, I see that.

Q. And what would a person of ordinary skill in the art understand O-allyl to refer to in terms of a particular compound?

A. Well, Metzker draws it, they would go to the figure.

Q. Why would they go to the figure?

A. Well, because it has it here. And they would go to Figure 2 and see that compound three is propenyl group.

Q. Do you have any explanation for why you were the only person we have calling this a propenyl group?

MR. SCHWARTZ: Objection, form.

A. The only person where?

Q. In any of the materials we

DR. STEVEN MENCHEN, Ph.D.

have looked at.

A. Yeah. I guess I haven't seen all your materials.

Q. I'm referring to your materials considered. In your materials.

A. Sir, in my declaration I use the term "propenyl group."

Q. I know you use it. I'm asking why you are the only one that uses the term "propenyl group" to refer to the O-allyl?

A. So that I don't have to say allyl and then say propenyl afterwards. Because in all these other references or most of these other references when they use the term "allyl" they draw a structure, that's what they do.

MR. SCHWARTZ:

Mischaracterizes the references.

Q. If you turn to Figure 4, please. And the description and you'll see like about six lines down

DR. STEVEN MENCHEN, Ph.D.

it says one mm. Can you describe what one mm refers to?

A. Figure 4. How -- this is the legend? The legend?

Q. Yeah.

A. Eight to ten. 1 millimolar.

Q. And let's take the 5 millimolar, that's how many times more than 250?

A. That would be 250, 20 times.

Q. Do you consider 5 millimolar to be a lot or a little in the context of this experiment?

MR. SCHWARTZ: Objection.

A. Yeah, I mean that's a whopping amount.

Q. You'll agree compared to the amount of terminated nucleotides in -- used in Exhibit 4 the 250 micromole is relatively small?

A. Could -- could we -- could I find on -- in these figures could

DR. STEVEN MENCHEN, Ph.D.

I look at this data?

Q. Oh, yeah. I mean you can look at -- you mean if you have it. I mean I don't have anything to add to you but if you want time to look at the document, please.

A. Yeah. And this is which, which polymerase, can you tell? Figure 4. Oh, this is -- this is the Sanger experiment. Okay. Yeah.

I don't -- yeah, so this -- this has nothing to do with the -- this is for Sanger sequencing. This has nothing to do with the SBS application, this particular reference to this 1 millimolar, 2.5 millimolar and 5 millimolar. This refers to 4A I'm pretty sure.

Q. So your view is that 5 millimolar for Sanger sequencing is not a lot?

A. Oh, no, I didn't say that. I'm just saying that it has nothing to do with the sequencing by

DR. STEVEN MENCHEN, Ph.D.

synthesis, this experiment.

Q. 4B?

A. Is this 4B or 4A?

MR. SCHWARTZ: You are jumping around.

A. Yeah. So what does this refer to?

MR. REINES: I'm asking him questions.

A. Yeah. I'm trying to figure this out.

Q. Please take the time that you need in order to answer most accurately.

A. Figure 4A --

MR. SCHWARTZ: I'm also confused. Are you referring to the 1 millimolar or are we referring to something else now? I just don't even know where you are.

A. Yeah. So this -- this definitely refers to 4A, which is Sanger sequencing and not designed for sequencing by synthesis. So I

DR. STEVEN MENCHEN, Ph.D.

don't really have any comment on these concentrations because, yeah, I just -- I don't know.

Q. In terms of the norms of concentration for Sanger versus single molecule sequencing do you have any understanding as to whether there's a correlation?

A. Single mole- -- what do you mean single molecule sequencing?

Q. I mean --

A. Sequencing by synthesis?

Q. Sequencing by synthesis, excuse me.

A. I don't know.

MR. SCHWARTZ: Asked and answered.

Q. Are you surprised to see Metzker teach 5 millimolar concentrations in the context of Sanger sequencing?

A. No. I don't have any opinion.

Q. Do you have any opinion on

DR. STEVEN MENCHEN, Ph.D.

what the norms are for the different concentration levels that are appropriate for sequencing by synthesis in the 1990s?

A. In the 1990s?

Q. Yes.

A. I mean it's -- it's taught by Tsien to be 30 micromolar. That's all -- that's all I have.

Q. At the bottom of Figure 4 do you see the reference to 500 micromolar?

A. Yeah, I do see that.

Q. And that's referring to a sequencing by synthesis experiment; is that correct?

A. So this is -- yeah, it -- it's one of these. I can't figure out which one. C. So this goes to Figure C. So this is a titration, okay. So that's good. And it is AmpliTaq. AmpliTaq. Yeah, okay, I see that. Go ahead and ask your question.

DR. STEVEN MENCHEN, Ph.D.

Q. Yes. Do you see that Metzker teaches the use of a 500 micromolar concentration for sequencing by synthesis?

A. So this is figure -- this is AmpliTaq -- this AmpliTaq Figure 4C and it's lanes 7 to 9. And he doesn't teach that. What he does is he shows a titration of 20 micromolar, a hundred micromolar and 500 micromolar for AmpliTaq DNA polymerase. And you can see that every one of these bands is the same. So what he's showing is it doesn't matter how high you go, nothing is going to change.

Q. Okay. And in B he shows 500 micromolar and that's --

A. Which polymerase?

Q. Vent(exo-) I think.

A. That's --

Q. I'll let you be the judge.

A. This is really hard. Okay. So how many lines -- which line are

DR. STEVEN MENCHEN, Ph.D.

you referring to?

Q. You see where it says 20, 100 and 500 micromolar?

A. 20 -- 20. Yeah, I see it. Yeah.

Q. Okay. So let me ask the question. In 4B Metzker teaches the use of 500 micromolar concentration of terminators for sequencing by synthesis?

A. So all this -- sorry. All this is, it's another titration. So he's doing 20 micro -- so if you look at lanes 7, 8 and 9 you can see at 20 micromolar, you see a lot of failures. At 800 micromolar you see it's almost complete.

So all he's doing is running at the highest concentration he can run, but it's obvious that if you look at 20 and a hundred and then 500 that at 250 it was probably complete.

And if you look back at the

DR. STEVEN MENCHEN, Ph.D.

table this is Vent with 3'O-methyl-dTTP. And if you go back to the table you go to Vent and dTTP you can see that's compound A, at 250 micromolar he gets complete termination.

So he's not really teaching 500 micromolar, he's just showing what happens is he does the titration.

Q. He's teaching titration, right?

A. That's right.

Q. And a person of ordinary skill in the art would understand that Metzker is teaching titration to the concentrations of terminators to improve efficiency?

A. No. They wouldn't assume that at all.

Q. I didn't ask what they would assume, I asked what he's teaching.

A. He's teach- --

DR. STEVEN MENCHEN, Ph.D.

Q. Metzker teaches titration of the concentrations of terminators, correct?

A. This is what he's showing, yes.

Q. And what he's showing until there's 100 percent efficiency you can expect improved efficiency, correct, with increases?

A. Yeah, that's -- that's -- no, he doesn't show. What he shows is when he -- he has not looked at any terminator here that didn't pass his screening test in Table 2. So every one of these terminators already showed complete incorporation at 250 micromolar. And then he goes back and he does his titration. That's what he's showing.

Q. Metzker is showing that there's a correlation between increasing the concentration and increased efficiency, correct, that

DR. STEVEN MENCHEN, Ph.D.

much you'll admit?

A. For up to 250 micromolar. Anything past that it's already in. So.

Q. You mean for the experiments that he shows you?

A. That's right.

Q. Yeah, okay. And is titration such as Metzker shows a common way to perform experiments in this field, field of atoms?

MR. SCHWARTZ: Objection to form.

A. So what Metzker teaches is you do an initial screen which is shown in Table 2 and then you go ahead and titrate to see how low you can go. That's what a POSA would see in this.

Q. And do you have any idea why Metzker was repeatedly showing titrating up to 500 micromolar; do you have any story on that?

A. He doesn't comment on that.

DR. STEVEN MENCHEN, Ph.D.

Q. Do you have any -- what would a person of ordinary skill in art understand as to why Metzker was titrating up to 500 micromolar concentrations of terminators?

A. A POSA would see that, read through the article and understand that Metzker didn't defend it, he was just showing it.

Q. If you turn back to the Ju patent, please, which is Exhibit 1075. And turning to column 26, please.

A. Okay.

Q. Would a person of ordinary skill in the art reading the paragraph at lines 12 through 29 understand that Ju is saying that MOM and allyl can be used for his invention?

MR. SCHWARTZ: Objection, scope.

A. I'm sorry, could you repeat that question?

DR. STEVEN MENCHEN, Ph.D.

Q. Would a person of ordinary skill in the art reading the paragraphs at lines 12 through 29 understand that Ju is saying that MOM and allyl could be used for his invention?

MR. SCHWARTZ: Same objection.

THE WITNESS: What was the objection?

A. So a person ordinarily skilled in the art would look at this paragraph and see that he is describing as his specification which is -- meets -- you know, it's in the present tense, caps all four nucleotide analogs --

So he's speaking in the present tense which means he is -- it says part of the specification is his statement 3'-OH is capped in all four nucleotide analogs which can then be mixed together with DNA polymerase and used to evaluate the sequencing system used in scheme

DR. STEVEN MENCHEN, Ph.D.
Figure 9. So, again, this is his specification.
The MOM or the allyl which he draws propenyl group is used to cap the 3' -- okay, is used to cap it with well established synthetic procedures. Again, he is speaking in the present tense and he's referring back to historical data from Fuji and Metzker, okay.
So he can make them, that's -- that's what a POSA would think.
"These groups can be removed chemically with high yield as shown in Figure 14." And a POSA would look at that and they would look at Figure 14 and see that what he -- he refers to Kamal. Again, he's speaking in the present tense so he's referring to Kamal.
They would look at Kamal and see that Kamal does not describe any nucleotides in the, you know, in their paper. And that what Metz- --

DR. STEVEN MENCHEN, Ph.D.

what Ju is showing here in Figure 14 is that he can protect and deprotect a nucleotide triphosphate but he doesn't show that he can protect -- or that he can deprotect a -- the N of a chain of a double strand piece of DNA under the conditions of SBS.

So that's what he shows here, so yeah.

MR. REINES: Would you read my question back, please.

(Record read.)

A. And a person skilled in the art would not see that -- that you can cleave the allyl under SBS conditions. He doesn't really show that in this paragraph.

Q. What would a person of ordinary skill in the art conclude as to whether or not Ju is stating that MOM and allyl can be used for his inventions that are claimed?

A. They would conclude that he doesn't really show that, you

DR. STEVEN MENCHEN, Ph.D.

know -- he doesn't show here that he has cleavage conditions that are compatible with SBS.

Q. How would a person of ordinary skill in the art in 2000 who hasn't figured out the conditions for cleavage that are compatible with SBS if it's not shown in the two patents?

MR. SCHWARTZ: Outside the scope.

A. I can't speculate what a POSA would do, how they would figure that out.

Q. Would you know what the conditions are?

MR. SCHWARTZ: Objection to form.

Q. Or do you know what the conditions are?

A. The conditions for what?

Q. Do you know what the conditions are for chemically cleaving allyl consistent with SBS

DR. STEVEN MENCHEN, Ph.D.

conditions?

A. I wouldn't know prior to 2000.

Q. Do you know now?

A. Ju has published a paper that shows the conditions.

Q. I'm saying but do you know now sitting here now?

A. Do I know now, have I read the paper, is that what you are asking?

Q. What paper are you referring to?

A. He has a couple of papers that describe this.

Q. And that's --

A. After 2000.

Q. Right. But you can't testify about those because of your confidentiality obligations; is that correct?

A. What do you mean?

Q. Can you testify about your review of the Ju literature that you

DR. STEVEN MENCHEN, Ph.D.
performed during the course of your work at Applied Biosystems and Life Tech?
A. So this is open -- open literature.
Q. I know.
A. Published.
Q. But before you were consistent that you could not even testify about your review of open literature. Do you recall that at the beginning of the deposition?
MR. SCHWARTZ: Objection to form.
A. I don't remember saying that.
Q. I have taken a day of deposition in reliance on that.
A. What?
Q. I said I have taken a day of deposition in reliance on your statement you could not testify about your review of public literature because it was trade

DR. STEVEN MENCHEN, Ph.D.

secret information.

A. No, I could not testify as to my interactions.

Q. Are you aware of any disclosure of conditions that would make allyl or MOM workable as caps in the Ju claimed inventions earlier than the Ju papers that you are referring to?

A. No, I don't.

Q. And when are the Ju papers?

A. I don't have those. I know they are out there. I have looked at them but -- yeah.

Q. Is it the ones you said in the 2006 time frame?

A. Something like that, yeah.

Q. In 2000 would you have known of what enzymes could be used with the claimed inventions of the '985 patent without reading the patents?

MR. SCHWARTZ: Objection. Objection, outside of scope.

DR. STEVEN MENCHEN, Ph.D.
Objection, asked and answered.
A. I wouldn't -- I wouldn't have known.
Q. Would you have known what would be good candidates?
A. I would have no idea.
MR. SCHWARTZ: Again, objection, outside of the scope to that question too.
Q. Would a person of ordinary skill in art have any idea what enzymes could be used to try to make the capping groups in the '985 patent work for the claimed inventions?
MR. SCHWARTZ: Objection to scope.
Q. In 2000?
A. Yeah, I don't know. I didn't -- I didn't look into that.
Q. Are there any small chemically capable viewable chemical groups that would meet R in the claims of the Ju patents that are

DR. STEVEN MENCHEN, Ph.D.
disclosed in the specification of the patent?
MR. SCHWARTZ: Objection to scope. Objection, legal conclusion. Objection to form.
A. Yeah, I was not -- I was not assigned the task to look into what a small group is.
Q. Did you review the Ju declaration in the prosecution history?
A. I reviewed the declaration that applied to the Y linker.
Q. The what?
A. The Y linker that connects the base with the tag.
Q. And in that declaration he states that MOM is a small group, correct?
MR. SCHWARTZ: Objection.
A. I didn't review that.
Q. You only read part of his declaration?
A. I read the part I was

DR. STEVEN MENCHEN, Ph.D.

supposed to read.

Q. When you say supposed to read, how do you know which part to read?

A. I read the part that applied to the Y linker, which was what I was supposed to cover.

Q. And why -- what is your basis for concluding that the only part of the prosecution history you needed to read was about the Y linker?

A. Because that was the task I was assigned.

Q. By counsel?

A. By counsel.

Q. Did counsel tell you not to read the prosecution history experts fully?

A. That's privileged information.

Q. I'd like to show you what's been marked Exhibit 10076 -- no, 1076. Correct that, 1076. Do you

DR. STEVEN MENCHEN, Ph.D.

have this prosecution history excerpt in front of you?

A. Yes, I do.

Q. And how did -- who decided what portion of the prosecution history you received, did you decide that?

A. The lawyers guided me to it.

Q. And then when you received this excerpt from the prosecution history, how did you decide what to read within this?

A. I was told by the lawyers which section to read.

Q. Which section did they tell you to read?

A. They told me to read the section -- the scope of Y.

Q. Which portion do you consider to be that section?

A. Section C.

Q. Page, please?

A. Oh, I'm sorry, page 20.

DR. STEVEN MENCHEN, Ph.D.

Q. Other than the three paragraphs in the scope of Y, did you read anything else in this prosecution history excerpt?

A. No, I didn't.

Q. As part of your assignment were you told not to read the other parts?

A. What?

Q. As part of your assignment were you told not to read the other parts?

MR. SCHWARTZ: I'm going to just object to this line of questioning where you are asking him what the attorneys told him to do. As long as you -- he can answer that question as long as you understand that that is not a waiver of privilege of any kind. Will you accept that?

MR. REINES: Yes.

MR. SCHWARTZ: Okay.

A. I'm sorry, could you repeat

DR. STEVEN MENCHEN, Ph.D.

the question?

Q. Were you told by counsel not to read the other portions of the Ju declaration beyond the three paragraphs in section C?

A. It was indicated to me that I should just focus on the scope of Y.

Q. And did you read the rest of it for context?

A. No, I didn't.

Q. If you turn to page 17 to 18, do you see where it says the -- at the very bottom of the page of 17 it says that the specification provides two -- only two examples of small capping groups, MOM and allyl?

A. Yeah, I see that.

Q. What's allyl ether, if you can describe that?

A. This comes out of Ju's patent, I assume, and allyl ether means propenyl on the 3'-hydroxyl on a nucleoside. That's what I assume.

DR. STEVEN MENCHEN, Ph.D.

Q. And you've used different terminology relating to allyls. Do you know what Alloc is?

A. Alloc.

Q. A-L-L-O-C?

A. I'm not -- I'm not really -- I have never used that term.

Q. Are you familiar with it at all?

A. A-L-L-O-C. I think I have seen it.

Q. Do you have any idea what it means?

MR. SCHWARTZ: Objection, scope.

A. Yeah, no. You are going to have to tell me what it means.

Q. Do you have any reason to dispute Columbia's position that MOM and allyl are examples of small capping groups?

MR. SCHWARTZ: Objection, scope.

DR. STEVEN MENCHEN, Ph.D.

A. Yeah, I can't -- yeah, I can't give -- give an opinion on that.

Q. I'm just asking do you have any basis to contest that?

MR. SCHWARTZ: Objection, scope.

A. What do you mean by basis?

Q. Basis. Is there any evidence, any understanding you have in any of your expertise that's inconsistent with MOM and allyl being examples of small capping groups that within the scope of the inventions claimed in the Ju patents --

MR. SCHWARTZ: Objection, scope.

Q. -- at issue in this matter?

A. Yeah. I don't think I can dispute it.

Q. And I'd like to direct your attention to -- are you familiar with allyloxycarbonyl?

DR. STEVEN MENCHEN, Ph.D.

A. Yes, I am.

Q. And is that something -- do you know whether that's Alloc. Does that refresh your recollection that's what Alloc refers to, A-L-L-O-C?

A. I mean is that what it is?

Q. I believe that to be but --

A. Okay. Yeah, I think -- I think I have seen it and I think that's what it is.

Q. And based on all the work you've done in this case and your expertise in the field, do you have any reason to contest that statements of counsel that allyl would be an example of a capping group that meets the limitations of Claim 1 of the '985 patent?

MR. SCHWARTZ: Objection, scope.

A. Yeah.

MR. SCHWARTZ: Objection to legal conclusion.

DR. STEVEN MENCHEN, Ph.D.

A. I can't form an opinion on that.

Q. Do you have any information inconsistent with that or any basis to challenge it?

MR. SCHWARTZ: Same objections.

A. Yeah, I can't form an opinion on it.

Q. Why not?

A. Because it's not something that I was told to look at or review.

Q. Leaving aside whether you've formed an opinion or not, do you have any information based on all your work in this case or all of the expertise that you have coming to this deposition to contest that allyl would satisfy the scope of -- the requirements of Claim 1 of the '985 patent?

MR. SCHWARTZ: Objection, asked and answered. Objection to

DR. STEVEN MENCHEN, Ph.D.

scope. Objection, legal conclusion.

Q. If you have any basis, please identify it.

A. I can't form an opinion on that.

Q. Do you have any basis to challenge it? I'm not asking you to form an opinion.

MR. SCHWARTZ: Same objections.

A. Yeah. If -- if -- yeah, if that's a legal issue, I can't -- I can't even begin to address that.

Q. How about from a technical perspective?

A. I can't form -- I can't form an opinion.

Q. Can you identify any technical reason why allyl wouldn't be able to meet the requirements of Claim 1 of '985 patent?

MR. SCHWARTZ: Objection, scope. Objection, legal

DR. STEVEN MENCHEN, Ph.D.

conclusion.

A. So what are you asking me?

Q. Can you identify any technological reason why allyl wouldn't meet the requirements of Claim 1 of the '985 patent as a capping group?

MR. SCHWARTZ: Same objections.

A. Metzker. Metzker shows it is inefficiently incorporated.

Q. Anything else?

A. There's a -- there's no method for cleaving it. Nothing in the prior art that would satisfy SBS.

Q. Does the Ju patent teach anything that would make allyl more efficient to a person of ordinary skill in the art than it was in the hands of Metzker?

MR. SCHWARTZ: Objection, scope.

Q. And when I say it, I mean

DR. STEVEN MENCHEN, Ph.D.

allyl.

A. And I say propenyl. I'd have to review the patent.

Q. Based on all the review you've done so far are you aware of anything in there?

MR. SCHWARTZ: Same objection.

A. Yeah, so I'm not aware of anything but I have never read the -- the patent in that context.

Q. You've never read the patent --

A. In that context.

Q. You've never read the Ju patent to determine whether there's anything about whether allyl is efficiently incorporating?

MR. SCHWARTZ: Same objection.

Q. Let me -- let me withdraw the question and ask it this way. Did it ever cross your mind as to whether allyl would be within the scope of the invention claimed by Ju in the '985 patent? Is it something

DR. STEVEN MENCHEN, Ph.D.

that ever occurred to you in the process of your hundreds of hours working on this matter?

MR. SCHWARTZ: Objection, legal conclusion.

A. Yeah. I can't form an opinion on that.

Q. Why is that?

A. I would need to read through the patent within the context that you are describing.

Q. During the hundreds of hours of your work in this case did it ever -- did you ever consider at all whether allyl would be within the scope of what Ju is describing as his invention?

MR. SCHWARTZ: Objection, legal conclusion. Objection to scope. And objection, mischaracterizes testimony.

A. I can't give you an -- so could you repeat the question?

Q. It's not an opinion. I'm

DR. STEVEN MENCHEN, Ph.D.

asking you whether you considered something that's historical fact.

A. I don't remember. Like you say, it was a hundred hours. Or hundreds of hours.

Q. Can you identify any embodiment of the claimed inventions of the Ju patents?

A. I wasn't asked to look into that.

Q. Did you ever form an opinion one way or the other as to whether using allyl as the capping group would meet the fundamental requirements of -- for sequencing by synthesis.

A. Only from reading Metzker and looking at the cleavage conditions or what's in the -- what's in the prior art supplied by Illumina for cleavage conditions.

Q. Do you understand the '985 patent specification to be stating that allyl meets the requirements --

DR. STEVEN MENCHEN, Ph.D.

the fundamental requirements for a sequencing by synthesis system?

MR. SCHWARTZ: Objection, scope.

A. Yeah, could you repeat that?

Q. Sure. One of the things you considered in Ju is the statement of what the fundamental requirements are for sequencing by synthesis system that's in column 21.

A. Oh, in the patent, column 21?

Q. Yes.

MR. SCHWARTZ: Objection, mischaracterizes statements. Objection, scope.

A. Column 21. So what are you asking me?

Q. As part of your work in this case did you consider Ju's statements of the fundamental requirements for a sequencing by

DR. STEVEN MENCHEN, Ph.D.

synthesis system described in column 21?

A. I'm sorry, one more time. One more time and that's it.

Q. That's all right. As part of your work in this case did you consider Ju's statements of the fundamental requirements for a sequencing by synthesis that he sets forth in column 21?

A. I didn't really consider those statements. I only considered the statements of Tsien and Dower.

Q. You are saying in your --

A. And Metzker. Sorry.

Q. And Metzker?

A. Right. Tsien, Dower and Metzker for the fundamental requirements. And it's summarized in my -- when I considered the fundamental requirements, it's summarized in my report as -- on page 4, 5 and 6.

Q. Okay. In terms of the

DR. STEVEN MENCHEN, Ph.D.

fundamental requirements for sequencing by synthesis you see the statements set forth in -- on page -- in column 21 of Ju, right?

MR. SCHWARTZ: Objection, mischaracterizes the document.

A. One more time.

Q. In the top of column 21 Ju sets forth the fundamental requirements for sequencing by synthesis.

Do you see that?

MR. SCHWARTZ: Objection, mischaracterizes the document.

You can answer.

A. Yeah, I can see that.

Q. Is that -- are the -- are the fundamental requirements set forth by Ju any different than the fundamental requirements disclosed in the prior art?

MR. SCHWARTZ: Objection, asked and answered.

A. Yeah, they are different.

DR. STEVEN MENCHEN, Ph.D.

Q. They are you say?

A. Yeah. There's -- when I read through this -- okay.

Q. Why don't you go through them one at a time and state whether you think the fundamental requirements for sequencing by synthesis disclosed in Ju are the same as those described in the prior art. Why don't you go through -- do it by number and break it down, that will be easier.

