

1 UNITED STATES PATENT AND TRADEMARK OFFICE
2 BEFORE THE PATENT TRIAL AND APPEAL BOARD

3
4 ALAMAR BIOSCIENCES, INC.,
5 Petitioner

6 v.

7 OLINK PROTEOMICS AB,
8 Patent Owner

9
10 Case IPR2024-01353
11 U.S. Patent No. 7,883,848
12

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14
15 DEPOSITION OF NORMAN C. NELSON, Ph.D.
16 San Diego, California
17 Tuesday, June 3, 2025
18 Volume 1
19

20
21 Reported by:

22 LESLIE JOHNSON

23 RPR, CCRR, CSR No. 11451

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25 PAGES 1 - 172

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17 DEPOSITION OF NORMAN C. NELSON, Ph.D., Volume 1, taken
18 on behalf of Patent Owner, at the office of Jones Day,
19 4655 Executive Drive Suite 1500, San Diego, California,
20 beginning at 8:59 a.m. and ending at 4:19 p.m., on
21 Tuesday, June 3, 2025, before LESLIE JOHNSON, Certified
22 Shorthand Reporter No. 11451.
23
24
25

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I N D E X

WITNESS

EXAMINATION

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BY MR. PLATT

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PRE-MARKED EXHIBITS REFERRED TO

NORMAN C. NELSON, Ph.D.

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NORMAN C. NELSON, Ph.D.

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1 San Diego, California; Tuesday, June 3, 2025

2 8:59 a.m.

3

4

EXAMINATION

5

BY MR. HOLMAN:

6

Q Good morning, Dr. Nelson.

7

A Good morning.

8

9

Q Please state your full name and place of residence for the record.

10

A Norman C. Nelson. San Diego, California.

11

12

Q Dr. Nelson, have you ever testified in a legal proceeding before?

13

A Yes.

14

Q How many times?

15

16

A This is a deposition, to be clear. It's either four or five times. I don't recall exactly.

17

18

Q So you've testified by way of deposition four or five times?

19

A Correct.

20

Q Have you ever testified in a trial?

21

A No.

22

23

Q In those depositions, what types of proceedings were those?

24

Were those patent cases?

25

A Yes, those were patent cases.

1 Q All of them?

2 A Yes.

3 Q What kind of technologies?

4 Let's start with -- let's just take them one
5 at a time. What kind of technologies did those
6 depositions relate to?

7 A They were all related to what I would call DNA
8 nucleic acid-based technologies.

9 Q All four or five of the depositions related to
10 DNA nucleic acid-based technologies?

11 A Yes.

12 Q And who were the parties involved in these
13 litigation matters?

14 A Yes. One was Enzo. Well, more than one was
15 Enzo. I think two were Enzo.

16 And I hate to say it, but I can't actually
17 recall the parties involved in the others at this point.

18 Q So two of the cases involved Enzo?

19 A Correct. Oh, and Enzo versus Gen-Probe,
20 G-E-N, hyphen, P-R-O-B-E.

21 Q So two of the cases were Enzo versus
22 Gen-Probe?

23 A Right. Two separate cases.

24 Q And you're not sure of the other two or three
25 cases?

1 A I can't recall. I really can't.

2 Q And in the Enzo versus Gen-Probe cases, is it
3 fair to say you represented Gen-Probe?

4 A Yes.

5 Q When was the last time you were deposed?

6 A It was approximately 2019. It was pre-COVID.

7 Q And which case was that in?

8 A That was neither of the Gen-Probe-Enzo cases.
9 It was one of those that I don't recall.

10 Q But it still was a case involving DNA and
11 nucleic acid-based technologies?

12 A Yes.

13 Q All right. You've been sworn in today.
14 Do you understand you're testifying under oath
15 and under penalty of perjury in the United States today?

16 A Yes, I do.

17 Q And you understand that means you're here to
18 testify truthfully and accurately regarding the
19 questions that I ask you today?

20 A Yes, I do.

21 Q Is there any reason you cannot testify
22 truthfully or accurately today?

23 A No, there is not.

24 Q We have a court reporter with us here today.
25 She's going to be transcribing our conversation for the

1 record in this case.

2 Do you understand that once the transcript
3 from today's deposition is entered into the record of
4 this case, it will become publicly available?