A. So number one, "The availability of four nucleotide analogs each labeled with a unique label and containing a chemical moiety" cap- -- "capping the 3'-hydroxyl group." That's not really a fundamental requirement that you need four with unique labels but it does satisfy sequencing by synthesis.

"The four nucleotide analogs need to be efficiently and

DR. STEVEN MENCHEN, Ph.D.

faithfully incorporated" --

MR. SCHWARTZ: Slow down so that the court reporter can type.

THE WITNESS: Oh, I'm sorry.

Q. Start with two again.

A. Two, "The four nucleotide analogs, AA, AC, AG, AT, need to be efficiently and faithfully incorporated by DNA polymerase as terminators of the polymerase reaction." That's a common requirement.

Q. When you say common requirement, common requirement to prior art?

A. To prior art, yeah.

"The tag and the group capping the 3'-hydroxyl need to be removed with high yield to allow the incorporation and detection of the next nucleotide." So that's incomplete.

Q. It's incomplete you say?

A. Yeah.

DR. STEVEN MENCHEN, Ph.D.

Q. What's incomplete about that statement?

A. "The prior art also specifies that it needs to be done under aqueous conditions and it needs to be fast."

"The growing strand of DNA should survive the washing, detection and cleavage processes to remain anneal to the DNA template." So that's not really in the prior art but I think that's implied.

Does that answer your question?

Q. For present purposes.

A. Okay.

Q. Now, would a person of ordinary skill in the art understand from Ju that allyl is the capping group satisfies the fundamental requirements for sequencing by synthesis that's set forth by Ju?

A. You are talking about propenyl.

DR. STEVEN MENCHEN, Ph.D.

Q. If that's what you would like to call it.

A. The propenyl capping group. They would look to Metzker and see that it's inefficiently incorporated. And then they would look to -- the references supplied by Illumina and see that there's no method to cleave it that are compatible with SBS.

Q. Would a person of ordinary skill in the art understand Ju to be stating that MOM meets the fundamental requirements of sequencing by synthesis?

MR. SCHWARTZ: Objection, scope. I'm going to object to the earlier question as scope.

A. I wasn't asked to evaluate MOM.

Q. Do you have any explanation as to why Ju would propose allyl as the capping group for his invention if Metzker taught otherwise?

DR. STEVEN MENCHEN, Ph.D.
MR. SCHWARTZ: Objection, scope.
A. I can't -- I can't explain how Ju made his decision.
Q. What would a person of ordinary skill in the art understand as to why Ju is directing people to Metzker and promoting allyl as a capping group if Metzker is stating that it's problematic?
MR. SCHWARTZ: Objection, scope.
A. Yeah, I don't know what a person -- a POSA, how they would react to that. I can't even speculate.
MR. SCHWARTZ: We have been going for a little bit more than an hour.
MR. REINES: Okay. Let's take a break.
THE WITNESS: That would be great. Thanks.
THE VIDEOGRAPHER: The time is

DR. STEVEN MENCHEN, Ph.D.

on the video monitor is 4:15 p.m. We off the record.

(Whereupon, there is a recess in the proceedings.)

THE VIDEOGRAPHER: We are back on the record. The time on the video monitor is 4:32 p.m. This is media seven.

Q. Turn to the prosecution history if you would. And specifically --

MR. SCHWARTZ: You are looking at Exhibit 1076?

MR. REINES: Yes, sir, page 30.

Q. Between 30 and over to 31 if you could read that paragraph 15, please.

A. Paragraph 15?

Q. Yeah. Let me know when you are done if you would.

MR. SCHWARTZ: Just so I'm clear what you want him to read is you want him to read paragraph 15

DR. STEVEN MENCHEN, Ph.D.

or all of paragraph 31?

MR. REINES: Just paragraph 15.

MR. SCHWARTZ: Just paragraph 15?

MR. REINES: That's correct.

MR. SCHWARTZ: Okay.

A. Yeah. Yeah, I'm done.

Q. And if you'll turn to page 58 and 59 now.

A. Okay.

Q. And this is the analysis referenced in Dr. Ju's paragraph 15. You see that?

A. Do you want me to read it?

Q. Yes, please. But do you see that? Just confirm that.

A. Do I see what?

Q. This Exhibit C is referred to in paragraph 15 of Dr. Ju's declaration.

A. Oh. Yeah.

Q. Why don't you read it.

A. Okay.

DR. STEVEN MENCHEN, Ph.D.

Q. The -- the available space within the active site of the polymerase to accommodate a 3 percent capped terminator is approximately 3.7 angstroms.

Do you see that in Dr. Ju's analysis?

A. Yeah, I see it.

MR. SCHWARTZ: Objection, scope.

Q. And do you have any reason to disagree that that's the space available?

MR. SCHWARTZ: Objection, scope.

A. For this polymerase?

Q. Yeah.

A. Yeah, I -- I don't have any reason to disagree.

Q. And this is something that a person of ordinary skill in the art would be able to know from Pelletier; is that correct?

MR. SCHWARTZ: Objection,

DR. STEVEN MENCHEN, Ph.D.

scope.

A. So I discuss that in my -- in my --

Q. Look at your declaration if you need to discuss that.

A. Yeah, in my declaration. And if I could turn to that. So it's page 44 in the declaration -- and do you want me to answer your question?

Q. Yes, please.

A. Could you repeat the question?

Q. A person of skill in the art would know of the -- the 3.7 angstroms size of the space available within the active site from Pelletier to be 3.78 percent with available software, commercially available software?

MR. SCHWARTZ: Objection, scope.

A. I'd need the Pelletier article.

DR. STEVEN MENCHEN, Ph.D.

Q. I think it might be -- look at the immediate preceding document.

A. So I would dispute that.

Q. On what basis?

A. That -- the first reason is that Pelletier describes this pol-beta as -- from the standpoint of drug discovery for -- for HIV. So a POSA wouldn't be looking in this -- in this literature for polymerases.

And the second reason is that a POSA would never consider this polymerase to be a polymerase for sequencing SBS. And for that I turn to footnote 22. And in footnote 22 -- are you there?

Q. No.

A. Okay. I'll read it slowly. It's pretty long.

Q. If you need to read it, read it.

Are you done?

A. Oh. Sorry. I was going to

DR. STEVEN MENCHEN, Ph.D.

read it -- I was going to read it out loud.

Q. Please do, if you want to.

A. So according to footnote 22 "Pol-beta is so efficient in incorporating mismatched base pairs that it was originally questioned whether pol-beta utilizes a template at all during DNA polymerization. Fueling the debate was the observation that the only other polymerase sharing sequence similarity with pol-beta terminal and deoxy transferase (TDT) is not a template directed polymerase."

So a POSA would never consider evaluating data from a polymerase that wouldn't be ever considered for SBS sequencing or any sequencing.

Q. And did Ju use that polymerase for his analysis in -- on page 58 and 59?

A. Yes, he did.

Q. And was that irrational?

DR. STEVEN MENCHEN, Ph.D.
MR. SCHWARTZ: Objection, scope.
A. Yeah. I'm not going to evaluate that. I'm just going to --
Q. Do you have any explanation why Ju would perform an analysis based on an enzyme that nobody in their right mind would consider for sequencing?
MR. SCHWARTZ: Objection, scope.
A. Yeah. I mean I have not spoken to Ju about that.
Q. Do you think the data based on the analysis -- the data and analysis performed by Ju in this Exhibit 3 at page 58 and 59 is meaningful if it used that enzyme?
MR. SCHWARTZ: Objection, scope.
A. So that's not really the crux of my argument. The argument is whether a POSA would consider using the data.

DR. STEVEN MENCHEN, Ph.D.

Q. My question isn't that. My question is whether it's meaningful information?

A. I can't comment on that.

Q. Why not?

MR. SCHWARTZ: Objection to scope to all those questions. Just give me a chance to object Dr. Menchen.

THE WITNESS: Okay.

A. Because I'm -- I'm not a crystallographer and I'm not an expert on polymerases. So I can't really evaluate, yeah, that analysis myself.

Q. You are aware that DNA sequencing researchers looked at polymerase crystal structures to develop nucleotide analogs in the 1990s?

MR. SCHWARTZ: Objection, scope.

A. Yeah, I'm not familiar with any of that.

DR. STEVEN MENCHEN, Ph.D.

Q. Do you have -- is that an area of expertise of yours that you wouldn't even know if they did?

A. Excuse me?

Q. Would you know -- are you -- do you know one way or the other whether DNA researchers in a sequencing -- sequencing area looked at polymerase crystal structures to develop nucleotide analogs?

MR. SCHWARTZ: Objection, form. Objection, scope.

Q. In the 1990s.

A. I believe that there's one reference that's in my declaration and it refers to Welsch. I believe it's Exhibit 1023. But I would have to...

Q. Okay. If you turn back to page 59 of the prosecution history.

A. Okay.

Q. Do you see where Dr. Ju states the diameters of five -- "The diameters of five groups possibly

DR. STEVEN MENCHEN, Ph.D.

useful as 3'-oxygen capping groups for nucleotide analog." And then he identifies allyl, MOM, methylthiomethyl, azidomethyl and 2-nitrobenzyl.

Do you see that?

A. I see that.

Q. Do you have any reason to dispute Dr. Ju's testimony that there are five groups possibly useful as a 3'-oxygen capping groups for nucleotide analog?

MR. SCHWARTZ: Objection, scope. Objection, mischaracterizes the document.

A. Sir, can you show me where Ju states that there are five?

Q. It's -- I'm sorry if I didn't already. It's on page 59.

A. Yeah, I'm on 59.

Q. And do you see the first sentence of the first full paragraph?

A. Yeah, I see the first

DR. STEVEN MENCHEN, Ph.D.

sentence.

Q. All right. And you see that Dr. Ju identifies five groups possibly useful as 3'-oxygen capping groups for nucleotide analog?

MR. SCHWARTZ: Objection, scope. Objection, mischaracterizes the document.

A. Yeah, that -- that's not what he says.

Q. So you are denying that Ju says there are five groups possibly useful as 3'-oxygen capping groups for nucleotide analog, and if you do deny it, what's your basis?

MR. SCHWARTZ: Objection, scope. Objection, mischaracterizes the document. You are not reading the sentence.

MR. REINES: You're -- you're way over the line with your objections. You are coaching like crazy and this is a perfect example.

DR. STEVEN MENCHEN, Ph.D.
MR. SCHWARTZ: I can say that you are not reading the sentence.
MR. REINES: You can certainly not coach.
MR. SCHWARTZ: I'm not coaching.
MR. REINES: While you are misstating the evidence, all stuff, it's transparent. Hopefully anyone reading this transcript can see it themselves.
MR. SCHWARTZ: Okay.
A. So what the sentence says is "The diameters of five groups possibly useful as 3'-oxygen capping groups for a nucleotide analog, allyl, methoxy methyl, MOM, methylthiomethyl, azidomethyl and two nitrobenzyl whose structures are shown below were calculated."
Q. Okay. So will you agree with me now that you read it that Dr. Ju identifies five groups possibly useful as 3'-oxygen capping

DR. STEVEN MENCHEN, Ph.D.

groups for a nucleotide analog? Or do you still deny that?

MR. SCHWARTZ: Objection, scope. Objection, mischaracterizes the document.

A. Ju just -- he did calculations.

Q. Do you still deny it?

A. That what?

Q. That's what I want to memorialize. You deny that Ju identifies five groups as possibly useful as 3'-oxygen capping groups for nucleotide analog?

MR. SCHWARTZ: Same objections.

Q. In his Exhibit C, you and counsel I suppose.

A. What he identifies are the groups that he's going to do calculations on.

Q. And he defines that group as those that are possibly useful as 3'-oxygen capping groups for

DR. STEVEN MENCHEN, Ph.D.
nucleotide analog; is that correct?
MR. SCHWARTZ: Same objections.
A. Yeah, that's what he says. That's what he writes.
Q. Are you sure?
A. The diameters of five groups possibly useful as three -- yeah, that's what he says.
Q. And do you feel like you are mischaracterizing it when you say that?
A. Mischaracterizing what?
Q. The document.
A. No.
Q. Do you have any reason to dispute Dr. Ju's testimony that these five groups are possibly useful as 3'-oxygen capping groups for nucleotide analog?
MR. SCHWARTZ: Same objections.
A. Yeah, I haven't done -- obviously this isn't in my report.

DR. STEVEN MENCHEN, Ph.D.

I didn't do analysis of this.

Q. You cited the prosecution history and in there it has the inventors' analysis of the claimed inventions and so forth. So I think it's more than fair grounds for me to be asking you questions and more than fair grounds for you to be -- assume to be knowledgeable about it. So that's the basis -- my basis for going forward. You deserve a response and that's the response.

Do you have any reason to dispute that these five groups are possibly useful candidates as 3'-oxygen capping groups for nucleotide analog?

MR. SCHWARTZ: Same objections.

A. I don't dispute that Ju said that.

Q. That's a --

A. I do dispute that -- that all of these five compounds are

DR. STEVEN MENCHEN, Ph.D.

possible candidates.

Q. And which ones do you dispute in particular? All of them or just a subset?

A. The only one that -- sorry. The only one that there's data for is the nitrobenzyl -- well, okay. I take that back. The only two that there are data for are the -- actually that's wrong too. The only one that there is data for is the two nitrobenzyl. In fact -- okay. I have to rephrase my answer. I apologize.

Q. Sure.

A. So if you go to --

Q. Let me repeat the question just so we have a little bit of a cleaner record.

A. Okay.

Q. Of the five groups that Dr. Ju identifies as possibly uses full as 3'-oxygen capping groups for a nucleotide analog in his

DR. STEVEN MENCHEN, Ph.D.

declaration which ones do you agree are possibly useful?

MR. SCHWARTZ: Objection to scope. Objection, mischaracterizes the document. I'll maintain that objection every time you ask those questions.

MR. REINES: It's the speaking that's the problem.

MR. SCHWARTZ: Okay, well.

A. So I will say that there are -- there's data for none of these before 2000. So there's no reason to select any of them.

Q. Is data necessary in order to establish that a 3'-oxygen capping group will work for its intended purpose?

A. If you are going to make a selection, yeah, you need some data.

Q. And you know that the conclusion is -- well, let me ask you the 2-nitrobenzyl, was the -- the data showed that it would work,

DR. STEVEN MENCHEN, Ph.D.

it would incorporate efficiently and work or not?

A. There's no data on the C compound which is shown here.

Q. And you understand that Dr. Ju's testimony was that the allyl, MOM, methylthiomethyl and azidomethyl groups would fit but that the nitrobenzyl would not?

MR. SCHWARTZ: Objection to scope.

Q. Correct?

A. I believe that's what he said.

Q. Do you have any reason to disagree with that?

MR. SCHWARTZ: Objection, scope.

A. With that statement?

Q. Yeah.

A. I can't really -- so I can't agree or disagree with that statement.

Q. Okay.

DR. STEVEN MENCHEN, Ph.D.

A. I don't have any -- I'm not a crystallographer.

Q. And that the fact that Ju has it in a declaration of his, is that a basis -- would you assume that it's true if he put it in there?

MR. SCHWARTZ: Objection, scope.

A. I mean those are his opinions.

Q. Is there any disclosure of thio methylthio -- methylthiomethyl in the Ju patent?

MR. SCHWARTZ: Objection, scope.

A. I didn't look at the Ju patent for anything except for the allyl -- or the propenyl group.

Q. Why did you review the Ju patent to analyze the allyl group as a potential capping group?

A. I was asked to.

Q. For what purpose?

DR. STEVEN MENCHEN, Ph.D.

A. To determine --

MR. SCHWARTZ: Again, to the extent that your disclosure of -- to answer counsel's question requires that you divulge conversations with attorneys, I instruct you not to answer.

THE WITNESS: Okay.

Q. Let me ask you this way. Based on the instruction from counsel to review the Ju patent for its disclosure on allyl capping group, when you executed your work in response to that, what were you looking for with respect to the allyl capping group?

A. I was just looking for his statements about the allyl capping group.

Q. For what purpose?

A. To see if -- what was taught, you know, in the speci- -- what was in the specifications.

Q. Based on your investigation

DR. STEVEN MENCHEN, Ph.D.

of the Ju patents to determine what was taught about the allyl capping group did you determine whether or not that would work for the claimed inventions in the Ju patents?

MR. SCHWARTZ: Objection, form.

A. I wasn't asked to make a determination like that. I was just asked to read through the patent and look at the statements.

Q. You looked at the Ju patents and you specifically focused primarily on what was disclosed about allyl capping groups to see what was taught. Do you recall that?

A. That's right.

Q. And was it taught whether -- how allyl groups could be cleaved?

A. Excuse me?

Q. Was it taught how allyl groups could be cleaved?

DR. STEVEN MENCHEN, Ph.D.
MR. SCHWARTZ: Objection, scope.
A. I didn't -- he suggested a cleavage method.
Q. What did Ju teach about the incorporation efficiency of the allyl groups?
MR. SCHWARTZ: Objection, form.
A. He taught that they should be incorporated efficiently.
Q. Did he teach how that should be done?
MR. SCHWARTZ: Objection, scope.
A. Yeah, I don't -- I don't remember seeing that.
Q. Did Ju -- do you believe that a person of ordinary skill in the art following the Ju disclosure that you were investigating would be able to have the allyl capping group efficiently incorporated?
MR. SCHWARTZ: Objection,

DR. STEVEN MENCHEN, Ph.D.

scope. Objection, form.

A. Yeah, could you give me a time frame?

Q. In 2000 would a person of ordinary skill in the art with the Ju patent in front of them be able to use the allyl capping group for efficient incorporation? You said he taught to use them efficiently.

A. That's right.

Q. Would they be able to do that --

MR. SCHWARTZ: Objection --

Q. -- a person of ordinary skill in the art?

MR. SCHWARTZ: Objection, scope. Objection, form.

A. Yeah, I don't know.

Q. Weren't you -- weren't you -- you were looking to see what was taught about the allyl capping group in Ju, right?

THE WITNESS: That's right.

Q. So how come you don't know?

DR. STEVEN MENCHEN, Ph.D.

A. Because I don't know what a POSA would do with that exactly.

Q. Do you believe based on your work in this case that you have a solid understanding of what a person of ordinary skill in the art would do in terms of selecting polymerases for sequencing by synthesis?

MR. SCHWARTZ: Objection, scope.

A. Yeah, I wasn't asked to cover that or to evaluate that.

Q. Do you have an opinion regarding whether a person of ordinary skill in the art, what capping groups they would select for a sequencing by synthesis process?

MR. SCHWARTZ: Objection to scope. Objection, form.

A. No. I don't -- I can't -- I can't really say what that would be.

Q. Do you have an opinion as

DR. STEVEN MENCHEN, Ph.D.
to -- well, actually let me move to -- if you could open up your declaration, which is Exhibit 2114.
Actually, just one more question to follow up. Do you have an opinion as to what preferences a person of ordinary skill in the art would have in 2000 as to capping groups for sequencing by synthesis?
MR. SCHWARTZ: Objection, scope.
A. I thought I answered that.
Q. What's that? Do you have any opinions on that?
A. Yeah, no, I don't have any opinions on that.
Q. Let me -- one second, sorry.
Do you have an opinion as to what the reasonable expectation of success a person of ordinary skill in the art would have in the year 2000 with an allyl group in terms of using that as a capping group in the

DR. STEVEN MENCHEN, Ph.D.

context of the Ju claimed inventions?

A. Yes, I have an opinion on that and it is covered in my declaration.

Q. Would a person of ordinary skill in the art in 2000 be motivated to attempt to develop a sequencing by synthesis system?

MR. SCHWARTZ: Objection, scope.

A. I would say there are a lot of people doing that, trying to develop it.

Q. And what capping groups would persons of ordinary skill in the art have been motivated to pursue in 2000?

A. I don't know.

Q. What polymerases would they -- would a person of ordinary skill in the art have been motivated to pursue?

A. Yeah, I don't know that

DR. STEVEN MENCHEN, Ph.D.

either.

Q. Would a person of ordinary skill in the art have been motivated to use azidomethyl as a capping group in 2000?

MR. SCHWARTZ: Objection, scope.

A. Yeah. I don't know anything about that. That --

Q. Would a person of ordinary skill in the art have been motivated -- do you know one way or the other whether a person of ordinary skill in the art would have been motivated to attempt to use the five different blocking groups identified by Dr. Ju in his declaration?

MR. SCHWARTZ: Objection --

Q. For sequencing by synthesis in -- in the year 2000?

MR. SCHWARTZ: Objection, scope.

Q. Without the benefit of the

DR. STEVEN MENCHEN, Ph.D.

patents.

A. Sure. The only thing that there was data on was Metzker. So if you look at Metzker, they wouldn't use -- they wouldn't be motivated to use allyl. However, if you look at Metzker the only group that was -- showed positive results was the -- the nitrobenzyl.

Q. Was it your -- is it your opinion that before Metzker in 1994 people would have been motivated to use allyl as a blocking group?

MR. SCHWARTZ: Objection, scope.

A. Yeah, I have no idea.

Q. What is the role of the motivation to combine in the obviousness analysis?

MR. SCHWARTZ: Objection, legal conclusion. Objection, scope.

A. The role of the?

Q. Motivation to combine.

DR. STEVEN MENCHEN, Ph.D.

A. Motivation to combine?

MR. SCHWARTZ: Same objections.

A. And what's the question?

Q. What is the role of the motivation to combine in the obviousness analysis you performed?

A. Yeah, that's a -- a legal term I'm not -- I'm not familiar with.

Q. What is the role of reasonable expectation of success in the obviousness analysis that you applied?

MR. SCHWARTZ: Same objections.

A. Those are legal terms.

Q. Are you familiar with them?

A. Which?

Q. Reasonable expectation for success is my question.

A. I'm familiar with reasonable expectation of success.

Q. And what was the role of

DR. STEVEN MENCHEN, Ph.D.

reasonable expectation of success in your analysis?

MR. SCHWARTZ: Same objections.

A. Could you ask that in a different way.

Q. You say you are familiar with reasonable expectation of success, correct?

A. That's right.

Q. How did you apply that in this case?

A. I -- I looked -- so there were two things that I looked at, the viability of the propenyl group as a substrate and the viability of being able to cleave -- cleave the propenyl group to release the 3'-hydroxyl.

Q. And whether or not the allyl group disclosed in Ju would actually -- was viable or not, that's something you don't have an opinion on, right, you've been

DR. STEVEN MENCHEN, Ph.D.

through that?

Whether or not the allyl would work as a capping group for sequencing by synthesis that's something you don't have an opinion on? I think we have been through that a couple times.

MR. SCHWARTZ: Objection. Mischaracterizes the witness's testimony.

A. Yeah, I think that was based on my reading of the -- of the Ju patent. However, looking -- so this was clearly looking at the -- at the prior art, Metzker and the cleavage conditions based on the -- the references supplied by Illumina and when I -- and when I combine those. When I looked at those individually there's no reasonable expectation of success.

Q. As to whether or not allyl actually works as a capping group for sequencing by synthesis under

DR. STEVEN MENCHEN, Ph.D.

the fundamental requirements disclosed in Ju, do you have an opinion on that? I'm talking about actually working.

MR. SCHWARTZ: Objection, scope.

A. So it was under the requirements of Dower and Tsien, that was the way I did the analysis.

Q. So let me ask the question again. Under the requirements of Dower and Tsien, does allyl work as a capping group in sequencing by synthesis actually, not what you think people might have gathered from prior art but in terms of the technical truth?

A. The technical truth?

Q. Yes.

A. I mean it all comes from the prior art.

Q. Okay. So what's your answer. Let's get it on the record.

A. My ans- -- my answer is

DR. STEVEN MENCHEN, Ph.D.

that there was no reasonable expectation of success using that group for sequencing by synthesis.

Q. That's not responsive. I'm not asking for what you think people might have thought. I'm asking you for whether in fact allyl would work for sequencing by synthesis as a capping group?

A. Prior -- prior to 2000?

Q. It's just -- it's just a technical truth. I don't know why -- obviously I'm not communicating.

MR. SCHWARTZ: Objection to form.

A. I mean the -- the way I did the analysis was prior to 2000 and that's the only literature that I looked at prior to 2000. So that's what I'm basing my opinion on.