5 A I do understand that.

6 Q And because the court reporter is transcribing
7 our conversation today, it's going to be important that
8 we not talk over each other, right? So I'm going to do
9 my best to wait until you've finished your answer before
10 I begin my next question. Okay?

11 A Yes.

12 Q And I ask that you wait until I finish asking
13 my question before you begin your answer. Is that fair?

14 A Yes.

15 Q Okay. Great.

16 So today, Dr. Nelson, I expect you're going to
17 understand the meaning of my questions. However, if you
18 don't understand a question, please just let me know.
19 I'll do my best to clarify it for you. Okay?

20 A Okay.

21 Q If you do answer my question, I'm going to
22 assume that you understood the question that I asked
23 you. Is that fair?

24 A That is fair.

25 Q If you don't understand a question, do you

1 understand you must ask me for clarification rather than
2 your counsel?

3 A Yes, I do.

4 Q Okay. And you agree to do that?

5 A Yes.

6 Q So during today's deposition, you're not
7 permitted to speak with anyone else about substance of
8 your testimony today, including during breaks.

9 Do you understand that?

10 A Yes.

11 Q And you agree to do that?

12 A Yes.

13 Q Speaking of breaks, we'll try to take breaks
14 at reasonable intervals today. If you need a break,
15 just let me know. We'll be happy to take one. I'll
16 ask, if there's a question pending, that you answer the
17 before we break. Okay?

18 A Okay.

19 Q During today's deposition, your counsel may
20 object to some of my questions. There may be objections
21 raised.

22 If your counsel objects to a question, you
23 understand that you still must answer my question,
24 unless you're specifically instructed not to answer by
25 your counsel?

1 A Yes. I'm going to silence my phone. I
2 apologize. I should have done that earlier.

3 Q Thank you.

4 A Done.

5 Q All right. Do you have any documents with you
6 today?

7 A I do. I have a copy of my declaration.

8 Q All right. Do you have any other exhibits
9 with that declaration?

10 A No.

11 Q Is it a clean copy?

12 A It is a clean copy. It has some tabs,
13 according to the table of contents, just so I can find
14 my place easier.

15 Q Do you mind if I take a look at it?

16 A I do not mind.

17 Q Okay. Thank you.

18 A You're welcome.

19 Q All right. So aside from the copy of your
20 declaration, do you have any other personal notes with
21 you, any other documents at all?

22 A I do not.

23 Q Okay. All right. You understand you're here
24 to provide testimony in a legal proceeding known as an
25 Inter Partes Review or an IPR?

1 A Yes.

2 Q Do you understand what an IPR is?

3 A Yes.

4 Q What is your understanding?

5 A It is a challenge to the validity of a patent,
6 in this case the '848 patent owned by Olink.

7 Q Do you understand that the IPR -- the IPR
8 proceeding takes place in front of the United States
9 Patent and Trademark Office?

10 A When you say takes place in front of, what do
11 you mean by that?

12 Q It's a proceeding held before the USPTO, as
13 opposed to a district court.

14 Do you understand that?

15 A Yes.

16 Q And I think you said you understand that this
17 IPR concerns the '848 patent owned by Olink, correct?

18 A Correct.

19 Q When did Alamar first contact you to retain
20 your services as an expert?

21 A Alamar did not. Their representative, Jones
22 Day, did. And that was in the early part of 2024.

23 Q Who contacted you from Jones Day?

24 A Laura.

25 Q Before Laura contacted you, were you aware of

1 a patent dispute between Alamar and Olink?

2 A I was not.

3 Q Before you started your consulting work on
4 this case, were you aware of Alamar Biosciences?

5 A I was not.

6 Q Before you started your work on this case,
7 were you aware of Olink Proteomics?

8 A I believe I've heard of them, but it's a vague
9 memory.

10 Q Aside from your work on this present case, do
11 you have any other professional relationship with
12 Alamar?

13 A I do not.

14 Q Have you ever done any other consulting work
15 for Alamar?

16 A I have not.

17 Q Have you ever had any research funding from
18 Alamar?

19 A I have not.

20 Q Research collaborations with Alamar?

21 A No.

22 Q Have you ever communicated with anyone at
23 Alamar, other than counsel?

24 A No.

25 Q Are you being compensated for your work on

1 this case?