Q. Do you know if -- whether someone if they actually performed an experiment using allyl as a

DR. STEVEN MENCHEN, Ph.D.

capping group, whether that would work or not, actual not expectations, actualities? Do you understand the difference?

A. Repeat -- repeat the question.

Q. Sure. I want you to focus not to expectations but on actualities. If someone performed an experiment using allyl as a capping group, do you believe that it would work for successful sequencing by synthesis?

MR. SCHWARTZ: Objection, form.

A. Prior to 2000? I really don't get the question because after 2000 it was demonstrated so. Yeah, I -- I don't understand the question at all.

Q. At some point it was demonstrated that allyl would work as a capping group for the claimed inventions of the Ju patents,

DR. STEVEN MENCHEN, Ph.D.

correct?

A. That's -- that's correct.

MR. REINES: Okay. I think we are a little after 5:00. Unless someone has a problem stopping now why don't we stop now. Does that work? Thank you.

THE WITNESS: Oh, that's it.

MR. REINES: Well, until tomorrow.

THE WITNESS: That's too bad. Thanks.

THE VIDEOGRAPHER: We are going off the record at 5:13 p.m. This concludes today's deposition of Dr. Steven Menchen. The total number of media units used was seven and will be retained by Veritext. We off the record.

(Time noted: 5:13 p.m.)

STATE OF NEW YORK)
) :ss
COUNTY OF NEW YORK)

I, STEVEN M. MENCHEN, PH.D., the witness herein, having read the foregoing testimony of the pages of this deposition, do hereby certify it to be a true and correct transcript, subject to the corrections, if any, shown on the attached page.

_____
STEVEN M. MENCHEN, PH.D.

Sworn and subscribed to before me, this _____ day of _____, 2019.

_____
Notary Public

STATE OF NEW YORK)
ss.:
COUNTY OF NEW YORK)

I, ERICA L. RUGGIERI, RPR and a Notary Public within and for the State of New York, do hereby certify:

That I reported the proceedings in the within-entitled matter, and that the within transcript is a true record of such proceedings.

I further certify that I am not related by blood or marriage, to any of the parties in this matter and that I am in no way interested in the outcome of this matter.

IN WITNESS WHEREOF, I have hereunto set my hand this 16th day of January, 2019.

ERICA L. RUGGIERI, RPR, CSR, CLR

---------- I N D E X ----------

WITNESS	PAGE
STEVEN M. MENCHEN, PH.D.	
By: Mr. Reines	6

---------- EXHIBITS ----------

ILLUMINA	FOR I.D.
Exhibit 1091, U.S. Patent No. 6,111,116	58
Exhibit 1092, '884 patent	152

*** EXHIBITS ATTACHED ***

INSTRUCTIONS TO WITNESS

Please read your deposition over carefully and make any necessary corrections. You should state the reason in the appropriate space on the errata sheet for any corrections that are made.

After doing so, please sign the errata sheet and date it.

You are signing same subject to the changes you have noted on the errata sheet, which will be attached to your deposition.

It is imperative that you return the original errata sheet to the deposing attorney within thirty (30) days of receipt of the deposition transcript by you. If you fail to do so, the deposition transcript may be deemed to be accurate and may be used in court.

E R R A T A

I wish to make the following changes, for the following reasons:

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STEVEN M. MENCHEN, PH.D. DATE

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&

& 3:8,19 5:25

1

1 106:13 139:21 143:22 144:9,13 145:13 146:4,20 147:6,14 148:12 148:20 149:6,19 150:11,14,15,18 150:22 172:18 173:2,4,19,23,25 174:25 175:7 176:10,17 180:18 183:23 184:14 195:3,12,13,14 196:15 197:13,15 198:7 199:6,20 202:17,19 222:7 223:17 224:19 248:20 249:22 250:23 251:7
1,009 16:3
10 155:16,20 163:2 163:6,17 210:2
100 124:7 125:16 125:18,19,21,24 126:5 228:4 230:8
1001 150:9
10076 242:24
10104 3:13
1016 190:21 219:24
102 184:17
1021 33:6
1023 271:18
1037 124:25
1075 46:13 100:6 112:21 232:13
1076 242:25,25 263:14
1091 58:10 300:9
1092 152:14,17 300:11
10:04 43:3
10:21 43:9
11 156:15
116 64:10 65:14 68:6,17,21 69:11 71:25 72:9 76:2,8 78:19 83:7,15 84:14 87:15 96:4 96:21 97:6,18 98:3 99:23 153:14 153:25 154:18,25
11:00 183:19
11:11 94:20
11:28 95:2
12 112:10,11,19,25 196:5,11 215:11 232:18 233:4
120 33:6
12790 3:5
1290 2:8 3:13 5:2
12:17 135:13,16
12:59 136:3,8
13 139:22 196:5,12 215:11
14 1:19 2:2 4:4 126:10,20 127:2,6 129:17 130:15,20 196:5,12 206:4,5 206:11,21 210:13 210:14,14 211:9 215:11 234:16,18 235:2
15 131:21 263:18 263:20,25 264:4,6 264:14,21
152 300:11
16 155:20
16th 299:21
17 107:18 195:2,4 195:9,19 245:13 245:15
18 107:2 108:17 200:17 206:21 245:14
1985 31:7
1989 40:3
1990s 156:22 218:24 219:3,6,10 226:5,6 270:21 271:14
1994 35:8,15,24 37:13 38:2,7,14 39:10 116:14,20 116:21,24 156:18 164:25 166:24 167:5 188:15,22 190:22 191:10 195:15 197:24 211:5 219:23 290:12
1997-1998 60:17
1998 65:15,15 66:25 72:2,8 76:8 78:20 83:12,16 84:15 85:4 90:18 97:8 98:18 99:14 210:7 211:19 212:15
1998-1999 90:8 91:10 92:7
1999 90:18 115:5 156:5 157:21 160:16
1:54 181:20

2

2 40:6 46:5 60:9 66:9 81:15,17,18 85:24 86:7,9 155:24 183:23 184:23,25 185:3,4 190:24 192:3,13 193:24 194:11,18 206:4,4,12,21 210:3,15 211:8 216:2 220:3,16 230:15 231:17 272:6 279:24
2.5 223:18
20 9:10 107:2 113:16,17 114:7,8 114:16 115:13,24 115:24 131:18,19 136:13 168:5 193:12 222:12 227:10 228:3,5,5 228:14,16,22 243:25
2000 42:20 48:19 117:10 118:6,22 120:13 132:25 134:9,17 137:14 138:25 142:25 145:20 147:18 148:19 151:3 168:21 188:21 190:11 217:3 236:6 237:4,18 239:19 240:19 279:14 285:5 287:9,24 288:8,19 289:6,22 295:11 295:19,21 296:17 296:19
2006 20:16 23:11 23:12 24:14 146:14 148:13 239:17
2006-2007 24:25 37:17 218:23

201 3:9 302:23
2015 30:25
2018 8:23 9:4
2018-00291 4:22
2019 1:19 2:2 4:4 298:22 299:22
2084 187:13
21 136:12 139:21 141:7 255:13,15 255:20 256:3,11 257:5,9
2108 13:25 40:9,17 40:19 41:6
2114 8:14 9:24 85:20 182:6 287:4
2115 183:8
22 130:12 267:17 267:18 268:5
24 121:14 156:17
25 50:18,19,20,24 59:3 100:9,12 156:17 202:18 203:2
250 203:13 216:13 216:19 217:3,9,25 217:25 218:6 222:11,12,22 228:23 229:6 230:18 231:3
25th 8:23 9:4
26 112:8,17,25 114:14 115:14,24 130:11 131:9 232:14
29 112:11,11 113:2 121:15 186:10,12 232:18 233:4
2:12 182:2
2:58 219:14

3

3 60:9,24 61:9 63:19 64:12 65:3 65:25 67:24 68:9 69:19,24 70:15 71:8 72:4,11 74:23 76:11 78:22 79:9 80:25 81:17 81:18 82:5,16 83:6,19 84:17 85:4 87:4,13 90:10,20 91:9 92:9 93:18 95:5 96:24 97:5 99:13 99:22 102:2,8 105:23 107:2,18 108:17 109:9 110:18 115:6 116:7,16 117:2,12 118:5,20,24 119:20,24 120:18 131:22,24 133:20 144:15 145:12 155:24 156:8 162:9,20 163:16 164:3,20 165:14 166:3,19 167:7 189:7,17 191:17 191:25 196:4,6 201:23 202:4,7 233:21 234:6 245:24 258:19 259:19 265:4 269:18 272:2,12 273:5,14 274:16 274:25 275:14,25 276:20 277:17 278:24 279:17 292:20
3'o 229:3
3.7 265:6 266:16
3.78 266:19
30 112:11 226:9 263:16,17 301:19
31 263:17 264:2
318 4:22
322 4:22
33 126:6
34 150:16
35 171:16
385 4:22
3:21 219:20
3b 196:4,7,11 198:25 204:15,16 204:18,25 205:14 205:21 215:10,13

4

4 106:8 201:12 221:23 222:4,22 223:10 226:11 256:24
40 59:10
41 102:10 107:8
4263 190:23
43 155:25 163:5,22
44 107:8 156:2 163:22 266:9
4:15 263:2
4:32 263:8
4a 223:19 224:4,16 224:23
4b 201:24 203:16 204:5,8 212:18 224:3,4 228:8
4c 227:8

5

5 58:18,20 87:14 87:20,25 95:15 97:18 202:17,21 222:9,14 223:18 223:20 225:20 256:24
50/50 202:23
500 170:12 226:12 227:3,12,19 228:4 228:9,23 229:9 231:23 232:5
5025 299:24
51 95:17 186:13,16 187:13
54 107:3,19 108:17
55 59:14,19 60:2
58 87:24,25 264:11 268:23 269:18 300:9
59 264:11 268:23 269:18 271:21 272:20,21
5:00 297:5
5:13 297:15,21

6

6 40:5 256:24 300:5
6,111,116 58:9,11 300:10
6.1 183:15,16
65 141:7

7

7 41:20 50:18 51:8 100:9 201:25 202:2,19 227:8 228:15
76 182:7
768 6:15
797 4:22

8

8 202:15,21 203:16 203:20 228:15
800 228:17

852 150:10,18,22
884 152:15,17 154:18,24 155:6 163:25 300:11

9

9 202:2,2 203:22 203:23 204:4 227:8 228:15 234:2
92130-2008 3:5
93 122:8,21 123:11 123:17 124:11,19
94065-1175 3:9
98 140:14,15
985 46:14 100:4 114:11 136:13 143:22 146:7 147:14 148:12,20 149:6,18 171:11 172:19 173:11 174:25 175:8 176:10,18 239:22 240:14 248:20 249:23 250:23 251:7 252:25 254:23
99 126:4
9:21 1:20 2:3 4:3

a

a.m. 1:20 2:3 4:3 43:3,9 94:20 95:2
aa 259:8
abi 17:25
ability 58:3 79:3
able 130:24 250:22 265:23 284:23 285:7,12 292:18
absence 160:23
absolutely 74:9
ac 259:8
accept 244:22
accommodate 265:4
accomplished 79:21
accord 15:17
accurate 12:5 301:23
accurately 139:8 224:15
acetylenes 185:22
acid 61:21
acknowledge 87:9 109:14
acknowledgment 121:11
acquisition 21:20
acting 174:3
active 202:20 265:3 266:18
activities 141:17
actual 126:15 127:18 195:15 296:3
actualities 296:4 296:10
add 33:2 223:5
adding 98:24
address 6:11,13 162:16 250:15
admit 54:20 63:8 231:2
advantage 66:14 66:17
affect 11:8
afternoon 209:12
ag 259:8
ago 8:11
agree 4:14 69:15 69:22 115:4,17 117:9,21 157:21 187:25 222:20 274:22 279:2 280:23
agreed 69:16 158:4
agreement 6:18,23
agreements 26:5
agrees 135:9
ahead 189:25 226:24 231:18
alcohols 130:24
alkamino 89:14,17
alkoxy 63:23,25 88:15
alloc 246:4,5 248:4 248:6
allow 15:15 259:20
allows 169:21
allyl 44:7,11 45:4 46:7,17,21 47:3,10 47:14,17 48:8,20 49:15 50:2,8,14 51:12,15,17,19,23 51:24 52:4,5,14,17 52:21 53:17 54:9 55:3,6 90:7 100:14,19,23 101:2 103:9,12 104:5,8,18 105:11 109:11 110:5,9 111:3 113:11 114:22 115:5 116:6,15 117:2,11 118:4 119:23 120:16 121:4,20 122:7,19 123:9 124:9,17 127:11 127:19 128:7,23 129:8,25 131:10 132:6,14 133:3,19 134:8,21 141:13 141:22 142:13 143:15 144:14,16 176:16 182:13 188:7,16,24 189:2 189:6,12,16 190:5 190:13 191:11,24 193:20 194:8,13 194:20 220:5,9 221:13,15,19 232:20 233:6 234:4 235:16,22 236:25 239:7 245:18,20,23 246:22 247:13 248:17 249:21 250:21 251:5,19 252:2,17,23 253:16 254:14,25 260:20 261:23 262:9 272:4 274:18 280:8 281:20,22 282:13 282:17,19 283:3 283:16,21,24 284:8,23 285:8,22 287:24 290:7,14 292:22 293:3,23 294:13 295:8,25 296:11,23
allyloxy 43:12 44:4,6,12,16 45:5 45:19,23 46:4,8,18 47:4,5,11,16,19,22 48:9,11,16,21 49:6 50:4,5,9 53:18 54:10,23 55:4,7,9 55:19,22 60:14

63:19,24 64:2,5,11 66:3 67:11,23 68:8 69:4,17,23 70:13 72:3,12 74:11,22 76:5,10 78:21 79:7 82:4 82:15 83:5,17 84:16 85:3 87:3 90:4,11,21 92:8 93:3,17 155:25 156:6 162:19 163:14 164:2,18 165:3,8,13 166:2 166:18 167:6
allyloxycarbonyl 247:25
allyloxys 55:14,16 60:19,23 61:8 91:8 162:8
allyls 246:3
americas 2:8 3:13 5:3
amino 89:14,17
amount 197:4,15 197:21 198:2,3,5 199:8,22 216:21 216:24 217:4 218:2,7,8 222:19 222:21
amplitaq 201:25 202:16 226:23,23 227:7,7,12
amv 196:19,20
analog 68:19 70:8 79:23 80:6 97:20 97:22 117:5,7 177:13 272:3,13 273:6,15 274:17 275:2,15 276:2,21 277:18 278:25
analogs 55:13 59:6 59:7,13,13,16,23 60:3,6 62:20,20 63:6,13 77:19,25 97:17,23,24 98:15 109:5 112:15 113:4,8,25 117:6 131:23 132:2,14 133:3,19 155:17 155:19 233:17,22 258:16,24 259:8 270:20 271:11
analysis 159:15 212:14 264:13 265:8 268:22 269:7,16,17 270:15 277:2,5 290:20 291:8,14 292:3 294:10 295:19
analyze 281:22
analyzed 151:22
angstroms 265:6 266:17
anneal 260:11
ans 294:25
answer 15:16 22:2 29:14 46:25 48:8 53:14,22,23 67:19 83:24 100:2 105:17 123:2,5 139:7 144:25 151:16,23 153:5,7 153:10 154:9 159:12 166:6,16 171:4,7,9,10 172:9 224:14 244:19 257:16 260:14 266:10 278:14 282:5,8 294:24,25
answered 103:17 108:3 149:9 181:5 214:16 216:8 225:18 240:2 249:25 257:24 287:13
answering 54:4
answers 151:8
anybody 23:5
anyway 54:20
apologize 278:15
appeal 1:3
appearances 5:9
application 57:15 66:20 99:15 106:18 109:4,25 119:23 156:5 160:2 223:16
applications 62:3 127:12 160:6
applied 7:18 17:19 18:13 19:4,13 21:21 29:25 30:19 31:5,8,24 36:22 38:16 238:3 241:14 242:7 291:15
apply 292:12
appreciate 15:19
approach 109:3 109:24 136:16
appropriate 11:17 226:4 301:7
approximately 9:13,14 265:6
aqueous 137:19 138:14 260:6
area 28:13 77:19 77:25 96:23 200:11 271:3,9
argument 55:10 192:11 269:23,23
art 29:7 30:18 34:7,12,13,14 36:8 42:20 48:18 63:11 65:14 68:6,16 70:2,7,19 71:25 72:8 74:12 76:2,7 78:19 83:15 84:14 84:25 85:8 86:5 86:13,23 90:15 92:6 93:16 94:10 97:7,13,20 98:18 99:4,8,16,25 102:22 105:24 107:4,9,11,23 108:5,15 109:17 109:20 110:19,25 114:23 118:12 120:13,15 121:2 122:4 126:16 127:7,8 131:7 132:4,25 133:16 134:20 138:25 139:10,16,18 142:11,22 149:23 157:4,22 158:18 160:19 168:19 175:7,14,24 176:15 188:14,21 190:11 217:3 220:8 229:16 232:4,17 233:3,12 235:15,20 236:6 240:12 251:16,21 254:21 257:22 258:11 259:16,17 260:4,13,19 261:13 262:7 265:23 266:16 284:21 285:6,16

286:7,17 287:8,23 288:8,18,23 289:4 289:12,15 293:16 294:17,22
article 35:8,15,15 35:25 38:14 39:2 39:7,10 156:18,22 162:11,18 164:11 164:15 166:24 167:6 190:22 232:8 266:25
articles 27:12 33:7
aside 147:20 194:18 249:15
asked 25:17 29:19 47:10 59:24 103:16 108:2 119:9,13,17 120:7 127:13 132:18,19 133:9,21 141:16 149:9 173:9 179:3 179:16,17,20 180:22 181:5 194:7 214:16 216:8 225:17 229:23 240:2 249:25 254:10 257:24 261:20 281:24 283:9,11 286:13
asking 11:21 24:3 30:12 31:19 51:5 51:22 59:20 75:18 105:5 119:15 145:21 147:5 148:9 163:12 173:22 192:11 221:11 224:9 237:12 244:16 247:5 250:9 251:3 254:2 255:21 277:8 295:6,7
aspect 11:23
assay 203:12 214:6 216:12
assigned 241:8 242:15
assignment 8:5 122:18 143:20 144:12 244:7,11
assume 11:3,25 25:5 72:2,11 76:3 76:9 84:15 138:8 207:6 229:20,23 245:23,25 277:10 281:6
asterisk 213:19,24 214:14 215:14 216:2
atlantic 183:5
atmosphere 184:22,24 185:2
atom 43:20
atoms 111:25 112:5 231:12
attached 298:13 300:15 301:14
attempt 58:4 288:9 289:16
attempted 68:21
attempting 96:22 108:16,20
attention 18:23 20:5 182:5 247:24
attorney 301:18
attorneys 3:4,12 153:9 244:17 282:7
audio 4:11,12
availability 258:15
available 265:2,14 266:18,20,21
avenue 2:8 3:13 5:3
aware 17:11,17,21 17:24 19:19,25 20:2,7 22:19 26:19,21 33:14,18 35:2,4,7 127:24 128:5 149:14 206:19 239:5 252:6,9 270:17
awareness 25:18 29:6,23
azidomethyl 272:5 274:19 280:9 289:5

b

b 123:23 196:8 227:18
back 23:10 33:4 43:7 68:19 76:5 94:24 95:7 100:4 100:8 109:19 126:19 130:10 136:6 145:7 162:8 181:24 182:5 193:22,22 219:18 228:25 229:3 230:19 232:11 234:10 235:12 263:6 271:20 278:9
background 9:25 10:7 106:13,19 108:6,22 142:4
backup 113:21,22
bad 201:13 207:17 216:11,17 297:12
band 202:13,14 203:5,7 210:16,17 210:21,25 211:3,9 211:11 212:23
bands 196:25 197:10,11 227:14
base 16:15 59:23 197:2 201:3 241:17 268:7
based 26:2 49:21 51:25 53:4 59:8 72:12 74:24 75:12 76:12 78:23 79:2 91:6,17 92:6 117:23 127:16,22 133:6,6,7,16 141:23 143:10 178:2 179:4 201:5 206:23 208:18 216:24 248:13 249:17 252:5 269:8,15 282:11 282:25 286:4 293:13,17
basic 11:4 133:7 133:17
basically 107:14 185:19 196:2 207:3 210:8
basing 74:13 217:13 295:22
basis 37:23 101:20 151:17 152:9 242:10 247:6,9,10 249:5 250:4,8 267:5 273:16 277:11,11 281:6
beckman 7:9
began 36:16
beginning 42:14 238:13
behalf 5:11,13

belief 100:22 206:25
believe 35:11 37:23 38:4,9,23 52:3 65:10 71:17 75:24 76:6 82:14 83:3 99:12,21 118:2 120:3 158:21 187:3 190:4 191:9 248:9 271:15,17 280:14 284:19 286:4 296:12
believed 70:13 79:6 159:25
benefit 289:25
benson 58:14 75:2 154:14 158:22
best 8:7 9:8 12:5 15:15 24:23 41:14 46:25 58:3 86:16 91:14,16 92:8,14 92:16,18 93:10,13 93:22 94:3 172:17 172:25
beta 267:8 268:6,9 268:14
beyond 7:4 79:16 101:19 194:17 208:15 218:14 245:5
bio 7:13
biosystems 7:18 17:19 18:14 19:5 19:13 21:21 30:2 30:19 31:5,9,24 36:23 38:16 238:3
birch 3:20 5:14,14
bit 170:14 197:8 262:19 278:19
blocking 289:17 290:14
blood 299:16
board 1:3 118:2
bolded 187:20,22
bond 66:8
bonds 66:10,15 95:6,13,20,21,24
book 183:10,12,13
bottom 51:2 100:15 136:14 226:11 245:15
bound 30:11,13
brackets 101:8
break 42:24 94:18 181:18 219:12 258:12 262:22
bring 25:16
broadly 190:11 191:10
bunch 191:2,4
butene 91:23
butenyl 93:6
butoxy 64:4 88:25 89:6 91:20

c

c 3:2 6:4 131:12 136:4 226:20,21 243:23 245:6 246:6,12 248:7 264:20 275:18 280:4
calculated 274:21
calculations 275:8 275:22
california 3:5,9 6:16
call 43:23 44:7 48:15 51:24 89:21 123:19,23,25 203:4,6 211:2,10 261:3
called 6:5 19:9 66:3 95:13 212:20
calling 49:15,19 87:24 212:22 220:21
calls 51:18,23 189:10,12
camino 3:5
candidate 64:17 64:20 67:11,24 69:18,24 70:14 71:5 72:4,10,24 73:7,15,25 74:14 74:22 75:10 76:10 78:21 79:7 83:5 83:18 87:3,13 95:4 99:12,21 156:7 162:20 163:15 164:3,19 165:14 166:2 191:25
candidates 65:7,9 65:17 66:4 70:22 71:14 76:4 90:10 90:20 91:9,13,14 91:16 92:9,14 93:11,13 95:24 97:4 155:23 162:9 192:7 240:6 277:16 278:2
cap 102:13 104:8 111:11 117:2,12 118:20 119:24 132:6 134:4 234:5 234:6 258:18
capable 160:12 240:23
capped 109:9 131:22,25 191:2 196:13,14,17 197:9 218:18 233:21 265:5
capping 60:24 104:4,6,15,19 105:9,11 115:6 116:7,16 118:4 119:19 138:2,15 139:12 142:24 144:14 145:11 146:2,19 147:12 147:24 148:10,17 149:6,18 150:21 162:21 166:19 167:7 193:25 194:3 240:14 245:18 246:23 247:14 248:18 251:8 254:14 258:18 259:18 260:20 261:4,24 262:10 272:2,12 273:5,14 274:16 274:25 275:14,25 276:20 277:17 278:24 279:18 281:23 282:13,17 282:19 283:3,16 284:23 285:8,22 286:18 287:9,25 288:16 289:5 293:4,24 294:14 295:10 296:2,12 296:24
caps 233:16 239:7
capture 99:3
carbon 43:20
careful 29:20
carefully 200:13 301:5
cartoon 195:17,18 195:24,25 200:17

206:4,12,21 210:3 210:15 211:8
case 7:9,13 16:20 52:3 53:5 144:8 179:5 248:14 249:18 253:14 255:23 256:7 286:5 292:13
catalyst 184:19 186:2
caution 67:15
cellphones 4:8
certain 207:17
certainly 32:5 129:19 274:4
certify 298:9 299:9,15
ch2 109:12
ch2ch 109:11
ch2och3 109:11
chain 109:12 235:7
challenge 249:6 250:9
chance 270:9
change 205:16 227:17 302:9,11 302:13,15,17
changes 301:13 302:5
channel 206:20
characterization 122:12,22 127:6
characterizing 23:22 49:2 124:20 158:17
checked 141:4
chemical 16:14 73:7 87:18 88:7,8 88:11,13,16 89:12 100:19 101:9 102:24 103:13 110:5,10 111:6 118:14 121:4,19 147:22 171:19 240:23 258:17
chemically 109:9 111:14 120:17 130:13 171:18 173:25 234:15 236:24 240:23
chemist 77:12 107:12 130:23
chemistries 65:25 75:11
chemistry 43:18 43:19 65:5 66:3 72:25 73:15 74:2 74:24 79:10,23 80:7 81:12 93:23 97:20 118:22 123:22 134:8,20 155:3 156:9 185:20 191:12
chen 3:21 6:2
chloride 182:14,16
circumvent 186:19,22,25 187:6,9 192:22
citation 10:13
citations 130:19
cite 161:25 211:22
cited 10:10 13:8 13:10 157:8,17 277:3
cites 130:15
citing 156:25 160:18
city 1:9 4:21
claim 143:22 144:9,13 145:13 146:4,20 147:6,14 148:12,20 149:6 149:19 150:11,14 150:15,18,22 172:18 173:2,4,19 173:23,25 174:9 174:25 175:7 176:10,17 180:11 180:18 181:2,13 248:20 249:22 250:23 251:7
claimed 235:23 239:8,21 240:15 247:16 252:24 254:8 277:5 283:5 288:2 296:24
claims 151:24 173:14 177:2,3,21 178:13,24 179:11 179:12,15 180:12 181:3,14 240:25
clarification 13:21
clarify 73:4
cleaner 278:20
clear 35:13 52:22 152:20 263:24
clearly 293:15
cleavable 42:4 109:6,10 171:19 174:2
cleavage 121:4,19 122:6,19 123:9 124:9,16 132:20 139:11 149:23 236:3,8 254:19,22 260:10 284:5 293:17
cleave 235:16 261:10 292:18,18
cleaved 111:14 125:11 283:22,25
cleaving 236:25 251:15
close 125:11,17,21 125:23 126:4 140:15
clr 299:25
coach 274:5
coaching 23:25 49:3 273:23 274:7
colleagues 61:24
columbia 1:8 3:20 3:21,21 4:20 5:21 6:3 8:13 13:24
columbia's 246:21
column 50:24 51:6 58:17,20 87:14,20 87:25 95:15 97:18 102:2,8 105:23 106:8,13,25 107:18 108:17 112:8,17,25 114:14 115:14,23 115:24 130:11 131:8 136:12,13 139:21 141:6 150:16 155:16,20 156:14 163:2,6,17 171:16 210:13,14 232:13 255:12,14 255:20 256:2,11 257:5,9
combine 290:19 290:25 291:2,7 293:19
come 14:4 64:21 65:25 86:17 90:3 95:23 189:5 191:23 192:11 211:22 285:25
comes 108:19 245:22 294:21

comfortable 49:14 49:19 69:7,10 209:17,23
coming 67:8 93:8 198:22 249:19
comment 142:17 143:5 149:10 159:3 165:10 176:13,22 225:2 231:25 270:5
commercially 266:21
commission 302:25
common 231:11 259:12,14,15
commonality 111:5,9
communicating 295:15
company 25:2 183:6
compared 66:9,15 177:15 222:20
compatible 236:4 236:9 261:11
competency 94:9 133:7,17
competing 169:14
complete 15:15 202:12 228:18,24 229:6 230:17
completely 80:17
compound 79:4 96:11 103:7 116:19 123:22,23 125:4,6 147:22,23 149:4,16 172:12 188:12 199:3 220:3,10,17 229:5 280:5
compounds 45:5,6 45:8,15 146:14 163:7 165:2,22 168:4 198:11 199:16,18 277:25
concentration 201:22 202:8 204:10,19,25 205:7,22,23 207:2 207:17 208:14 216:14 217:12 225:6 226:3 227:4 228:9,20 230:24
concentrations 205:17 225:3,21 229:18 230:3 232:6
concept 159:7
concerned 21:3,6
conclude 22:9 78:20 235:20,24
concludes 297:16
concluding 242:10
conclusion 20:25 26:10,14 27:17 82:20 83:9,22 84:22 144:23 146:24 147:8 148:24 149:12 150:25 159:11,19 161:16 174:20 213:15 241:6 248:25 250:3 251:2 253:6,20 279:23 290:22
conclusions 18:14 18:17 29:2 38:14 38:25 39:19
conditions 235:8 235:17 236:3,8,17 236:21,22,24 237:2,7 239:6 254:20,22 260:6 293:17
confidence 146:18 148:16
confident 48:13
confidential 6:21 25:14,15 27:16,19 27:21 28:5,16 30:5 35:12,17 37:21,23
confidentiality 26:5 30:11,14,23 38:10 237:21
confirm 8:21 101:5 264:18
confused 224:18
connection 22:6 22:20 23:14 24:14 25:22
connects 16:15 241:16
consider 14:11 15:3 21:18 29:9 30:13 31:9 35:16 40:15 41:5 72:23 73:5,10,14,24 77:4 77:11 93:9 159:18 174:16 199:21 222:14 243:22 253:15 255:23 256:8,12 267:14 268:17 269:9,24
considered 14:2,5 14:20,20 15:8 30:3 33:5 40:8 83:11 153:13,24 221:6 254:2 255:9 256:13,21 268:19
consistent 236:25 238:10
cont'd 136:10
contained 10:18
containing 258:17
contaminant 199:5
contamination 196:16 197:5,21 199:21 200:15 212:21
content 38:5
contest 247:6 248:16 249:20
context 17:16 34:5 35:10 42:3 43:17 44:2 56:19 61:11 61:15 62:10 78:3 78:10,15 82:10 83:20 84:3,4,17 87:5 92:10 94:4 98:15 106:7 116:8 120:22 124:12 131:4,16 134:16 134:16,21 147:2,4 147:6 149:22 166:23 169:4,25 174:24 175:8 182:25 183:2 187:2 190:14 191:16 222:16 225:21 245:11 252:11,14 253:12 288:2
continue 4:13 18:20 54:21
continued 191:23
continuing 162:19
convention 101:16 101:19
conversation 67:18

conversations 4:7 38:12 123:3 282:7
convert 134:2
converted 184:15
cooper 3:19 5:25
copper 183:23,23 183:25 184:9,18 184:21,23,25 185:3,7,10,17,24 186:2,5,7
copying 196:3
corner 50:21 183:19
correct 7:10,13,15 17:14,15 19:17,18 27:4,10,25 28:2,17 29:10 30:4,9 31:16,25 32:8,15 35:19 36:12 38:10 39:12,22 40:12 41:15,25 44:23 48:21 49:23 50:14 51:15 52:24 53:19 56:3,23 57:21 58:6,15,16,23 60:10,20 61:21,22 61:25 62:2,5,6,11 62:22 63:9,14,15 63:20 64:12,13 69:4,5,20,21 74:17 80:9 86:5,14 88:19,20 91:3 93:22 97:21 98:6 98:12,19 99:5 103:20 104:6 105:12,19,25 107:4,25 112:16 113:4 114:2 116:11,12 120:19 123:14 128:12,17 128:24 130:3 134:12 148:14 151:12,23 152:24 153:14 154:2,16 155:8,9 156:9 157:5 162:2 163:16 164:5,13 166:20 167:8 168:8 172:19 173:12,13 179:9 179:10 180:6,18 181:3 195:16 204:6 209:18 210:23 213:11 215:15 216:21 218:2,10 226:17 230:4,10,25 237:22 241:20 242:25 264:7 265:24 276:2 280:13 292:10 297:2,3 298:10
corrections 298:12 301:6,9
correctly 39:19
correlates 165:7
correlating 164:15
correlation 225:9 230:23
corresponds 206:11,20 210:5
coulter 7:9
counsel 4:17 5:8 6:19,24 11:8 154:7 242:16,17 242:18 245:3 248:17 275:19 282:12
counsel's 282:5
county 298:4 299:4
couple 8:19 185:22 237:15 293:8
course 9:22 11:13 11:20 30:8 46:12 238:2
court 259:4 301:23
cover 144:10,13 242:8 286:14
covered 30:23 144:10 288:5
covers 150:18 175:11
crack 61:18
crazy 273:24
create 75:10
created 14:8 215:5
cross 252:22
crux 269:23
crystal 270:19 271:10
crystallographer 270:13 281:3
csr 299:25
cu 183:18,21
current 6:21

d

d 3:15 300:2
da 188:11 189:3 190:7 196:13,14 196:16
darker 204:25
data 72:25 73:8,16 74:3 195:20 206:10,19 210:4 213:23 215:4 216:3 223:2 234:10 268:18 269:15,16,25 278:7,10,12 279:13,16,21,25 280:4 290:4
date 58:12 66:24 152:19 301:11 302:20
day 9:13 12:17 67:6 238:18,21 298:21 299:21 302:23
days 9:7,10,12,17 9:19 12:10,12,13 12:18 53:6 128:11 180:4,7,16 301:19
deadline 212:7
debate 268:11
debating 51:21
decide 14:10 16:3 93:13 243:7,13
decided 16:6 243:5
decision 262:5
declaration 8:22 13:3,11,17 15:4 16:21 40:6 41:11 41:17 85:10,13,22 86:8,24 139:3 152:12 153:22 182:5 195:8,10 210:11 212:3,5,13 221:8 241:11,13 241:18,24 245:5 264:22 266:5,7,9 271:16 279:2 281:5 287:4 288:6 289:19
deemed 301:22
defend 232:9
define 56:13 58:22 140:22,25
defined 85:9 86:23 140:13

defines 140:20 275:23
defining 110:13
definitely 51:14 189:10 224:23
definition 68:18 70:8 85:12 86:12 86:17,20 97:17 98:14 155:18 156:14
definitions 68:20 98:9 155:11
degrade 121:6,21
degree 142:14 146:18 148:16
demonstrate 157:2
demonstrated 296:19,23
dense 59:25
deny 273:16 275:3 275:9,12
denying 273:12
deoxy 268:15
dep 153:20
depends 56:13 125:23 131:4 140:19 178:17
deposing 301:18
deposition 1:16 2:5 4:10,16 7:5,17 7:23 11:2,5,14,21 12:9,21,25 13:9,12 13:15 15:13 28:17 40:18 41:4,9 53:7 53:13 67:9 119:10 128:12 142:20 143:9 152:23 153:12,23 166:12 171:3,6 180:5,8,15 194:9 238:13,19 238:22 249:20 297:16 298:9 301:4,15,20,21
deprotect 130:24 235:3,6
derivative 44:10
describe 14:7 16:17 37:2 50:7 108:18,21 132:11 163:8 165:8 185:12 211:6 222:2 234:23 237:16 245:21
described 21:8 52:4 56:22 69:23 97:16 100:20 127:2 138:16 139:21 144:17 184:16 208:4 256:2 258:10
describes 43:19 107:14 108:4 111:10 113:3 146:13 185:21 267:7
describing 52:11 62:8,13 97:19 98:17 105:24 107:3,9,10,23 109:16 112:14 124:12 183:10 233:14 253:12,17
description 86:4 99:24 106:19 126:21 201:15 221:24
deserve 277:12
design 73:7
designed 224:24
details 201:16
detection 136:20 259:21 260:10
determination 283:10
determine 122:18 127:14,21 128:3 132:18,19 142:5 179:17 252:16 282:2 283:2,4
develop 37:9 270:20 271:11 288:9,15
developing 37:4 113:25
deverell 3:23 5:5
diameters 271:24 271:25 274:15 276:8
diego 3:5
difference 140:7 140:17 296:5
different 19:14 44:6 45:14 46:24 54:5 57:5 65:2,24 68:20 89:5 93:20 141:10 176:25 177:3,3 178:9,10 187:16 189:15 191:4,6 192:19 201:21,22 205:17 226:2 246:2 257:20,25 289:17 292:7
direct 182:4 247:23
directed 98:4 268:16
directing 262:8
directly 48:7
directs 114:20
disagree 117:21 265:13,20 280:17 280:23
disclose 30:7 38:11,13 88:4 116:14,24 117:5 162:19 164:2
disclosed 21:10 27:2,9 46:7,17,21 47:3,10,13,18 48:8 48:11 50:3,8 53:17 64:25 66:20 69:17 107:15 109:3,24 110:11 111:15 148:18 160:2 162:25 163:14 241:2 257:21 258:9 283:15 292:22 294:3
discloses 50:14,15 51:14,16 88:3 105:7 110:17 117:4 121:3 166:17 167:6
disclosing 113:23 164:12 165:25
disclosure 51:12 67:3,6,10 79:8 82:15 83:17 85:2 87:2,16 104:3,5,14 104:18 105:7,8,10 110:14 111:2,4 126:14 131:8 142:12 165:13 239:6 281:13 282:4,13 284:21
disclosures 22:6 42:21
disconnect 153:21

discourages 191:10
discovery 267:9
discriminate 165:5
discuss 7:3 35:18 35:23 36:3,4,9 37:12,25 38:24 41:10 266:3,6
discussed 38:6 39:6,13
discussions 25:17 39:4
dispute 246:21 247:22 267:4 272:10 276:18 277:15,21,24 278:4
disruptive 80:17
dissuaded 162:18 164:12
distance 8:19
divulge 29:17 153:8 282:6
divulging 29:21
dna 42:6 80:9,12 80:17 109:13 121:6,22 136:19 136:23 161:12 177:14 182:25 185:8 193:14 227:12 233:23 235:8 259:10 260:8,11 268:10 270:17 271:8
doctor 210:11
document 60:17 152:24 175:9 223:7 257:7,15 267:3 272:16 273:9,19 275:6 276:15 279:6
documents 14:2 14:19,21 40:9,16 41:5,12 57:24 58:5 128:16,19 153:12,24 159:24 175:10 176:2
doing 18:25 23:15 27:14 37:19 123:22 131:5 197:20 214:4,8 228:14,19 288:14 301:10
double 66:8,10 235:7
dower 35:2,5 256:14,18 294:9 294:13
dr 4:17 6:1 7:1 8:1 9:1 10:1 11:1 12:1 13:1 14:1 15:1 16:1 17:1 18:1 19:1 20:1 21:1,25 22:1 23:1 24:1 25:1 26:1,3 27:1 28:1 29:1,13,16 30:1 31:1,9 32:1 32:14,19 33:1 34:1 35:1 36:1 37:1,13,25 38:1,6 39:1 40:1 41:1 42:1 43:1 44:1 45:1 46:1 47:1 48:1 49:1 50:1 51:1 52:1 53:1 54:1 55:1 56:1 57:1 58:1 59:1 60:1 61:1 62:1 63:1 64:1 65:1 66:1 67:1 68:1 69:1 70:1 71:1 72:1 73:1 74:1 75:1 76:1 77:1 78:1 79:1 80:1 81:1 82:1 83:1 84:1 85:1 86:1 87:1 88:1 89:1 90:1 91:1 92:1 93:1 94:1 95:1 96:1 97:1 98:1 99:1 100:1 101:1 102:1 103:1 104:1 105:1 106:1 107:1 108:1 109:1 110:1 111:1 112:1 113:1 114:1 115:1 116:1 117:1 118:1 119:1 120:1 121:1 122:1 123:1 124:1 125:1 126:1 127:1 128:1 129:1 130:1 131:1 132:1 133:1 134:1 135:1 136:1 137:1 138:1 139:1 140:1 141:1 142:1 143:1 144:1 145:1 146:1 147:1 148:1 149:1 150:1 151:1 152:1 152:6,7 153:1 154:1 155:1 156:1 157:1 158:1 159:1 160:1 161:1 162:1 163:1 164:1 165:1 166:1 167:1 168:1 169:1 170:1 171:1 172:1 173:1 174:1 175:1 176:1 177:1 178:1 179:1 180:1 181:1 182:1 183:1 184:1 185:1 186:1 187:1 188:1 189:1 190:1 191:1 192:1 193:1 194:1 195:1 196:1 197:1 198:1 199:1 200:1 201:1 202:1 203:1 204:1 205:1 206:1 207:1 208:1 209:1 210:1 211:1 212:1 213:1 214:1 215:1 216:1 217:1 218:1 219:1 220:1 221:1 222:1 223:1 224:1 225:1 226:1 227:1 228:1 229:1 230:1 231:1 232:1 233:1 234:1 235:1 236:1 237:1 238:1 239:1 240:1 241:1 242:1 243:1 244:1 245:1 246:1 247:1 248:1 249:1 250:1 251:1 252:1 253:1 254:1 255:1 256:1 257:1 258:1 259:1 260:1 261:1 262:1 263:1 264:1 264:14,21 265:1,7 266:1 267:1 268:1 269:1 270:1,10 271:1,23 272:1,10 273:1,4 274:1,24 275:1 276:1,18 277:1 278:1,23 279:1 280:1,7 281:1 282:1 283:1 284:1 285:1 286:1 287:1 288:1 289:1 289:18 290:1 291:1 292:1 293:1 294:1 295:1 296:1 297:1,17
draw 44:25 221:19

draws 51:20 52:12 220:11 234:5
dropping 88:21
drug 267:9
dttp 201:23 202:7 229:3,4
duly 6:6
dunham 3:19 5:25
dye 77:12 96:11 96:14,15,22 153:13,25
dyes 61:20 62:4,9 63:14 98:5,10 109:8 155:2,5

e

e 3:2,2 6:4,4,4,4 136:2,2,4,4,4,4 300:2 302:1
earlier 54:8 156:21 239:8 261:19
easier 258:13
easiest 15:21
easy 80:20 103:23
edward 3:10 5:10
edward.reines 3:10
efficiency 169:22 170:19 188:16,23 193:19,25 194:3 194:13,20 203:5,6 204:11 205:9 207:2 210:20 211:10,11 212:23 229:19 230:8,9,25 284:7
efficient 54:25 167:17,21,22 168:6,12,23 169:2 192:16 203:17,19 204:4 207:4 251:20 268:6 285:9
efficiently 196:22 252:18 258:25 259:9 280:2 284:12,24 285:10
effort 174:7
eight 9:16,19 12:12,15,16,17 53:6 128:10 180:4 180:7,15 191:6 222:7
either 109:10 176:22 289:2
el 3:5
element 45:12,13 47:21 48:2 51:17 55:5,7,19 89:8
elements 45:17 63:25 64:2,3,6,7 90:6
embodiment 254:8
employer 6:21
employing 49:25
ends 170:11,12
entered 6:18
entitled 299:11
enzyme 193:2 196:18 215:18 269:8,19
enzymes 141:10 142:7,12 193:3,4 239:20 240:13
enzymologist 141:19
erica 1:23 2:10 299:6,25
errata 301:8,11,14 301:17
errors 13:16
esq 3:6,10,14,15 3:16
essentially 212:10
establish 279:17
established 113:12 114:2,7,18,23 115:7,11,13,17,22 116:6,10 117:10 117:20 118:3,9,21 119:25 120:4 131:11 132:7 234:7
estimate 7:22 8:8 24:23
ether 245:20,23
ethoxy 63:22 88:19
evaluate 17:3 21:19 120:8 141:16 233:24 261:20 269:5 270:15 286:14
evaluated 23:13 24:6
evaluating 16:25 268:18
evaluation 29:5,22 145:9
everybody 135:9
evidence 127:18 128:5,8,22 129:6 129:12 130:22 205:12 247:11 274:9
exactly 14:9 65:22 68:12 87:22 99:9 146:15 186:9 286:3
examination 6:8 136:10
examined 6:7
example 74:7 122:6 131:12 143:16 165:20 201:23 206:7 214:22 248:18 273:25
examples 72:15 245:17 246:22 247:14
excerpt 243:3,12 244:5
excerpts 15:25
exclude 64:6,8
excuse 13:9 109:23 157:12 203:24 207:10 215:17 218:8 225:15 271:5 283:23
executed 57:17 282:14
exemplary 59:15 59:16,22 60:2,5
exhibit 8:14 9:24 13:25 33:4,6 40:9 40:17 41:6 46:13 58:10 85:20 95:8 100:6 112:21 124:25 152:14,17 182:6 183:8 187:13 190:21 215:13 219:24 222:22 232:13 242:24 263:14 264:20 269:18 271:18 275:18 287:4 300:9,11
exhibits 8:18 152:5 153:16 300:7,15

existing 210:16 211:11,14
exo 188:11 190:15 191:21 193:14 227:21
expect 197:16 198:6 205:6 212:21 230:9
expectation 207:8 207:12 287:21 291:13,21,24 292:2,9 293:22 295:3
expectations 296:4,9
expecting 170:10
expended 9:15
experience 57:5
experiment 169:18 170:9,13 190:25 197:25 198:17,24 199:8 199:12,15 201:4 204:12 213:3 222:16 223:11 224:2 226:16 295:25 296:11
experimental 206:9,10,18 207:9 207:13 210:4
experimentation 219:2
experiments 127:10,19 128:6 128:23 129:7,14 130:3 200:9 201:6 201:10,18 214:4,9 214:19 231:7,11
expert 8:2 77:5 117:25 145:10 147:12 149:14 270:14
expertise 49:22 50:2 52:2 74:25 75:13 76:12,16,18 76:22,24 77:16,19 77:25 78:10,14,24 79:3,6 91:7,18 117:24 141:24 143:11,13 198:13 198:14 206:24 218:14 247:12 248:15 249:19 271:3
experts 242:19
expires 302:25
explain 72:19 169:19 262:4
explanation 138:12 169:2,9,10 220:19 261:22 269:6
extent 26:4 29:12 29:17 122:25 282:4

f

f 136:2
face 96:9
fact 41:22 79:17 79:19 80:15 145:24 182:24 185:11 213:20 254:3 278:13 281:4 295:8
factual 75:19
fail 80:22 301:21
failed 81:25
fails 200:25
failure 202:14,25 203:7
failures 228:17
fair 12:2,3 53:25 75:25 76:6 78:18 277:7,9
fairly 56:22 121:5 121:20
faithfully 259:2,9
familiar 8:15 10:20,24 17:12 36:15,19 55:13,18 57:3,7,9,10 60:18 75:17,20,22 106:17 143:12 146:15 156:21 183:3 186:21 246:10 247:24 270:24 291:10,19 291:23 292:8
far 148:12 252:6
fast 260:7
faster 197:8
feel 171:10 210:10 276:11
felt 13:20
field 20:6 22:18 26:12 77:6,7,8 141:24 158:8 231:12,12 248:15
figure 50:18 51:5 51:8 100:9 126:9 126:10,20 127:2,5 129:16 130:14,20 183:15,16 195:3 195:12,13,14,15 196:3,4,9,24 199:19 201:12,24 203:16 204:5,8 206:4 212:18 215:10 220:12,14 220:16 221:23 222:4 223:10 224:11,16 226:11 226:19,21 227:6,7 234:2,16,18 235:2 236:14
figured 236:7
figures 102:6 126:21 196:2 222:25
filed 4:23 66:24 156:5
find 13:16 147:9 183:8 187:23 222:25
fine 12:11 87:9 164:10 166:5,7 193:6
first 15:2,2,8 20:8 23:18 31:4 82:3 82:13 154:15 155:12 158:23 159:4 172:15 197:12 202:6,19 210:20 267:6 272:22,23,25
fit 280:9
fits 178:18,23
fitzpatrick 2:7 3:12 5:2,20,24
five 7:24 182:3 191:5 271:24,25 272:11,18 273:4 273:13 274:15,24 275:13 276:8,19 277:15,25 278:22 289:17
fixed 178:5,7
floyd 3:22 5:16
fluorescent 98:5 109:7
focus 174:6 245:8 296:8

focused 180:11 283:14
folks 42:25
follow 115:21 219:4 287:6
followed 185:20
following 284:21 302:5,6
follows 6:7 136:5
footnote 267:17,17 268:5
foregoing 298:8
form 9:6 10:23 19:23 22:13,24 33:2,22 38:18 43:15 44:9,15 45:10,22 46:10,20 47:24 48:4 49:18 61:2,13 62:17,24 64:15 65:19 68:2 68:11 69:9 70:5 70:18 75:5 78:7 80:11 82:8,19,24 83:9,22 84:10,22 85:6 87:7 90:13 90:24 92:12 94:7 96:6 97:11 98:21 99:18 101:12 103:22 104:21 105:15 106:3 107:7 111:8 114:4 115:3 117:15 121:17 122:15,25 123:16 126:18 134:24 140:9 142:16 143:3,24 146:23 154:20 157:7 161:7,16 162:13,23 163:20 164:7,24 166:22 167:2,10 172:22 174:20 189:23 191:14 193:16 194:6,15,22 213:5 213:13 214:11 216:9 220:23 231:14 236:19 238:15 241:6 249:2,9 250:6,10 250:18,19 253:7 254:12 271:13 283:8 284:10 285:2,18 286:21 295:17 296:16
formally 20:11
formed 25:7 249:16
formula 100:19 101:9 110:10
forth 9:23 256:11 257:4,10,20 260:23 277:6
forward 36:5 73:12,12 277:12
four 13:6 131:23 132:13 133:2,18 136:9 137:6 139:18,24 151:20 183:4 191:5 233:16,22 258:15 258:21,24 259:7
frame 12:19 24:22 24:24 26:23 28:19 33:23 72:2 145:16 145:19 146:9,10 146:11 168:20 178:14,16 239:17 285:4
free 38:24 210:10
freemont 6:15
front 40:23 51:9 58:19 112:12 139:4 152:5 171:12 182:8 189:19 219:23 220:3 243:3 285:7
fueling 268:11
fuji 113:21 234:11
full 272:23 278:24
fully 242:20
function 212:8
fundamental 137:4,10,13 138:13,20 254:15 255:2,10,24 256:9 256:19,22 257:2 257:10,19,21 258:7,20 260:21 261:15 294:2
further 7:4 52:13 299:15

g

g 131:13
garrett 3:16 5:23
gather 188:14,22
gathered 294:16
gel 211:12 213:16 213:18 214:13,18 215:3
general 149:24,25 150:5
generally 10:11 17:17 36:7,14 57:3 78:13 168:18 209:14,20
generated 14:17
genus 44:17,24 45:3,4,6,8,14,15 45:18,23 52:12,21 55:6,7,9 66:6 88:6 88:11,15,17,22,25 89:3,5,12,13,15,18 90:5,11 100:25 101:3,8,14 102:18 102:25 103:14,18 110:9
getting 28:12 57:9 167:17,20 202:22 202:24 204:22
give 8:18 12:5 21:25 106:6 134:15 201:15 247:3,3 253:23 270:9 285:3
given 164:21,21
go 4:14 11:5 54:22 109:19 126:19 154:22 156:13 189:25 190:23 196:24 201:12,16 217:18 218:6 220:12,13,16 226:24 227:16 229:3,4 231:17,19 258:5,11 278:17
goes 202:15,16 226:20 230:19
going 4:3 8:17 21:11 32:25 58:8 67:14 80:2,22 106:6 152:4 162:5 171:4 177:16 198:18,19 201:13 207:8,12 227:17 244:14 246:18 261:18 262:19 267:25 268:2 269:4,5 275:21 277:12 279:20 297:15
good 15:24 60:7 64:17,20 65:7,9 67:23 69:23 70:14 70:21 71:4,5,5