2 A Yes.

3 Q What is your current consulting rate for this
4 work?

5 A \$500 an hour.

6 Q How many hours would you say you spent
7 preparing your declaration for this case?

8 A Somewhere between about 150 and 200 hours.

9 Q Have you submitted any invoices for your work
10 in this case?

11 A Yes.

12 Q Approximately how much were the invoices for,
13 do you recall?

14 A Probably between 10 and \$18,000 apiece,
15 depending on the interval, approximately.

16 Q Do you bill it monthly?

17 A Approximately monthly, yes.

18 Q Did you prepare for today's deposition?

19 A Yes.

20 Q What did you do to prepare?

21 A Well, I studied my declaration, other
22 documents, and we had two meetings with counsel
23 beforehand as well.

24 Q Who did you meet with when you met with
25 counsel?

1 A The first meeting was -- they were both with
2 Christian and Laura. And Ellie was here as well. And
3 the first one Laura was remote, and the second one she
4 was in person. And Christian was present at both in
5 person.

6 Q These were two meetings --

7 A Yes.

8 Q -- with counsel, right?

9 A Yes.

10 Q Approximately how long were the meetings?

11 A Approximately five hours each.

12 Q Each meeting was five hours?

13 A Each meeting.

14 Q So aside from Christian, Laura and Ellie, was
15 anyone else present at these meetings?

16 A No.

17 Q You mentioned you studied your declaration and
18 documents; is that right?

19 A That is correct.

20 Q In preparation for today's deposition.
21 What documents did you study to prepare?

22 A Those documents cited as exhibits in my
23 declaration.

24 Q In preparing for today's deposition, did you
25 review any documents that are not cited in your

1 declaration?

2 A No.

3 Could you repeat that last question precisely?
4 I'm listening to it back in my mind and wonder if you
5 said that.

6 Q Sure.

7 In preparing for today's deposition, did you
8 review any documents that are not cited in your
9 declaration?

10 A Okay. Same answer.

11 Q The answer is "no"?

12 A That's correct.

13 Q Okay. You have a copy of your declaration
14 there. We have copies as well. You're welcome to work
15 from your copy. I understand you have it tabbed for
16 easy navigation. We have copies for counsel. We can
17 give you those.

18 So, in your declaration, if you could please
19 turn to the last page, the back page, 144.

20 Let me know -- are you there?

21 A I'm there.

22 Q Could you confirm that's your signature there?

23 A Yes.

24 Q And you signed it on August 3, 2024; is that
25 correct?

1 A Yes, I did.

2 Q Did you review your declaration before you
3 signed it?

4 A Yes.

5 Q Did you review the entire declaration before
6 you signed it?

7 A Yes.

8 Q Cover to cover?

9 A Yes.

10 Q And sitting here today, do you still stand by
11 all the opinions set forth in your declaration?

12 A Yes.

13 Q Okay. Did you meet with anyone in preparing
14 your declaration?

15 Earlier I was asking you about your deposition
16 preparation. Now I'm asking about your declaration.

17 Did you meet with anyone to prepare your
18 declaration?

19 A Mostly virtually, but yes, Laura and
20 Christian, again.

21 Q Anybody else you met with besides Laura and
22 Christian?

23 A There may have been one or two others which
24 popped into the meeting for a short time, but nothing
25 substantive.

1 Q Who were the one or two others that popped in
2 you said?

3 A I can't remember. I believe that they were --
4 this was back in 2024. I believe one's name was
5 Patricia. I can't recall for sure. And I don't recall
6 the other one.

7 Q Do you know if they were attorneys, Patricia
8 and the other?

9 A I believe Patricia was. I honestly can't
10 recall with the other one.

11 Q Is it your understanding that they were with
12 Jones Day?

13 A Yes.

14 Q How many times did you meet with Laura and
15 Christian and these other folks in preparing your
16 declaration?

17 A Rough estimate, between 20 and 30 times.
18 Again, this is mostly remote.

19 Q Uh-huh.

20 A Somewhere in there. It's just an estimate.

21 Q And this was in 2024; is that correct?

22 A Correct.

23 Q About what time frame of 2024 were these
24 meetings?

25 A Between March and August.

1 Q Including these meetings, what would you say
2 is the total amount of time you spent to prepare your
3 declaration?

4 A Probably between about 150 and 200 hours,
5 approximately.

6 Q All right. In preparing your declaration, did
7 you review any documents to inform your opinions?

8 A Yes.

9 Q What documents did you review to prepare your
10 declaration?

11 A Those that are cited in my declaration, as
12 well as others during my research phase, which I deem
13 not -- I did not use to form my opinion. And I don't
14 recall those exact documents.