123:17 135:8 138:11 144:8 169:12 187:8 226:22 240:6
gotshal 3:8
granted 17:5
great 262:24
greater 169:21
grounds 277:7,9
group 42:4,5 43:21 44:13,22 45:7,11,14,20,25 46:4 47:8,14,21 48:2,6 55:20 60:24 78:25 87:17 89:7,17 90:22 91:24 92:8 93:3,8 93:20 102:17 104:4,6,9,15,19 105:9,11 107:11 107:15 110:6,16 111:3,11 113:10 113:11,17 115:6 116:7,16 117:2 118:4,5,20,24 119:20,24,24 120:16,16 121:4 122:7,20 123:9 124:10,17 125:10 125:10 127:11 129:25 132:6,14 133:3,19 138:2,15 139:12 141:13 142:13 144:14,15 144:16 145:12 146:2,19 147:13 147:24 148:11,18 149:6,18 150:21 162:21 166:19 167:7 171:19 191:17 194:8 220:18,21 221:9 221:12 234:5 241:9,19 248:19 251:8 254:15 258:19 259:18 260:21 261:4,24 262:10 275:23 279:18 281:20,22 281:23 282:14,17 282:20 283:4 284:23 285:8,23 287:24,25 289:6 290:8,14 292:16 292:19,22 293:4 293:24 294:14 295:4,10 296:2,12 296:24
group's 189:2
groups 44:17 52:12,21 102:12 102:16,23 103:9 103:12 104:8 115:6 117:11 121:20 127:19 130:13 134:9,21 142:24 143:15 188:7,17,24 189:6 189:16 190:5,13 191:11,24 193:20 193:25 194:4,13 194:20 234:14 240:14,24 245:18 246:23 247:15 271:25 272:2,11 272:12 273:4,6,13 273:14 274:15,17 274:24 275:2,13 275:14,21,25 276:9,19,20 277:15,17 278:22 278:24 280:9 283:16,21,25 284:8 286:18 287:10 288:16 289:17
growing 109:12 136:22 260:8
guess 61:14 66:24 151:7 158:9 211:2 221:3
guided 243:9

h

h 6:4 136:4
h2o 184:5,6,7
half 87:23
hand 50:21 183:18 299:21
hands 251:22
happen 185:7 207:18
happens 200:21 208:13 229:10
hard 196:10 227:24
heard 43:11
hearing 34:3,6
heights 187:17 192:20
held 2:6
help 187:23
hereunto 299:21
high 104:9,15,18 105:9 111:14 120:17 123:13,19 123:24,25 124:2 130:14,25 131:3 138:6,9 140:5,12 140:17,20,22,25 198:5 199:7,22 200:2 216:14,23 217:11 227:16 234:15 259:20
higher 140:13,14
highest 228:20
historical 130:21 234:10 254:3
history 16:2,4,9,11 16:19 17:2 241:12 242:11,19 243:2,7 243:13 244:5 263:11 271:21 277:4
hiv 267:9
holding 194:17
hopefully 274:10
hour 9:16,19 262:20
hours 9:14 12:15 12:17 253:3,14 254:5,6
hplc 199:5
hui 3:21 6:2
human 15:22
hundred 56:10,15 56:21 57:5 106:16 125:12 140:12 159:18,23 204:19 207:3 227:11 228:22 254:5
hundreds 56:18 253:3,13 254:6
hydrogen 87:16 88:3,4,5
hydrogens 112:2,4
hydroxy 88:10
hydroxyl 118:25 245:24 258:19 259:19 292:20

i

i.d. 300:8
ibs 24:19 25:10,17
idea 52:8 68:8 91:2,7 119:8,12,18

133:11,14,23 142:6,9,21 172:5 199:23 213:18,25 214:7,17,20 215:2 215:23,25 216:5 231:21 240:7,12 246:14 290:17
identification 58:12 152:18
identified 89:19 148:13 189:6 289:18
identifies 272:4 273:4 274:24 275:13,20 278:23
identify 52:13 59:14 92:20,25 111:18,22 146:2 146:17 147:12,20 147:22 148:10 150:20 155:24 172:11 178:20,22 180:16,24 181:12 189:16 209:8 250:5,20 251:4 254:7
identity 136:21
illumina 1:5 3:20 4:19 5:15 10:3,5 20:3,11,14,19 21:8 21:17 254:22 261:9 293:18 300:8
illustrating 114:21
immediate 267:3
imperative 301:16
implied 260:13
important 53:21 128:16,19 167:22 173:15
improve 229:19
improved 230:9
inappropriate 54:4
include 59:16 63:24 64:3,17 72:24 73:6,8,15,25 79:7 83:4 90:6 91:20 92:5 95:23 157:11,14,23 158:12,24 164:18 180:9 209:4
included 64:2,21 64:23 75:7 81:3 98:8 162:8
includes 89:4,6 165:2
including 63:18 67:16 72:25 76:4
inclusion 72:3,12 74:11,21 76:9 78:21
incompatible 81:4
incomplete 259:23 259:24 260:2
inconsistent 81:11 165:12,25 247:13 249:5
incorporate 109:5 143:15,18 191:18 201:2 213:9 280:2
incorporated 4:19 136:22 165:4 188:8,10 189:4 190:6,8 191:20 196:23 251:12 259:2,10 261:7 284:12,24
incorporating 252:18 268:7
incorporation 164:4 167:13,18 167:21,22 168:3,6 168:13,24 169:3 169:12,17,22 177:18 187:15 188:3,16,23 189:22 190:12 192:14,17,19 193:5,20,24 194:3 194:12,19 200:23 202:9,24 203:5,17 204:5,11,20 205:24 230:18 259:21 284:7 285:9
increase 205:8 208:14
increased 230:25
increases 204:10 205:2 207:2 230:10
increasing 204:9 205:7,21,23,24 206:25 230:24
indented 186:15
independent 9:20 17:4 121:11
indicated 245:7
individually 39:16 293:21
industry 79:24
inefficiencies 169:16
inefficiency 170:16
inefficient 187:15 188:2 189:21 190:13 192:18 193:5 200:22 202:10
inefficiently 188:7 188:10 189:3 190:6,8 191:20 251:12 261:6
information 29:18 29:21 30:15 31:21 39:21 113:22 153:8 154:4 217:22 239:2 242:22 249:4,17 270:4
informed 6:25
initial 231:16
innovate 96:23 97:15
innovating 97:9
innovation 83:20
innovative 83:4
institute 3:22 5:18
instruct 123:4 153:10 282:8
instruction 282:11
instructions 301:2
intellectual 22:11
intended 279:19
intends 116:10
intensities 187:16 192:20
interactions 239:4
intercourse 15:23
interested 219:9 299:18
interfere 4:10 80:8 177:12
interposed 154:7
interpretation 177:24
interrupt 108:12
invent 159:7
invented 159:25 160:10,14,17

161:2,10,23
invention 75:12 81:5 84:19 96:3 105:25 106:10,14 106:20,23 107:5 107:24 108:7,18 108:21,23 109:18 109:22 110:15 158:16 232:21 233:7 252:24 253:18 261:24
inventions 96:4 192:2 235:23 239:8,21 240:16 247:16 254:8 277:6 283:6 288:3 296:25
inventive 82:17,22
inventor 56:21 75:14 154:15
inventors 57:12 76:13 277:5
inventorship 57:13 69:13 71:10 78:24 159:17 160:7
investigating 284:22
investigation 282:25
involve 39:5
involved 36:24 37:2 55:25
involvement 26:8 32:12 35:25 39:24
involves 136:20
iodo 185:22
ion 19:11,15 22:8 22:21
ipr 4:21
ipr2018-00291 1:12
ipr2018-00318 1:12
ipr2018-00322 1:13
ipr2018-00385 1:13
ipr2018-00797 1:14
ireland 104:2,13 105:8 130:15,19 131:3,5
irrational 268:25
isobutenyl 93:7
isobutoxy 64:5 89:4,7
isopropoxy 88:22 89:22 91:20
isopropyloxy 64:4
issue 27:3 41:19 41:24 42:8 75:16 75:19,19 77:9 84:6 247:20 250:14
issued 66:23
issues 192:14

j

jacket 54:2
january 1:19 2:2 4:4 299:22
jeff 5:25
jeffrey 3:20
jmurnane 3:15
joe 58:15 75:2 154:13,14 158:22
john 3:15,19 5:22 5:24
ju 10:21 17:2,10 18:5,7,13,22 19:3 20:21 21:10 22:5 22:10,10,16 23:13 24:4,13,18 25:18 25:22 26:2,10,17 27:20 28:10,14 41:23 42:7,13,21 46:8,18,22 47:4,11 47:18 48:9,12,19 49:8,15 50:3,8,13 51:9,14 52:4,16 53:14,18 55:3 103:19 105:23 106:4 107:5 110:25 111:9 113:23 114:20 115:4,12,21 116:5 117:9,18 119:22 121:10 122:11 123:8 124:8,16 125:5,10 126:13 126:25 127:9,17 128:5,17,22 129:7 129:14 130:2 131:22 132:11 137:11 138:13,25 139:17 140:22,25 142:11 144:17 146:12,20 147:17 147:24 148:17 176:25 177:22 178:13,25 179:11 179:12,15 180:12 180:21 181:3,8,13 232:11,19 233:5 235:2,21 237:6,25 239:8,9,12 240:25 241:10 245:5 247:16 251:18 252:15,24 253:17 254:9 255:9 257:5 257:9,20 258:9 260:20,23 261:13 261:23 262:5,8 268:21 269:7,14 269:17 271:23 272:18 273:4,12 274:24 275:7,12 277:21 278:23 281:4,15,18,21 282:12 283:2,6,13 284:6,19,21 285:7 285:23 288:2 289:18 292:22 293:14 294:3 296:25
ju's 16:21 26:25 27:7,25 28:4 31:9 32:14,19 54:9 107:24,24 108:14 110:14 112:23 113:7 122:3,23 126:14,14 131:7 148:13 245:22 255:23 256:8 264:14,21 265:7 272:10 276:18 280:7
judge 227:23
judgment 92:16 92:18 160:21
jumping 224:5

k

kamal 40:2 103:20 103:25 104:4,17 104:23 105:4,5,10 107:15 111:15 121:3 122:12,22 124:15,15,20,23 124:25 125:4,6,7 130:16,19 131:3,5 234:19,21,22,23
kamal's 125:8

karyn 3:21 6:2
keep 6:20 26:6 52:18 184:2,22
keeps 185:3
kestler 3:20 6:2
kind 10:11 22:17 37:7 166:10 244:21
kinetics 185:5
kit 186:19,22,25 187:10 192:23
knew 10:25 20:13 21:17 80:16,22 157:22 209:2
knobbe 3:4
knobbe.com 3:6
know 11:16,24 24:5,6,8 31:20 33:13 36:5,22 47:15 48:5 52:7 53:25 58:18 61:10 64:16,19 66:12,16 67:9 74:12,18,20 75:8,9 76:17 82:12 83:12 84:20 86:25 87:8,9,11,21 90:25 91:12 92:14 99:7,9 100:3 101:15 102:19,19 114:9 117:17,19 118:11 119:7,21 126:24 127:3,5,9 129:17,18,18,25 130:7,9,18,22,23 132:21,25 133:8 133:13,17 137:16 138:7,19 139:18 140:2 141:12,21 142:12,23 143:10 143:17,25 144:3 144:21 145:11,17 146:14 148:17 149:12 151:11 157:8 158:2,3,11 159:2,6 160:24 164:17 166:11 168:9,12,17 170:24 172:15,16 173:14 176:6,7,14 177:11 178:11 179:5,6,13,19,24 179:25 180:6 182:8,22 186:3,4 186:23,24,25 187:5 188:17,24 191:4 193:2,4 198:8 199:13 200:7,8 203:13 210:25 212:20 213:16 217:5,8 221:10 224:21 225:4,16 233:15 234:24 236:2,16 236:20,23 237:3,5 237:8,10 238:7 239:13 240:20 242:4 246:4 248:4 262:14 263:21 265:23 266:16 271:4,6,7 279:22 282:23 285:19,25 286:2 288:20,25 289:9,13 295:13 295:23
knowing 164:17
knowledge 164:21 194:2,12,16,19
knowledgeable 277:10
known 33:11 103:24 104:7 106:5 109:15 119:19 120:14 138:23 157:4 209:12 239:20 240:4,5

l

l 1:23 2:10 3:16,20 246:6,6,12,12 248:7,7 299:6,25
label 210:24 258:17
labeled 109:6 203:18 205:4,5,5,7 258:16
labels 109:7 258:22
lam 58:15 75:3 154:14,15 158:22
lane 202:6,15,19 202:21 203:16,20 203:21,23 204:4 206:4,5,6,11 210:2 210:14 211:9
lanes 201:25 215:11 227:8 228:15
large 217:25 218:8
lawyer 67:19 123:4
lawyers 29:19 243:9,15
lead 192:19
leads 187:15
learn 28:9 60:22 61:7
learned 22:4,19 28:14 67:17,23
learning 68:3
leaving 147:20 249:15
left 183:18 199:6
legal 5:6 16:7,7 26:13 27:17 75:16 75:19 82:19,22 83:9,22 84:6,22 144:23 145:8 146:24 147:8 148:23 149:12 150:25 159:11,14 159:19 161:16 174:19 241:5 248:25 250:2,14 250:25 253:6,20 290:22 291:9,18
legend 204:2 222:5,5
legends 196:9
legs 11:15
letters 40:3
level 139:17
levels 226:3
lexicons 105:2
license 36:23
licensed 37:6
life 19:12 25:14 28:25 29:8 30:2 30:20 38:16 238:3
limitation 118:15
limitations 175:21 178:19 248:19
limited 59:17
limiting 118:13
line 19:20 21:12 59:3,9,10,14,19 60:2 87:23 102:4 102:10 107:2,18 107:19 112:10,19 112:25 113:16,17 114:7,8,16 115:13 115:24 130:12 131:18,19,21 139:21 141:7

155:20,25 156:17 163:2,5,22 204:24 227:25 244:15 273:22 302:8
lines 108:17 121:14 196:5,11 221:25 227:25 232:18 233:4
link 16:14
linker 179:13 180:17,25 241:14 241:16 242:7,13
linkers 180:20 181:8,12 185:19 185:20
list 13:25 14:5 33:5 40:22 71:7 72:10 75:10 76:3 87:12 89:20 91:19 97:4 99:12,21 141:9 153:15
listed 40:9,16 41:5 80:18 95:11 137:11
lists 137:6
literature 9:21 26:18,19,22,25 27:7,21,25 28:4,10 28:15,24 29:5,23 30:16 31:15,23 36:9 134:5 148:18 170:25 183:9 200:11,13 208:20 209:9,13 219:5 237:25 238:6,12 238:25 267:11 295:20
little 8:17 39:6 59:25 170:14 189:14 202:6,12 222:15 262:19 278:19 297:5
llp 3:8
located 5:2
location 60:10 61:9 64:12 69:19 69:25 70:16 71:8 72:5,11 76:11 78:22 79:9 83:6 84:17 85:4 87:4 87:14 93:18 95:5 96:24 99:22 115:7 116:8,16 117:3,12 118:5,20 119:20 120:18 144:15 145:12
locations 65:3
logic 72:20
long 166:5 184:13 185:6 244:18,19 267:21
longer 43:24
look 16:5,11,12,21 46:11 105:3 119:9 119:13,17 124:15 124:22 129:21 131:2 155:10 179:8,21 183:15 188:25 190:16 191:7 194:7 196:3 196:4,20 201:24 201:25 213:17 214:18,21 215:4 223:2,4,6 228:15 228:22,25 233:12 234:17,17,22 240:21 241:8 249:13 254:10 261:5,8 266:5 267:2 281:18 283:12 290:5,8
looked 10:15 18:7 18:12 24:7 100:10 132:23 134:11,25 193:8 198:9 207:21,25 208:21 209:15,21 213:18 213:20 216:11,17 221:2 230:13 239:14 270:18 271:9 283:13 292:14,15 293:20 295:21
looking 16:9,19 72:9 114:10 129:20 152:23 180:9 254:19 263:13 267:10 282:16,18 285:21 293:14,15
looks 8:14 205:3 205:15 216:3
lot 54:23 64:23 102:5 128:13 133:25 202:13,25 208:19,20 222:15 223:22 228:16 288:13
loud 268:3
low 199:8,22 202:8 216:20 231:18
lower 50:20
luman 3:6 5:12,12
lunch 135:8
luncheon 135:15

m

m 1:17 2:6 6:4,4 136:4,4 298:6,16 300:4 302:20
maintain 279:6
making 117:4
manges 3:8
marcus 3:20 5:14
marked 8:13 13:24 46:13 58:11 150:9 152:13,18 242:24
marriage 299:16
martens 3:4
mass 109:8
match 87:22
material 14:18 106:25
materials 13:8,10 14:5,11,15 15:3,9 33:5 220:25 221:4 221:6,7
matter 4:18 8:5 35:7 120:14 139:17 160:22 208:13,22,24 209:22 227:16 247:20 253:4 299:12,17,19
mean 10:8 13:9 14:9 25:4 31:3 32:2 37:3 48:5 55:8 64:8 68:13 68:14 71:22 72:6 76:15 77:2 79:22 82:21 91:4,13 92:13 96:7 108:12 115:10 137:9 139:23 144:2,3 145:19,20,22,23 146:8,12 147:5 150:4 151:7,24 172:24 174:14 177:4 178:7 197:14 199:11 205:4 208:19

210:14 213:6 215:6 216:10 217:17 222:18 223:3,4,5 225:11 225:12 226:8 231:6 237:23 247:9 248:8 251:25 269:13 281:11 294:21 295:18
meaningful 140:10,16 269:19 270:3
means 33:24 78:15 115:13,20 116:3,9 116:10 117:19 140:11 171:23 173:4,6 174:17,24 176:3 177:11,15 233:19 245:24 246:15,19
meant 173:2
media 4:15 43:10 95:3 136:9 182:3 219:21 263:9 297:18
meet 145:13 146:3 180:25 181:12 240:24 250:22 251:6 254:15
meets 146:19 147:13 148:11,19 149:5,17 150:21 178:24 180:17 233:15 248:19 254:25 261:14
member 44:12,16 45:19,24 46:3,6 47:7 55:8
members 88:18 93:20
memorialize 275:12
memory 53:3 160:23
menchen 1:17 2:6 4:17 6:1,12 7:1 8:1 9:1 10:1 11:1 12:1 13:1 14:1 15:1 16:1 17:1 18:1 19:1 20:1 21:1,25 22:1 23:1 24:1 25:1 26:1,3 27:1 28:1 29:1,13 29:16 30:1 31:1 32:1 33:1 34:1 35:1 36:1 37:1 38:1 39:1 40:1 41:1 42:1 43:1 44:1 45:1 46:1 47:1 48:1 49:1 50:1 51:1 52:1 53:1 54:1 55:1 56:1 57:1 58:1 59:1 60:1 61:1 62:1 63:1 64:1 65:1 66:1 67:1 68:1 69:1 70:1 71:1 72:1 73:1 74:1 75:1 76:1 77:1 78:1 79:1 80:1 81:1 82:1 83:1 84:1 85:1 86:1 87:1 88:1 89:1 90:1 91:1 92:1 93:1 94:1 95:1 96:1 97:1 98:1 99:1 100:1 101:1 102:1 103:1 104:1 105:1 106:1 107:1 108:1 109:1 110:1 111:1 112:1 113:1 114:1 115:1 116:1 117:1 118:1 119:1 120:1 121:1 122:1 123:1 124:1 125:1 126:1 127:1 128:1 129:1 130:1 131:1 132:1 133:1 134:1 135:1 136:1 137:1 138:1 139:1 140:1 141:1 142:1 143:1 144:1 145:1 146:1 147:1 148:1 149:1 150:1 151:1 152:1,6 153:1 154:1 155:1 156:1 157:1 158:1 159:1 160:1 161:1 162:1 163:1 164:1 165:1 166:1 167:1 168:1 169:1 170:1 171:1 172:1 173:1 174:1 175:1 176:1 177:1 178:1 179:1 180:1 181:1 182:1 183:1 184:1 185:1 186:1 187:1 188:1 189:1 190:1 191:1 192:1 193:1 194:1 195:1 196:1 197:1 198:1 199:1 200:1 201:1 202:1 203:1 204:1 205:1 206:1 207:1 208:1 209:1 210:1 211:1 212:1 213:1 214:1 215:1 216:1 217:1 218:1 219:1 220:1 221:1 222:1 223:1 224:1 225:1 226:1 227:1 228:1 229:1 230:1 231:1 232:1 233:1 234:1 235:1 236:1 237:1 238:1 239:1 240:1 241:1 242:1 243:1 244:1 245:1 246:1 247:1 248:1 249:1 250:1 251:1 252:1 253:1 254:1 255:1 256:1 257:1 258:1 259:1 260:1 261:1 262:1 263:1 264:1 265:1 266:1 267:1 268:1 269:1 270:1 270:10 271:1 272:1 273:1 274:1 275:1 276:1 277:1 278:1 279:1 280:1 281:1 282:1 283:1 284:1 285:1 286:1 287:1 288:1 289:1 290:1 291:1 292:1 293:1 294:1 295:1 296:1 297:1,17 298:6,16 300:4 302:20
mention 28:16
mentioned 139:13
mere 79:17 80:15
merely 79:19
method 251:15 261:10 284:5
methoxy 63:22 88:19 103:4 274:18
methyl 103:5 196:21 197:8 201:23 202:4,7 214:23 229:3 274:18
methylthio 281:14
methylthiomethyl 272:5 274:19

280:8 281:14
metric 126:2,3
metz 234:25
metzger 37:13
metzker 35:7,14 35:24 37:13,25 38:6,25 39:10 113:21 114:18,21 116:13,14,21,24 118:10 156:18,22 157:2,18 161:25 162:4,6,10,18 164:11,15,22,25 165:7,12,24 166:17 167:5,19 188:6,15,22,25 189:9,18,22 190:4 190:9,17,21 191:9 192:3 195:15 198:22 201:19 205:13 206:14,24 210:6,24 211:13 211:20 212:15 213:21,22 215:5 219:22 220:11 225:20 227:3 228:8 229:17 230:2,22 231:10 231:15,22 232:4,9 234:11 251:11,11 251:22 254:18 256:16,17,19 261:5,25 262:9,10 290:4,5,8,12 293:16
metzker's 39:8
micro 228:14
micromolar 202:17,17,18,20 202:21 203:2,13 216:13,20 217:4,9 217:25 218:7 226:9,13 227:4,11 227:11,12,19 228:4,9,16,17 229:6,9 230:18 231:3,23 232:5
micromole 222:23
micromoles 200:3
microphones 4:5,9
mild 121:5,20 139:13
millimolar 222:8 222:10,15 223:17 223:18,18,21 224:19 225:20
mind 26:6 47:2 54:7 252:22 269:9
minus 211:2,3
minutes 122:7,20 123:10 124:10,18
mischaracterized 48:23
mischaracterizes 17:8 23:7 54:13 71:12 79:13 92:24 121:17 129:3 174:19 190:2 192:5 221:22 253:22 255:18 257:7,15 272:15 273:8,18 275:5 279:5 293:10
mischaracterizing 23:20,24 276:12 276:14
misincorporation 208:17
mismatched 268:7
missing 137:15,17 137:20,23,25
misspoke 203:21
misstating 274:9
mistake 215:22
mistakes 13:16
misunderstood 205:20
mixed 233:23
mixture 198:23 202:23
mm 222:2,3
modification 60:23 64:11 69:19 69:24 70:15 72:4 74:23 76:11 78:22 79:9 82:16 83:6 83:18 84:16 85:3 87:4 90:10 91:10 92:9 93:18 110:18 156:7 163:15 164:3,20 165:15 166:3 191:25
modifications 60:9 60:13,19 61:9 63:17 65:2,21 71:7 72:10 77:20 78:2 80:25 87:13 90:21 95:5 96:24 97:5 99:13,22 162:9
modified 59:8
modifier 189:7
modifiers 189:17
moieties 59:8
moiety 109:10 110:5 121:7,22 258:18
mole 225:10
molecule 225:7,11
molecules 96:12
mom 102:10,12,16 102:20,23 103:4 104:3,7,14 105:9 109:10 110:15 111:3 113:10,17 118:19,24 119:19 119:23 120:16 121:19 125:9,10 129:15,20,25 142:7 176:8 232:20 233:6 234:4 235:22 239:7 241:19 245:18 246:21 247:13 261:14,21 272:4 274:18 280:8
moment 22:2
monitor 43:3,9 94:20 95:2 135:13 136:8 181:20 182:2 219:14,20 263:2,8
months 12:23
motivated 288:9 288:18,23 289:4 289:13,16 290:7 290:13
motivation 290:19 290:25 291:2,7
move 287:2
moving 36:5
mulv 214:23 215:20
murnane 3:15 5:23

n

n 3:2 6:4,4,4 136:2 136:2,2,4,4,4 235:6 300:2
name 5:5 6:10 210:21

named 154:15
naming 103:6
nate 5:12
nate.luman 3:6
nathaniel 3:6
natural 90:9,20 91:9,13 169:14,20 170:18 177:16 197:5,7,17 198:3 198:15 212:19 213:2,8
necessarily 70:21 107:13 116:4 207:14
necessary 279:16 301:6
need 7:4 15:13 16:12 57:12 93:19 93:25 101:23 124:22 139:7 143:21 153:20 155:12 169:11 201:16 224:14 253:10 258:21,25 259:8,19 266:6,24 267:22 279:21
needed 41:9 242:12
needs 80:7 138:2 139:11,12 260:5,7
negative 128:9 129:10
neither 200:12
never 23:12 32:13 44:5 81:13 165:21 168:2 193:17 218:16 246:8 252:10,12,15 267:14 268:17
new 1:9,18,18 2:8 2:9,12 3:13,13 4:21 5:3,4 98:4,24 152:4 298:2,4 299:2,4,8
nine 12:13 53:6 128:11 180:4,7,16
nitrobenzyl 165:6 272:6 274:20 278:8,13 279:24 280:10 290:10
noh 107:11,14
normal 15:22 197:13,15
norms 225:5 226:2
notary 2:11 6:6 298:24 299:7 302:25
note 4:4 62:18 152:3
noted 136:3 297:21 301:13
notice 2:9
notwithstanding 192:2,12
ntps 200:3
nuances 200:14
nucleic 61:21
nucleoside 59:2,3 134:3,4 157:11,12 245:25
nucleosides 59:7 98:11
nucleotide 61:10 80:6 107:13 109:5 113:4 119:3 131:23 132:13 133:2,18 134:3 136:21 157:3,13 157:15 158:24,25 169:14 177:16 197:6,7,17 198:16 201:2 233:17,22 235:4 258:15,24 259:7,22 270:20 271:11 272:3,13 273:6,15 274:17 275:2,15 276:2,21 277:18 278:25
nucleotides 55:14 60:8 62:8,14,19 63:7,13,18 65:4 77:20 78:2 98:11 98:16 169:20,23 170:18,20 177:5 191:3 212:19 213:2,9 222:21 234:24
number 51:2 258:12,14 297:18
numeral 85:25 86:9,11
numerically 13:5 124:6

o

o 136:2,2,2 196:21 201:23 202:4,7 214:23 220:5,9 221:13 246:6,12 248:7
oath 57:13 69:12 71:10 159:17 160:7
object 21:12 22:2 152:4 244:15 261:18 270:9
objection 9:5 10:22 17:7 18:19 18:24 19:22 21:23 22:12,13,23,24 23:19,25 24:11,16 25:11 26:14,15 27:15,16,17 31:11 31:17 32:21 33:2 33:21 38:17 43:14 44:8,14 45:9,21 46:9,19 47:23 48:3 60:25 61:12 62:16,23 64:14 65:18 67:25 68:10 69:8 70:4,10,17 71:11 75:4,15 78:6 79:12 80:10 82:7,18,19,23 83:8 83:9,21,22 84:9,21 84:22 85:5 87:6 90:12,23 92:11,23 94:6 96:5 97:10 98:20 99:6,17 101:11 103:2,21 104:20 105:14 106:2 107:6 110:22 111:7 114:3 115:2,8 116:18 117:14,15 118:7 119:4 120:5 120:20 121:16,17 122:14,24 123:15 126:17 131:14 132:15 133:4 134:14,23,24 138:17 140:8 141:14,25 142:8 142:15,16 143:2,3 143:23 144:19,22 145:14 146:5,22 146:23,24 148:3 148:22,23 150:2 154:7,19 156:10 157:6 159:10 161:6,15,16 162:12,22 163:19 164:6,23,24 166:8 166:21,25 167:9 167:24 168:10

169:7 170:5,21 171:24 172:7,14 172:21 173:7,20 174:18,19,20 175:12,18 176:4 176:11,19 181:4,7 191:13 193:15 194:5,14,21 198:4 199:10 200:5 213:4,12 214:10 214:15 216:7,8,22 220:22 222:17 231:13 232:22 233:8,10 236:18 238:14 239:24,25 240:2,9,17 241:4,5 241:6,21 246:16 246:24 247:7,18 248:21,24 249:24 249:25 250:2,24 250:25 251:23 252:8,19 253:5,19 253:20,21 255:4 255:17,19 257:6 257:14,23 261:17 262:2,12 265:10 265:15,25 266:22 269:2,11,20 270:7 270:22 271:12,13 272:14,15 273:7,8 273:17,18 275:4,5 279:4,5,7 280:11 280:18 281:9,16 283:7 284:2,9,15 284:25 285:2,14 285:17,18 286:11 286:20,21 287:11 288:11 289:7,20 289:23 290:15,21 290:22 293:9 294:6 295:16 296:15

objections 11:10 23:17 105:16 129:4 145:5 147:16 149:8,21 150:25 151:6 175:3 249:8 250:12 251:10 273:23 275:17 276:4,23 277:20 291:4,17 292:5

objects 11:8

obligated 35:18

obligation 11:9 30:24

obligations 237:21

observation 268:12

observe 21:7

obtain 184:11

obtained 58:14

obtaining 55:25

obvious 174:15,17 174:23 175:5 228:21

obviously 11:22 91:21 197:7 276:25 295:14

obviousness 290:20 291:8,14

occurred 253:2

october 8:23 9:4

offhand 82:2

office 1:2 4:24 17:5

offices 2:7 4:25

officially 143:18

oh 40:24 51:3 59:22 60:5 104:9 109:9 111:11 131:24 184:7 223:3,10,23 233:21 243:25 255:14 259:5 264:23 267:25 297:9

okay 10:18 14:24 15:12,24 26:7 28:7,12 32:11 38:22 39:18 46:23 49:14,21 50:16 51:7 55:12,24 56:11 59:11 60:5 61:17 63:10,16 67:8,21 69:6 78:8 78:17 84:8 85:18 85:23 86:11 87:12 94:16 95:18 97:25 106:12 107:22 108:10,16,25 110:8 111:21 114:20 123:13 126:8 137:8 147:19 150:15 154:8,9,12 155:10 155:22 158:7 160:20 163:23 171:15 175:22 176:7 186:17 187:25 199:18 203:23 206:3 210:12 223:11 226:22,23 227:18 227:24 228:7 231:9 232:15 234:6,11 244:24 248:10 256:25 258:4 260:17 262:21 264:8,12 264:25 267:20 270:11 271:20,22 274:13,22 278:8 278:13,21 279:11 280:25 282:9 294:23 297:4

olefin 43:20,21,25 182:15

omitted 138:13

once 36:10 184:14 184:14 207:16

ones 18:4 93:21 94:2 141:12 203:14 239:16 278:3 279:2

open 150:10,13 177:23 238:5,5,11 287:3

opinion 120:9 147:9 149:2,3 151:14 193:9 199:9 225:24,25 247:3 249:2,10,16 250:6,10,19 253:8 253:25 254:13 286:15,25 287:7 287:20 288:4 290:12 292:25 293:6 294:4 295:22

opinions 9:23 208:12 209:5 281:12 287:15,17

opposing 6:19

order 7:2 80:5 93:21 94:2 123:2 185:18 224:14 279:16

ordinarily 85:7 233:11

ordinary 42:19 48:18 63:11 65:13 68:5,16 70:2,7 71:24 72:7 74:12

75:24,25 76:7 78:18 83:14 84:13 84:25 86:4,13,22 90:14 93:15 94:10 102:21 110:19,24 120:12 131:6 132:24 133:15 138:24 139:15 142:10,22 175:6 175:24 176:15 188:14,21 190:10 217:2 220:8 229:15 232:3,16 233:2 235:20 236:6 240:11 251:20 260:19 261:12 262:7 265:22 284:20 285:6,15 286:7,17 287:8,22 288:7,17 288:22 289:3,11 289:15
organic 77:3 130:23
original 301:17
originally 268:8
outcome 299:19
outside 18:18 116:17 117:15 134:13 138:18 152:10 197:18,19 236:11 239:25 240:9
overall 175:15 213:10
overlap 19:2
owner 1:10 3:12
oxidation 184:11
oxy 47:20,25 48:12 50:6 53:20 55:19
oxygen 43:22 184:22,24 185:2,6 272:2,12 273:5,14 274:16,25 275:14 275:25 276:20 277:17 278:24 279:17

p

p 3:2,2
p.m. 135:13,16 136:3,8 181:20 182:2 219:14,20 263:2,8 297:15,21
p32 205:5,5
page 40:6 50:17,20 50:25 51:4 85:24 86:6,7,9 100:9,12 126:6 184:17 186:10,12 190:23 195:2,4,9,19 200:17 206:21 243:24,25 245:13 245:15 256:24 257:5 263:15 264:10 266:9 268:23 269:18 271:21 272:20 298:13 300:3 302:8
pages 298:8
pairs 268:7
palladium 182:14 182:16 184:3,14 184:19 185:3,24
paper 37:13 38:3,7 103:20,25 104:4 164:25 189:12,13 205:13 206:14,24 208:3,5 209:9 210:7 211:3,4,5,13 211:15,17,20,23 212:15 219:23 234:25 237:6,11 237:13
papers 128:14 237:15 239:9,12
paragraph 40:5 41:20 107:17,20 107:22 108:7,9 112:10 113:2 130:11 131:8 140:24 155:19 182:7 186:13,14 186:15,16 187:13 232:18 233:13 235:18 263:18,20 263:25 264:2,3,5 264:14,21 272:24
paragraphs 233:4 244:3 245:6
parkway 3:9
part 16:3 50:9 55:4 73:10 84:18 119:10 122:17 127:14 138:23 143:19 144:7,11 152:6 158:16 161:24 174:2 187:12 233:20 241:23,25 242:4,6 242:11 244:7,11 255:22 256:6
particular 34:9,15 39:7 180:25 220:10 223:16 278:4
particularly 17:12 200:2
particulars 11:6
parties 4:14 7:2 299:17
parts 244:9,13
pass 230:14
passed 196:21
patent 1:2,3,10 3:12 4:23 17:3,5 17:10 19:3 20:22 22:5,5 23:13 24:14,18 25:19,23 26:2 35:3,5 41:18 42:21 46:8,14,18 46:22 47:4,11 48:9,12,19 49:6,8 49:15 50:3,8,13,23 51:9 52:23 53:2 53:14 56:2,20 57:11,15,24,24 58:5,9,10,13,22 60:17 61:19 63:12 64:10,18 65:15 66:19,22,23 67:3,5 68:7,17,21,24 69:11 72:2,9 73:6 73:16 74:2 76:3,8 78:20 79:8 83:7 83:16 84:15 87:15 96:4,15,22 97:6,18 98:4,17 99:14,23 100:5 106:18 111:2 114:11 124:9 126:13 127:12,21 128:3 128:17 132:23 136:14 139:2,17 141:5 143:22 144:18 146:7,21 147:14 148:12,21 149:7,18 150:10 150:18,23 152:11 152:16,17,21,25 153:13,14,25,25 154:18,18,24,25

155:6 160:6 163:25 171:12 172:19 173:12 174:25 175:8,9,10 175:25 176:10,18 178:13 180:21 181:3,9,14 189:15 192:7 232:12 239:22 240:15 241:3 245:23 248:20 249:23 250:23 251:7,18 252:4,11,13,16,25 253:11 254:24 255:14 281:15,19 281:22 282:12 283:11 285:7 293:14 300:9,11
patented 22:16
patenting 57:2,4,8
patents 10:21 17:22,24 18:13,22 24:5,7 26:10,11,18 27:3,9 31:15,23 32:7,10,14 36:20 41:23 42:8,14 56:2,6,23 57:6,9 77:8 106:17 127:17 128:14 129:23 151:21 152:15 159:18,24 176:25 177:6,22 178:25 189:8 236:10 239:23 240:25 247:17 254:9 283:2,6,14 290:2 296:25
pcr 197:13,21 198:17 200:4,9,14
pd0 184:15
peak 187:16 200:25,25 201:3 203:8
peek 192:20
pelletier 33:7 265:24 266:19,24 267:7
people 13:4 37:7 44:7 56:17 63:11 82:13 157:21 158:2,8,10 186:6 262:8 288:14 290:13 294:16 295:6
percent 122:8,21 123:11,17 124:7 124:11,19 125:12 125:16,18,19,21 125:24 126:4,5 140:12,14,15 196:15 197:13,15 198:7,15 199:6,20 204:20 207:4 230:8 265:5 266:19
perfect 273:24
perfectly 35:13
perform 200:9 231:11 269:7
performed 126:25 127:4,10,18 128:6 128:22 129:7,14 130:2 238:2 269:17 291:8 295:24 296:10
performing 214:19
period 60:18 65:16 90:9,19 91:11 97:21 134:9 134:18 137:14 142:25 156:23
person 42:19 48:18 65:13 68:5 68:16 69:25 70:6 70:19 71:24 72:7 74:11 75:23,25 76:7 78:8,17,18 82:3 83:14 84:13 84:24 85:7,15 86:4,13,22 90:14 93:15 94:9 102:21 110:19,24 120:12 131:6 132:24 133:15 138:24 139:15 142:10,22 168:18 175:6,14 175:23 176:15 188:13,20 190:10 217:2 220:7,20,24 229:15 232:3,16 233:2,11 235:14 235:19 236:5 240:11 251:20 260:18 261:12 262:6,15 265:22 266:15 284:20 285:5,15 286:7,16 287:8,22 288:7,22 289:3,11,14
personal 218:14
personally 193:13
persons 288:17
perspective 250:17
petitioner 1:6 3:4 4:18 5:11,13
petitioners 6:24
petrochemical 183:6
ph.d. 1:17 2:6 3:6 3:14 6:1 7:1 8:1 9:1 10:1 11:1 12:1 13:1 14:1 15:1 16:1 17:1 18:1 19:1 20:1 21:1 22:1 23:1 24:1 25:1 26:1 27:1 28:1 29:1 30:1 31:1 32:1 33:1 34:1 35:1 36:1 37:1 38:1 39:1 40:1 41:1 42:1 43:1 44:1 45:1 46:1 47:1 48:1 49:1 50:1 51:1 52:1 53:1 54:1 55:1 56:1 57:1 58:1 59:1 60:1 61:1 62:1 63:1 64:1 65:1 66:1 67:1 68:1 69:1 70:1 71:1 72:1 73:1 74:1 75:1 76:1 77:1 78:1 79:1 80:1 81:1 82:1 83:1 84:1 85:1 86:1 87:1 88:1 89:1 90:1 91:1 92:1 93:1 94:1 95:1 96:1 97:1 98:1 99:1 100:1 101:1 102:1 103:1 104:1 105:1 106:1 107:1 108:1 109:1 110:1 111:1 112:1 113:1 114:1 115:1 116:1 117:1 118:1 119:1 120:1 121:1 122:1 123:1 124:1 125:1 126:1 127:1 128:1 129:1 130:1 131:1 132:1

133:1 134:1 135:1
136:1 137:1 138:1
139:1 140:1 141:1
142:1 143:1 144:1
145:1 146:1 147:1
148:1 149:1 150:1
151:1 152:1 153:1
154:1 155:1 156:1
157:1 158:1 159:1
160:1 161:1 162:1
163:1 164:1 165:1
166:1 167:1 168:1
169:1 170:1 171:1
172:1 173:1 174:1
175:1 176:1 177:1
178:1 179:1 180:1
181:1 182:1 183:1
184:1 185:1 186:1
187:1 188:1 189:1
190:1 191:1 192:1
193:1 194:1 195:1
196:1 197:1 198:1
199:1 200:1 201:1
202:1 203:1 204:1
205:1 206:1 207:1
208:1 209:1 210:1
211:1 212:1 213:1
214:1 215:1 216:1
217:1 218:1 219:1
220:1 221:1 222:1
223:1 224:1 225:1
226:1 227:1 228:1
229:1 230:1 231:1
232:1 233:1 234:1
235:1 236:1 237:1
238:1 239:1 240:1
241:1 242:1 243:1
244:1 245:1 246:1
247:1 248:1 249:1
250:1 251:1 252:1
253:1 254:1 255:1
256:1 257:1 258:1
259:1 260:1 261:1
262:1 263:1 264:1
265:1 266:1 267:1
268:1 269:1 270:1
271:1 272:1 273:1
274:1 275:1 276:1
277:1 278:1 279:1
280:1 281:1 282:1
283:1 284:1 285:1
286:1 287:1 288:1
289:1 290:1 291:1
292:1 293:1 294:1
295:1 296:1 297:1
298:6,16 300:4
302:20

pharmaceutical 79:24

phenoxy 89:11 91:21

phenyl 91:24 93:7

pick 4:6 201:14

piece 183:9 235:7

place 4:8,13 184:8

please 4:4,8 5:9 6:10,14 8:24 22:3 26:5 29:20 40:7 46:24 49:3 50:7 58:18 92:25 102:3 105:17 108:11 112:9 126:7 129:4 130:11 136:12 137:22 141:7 150:11 169:19 171:16 182:9 183:15 185:13 186:11 195:3 215:9 219:23 221:24 223:7 224:13 232:12,14 235:12 243:24 250:5 263:19 264:17 266:12 268:4 301:4,10

plus 184:3,23,25 185:4 215:14 216:2

point 26:24 27:6 27:24 296:22

pointed 68:15

pointing 165:6

pol 267:8 268:6,9 268:14

polymerase 42:6 136:23 177:14 178:11,12,23 190:7,15 193:14 193:18 207:19 223:9 227:13,20 233:24 259:10,11 265:4,17 267:15 267:15 268:13,16 268:18,22 270:19 271:10

polymerases 141:17,22 142:23 143:14 178:10 179:3 191:7,19 267:12 270:14 286:9 288:21

polymerization 268:10

portion 58:21 243:6,21

portions 245:4

posa 231:19 232:7 234:13,16 236:14 262:15 267:10,14 268:17 269:24 286:3

position 28:18 43:24 60:24 63:20 66:2,9 67:24 68:9 74:23 80:25 81:16 82:5,16 83:19 99:13 122:10 133:20 155:24 156:8 163:16 164:20 166:19 167:8 189:7,17 246:21

positive 128:9 129:9 290:9

possibilities 70:21 70:23

possibility 67:12 67:13

possible 71:13 192:7 278:2

possibly 271:25 272:11 273:5,13 274:16,25 275:13 275:24 276:9,19 277:16 278:23 279:3