15 Q So the documents that are not cited in your
16 declaration, I think you said they did not inform your
17 opinion; is that correct?

18 A That is correct.

19 Q So it's fair to say, if a document were
20 important for your opinions in your declaration, you
21 would have cited it in your declaration; is that right?

22 A That is generally correct, yes.

23 Q All right. I'm going to give you a copy of
24 your CV. It's Exhibit 1006.

25 Do you recognize this document?

1 A Yes.

2 Q And this is your CV that you submitted in this
3 proceeding, correct?

4 A Correct.

5 Q On page 5., it says you have a Ph.D. in
6 chemistry from University of California at San Diego; is
7 that correct?

8 A That is correct.

9 Q What year did you complete your Ph.D.?

10 A 1982.

11 Q Okay. And then, after you finished your
12 Ph.D., is that when you joined Gen-Probe?

13 A No. I had another job for about two and a
14 half years before joining Gen-Probe.

15 Q What job was that?

16 A That was with a small company named BioLink,
17 which was then acquired by Westbridge Research Group.

18 Q After BioLink, that's when you joined
19 Gen-Probe in '85; is that right?

20 A Correct.

21 Q What role did you have when you joined
22 Gen-Probe in 1985?

23 A Scientist.

24 Q And then you stayed at Gen-Probe until
25 2012; is that right?

1 A That is correct.

2 Q Did you -- were you -- did you work as a
3 scientist the whole time that you were at Gen-Probe?

4 A Well, I was promoted. So scientist, senior
5 research scientist, et cetera.

6 Q Throughout the promotions, were you still
7 actively involved in laboratory research?

8 A Yes. I was in the science aspect of it, that
9 is correct.

10 Q And would you say -- what would you say was
11 the nature of the laboratory research that you did at
12 Gen-Probe?

13 A Gen-Probe, it was Gen-Probe's primary
14 business, which is molecular diagnostics.

15 Q What kind of work did that involve? What kind
16 of laboratory work did that involve.

17 A That would involve the design and testing of
18 DNA probe-based assays.

19 Q We have page 2 of your CV under "Professional
20 Experience" a company called NCN Enterprises?

21 A Yes.

22 Q It says you've been involved with NCN from
23 2012 to present; is that correct?

24 A Correct.

25 Q What is NCN Enterprises?

1 A It is a sole proprietorship consulting
2 business of my own.

3 Q So do you own NCN Enterprises?

4 A Yes.

5 Q And what is your role at NCN Enterprises?

6 A Consultant.

7 Q Is this technical consulting services?

8 A Yes.

9 Q In the description on page 2, you include
10 intellectual property as one of the topics you provide
11 consulting on; is that correct?

12 A That is correct.

13 Q What's the nature of your IP consulting
14 services?

15 A Yes. Mostly what we're doing here today,
16 which is serving as an expert witness. And with other
17 contracts that I have, I also consult as far as patent
18 preparation and prosecution.

19 Q Do you have a background in law?

20 A No. So it's always from a technical
21 standpoint.

22 Q Are you compensated for your work at NCN
23 Enterprises?

24 A Yes.

25 Q And how much of your total annual income would

1 you say, ballpark, comes from your work with NCN
2 Enterprises?

3 A Could you repeat that question, please?

4 Q How much of your total annual income would you
5 say comes from your work for NCN Enterprises?

6 A Yes. Essentially 100 percent of my technical
7 work is the income I have. I mean, I have some other
8 income from rental properties, et cetera. But I don't
9 think you were referring to that. So all my income from
10 a technical standpoint is through NCN Enterprises.

11 Q What is -- this is on page 3 of your CV.
12 What is AEGEA Biotechnologies?

13 A A small startup company here in San Diego.

14 Q Did I pronounce that correctly?

15 A Yes.

16 Q Does A-E-G-E-A -- is that an acronym?
17 Does it stand for something?

18 A It's not. I asked the founder a few times,
19 but I do not think it is, no.

20 Q It says here you're VP of operations and
21 developing for Aegea; is that right?

22 A Yes. But let me give you some context here.
23 That was a title given when there was three or four
24 people in 2013, and it hasn't changed, even though I --
25 that's how I'll leave my answer. Yeah.