potential 21:20 70:15 71:7 85:3 281:23

preceding 267:3

precise 48:11 55:23 57:25 58:4 68:22,23

predict 79:25

preexisting 120:15

preferences 287:7

preparation 13:11 40:17 41:3 53:6

prepare 12:24 57:23 58:5 127:24 142:19 153:22 170:23,24

prepared 14:21 41:10 53:12,13

60:16 152:22 166:11 171:6 172:3 180:15
preparing 9:22 12:9,20 13:15 128:11 143:8 153:11 180:5,8
presence 169:20 170:17 212:19,25
present 3:18 6:20 13:5 106:4 109:4 109:25 112:23 113:6,19 121:24 233:16,19 234:9 234:20 260:16
presented 118:18
presenting 117:24
pretty 123:17 151:25 174:15 216:11 223:19 267:21
primarily 283:15
primary 77:15
primer 201:19 202:5
prior 10:19 17:13 26:8 28:21 33:15 33:19 34:7,8,12,13 34:14,25 35:6,15 35:25 36:8 39:11 39:24 109:14,17 118:12 122:4 126:16 127:6,8 132:4 138:23 139:10 149:23 151:3 160:18 237:3 251:16 254:21 257:22 258:10 259:16,17 260:4,12 293:16 294:17,22 295:11 295:11,19,21 296:17
priority 66:24
private 4:6
privilege 244:21
privileged 154:3,6 242:21
probably 8:10,14 9:10 12:12,16,22 20:16 24:25 25:8 80:23 216:10,16 228:23
prober 36:16,20 185:19,21
problem 28:13 98:3 279:10 297:6
problematic 188:4 262:11
procedure 114:17 114:22 116:15,25
procedures 113:13 113:24 120:2 131:9 132:8,12 234:8
proceed 41:24 182:17
proceedings 30:8 35:19 41:25 42:9 43:6 94:23 181:23 219:17 263:5 299:11,14
process 11:5 20:10 50:10 54:6 57:2,4 57:8,11 62:21 94:8 182:18,23 183:3,14,25 184:10 213:11 253:3 286:19
processes 47:18 55:4 80:9,12 260:10
product 19:6,8,10 19:14,20 57:24
products 21:9
professional 2:11
project 9:3 10:20 17:13 26:9 28:22 32:12,13,18 33:16 33:20,25 34:20 35:2,16 36:2,6,11 36:17 37:8 39:3 39:11,25 143:20 182:22 208:2 209:16
projects 21:16
promote 191:24
promoted 187:4
promoting 262:9
prop 89:22
propanol 89:25
propene 46:22 91:23
propenyl 42:3,5 44:13,18,20,22,22 45:7,11,20,24 46:3 46:5 47:20,25 48:12 49:8,10,12 49:16,18,20 50:6 50:15 51:16,20 52:6,18,19,24 53:10,15,20 55:5,6 55:19 89:19,23 90:4 93:6 101:4 104:22,24 110:13 110:16 189:11 191:16 196:14,15 196:17 220:18,21 221:9,12,15 234:5 245:24 252:3 260:25 261:4 281:20 292:16,19
propenyloxys 55:15
property 22:11
propose 63:6,16 82:4,13 261:23
proposed 64:10 155:6
proposing 65:17 65:20 156:6
proposition 157:18 162:2,6
prosecution 16:2,4 16:9,11,19 17:2 56:3 241:11 242:11,19 243:2,6 243:12 244:5 263:10 271:21 277:3
protect 235:3,5
protective 7:2
protocol 15:18 207:9,13
proved 73:3
provide 30:15 31:20 38:8 39:21 151:14
provided 153:9
provides 245:17
proving 73:8,17 74:3
ptab 117:25
public 2:12 6:6 238:24 298:24 299:7 302:25
publication 10:13 33:12,15 40:2 104:2,13 146:12 147:25 148:14 189:19
publications 32:6

published 26:17 26:20 147:18 210:7 237:6 238:8
purchased 19:12 20:3
purified 199:3
purify 199:4
purines 185:23
purpose 16:8,10 16:18 25:9 27:13 37:18 42:9 156:25 183:24 184:4 208:23 279:19 281:25 282:21
purposes 6:20 98:16 171:5 207:25 208:22 209:21 260:16
pursuant 2:9 177:21
pursue 93:16 288:19,24
put 6:22 23:4 47:16 66:18 118:24 152:5 162:15 174:7 182:15 185:18 206:5 220:2 281:7
putting 118:15
pyrimidines 185:23

q

qualifications 66:19
qualified 77:5
qualifies 176:9
qualify 53:24 172:6
quantify 9:9
quantitative 124:4 125:15,20,22 138:6,8 140:6,11 140:15,18
question 11:23,24 12:2 14:12 15:16 22:15 27:23 29:15 33:3 35:21,23 38:20 39:9 40:25 46:16,24,25 48:4 50:12 53:22 54:5 54:8 61:16 64:9 67:16,20 73:13,19 73:21,23 80:20 82:25 85:17 90:17 92:4 97:24 104:10 107:17 115:14 116:22 119:16 123:5,7 126:23 131:20 147:3 148:9 150:7 153:5 153:7 161:9,18 163:13,24 166:6 166:16 167:4 174:22 180:23 189:14 198:20 217:23 226:25 228:8 232:25 235:12 240:10 244:19 245:2 252:21 253:24 260:15 261:19 266:11,14 270:2,3 278:18 282:5 287:6 291:5,22 294:11 296:7,18 296:20
questioned 67:10 115:20 268:8
questioning 21:13 53:25 244:16
questions 11:21 24:12 41:10 53:14 54:24 154:23 171:7,9 182:12 224:10 270:8 277:8 279:8
quick 42:24
quicker 155:15
quite 22:14 197:8
quote 186:19 187:12

r

r 3:2,6,10 43:21 136:2 171:17 192:6 240:24 302:1,1
rad 7:13
radio 205:4,5
ran 212:13
rapidly 138:3,16
rate 177:17,17
rates 168:3
rea 101:6
reach 26:9
reached 39:2
reaching 20:25
react 262:16
reaction 136:24 184:8 185:5,7 186:5 259:12
reactions 82:6 127:2
reactivity 197:6
read 13:13 27:11 27:12,20,24 28:4 28:10,15,23 32:4,5 32:14 39:17,25 42:13 57:14 63:21 66:22 70:20 91:19 93:4 102:22 108:9 128:13 137:9 139:3,5,7 142:19 162:10 170:24 174:10 196:10 197:11 200:10,13 207:23 210:11,15 211:9 232:7 235:11,13 237:10 241:23,25 242:2,4 242:5,6,12,19 243:14,16,18,19 244:4,8,12 245:4 245:10 252:10,12 252:15 253:10 258:4 263:18,24 263:25 264:16,24 267:20,22,23 268:2,2 274:23 283:11 298:7 301:4
reading 32:10,17 48:19 63:12 65:14 68:6,17 70:7 72:8 76:2,8 78:19 83:15 84:14 110:25 121:8 131:7 134:5 138:25 139:16 142:11 174:11 175:7,24 232:17 233:3 239:22 254:18 273:19 274:3,11 293:13
real 3:5
really 18:3 21:18 39:5 73:18 79:25 81:8 101:13 139:13 142:17 143:4 146:25 147:6 161:17 165:10 172:3 186:7,8 187:11 192:8 193:11 196:10 198:8,8

201:13 209:2 217:19 225:2 227:24 229:8 235:17,25 246:8 256:12 258:20 260:12 269:22 270:15 280:22 286:23 296:17
reason 12:4,7 28:4 48:7 65:10 99:11 99:20 120:2 130:8 246:20 248:16 250:21 251:5 265:12,20 267:6 267:13 272:9 276:17 277:14 279:15 280:16 301:7 302:10,12 302:14,16,18
reasonable 37:22 142:14 146:18 148:16 151:17 287:21 291:13,21 291:24 292:2,9 293:21 295:2
reasons 302:6
recall 33:8 54:10 128:21 129:6 181:10 238:12 283:17
receipt 301:19
receive 8:4
received 243:7,11
recess 43:5 94:22 135:15 181:22 219:16 263:4
recognition 177:13
recognize 20:20 48:20 51:11 158:23
recollection 8:8 53:12 248:5
record 4:3,14 6:11 6:22 11:10 23:21 43:4,8 94:21,25 101:24 135:14 136:7 152:3 181:21,25 219:15 219:19 235:13 263:3,7 278:20 294:24 297:15,20 299:13
recorded 4:16
recording 4:12
redwood 3:9,9
refer 101:7 103:25 125:5 132:3 147:17 156:18 162:3 220:9 221:13 224:8
reference 34:13,15 34:23 59:2,6 100:13,14,24 101:2 102:9,22 103:9 106:9 111:15 125:2 155:17 183:17 186:18 218:9 223:17 226:12 271:16
referenced 264:14
references 10:2,4 10:9 221:17,18,22 261:8 293:18
referencing 112:8
referred 59:6 264:20
referring 101:13 102:24 103:13 104:25 105:2 110:8 114:18
147:21 183:21 192:21,22 206:6 208:6 221:5 224:18,19 226:15 228:2 234:10,21 237:14 239:10
refers 100:23 102:12 103:18,19 106:13 110:4 124:15 125:6 189:10 222:3 223:19 224:23 234:19 248:6 271:17
refines 101:3
reflected 198:24
reframe 198:19,20
refresh 170:25 184:19 248:5
regarding 155:19 171:7 176:24 193:24 286:16
registered 2:10
reines 3:10 5:10 5:10 6:9,17 8:16 23:18 42:23 48:25 87:21 94:17 95:9 135:7 136:11 152:9,13 181:17 219:11 224:9 235:11 244:23 262:21 263:15 264:3,7 273:21 274:4,8 279:9 297:4,10 300:5
rejected 216:15
related 21:9 26:18 154:17,21,25 299:16
relates 27:2,8
relating 246:3
relation 142:24
relatively 216:20 216:23 222:23
release 292:19
relevant 175:9,25 217:20,22 218:4 218:15
reliance 238:19,22
relied 41:12
rely 162:6
relying 217:24
remain 260:11
remember 8:6 18:3,5,6,8,10 19:24 20:23,24 22:25 23:3,9 24:17,21 25:3,7 26:16,22 31:13 32:9,16,24 34:3,6 53:16 66:21 67:22 68:3 75:6 83:13 95:25 96:2,8,10,19 99:9 123:7 141:3 158:19 160:16 164:14 165:9 181:14 208:8,11 219:8 238:16 254:4 284:18
remembered 161:5,14
removed 120:17 130:13 138:3,15 184:9 234:14 259:19
repeat 27:22 34:10 35:20 38:19 40:25 46:15 73:22,22 77:22 82:25 97:23 104:10 126:22 150:12 161:9

163:23 167:3 174:21 188:18 232:24 244:25 253:24 255:6 266:13 278:18 296:6,6
repeatedly 231:22
rephrase 144:5 278:14
report 14:14,16,17 14:22 152:7 186:11 195:7,19 209:6 256:23 276:25
reported 1:23 125:11 299:10
reporter 2:11 259:4
reports 125:10 152:8
representing 5:6
represents 171:18 202:3
reputation 22:18 24:4
required 13:20 184:18 186:8
requirement 137:16,18,23,25 138:14 168:7,13 168:15,19 169:3 172:13 178:13,24 180:11,17 258:20 259:13,15,15
requirements 137:4,6,11,13 138:21 139:19,25 140:3 145:13 146:3,20 147:13 148:11,20 149:5 149:17 150:22 168:23 179:14 181:2,13 249:22 250:22 251:6 254:16,25 255:2 255:11,25 256:9 256:20,22 257:2 257:11,19,21 258:8 260:22 261:15 294:2,9,12
requires 26:13 82:19 144:23 147:8 159:11,14 282:6
reread 13:7,10 32:6 52:25 53:8 66:22 127:20 128:2
research 3:22 5:17 18:21,25 185:9
researchers 270:18 271:8
reserving 7:3
residual 197:17 198:2
respect 56:25 116:13 125:9 129:24 163:10 175:22 194:24 210:2,13 282:16
respond 11:9
response 277:13 277:13 282:15
responsive 295:5
rest 66:9 174:8,14 245:10
result 19:6
results 38:2 193:3 290:9
resumed 136:5
retained 297:19
return 301:17
reveal 123:3
reversible 34:17 157:3,12,14,23 158:12,25 159:8 161:3,11,23 163:9 166:14 218:17,20
review 24:13 30:16 31:23 32:3 39:14,15 40:16 41:4 42:7 127:16 128:17 133:21 237:25 238:11,24 241:10,22 249:14 252:4,5 281:21 282:12
reviewed 26:25 27:7 31:14 39:10 40:8 241:13
reviewing 10:14 24:17 71:25 129:22
reviews 9:21
rhodamine 152:15
richfield 183:5
right 7:20 10:6,17 14:16,19,22,23 15:7 30:6,12,21 42:24 50:21 51:18 51:19 54:6 55:11 56:6 60:11 61:6 62:15 81:7 86:15 96:16,18,25 98:7 98:13 101:17,22 102:15 103:9 104:12,16 105:19 106:21,24 108:18 113:9 114:12,13 118:14 119:15 121:7 130:8,9,19 135:10 145:24 150:6 151:17,18 155:5 160:3,23,25 164:9 167:19 179:25 180:3,13 181:6,17 184:20 186:22 187:24 199:18 200:16 204:7 206:3 211:18,21 212:17 217:4 219:11 229:13,14 231:8 237:19 256:6,18 257:5 269:9 273:3 283:19 285:11,23 285:24 292:11,25
rights 7:3
robert 3:14 5:19
role 147:11 149:13 186:4 290:18,24 291:6,12,25
roman 85:25 86:9 86:11
romesberg 3:22 5:16,17
romesberg's 152:7
rpr 1:23 299:6,25
rschwartz 3:14
rt 196:19,20 214:23 215:20
ruggieri 1:23 2:10 299:6,25
rule 75:21
rules 15:12
run 184:21 197:14 228:21
running 228:19

s

s 3:2,14 6:4 136:2 136:2,2,4
san 3:5

sanger 37:9 81:19 81:21,25 82:11 85:11 155:4,7 156:11 157:24,25 158:9,10 159:9 162:24 163:4,7 164:8 165:16,18 166:4,13 167:23 168:4,7 169:5,13 169:17,25 170:7,9 171:2,7 185:15 187:2,4,6 188:4 192:8,15 193:6 197:22 217:18 223:11,14,21 224:24 225:6,22
satisfies 260:21
satisfy 138:9 172:12 178:12 179:14 249:21 251:16 258:22
saturated 205:11 205:15
saturation 205:13 208:15
saw 67:2,5,5 199:20,25 208:3
saying 28:3,14 49:11 56:19 71:6 71:15 79:18 80:14 92:21 115:16 161:22 165:16 189:20,20 192:13 199:17 211:16 223:24 232:19 233:5 237:8 238:16 256:15
says 59:15 60:2 70:24 102:16 109:23 111:17 114:5 121:10,18 122:5 124:8,16 125:17 130:12 131:22,24 136:15 136:19 137:3 157:10,13 171:17 220:4 222:2 228:3 233:20 245:14,16 273:11,13 274:14 276:5,10
sbs 81:20 123:24 124:2 137:11 166:14 223:15 235:8,16 236:4,9 236:25 251:17 261:11 267:16 268:20
scheme 233:25
schwartz 3:14 5:19,20 9:5 10:22 17:7 18:18,24 19:22 21:11,23 22:12,23 23:6,16 24:11,16 25:11 26:3,13 27:15 29:11,16 31:11,17 32:21,25 33:21 38:17 43:14 44:8 44:14 45:9,21 46:9,19 47:23 48:3,22 54:12 60:25 61:12 62:16 62:23 64:14 65:18 67:14,25 68:10 69:8 70:4,10,17 71:11 75:4,15 78:6 79:12 80:10 82:7,18,23 83:8,21 84:9,21 85:5,21 87:6,19 90:12,23 92:11,23 94:6 95:7 96:5 97:10 98:20 99:6,17 101:11 103:2,16 103:21 104:20 105:14 106:2 107:6 108:2 110:22 111:7 114:3 115:2,8 116:17 117:14 118:7 119:4 120:5 120:20 121:16 122:14,24 123:15 126:17 129:2 131:14 132:15 133:4 134:13,23 138:17 140:8 141:14,25 142:8 142:15 143:2,23 144:19,22 145:4 145:14 146:5,22 147:15 148:3,22 149:8,20 150:2,24 151:5 152:2,10 153:4 154:19 156:10 157:6 159:10 161:6,15 162:12,22 163:19 164:6,23 166:8,21 166:25 167:9,24 168:10 169:7 170:5,21 171:24 172:7,14,21 173:7 173:20 174:18 175:2,12,18 176:4 176:11,19 181:4,7 189:25 191:13 192:4 193:15 194:5,14,21 195:4 197:18 198:4 199:10 200:5 210:10 213:4,12 214:10,15 216:7 216:22 220:22 221:21 222:17 224:5,17 225:17 231:13 232:22 233:8 236:11,18 238:14 239:24 240:8,17 241:4,21 244:14,24 246:16 246:24 247:7,18 248:21,24 249:7 249:24 250:11,24 251:9,23 252:8,19 253:5,19 255:4,17 257:6,14,23 259:3 261:17 262:2,12 262:18 263:13,23 264:5,8 265:10,15 265:25 266:22 269:2,11,20 270:7 270:22 271:12 272:14 273:7,17 274:2,6,13 275:4 275:16 276:3,22 277:19 279:4,11 280:11,18 281:9 281:16 282:3 283:7 284:2,9,15 284:25 285:14,17 286:11,20 287:11 288:11 289:7,20 289:23 290:15,21 291:3,16 292:4 293:9 294:6 295:16 296:15
science 33:7 61:21 98:24
scientific 145:24
scope 18:19 21:13 21:24 22:13,24 24:3,9,12 25:12 26:14 27:16 31:12

31:18 32:22 103:3 110:23 115:9 116:18 117:16 118:8 119:5 120:6 120:21 131:15 132:16 133:5 134:13,24 138:18 141:15 142:2,16 143:3,21 144:2,4 144:20 145:15 146:6,23 148:4,23 151:2 152:11 164:24 166:9 167:25 168:11 169:8 170:6,22 171:25 172:8,18 172:20,24 173:8 173:21 175:13,19 176:5,12,20 179:18 197:19 200:6 232:23 236:12 239:25 240:9,18 241:5 243:20 244:3 245:8 246:17,25 247:8,15,19 248:22 249:21 250:2,25 251:24 252:24 253:17,21 255:5,19 261:18 261:19 262:3,13 265:11,16 266:2 266:23 269:3,12 269:21 270:8,23 271:13 272:15 273:8,18 275:5 279:5 280:12,19 281:10,17 284:3 284:16 285:2,18 286:12,21 287:12 288:12 289:8,24 290:16,23 294:7

scott 58:14 75:2 154:14 158:22

screen 196:22 231:16

screened 191:2

screening 190:25 203:12 214:5 216:12 230:15

scripts 3:22 5:17

search 54:24

searches 10:2,8

sec 89:6

second 267:13 287:18

secret 28:6,7,11 29:2,9 30:3 39:20 239:2

section 108:7,23 155:11 243:16,17 243:20,22,23 245:6

see 13:19 33:8,10 40:10,11 41:19 47:5 49:5,7,9,11 50:25 51:4,22 53:9 59:2,4,11,15 59:18,20,22 60:4 60:14,15 63:22 72:14 85:25 86:2 86:10 88:2 89:25 93:21 94:2 95:21 100:14,17,18,21 102:9,13 103:8,11 106:8,11,12,15 107:20,21 108:25 109:25 110:3,6,7 110:20 112:13 113:14,16 114:6 115:23,25 122:5 123:8,12 125:13 125:14 126:9,11 130:12,17 131:21 132:9,10 136:14 136:17,25 137:2,7 137:9 140:7,16 141:8,10,11 155:16,18,21 156:3,15,16,19 157:10,13,16 171:16,20,21 182:19,20 183:17 183:20 186:18 187:18 189:2 191:8 195:12,13 196:21,25 197:9 202:11,22 203:2,3 205:12,16 208:3 210:18,19 212:22 214:24,25 220:4,6 220:17 221:25 225:19 226:12,14 226:24 227:2,13 228:3,5,15,16,17 229:5 231:18,20 232:7 233:13 234:18,23 235:15 245:14,19 257:3 257:13,17 261:5,9 264:15,18,19 265:7,9 271:23 272:7,8,22,25 273:3 274:11 282:22 283:16 285:21

seeing 111:2 128:21 129:6 204:23 284:18

seen 20:21 127:17 129:12 221:4 246:13 248:11

sees 203:10,11

segregate 105:20

select 279:15 286:18

selected 14:15

selecting 286:8

selection 279:21

sense 15:7 135:10

sensitive 4:5

sentence 104:25 109:15 110:2 122:19 131:18,19 136:18 137:3 182:12 272:23 273:2,20 274:3,14

sequence 268:13

sequencers 20:19

sequencing 17:20 17:23 18:2,21 19:5,16 20:9 22:7 22:21 23:14 24:15 26:12 29:7,24 30:18 34:16,22 37:10 61:11 62:4 62:10,21 65:4 66:2 69:25 74:24 78:4 79:10 80:7 80:18 81:11,19,21 81:25 82:5,11,17 83:19 84:18 85:11 87:5,14 92:10 93:19 94:3 97:6 98:5 99:14,23 117:3,12 118:6,23 120:23,24 124:13 134:22 136:15,19 138:21 139:20 155:2,4,7 156:8,11 157:25 158:11 159:9 161:4,12 162:24 163:4,8

164:4,8 165:15,17 165:18 166:4,13 167:23 168:4,8,14 169:4,6,13,18 170:2,7,9 171:2,8 185:9,15 187:2,5,7 188:4 192:9,15 193:6 197:23 217:19 218:25,25 219:9 223:14,21 223:25 224:24,25 225:7,11,13,14,22 226:4,16 227:5 228:10 233:25 254:16 255:3,11 255:25 256:10 257:3,11 258:8,23 260:22 261:16 267:16 268:20,20 269:10 270:18 271:9,9 286:9,19 287:10 288:10 289:21 293:5,25 294:14 295:4,9 296:14
series 91:5
served 7:25
set 9:23 98:8 154:23 257:4,19 260:23 299:21
sets 256:10 257:10
seven 191:4,6,19 263:9 297:19
sharing 268:13
sheet 301:8,11,14 301:17
shen 34:4,21
shores 3:9,9
short 8:17 52:10 52:10 181:18
shorter 201:4
shortly 25:8
show 8:12 13:23 16:13 46:12 58:8 73:16 74:3,6 150:8 183:7 200:20 206:17 213:22 215:9,22 216:4 230:12 235:5,17,25 236:2 242:23 272:17
showed 230:17 279:25 290:9
showing 73:2 124:24 190:20 227:15 229:9 230:5,7,21,22 231:22 232:10 235:2
shown 130:14 189:22 193:23 194:10 204:14 231:17 234:15 236:10 274:21 280:5 298:12
shows 125:4 196:11,12,17 200:21,23 203:17 210:8,15 215:6,13 227:10,18 230:12 231:7,10 235:9 237:7 251:11
sign 57:13 301:10
signature 299:24
signed 8:23 69:12 71:9 159:16,20,24 160:7
significance 23:4 34:21
significant 22:10 26:11 31:10 32:20 199:25
signing 301:12
similar 177:17,19
similarity 268:14
simple 115:14
simply 115:19
single 87:17 88:7,8 88:11,13,23,24,25 89:8,10,11,16 103:6,13 225:7,10 225:11
sir 221:8 263:15 272:17
site 265:3 266:18
sitting 53:12 75:8 127:22 128:4,20 129:5,11 130:3 145:18 151:11 180:23 237:9
situation 185:25
six 12:16 191:6 219:21 221:25
size 266:17
skill 42:19 48:18 63:11 65:14 68:6 68:16 70:2,7 71:25 72:8 74:12 76:2,7 78:19 83:15 84:14,25 86:5,13,23 90:15 93:15 94:9,10 102:22 110:19,25 120:12 131:7 132:25 133:15 138:24 139:16 142:11,22 175:7 175:24 176:15 188:14,21 190:10 217:3 220:8 229:16 232:3,17 233:3 235:20 236:6 240:12 251:21 260:19 261:13 262:7 265:22 266:15 284:20 285:6,16 286:7,17 287:8,22 288:8,17,23 289:4 289:12,15
skilled 70:19 85:8 139:18 157:21 168:18 175:14 233:12 235:14
slow 259:3
slowly 267:20
small 171:18,23 172:6,13,16 173:6 174:16,24 175:23 176:9,16 177:2 197:4 198:3 217:4 218:7 222:23 240:22 241:9,19 245:18 246:22 247:14
software 266:20 266:21
solexa 19:20,25 20:3,4,12 21:19
solid 19:9,15 20:15 22:8,21 286:6
solution 138:14
solutions 5:7
solvent 184:6,7
sorry 8:16 15:10 27:5 34:10 40:24 51:3 62:12 77:22 95:14 98:2 101:23 101:25 102:7 105:18 150:12 188:18 195:7,8 209:19 215:16,21 218:3 228:12