1 Q What's the size of AEGEA Biotech now?

2 A It's approximately 10 people.

3 Q And are you saying you're no longer the VP of
4 operations and development?

5 A I'm saying essentially that. I've kept that
6 title, but my involvement with that company is very low
7 now. Two hours a week at the most.

8 Q Are you compensated for your work at AEGEA?

9 A Not currently.

10 Q Again, it says under your description here
11 "Support of technology, assay and intellectual property
12 development."

13 How do you support intellectual property
14 development for Aegea?

15 A How do I support which now? I'm sorry.

16 Q Intellectual property development.

17 A Yes. And that's been quite some time since
18 I've done that, but it's -- as I was mentioning before,
19 helping prepare patent applications and then assisting
20 with the prosecution.

21 Q I think you said this earlier, but in your
22 contributions for this intellectual property support,
23 it's based on technical input --

24 A Correct.

25 Q -- not legal; is that correct?

1 A Correct.

2 Q Same page, you have a category of expert
3 witness?

4 A Yeah.

5 Q That's from 1998 to present day; is that
6 correct?

7 A That is correct.

8 Q And then we have here a list of several cases.
9 I see "Gen-Probe versus adverse party" are the first
10 two. That's the same Gen-Probe cases you were referring
11 to earlier today?

12 A That's just where my memory -- I apologize but
13 is somewhat shaky. I don't recall the adverse party in
14 those two exactly. And I will tell you preemptively,
15 the Hologic versus Enzo, those two were -- Hologic
16 purchased Gen-Probe, acquired Gen-Probe in 2012. So
17 it's still essentially Gen-Probe technology.

18 Q A then you have three additional IPRs. Party
19 names still confidential there from 2018 to 2020.

20 Do you see that?

21 A Yes.

22 Q Are those names still confidential today in
23 2025?

24 A I have not looked into that, and I wonder that
25 myself. I have not found out the answer to that

1 question.

2 Q Do you understand that IPR proceedings are
3 public record?

4 A Yes, I do.

5 Q Does "Becton Dickinson versus Enzo" sound
6 familiar?

7 A It does.

8 Q Do you think that might be one of the parties
9 involved in those cases?

10 A I believe so.

11 Q The last one there you list is one current IPR
12 project, 2024. Is it fair to say that's this present
13 proceeding?

14 A That is correct.

15 Q Is your work as an expert witness that you
16 have characterized here, is that all through NCN
17 Enterprises?

18 A No. The ones prior to the first two were when
19 I was with Gen-Probe.

20 Q Uh-huh.

21 How about the other ones? Were those through
22 NCN Enterprises?

23 A Yes.

24 Q So, if I asked you the question, "How much of
25 your total annual income comes from your work as an

1 expert witness?" it's the same answer as how much of
2 your income comes from NCN Enterprises; is that correct?

3 A Could you please restate that question?

4 Q Sure. I'll just -- let me just ask the
5 question --

6 A Okay.

7 Q -- in a clearer way.

8 How much of your total annual income would you
9 say comes from your work as an expert witness?

10 A It varies from year to year, but I would say
11 between 2016 and current, approximately 25 percent.
12 It's a rough estimate.

13 Q And would you say the remaining percentage --
14 notwithstanding rental properties or other income, the
15 remaining percentage comes from technical consulting --

16 A Yes.

17 Q -- on other cases?

18 A Other clients.

19 Q Other matter. Other clients.

20 A Yes. Thank you.

21 Q Did you prepare this document, Exhibit 1006,
22 yourself?

23 A Yes.

24 Q And sitting here today, it's your testimony
25 this is a true and accurate copy of your CV?

1 A Yes.

2 Q Dr. Nelson, do you consider yourself an expert
3 in nucleic acid chemistry?

4 A Yes.

5 Q Do you have an understanding of basic
6 principles of nucleic acid hybridization?

7 A Yes.

8 Q What is your understanding of nucleic acid
9 hybridization? Can you explain to me what that is?

10 A That is -- nucleic acid hybridization is when
11 two strands of nucleic acid form a double helix through
12 base pairing of the nucleotide bases G pairing with C
13 and A pairing with T in DNA or A pairing with U in RNA.

14 Q What makes these bases pair together?

15 A It's mostly through noncovalent forces or
16 ionic forces between functional groups on the nucleotide
17 bases. And there's some stacking energy too between the
18 rings of the nucleotide bases.

19 Q What type of conditions would you say would
20 potentially cause a hybridized pair of nucleic acids to
21 become unhybridized?

22 A The main factors affecting the stability of a
23 nucleic acid hybrid are the ionic strength of the
24 solution and the temperature thereof. So high
25 temperature or low salt can cause disruption of the

1 duplex.

2 Q Anything else other than ionic strength or
3 temperature that might cause a disruption of the duplex?

4 A Yes. There are a variety of other factors.
5 Other -- for example, other components of the solution,
6 such as denaturing components. Formamide is a solution
7 that tends to denature or break apart the double
8 strands. And other chemical compounds that are in the
9 solution of the DNA that can decrease the stability of
10 the duplex.

11 Q I think you mentioned ionic strength may be a
12 factor; is that right?

13 A Yes. Uh-huh.

14 Q How does ionic strength affect hybridization
15 of nucleic acids?

16 A Basically, you need counter-ions to the
17 negative charge in the phosphate groups. So,
18 classically, sodium is used as a counter-ion to bind
19 with the negative charge of the phosphate group to
20 minimize repulsion of the two strands. Magnesium is
21 another component that is used to do the same function.

22 Q And so is it fair to say that without these
23 counter-ions, the strands start to repel each other to
24 do a negative charge?

25 A Well, it depends on what else is in the

1 solution. But generally speaking, that would be a
2 reasonable statement.

3 Q Can you give us -- can you provide me any
4 examples of low ionic strength buffers or solutions that
5 would cause dehybridization of nucleic acids?

6 A Well, I wouldn't say "cause" because there are
7 other factors, as I mentioned, temperature and other
8 components in the solution.

9 But most basically speaking, low ionic
10 strength solutions with low sodium, low magnesium, for
11 example. But it depends on the other conditions as
12 well.

13 Q How about water? Would water cause
14 dehybridization of nucleic acid strands?

15 A Well, again, saying "cause dehybridization" is
16 too general. But water, which is zero ionic strength,
17 would certainly not support, in and of itself, stability
18 of the DNA duplex. But it depends on temperature and
19 other features.

20 Q All right. Would -- you said using the phrase
21 "cause dehybridization" you mentioned is too general
22 because temperature might be a factor as well. So how
23 about water at room temperature, would that cause
24 dehybridization of nucleic acids?

25 A Well, again, my answer is it depends on other

1 factors -- the length of the DNA, the GC content of the
2 DNA, are there modified nucleotides, modified bases
3 which increase the stability, is the backbone phosphate
4 or is it PNA, in which case water won't cause
5 dehybridization of PNA backbones, methoxy residues.

6 There are so many features that I can't make a
7 blanket statement that water at room temperature might
8 cause dehybridization. Too many variables. It depends
9 on all those other variables.

10 Q Understood.

11 It's fair to say that water definitely can
12 contribute to dehybridization of nucleic acid strands
13 due to its absence of ions; is that fair?

14 A Again, I would say it depends on all those
15 other factors. So I can't say that that's generally
16 true.

17 Q Well, my question is a little different than
18 the previous ones. I'm just asking, is it fair to say
19 that water can contribute to dehybridization of nucleic
20 acids?

21 A Depending on the other conditions, it is -- it
22 is a factor that could contribute to dehybridization,
23 depending on the other factors.

24 Q All right. In your declaration, if you could
25 please turn to paragraph 64.

1 A I'm there.

2 Q In this first sentence here, you state "For my
3 analysis, I have review and considered the '848 Patent's
4 specification claims, and prosecution history, along
5 with various pieces of relevant extrinsic evidence."

6 Do you see that?

7 A Yes.

8 Q What do you mean by "extrinsic evidence" here?

9 A The evidence that is captured in the other
10 exhibits, other pieces -- other patents, patent
11 applications and literature.

12 Q Why do you refer to it as "extrinsic
13 evidence"?

14 A Extrinsic to that list that's been recited,
15 the '848's specification claims and prosecution history.

16 Q All right. And when you say "various pieces
17 of relevant extrinsic evidence," what are the various
18 pieces you're referring to?

19 A Pieces would comprise patents, patent
20 applications, and scientific literature.

21 Q Which patents are you referring to?

22 A It's in the exhibit list. I could look at
23 that list and read them off if you like. But it's just
24 those claimed in the -- or cited in the exhibit list.