232:24 243:25 244:25 256:4,16 259:5 267:25 272:19 278:6 287:19
sounds 46:23
source 206:20
space 18:2 265:2 265:13 266:17 301:8
speak 15:14 24:18
speaking 209:14 233:18 234:8,20 279:9
spec 132:3
speci 282:23
special 66:5,7
specific 16:18 100:18,23 101:10 102:17 110:9,10 121:5,21
specifically 68:18 109:11 182:7 209:15 263:12 283:14
specification 63:2 69:11 70:24 73:11 233:14,20 234:3 241:2 245:16 254:24
specifications 61:4 198:10 282:24
specifies 260:5
speculate 92:19 134:6 236:13 262:17
speculating 65:8 65:11
speculation 71:9 71:18,20,21,23 72:5,13,18,24 73:6 73:14,25 74:5,9,15 93:10 134:10,18 135:5,6 216:17,18
speed 213:2
speeds 213:10
spend 9:3 12:8
spent 13:14 128:10 180:4,7
spirit 54:6
spoken 269:14
ss 298:3 299:3
standpoint 267:8
stands 103:4
star 216:13
start 31:2 43:10 100:8 102:3 115:19 136:9 158:6 203:24 207:18 208:16 259:6
started 31:3,4 33:24 36:11 39:3
starting 107:18 109:15
state 2:12 5:9 6:10 23:21 29:6 30:17 40:7 41:18 92:6 97:7,13,19 98:17 99:4,8,15,25 105:24 107:3,9,10 107:23 108:5,14 109:16,20 120:15 120:25 129:12 134:7,19,19 158:14 184:3,23 184:25 185:4 187:14 258:6 298:2 299:2,8 301:7
stated 158:20
statement 23:8 40:13 74:17 112:24 113:20 121:18 122:4,10 132:2 134:16 209:10 233:21 238:23 255:10 260:3 280:20,24
statements 48:24 54:13 248:17 255:18,24 256:8 256:13,14 257:4 282:19 283:12
states 1:2 109:21 109:23 113:10 116:5 119:22 121:14 123:8 132:5 187:14 241:19 271:24 272:18
static 205:25
stating 57:13 158:15,17 159:24 235:21 254:24 261:14 262:10
step 68:19 76:5 145:7 162:8 193:22
steve 6:12
steven 1:17 2:6 4:17 6:1 7:1 8:1 9:1 10:1 11:1 12:1 13:1 14:1 15:1 16:1 17:1 18:1 19:1 20:1 21:1 22:1 23:1 24:1 25:1 26:1 27:1 28:1 29:1 30:1 31:1 32:1 33:1 34:1 35:1 36:1 37:1 38:1 39:1 40:1 41:1 42:1 43:1 44:1 45:1 46:1 47:1 48:1 49:1 50:1 51:1 52:1 53:1 54:1 55:1 56:1 57:1 58:1 59:1 60:1 61:1 62:1 63:1 64:1 65:1 66:1 67:1 68:1 69:1 70:1 71:1 72:1 73:1 74:1 75:1 76:1 77:1 78:1 79:1 80:1 81:1 82:1 83:1 84:1 85:1 86:1 87:1 88:1 89:1 90:1 91:1 92:1 93:1 94:1 95:1 96:1 97:1 98:1 99:1 100:1 101:1 102:1 103:1 104:1 105:1 106:1 107:1 108:1 109:1 110:1 111:1 112:1 113:1 114:1 115:1 116:1 117:1 118:1 119:1 120:1 121:1 122:1 123:1 124:1 125:1 126:1 127:1 128:1 129:1 130:1 131:1 132:1 133:1 134:1 135:1 136:1 137:1 138:1 139:1 140:1 141:1 142:1 143:1 144:1 145:1 146:1 147:1 148:1 149:1 150:1 151:1 152:1 153:1 154:1 155:1 156:1 157:1 158:1 159:1 160:1 161:1 162:1

163:1 164:1 165:1 166:1 167:1 168:1 169:1 170:1 171:1 172:1 173:1 174:1 175:1 176:1 177:1 178:1 179:1 180:1 181:1 182:1 183:1 184:1 185:1 186:1 187:1 188:1 189:1 190:1 191:1 192:1 193:1 194:1 195:1 196:1 197:1 198:1 199:1 200:1 201:1 202:1 203:1 204:1 205:1 206:1 207:1 208:1 209:1 210:1 211:1 212:1 213:1 214:1 215:1 216:1 217:1 218:1 219:1 220:1 221:1 222:1 223:1 224:1 225:1 226:1 227:1 228:1 229:1 230:1 231:1 232:1 233:1 234:1 235:1 236:1 237:1 238:1 239:1 240:1 241:1 242:1 243:1 244:1 245:1 246:1 247:1 248:1 249:1 250:1 251:1 252:1 253:1 254:1 255:1 256:1 257:1 258:1 259:1 260:1 261:1 262:1 263:1 264:1 265:1 266:1 267:1 268:1 269:1 270:1 271:1 272:1 273:1 274:1 275:1 276:1 277:1 278:1 279:1 280:1 281:1 282:1 283:1 284:1 285:1 286:1 287:1 288:1 289:1 290:1 291:1 292:1 293:1 294:1 295:1 296:1 297:1 297:17 298:6,16 300:4 302:20

stop 184:16 297:7
stopping 297:6
story 231:24
straight 54:2
strand 109:12 136:23 235:7 260:8
stretch 11:15
structure 16:13 45:2 49:9 52:13 87:18 88:7,9,12,14 88:16,23,24 89:2 89:12 100:24 101:4 102:24 103:14 106:18 189:11 221:19
structures 89:16 89:16 111:6 192:6 270:19 271:10 274:20
studied 38:15 41:18,22 42:2 135:3 143:8 168:2 173:11
study 130:6 166:15 173:10 179:3,21
stuff 274:9
subfield 158:9
subject 143:12 193:10 195:2 209:5 298:11 301:12
submitted 160:5 160:15
submitting 127:11
subscribed 298:20 302:22
subset 278:5
substitute 138:5
substrate 42:5 174:3 177:14 207:19 292:17
success 287:22 291:13,22,24 292:2,10 293:22 295:3
successful 165:3 166:18 167:7,15 167:17 202:24 296:13
successfully 165:4
sufficiency 210:16
sugar 59:16 60:3,5
suggest 63:23
suggested 284:4
suggestion 74:14 93:17
suitable 162:20 163:14 164:2,19 165:14 166:2 189:7,16 191:24
summarized 129:16 256:20,23
summary 106:9 106:22 126:20
superior 66:11,13
supplied 10:3,4 254:21 261:8 293:18
support 195:22
supports 104:3,5 104:14,17,22 105:8 195:20,23 209:10
suppose 27:18 160:4 275:19
supposed 129:21 130:6 174:6 242:2 242:3,8
supposedly 195:20
sure 15:20 42:11 56:24 76:19 81:23 104:11 137:21 139:4 153:6 161:10 167:5 173:18,23,24 190:18 223:19 255:8 276:7 278:16 290:3 296:8
surprised 225:19
survive 260:9
sworn 6:6 298:20 302:22
synthesis 17:20,24 18:2,21 19:5,16 20:10 22:7,22 23:15 24:15 26:12 29:7,24 30:18 34:17,22 77:3 115:5 117:13 118:6,23 120:23 120:24 124:13 126:15 132:18 136:15,20 138:22 139:20 167:13 168:14 169:5 219:2,10 224:2,25 225:13,14 226:5 226:16 227:5 228:11 254:17 255:3,12 256:2,10 257:3,12 258:9,23 260:23 261:16 286:10,19 287:10

288:10 289:21 293:5,25 294:15 295:4,9 296:14
synthesize 112:15 113:3,8,9 116:6 117:11 118:3 133:2,18
synthesized 113:12
synthesizing 94:14 116:25 132:13 167:16
synthetic 59:7 61:8 62:20 63:17 64:11 69:18 107:12 113:13,24 114:22 116:15,25 118:21 119:25 123:22 130:23 131:9 132:8,12 134:8,20 234:7
synthetically 79:20 81:2
system 22:8,9 51:6 137:5 138:22 139:20 178:25 179:2 201:20 202:5 233:25 255:3,12 256:2 288:10
systems 19:16 20:11 22:22

t

t 6:4 131:12 136:2 136:4 191:3 197:2 204:24 302:1
table 190:24 191:8 192:3,13 193:24 194:11,18 196:19 215:25 220:2 229:2,4 230:15 231:17
tag 16:16 241:17 259:18
tags 109:8
take 4:13 11:14 24:10 42:23 61:17 85:2 94:17 96:9 135:8 139:6 145:7 165:19 181:18 193:21 196:11 214:22 219:12 222:9 224:13 262:21 278:9
taken 4:17 7:6,17 7:23 11:3 135:15 238:18,21
takes 122:7,20 123:10 124:10,17 184:8
talk 64:4
talked 25:4
talking 12:14 25:10 28:20 52:14 60:8 61:20 80:13 107:8 153:19,21 167:12 197:22,24 206:13 215:19 260:24 294:4
talks 196:12
task 127:14 241:8 242:14
tasks 141:18
taught 139:10 226:8 261:25 282:23 283:3,17 283:20,24 284:11 285:10,22
tdt 268:15
teach 188:6 190:9 191:21 225:20 227:9 229:25 251:18 284:6,13
teaches 105:10 138:8 188:9,11 190:5 191:8,15 204:9 227:3 228:8 230:2 231:15
teaching 105:23 216:24 229:8,12 229:17,24
teachings 217:15 218:11
team 16:7 25:10
tech 30:20 238:4
technical 37:7 49:22 50:2 74:25 75:13 76:12,16,17 76:21,23 77:18,24 78:9,14,23 79:3,6 91:6,18 117:23 141:23 143:11,13 145:9 147:11 149:13 217:5 250:16,21 294:18 294:19 295:13
technological 251:5
technologies 19:12 25:15 28:25 29:8
technology 20:21 21:8,20 22:17 25:25 27:2,8 30:2 37:5
tell 32:19 47:17 117:20 122:13 125:7 203:12 223:9 242:18 243:17 246:19
telling 63:10
template 121:6,22 201:20 202:5 260:11 268:9,16
ten 9:16,19 12:15 222:7
tense 106:5 112:23 113:6,19 121:24 121:25 233:16,19 234:9,20
teresa 3:21 6:2
term 9:12 43:12 49:5 52:5,17,19 53:9,15 55:17,22 64:5 69:3 78:14 82:22 90:3 115:22 175:23 176:2,9,17 221:9,12,19 246:9 291:10
termed 14:3
terminal 268:14
terminate 170:10 197:2
terminated 169:23 170:20 213:23 222:21
terminating 170:12
termination 170:15 200:24 202:13 213:19 214:14 216:2,13 229:7
terminator 169:15 191:11 205:8 230:14 265:5
terminators 34:18 37:9 109:13 156:14 157:3,4,11 157:14,15,22,23 158:11,13,24,25 159:8 161:3,11,23 163:10 166:14 188:3 218:17,20 228:10 229:18

230:4,16 232:6 259:11
terminology 246:3
terms 9:14 12:10 15:25 17:10 24:3 29:4,22 31:21 34:21 36:8 52:24 58:23 59:12 68:20 74:10 79:5 105:6 105:22 110:14 118:19 134:7 140:5 148:8 173:25 174:2 179:12 188:22 195:18 197:12 198:22 200:15 206:3 214:12,13 216:19 217:21,22 218:4 220:9 225:5 256:25 286:8 287:24 291:18 294:17
terrible 204:2
test 79:15,18 93:19 93:25 203:7 210:17,21 211:11 212:23 230:15
testified 6:7 54:9 136:5 156:20 180:19 181:11
testify 237:20,24 238:11,23 239:3
testifying 209:17 209:23
testimony 12:6 17:9 23:20,23,24 49:3 79:13 176:23 177:9,10 190:3 192:5 253:22 272:10 276:18 280:7 293:11 298:8
testing 94:11
tetrahedron 40:3
text 74:7
thank 135:10 297:8
thanks 102:2 262:24 297:13
theoretical 126:16
thing 10:11 11:7 15:2,21 114:10 116:23 118:11 139:9 166:11 210:9 217:18,23 218:5 290:3
things 10:10 21:18 36:10 62:7 63:5 64:23 71:16 77:13 81:24 105:7 129:21 133:25 147:21 173:17 174:5 179:8 180:10 203:14 207:18 211:14 255:8 292:15
think 7:11,14,14 25:25 36:3,13 37:20 39:23 40:20 53:23 54:18,19 56:15,21 65:5,6 68:15 69:16 70:6 71:3 74:8 78:16 80:21,24 81:6,8,9 81:22 82:2 83:23 93:12 95:9 97:12 98:25 100:2 108:20 114:5 124:22 139:24 140:4 144:24 146:3 154:5,6 159:5 160:13 161:5,12 165:24 174:23 175:4,15 177:23 178:4 186:6,8 202:15 205:20,25 207:5 208:9,10 212:16 215:3,8,10,12 227:21 234:13 246:12 247:21 248:10,11,11 258:7 260:13 267:2 269:15 277:6 293:7,12 294:16 295:6 297:4
thinking 20:25 23:10 73:11,12
thinks 109:22
thio 281:14
thirty 301:18
thought 15:23 35:14,24 36:10 160:9,17 161:22 204:22 205:18,18 205:19 287:13 295:7
three 43:24 85:25 86:10,12 95:3,6,12 111:25 112:5 117:6 122:7,20 123:10 124:10,18 131:25 151:21 191:5 220:4,17 244:2 245:5 276:9
throwing 8:20
time 5:8 7:8,12 9:2 11:17 12:8,19 13:14 15:14 24:22 24:24 26:23,24 27:7 28:19 29:25 33:23,24 43:2,8 54:19 60:18 61:24 65:15 67:2,4 72:2 83:2 90:8,19 91:10,18 92:7 94:19,25 97:7,21 116:23 120:4 134:9,17 135:8,12 136:3,7 137:14 139:6 142:25 145:16,19,23 146:8,10,11 151:4 154:14 156:22 159:16 160:6 167:4 168:20 170:8 178:14,16 181:19,25 212:9 212:14 219:13,19 223:6 224:13 239:17 256:4,5 257:8 258:6 262:25 263:7 279:7 285:4 297:21
times 7:17,21 222:10,13 293:8
titrate 231:18
titrating 231:23 232:5
titration 201:18 202:3 203:10 226:21 227:10 228:13 229:11,12 229:17 230:2,20 231:10
today 12:6 127:24 130:4 180:5,14 218:5
today's 297:16
told 243:15,19 244:8,12,17 245:3 249:13

tolerable 170:19
tolerance 169:21
tolerate 169:16 170:15
tolerated 177:21
tomorrow 297:11
top 197:10 257:9
topic 209:17
topics 209:20
torrent 19:11,15 22:8,21
total 71:8,21,22 72:5 297:17
trade 28:6,7,11 29:2,9 30:3 39:20 238:25
trademark 1:2 4:24
transcript 274:11 298:11 299:13 301:20,22
transferase 268:15
transferring 166:13
transparent 274:10
trial 1:3
tried 68:22 72:22 165:21
triphosphate 235:4
triple 95:13,20,21 95:24
true 7:19 36:8,14 97:3 121:12 167:11 170:3 209:24,25 281:7 298:10 299:13
trustees 1:8 4:20
truth 294:18,19 295:13
truthful 57:20
try 15:17 57:25 58:2,7 65:22 71:16 84:11 91:5 240:13
trying 48:10 54:2 55:23 97:3,14 99:2,3 187:23 224:11 288:14
tsien 138:7 140:13 168:16 216:25 217:15 218:2,9,12 226:9 256:14,18 294:9,13
tsien's 33:18
tube 201:21
tubes 201:21
turn 40:5 50:17 58:17,25 85:19,24 101:18 102:2 126:6 136:12 141:6 154:12 171:11,15 186:10 194:25 195:2 200:16 221:23 232:11 245:13 263:10 264:10 266:8 267:16 271:20
turning 100:4 130:10 232:13
twenty 40:21
two 12:23 13:6 43:10 63:23 64:2 66:14 88:18 111:5 174:5 184:3 191:5 211:13 236:10 245:17,17 259:6,7 274:20 278:9,13 292:15
type 259:4
typical 197:15
typically 200:4

u

u.s. 4:23 58:8,10 300:9
understand 11:11 11:18,22 20:9 22:15 39:18 42:16 42:18 50:11 57:12 57:14 61:15 65:16 67:12 68:7 70:9 70:11 73:19,21 76:15 78:9,13 83:16 84:2 86:19 87:2 102:23 111:4 115:12,15 116:2,9 131:10 143:21 147:2 150:17 159:22 161:18,20 171:22 172:18 173:2,3 175:10 176:16 179:7 186:7,9 192:10 198:21 200:14 220:8 229:16 232:4,8,19 233:5 244:20 254:23 260:19 261:13 262:7 280:6 296:5 296:20
understanding 11:4 17:4 30:17 34:20,24 52:16 84:24 101:7 126:12 137:12 144:9 160:8,13 173:6 174:8 175:17,20 177:25 187:9 225:8 247:11 286:6
understood 11:25 20:18 41:8 42:20 48:17 61:5 63:3 173:18,23,24
unique 109:7 258:16,21
unit 4:15
united 1:2
units 297:18
university 1:8 3:21,21 4:20 5:21 6:3
unsuccessful 167:20
unusually 198:3,5 199:7
upper 183:18
usable 110:18
use 52:17 55:22 60:13 61:8 63:19 71:3 82:4 84:15 118:4 119:19 144:14 146:13 155:2,7 161:3,11 166:18 176:25 185:9 187:4 191:10 221:9,10 221:18 227:3 228:9 268:21 285:8,10 289:5,16 290:6,7,14
useful 15:24 272:2 272:12 273:5,14 274:16,25 275:14 275:24 276:9,20 277:16 279:3
uses 53:9 106:4 113:20 115:22 221:12 278:23
usually 34:13

utilizes 268:9

v

v 6:4 136:4
value 96:9
vanda 6:15
variability 177:20
venable 2:7 3:12 5:2,20,24
venable.com 3:14 3:15,16
vent 188:11 189:4 190:7,15 191:21 193:14 227:21 229:2,4
verify 54:17 124:23
veritext 5:6 297:20
version 40:21,22
versus 4:19 140:6 225:6
viability 292:16,17
viable 292:23
video 4:12,16 43:3 43:9 94:20 95:2 135:13 136:8 181:20 182:2 219:14,20 263:2,8
videographer 3:23 4:2 43:2,7 94:19 94:24 135:12 136:6 181:19,24 219:13,18 262:25 263:6 297:14
videotape 1:16 2:5
view 23:23 108:14 113:7,19 178:5,7 223:20
viewable 240:23
virtues 79:11,14
vs 1:7

w

wait 95:12 102:5 137:24
waiver 244:21
walk 11:15
want 23:21 53:24 53:25 55:21 67:19 80:3,4 81:13 104:11 121:11 138:7 151:13 153:5 182:11 223:6 263:24,25 264:16 266:10 268:4 275:11 296:8
wanted 6:22 93:16
warranted 13:20
washing 260:9
water 182:14,16
way 6:15 9:8,11 46:2 47:17 50:17 52:10,11 54:21,25 67:17 84:11 120:10 122:17 153:6 162:15 176:7 182:15 199:19 205:3 231:11 252:21 254:13 271:7 273:22 282:10 289:13 292:7 294:10 295:18 299:18
weil 3:8
weil.com 3:10
welsch 271:17
went 13:2 151:19 152:21 203:3
whacker 182:18 182:23 183:3,14 183:25
whatsoever 91:3
whereof 299:20
whispering 4:6
white 3:19,23 5:5 5:25
whopping 222:19
wish 302:5
withdraw 150:6 252:20
withdrawn 85:17
witness 5:22 6:5 26:7 54:16 67:21 85:23 95:10 105:18 210:12 233:9 259:5 262:23 270:11 282:9 285:24 297:9,12 298:7 299:20 300:3 301:2
witness's 17:8 23:7 48:23 49:2 190:2 293:10
word 49:7,12,16 54:24 71:4,5 115:20
words 54:22 59:21 114:6
work 10:19 19:4 22:7,20 23:15 24:15 28:21 31:10 31:10 33:15,19,19 34:25 35:6,16 36:16 37:8 39:8 39:11 44:3 52:2 53:4 61:23 68:8 73:9 80:2 98:10 107:24 122:23 124:21 125:8,8 126:14 127:23 129:13 137:5 141:13,22 142:7 142:13,14 144:7 154:13,17,18 178:2 179:4 182:21 185:9 197:14 203:14,15 209:22 217:6,6,7 218:24 238:3 240:15 248:13 249:18 253:14 255:22 256:7 279:18,25 280:3 282:14 283:5 286:5 293:4 294:13 295:8 296:3,13,23 297:8
workable 239:7
worked 19:11 20:19 31:4 80:6 93:22 94:3 183:4 193:13,17 218:16 218:19
working 9:3 17:19 17:25 20:6,15 21:16 28:24 31:4 33:25 36:11 75:11 138:21 139:19 158:10 253:4 294:5
works 73:17 74:4 293:24
worth 54:18
writes 276:6
written 112:22 113:6,18 121:24 122:2
wrong 278:11
wrote 14:16 117:18 164:16

x

x 1:4,11 300:2

y

y 3:21 16:15 181:2 181:13 241:14,16 242:7,12 243:20 244:3 245:9
yeah 7:14 9:16 10:10 12:3 15:10 15:10,10,11 22:14 23:2,9 25:6 27:11 27:12 28:8,25 32:5,16 39:17 40:24 45:17 46:6 49:18 50:23 58:20 59:22 61:14 63:4 67:13 68:12,25 69:2 73:12,22 76:14 78:16 79:22 80:21 81:22 82:9 82:21 83:23 84:5 84:12 86:10 87:11 88:2 90:16 91:12 92:13 94:12 95:9 95:11,16,18,18,18 96:10,10 98:22 100:17 101:22,25 102:11 105:21 106:11,15 107:21 108:11,24 110:7 110:12,20 112:18 114:25 115:10,16 119:6 120:7 121:25 129:17 130:21 132:17 134:4 137:8,8,15 137:24 138:19 139:6 142:3 143:4 144:5,24 146:25 148:5,25 149:10 151:24 153:2 154:3 156:3 157:19,19 160:4 161:17 162:3 163:3,6,12,21 165:21 166:10 172:9,23 173:3,16 174:12,14 176:6 176:21 177:7,7,8 181:8 183:13,16 183:20 184:7 186:13 187:24,24 190:19 192:24 197:20 198:7 199:11 200:7,12 200:19 203:20 204:12,17 205:11 208:10 210:19 212:10 213:6,14 214:6,12,20,25 215:21 216:10,18 218:11 221:3 222:6,18 223:3,8 223:11,12 224:7 224:11,22 225:3 226:14,18,23 228:5,6 230:11 231:9 235:10 239:15,18 240:20 241:7 245:19 246:18 247:2,2,21 248:10,23 249:9 250:13,13 252:9 253:7 255:6 257:17,25 258:3 259:17,25 262:14 263:21 264:9,9,23 265:9,18,19 266:7 269:4,13 270:15 270:24 272:21,25 273:10 276:5,10 276:24 279:21 280:21 284:17 285:3,19 286:13 287:16 288:25 289:9 290:17 291:9 293:12 296:19
year 8:11 118:22 120:13 287:23 289:22
years 30:22 168:5 183:4 193:12
yep 119:2
yesterday 67:6,7
yield 104:9,15,18 105:9 111:14 120:17 122:8,21 123:11,14,18,20 123:24,25 124:2 124:11,12,19 125:5,12 130:14 130:25 131:3 138:6,9 140:5,12 140:17,20,23 141:2 234:15 259:20
york 1:9,18,18 2:9 2:9,12 3:13,13 4:21 5:3,4 298:2,4 299:2,4,8

z

zachary 3:16 5:23
zgarrett 3:16

Federal Rules of Civil Procedure

Rule 30

(e) Review By the Witness; Changes.

(1) Review; Statement of Changes. On request by the deponent or a party before the deposition is completed, the deponent must be allowed 30 days after being notified by the officer that the transcript or recording is available in which:

(A) to review the transcript or recording; and

(B) if there are changes in form or substance, to sign a statement listing the changes and the reasons for making them.

(2) Changes Indicated in the Officer's Certificate. The officer must note in the certificate prescribed by Rule 30(f)(1) whether a review was requested and, if so, must attach any changes the deponent makes during the 30-day period.

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COMPANY CERTIFICATE AND DISCLOSURE STATEMENT

Veritext Legal Solutions represents that the foregoing transcript is a true, correct and complete transcript of the colloquies, questions and answers as submitted by the court reporter. Veritext Legal Solutions further represents that the attached exhibits, if any, are true, correct and complete documents as submitted by the court reporter and/or attorneys in relation to this deposition and that the documents were processed in accordance with our litigation support and production standards.

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