25 Q So, when you say patents and scientific

1 literature as extrinsic evidence, you're referring to
2 patents and scientific literature which are cited in
3 your declaration --

4 A Correct.

5 Q -- is that correct?

6 A That is correct.

7 Q All right. Let's -- I'm going to give you a
8 copy of the '848 patent. It's Exhibit 1001.

9 Do you recognize this document, Dr. Nelson?

10 A Yes, I do.

11 Q And this is the '848 patent you discuss in
12 your declaration, correct?

13 A Yes.

14 Q All right. If you could turn to claim 1 on
15 the third to the last page of the document.

16 A Okay. I'm there.

17 Q Claim 1 begins -- recites "A method of
18 detecting functional interactions between at least two
19 molecules of interest."

20 Do you see that?

21 A Yes, I do.

22 Q Do you have an understanding of what a
23 molecule of interest is in the '848 patent?

24 A I do.

25 Q What is your understanding of molecule of

1 interest in the '848 patent?

2 A If you'll give me just a moment to look in my
3 declaration, I have included that at one point. Let me
4 see if I can find it.

5 Okay. If you'll look at paragraph 45 in my
6 declaration, this is my understanding. As stated in the
7 '848 patent, "The molecule of interest 'refers to a
8 molecule about which interactive information is
9 desired.'"

10 And that's in the '848 patent, Exhibit 1,
11 column 8, lines 53 through 55. So that's my
12 understanding.

13 Q And is it your opinion that would be the
14 ordinary and customary meaning of "molecule of interest"
15 in the '848 patent?

16 A It depends on the literature, the researcher
17 talking about molecule of interest.

18 Certainly a person of ordinary skill in the
19 art reading the '848 patent would read that definition
20 and understand what was meant by it in that context.

21 Q All right. Let's go back to claim 1.

22 Step (a), claim 1, recites "Forming a
23 plurality of interactors by coupling each molecule of
24 interest with at least one nucleic acid moiety, the
25 nucleic acid moiety comprising an identification

1 sequence element and an association element."

2 Do you see that?

3 A Yes.

4 Q Do you have an understanding of what a nucleic
5 acid moiety is in the '848 patent?

6 A Yes.

7 Q What is your understanding of "nucleic acid
8 moiety" in the '848 patent?

9 A Yes.

10 First, the general definition of "moiety" is a
11 subset of a larger molecule. So, in this case, the
12 nucleic acid moiety would be simply the nucleic acid
13 strand that is attached to the molecule of interest --
14 coupled to the molecule of interest.

15 Q So is it your opinion that the customary and
16 ordinary meaning of "nucleic acid moiety" is the nucleic
17 acid strand that is coupled to the molecule of interest?

18 A That would be the general understanding
19 thereof, that's correct, in this context.

20 Q And part of the claim step (a) recites that
21 "Nucleic acid moiety comprises an identification
22 sequence element and an association element."

23 Do you see that?

24 A I do.

25 Q Is it your understanding that the nucleic acid

1 moiety of the '848 patent requires an identification
2 sequence element and an association element?

3 A From the reading of this, that would be
4 generally understood by a POSA. It does -- yes, it does
5 include those two elements. Whether they're distinct or
6 coincident, it doesn't recite specifically.

7 Q All right. If you're still on step (a) of
8 claim 1.

9 A Yes.

10 Q It begins -- it says -- it recites "Forming a
11 plurality of interactors."

12 Do you have an understanding of what an
13 interactor is in the '848 patent?

14 A I do. I would like to take a moment to look
15 at my declaration again before I answer that question.

16 Yes. In paragraph 44 of my declaration, my
17 understanding is, as recited there, "The interactors
18 'comprise at least two distinct parts which are coupled,
19 one part is the molecule of interest and one part is the
20 nucleic acid moiety.'"

21 And that's column 10, lines 45 through 48.

22 That's my understanding in this context.

23 Q So you agree that an interactor requires at
24 least two parts, a molecule of interest and a nucleic
25 acid moiety?

1 A According to this -- the way it's written,
2 that is correct.

3 Q And is it your opinion that that would be the
4 customary and ordinary meaning of an "interactor" in the
5 '848 patent?

6 A In the context of the '848 patent, that would
7 be a common understanding of it. It could have other
8 meanings in other pieces of work, that is correct.

9 Q If you could back to claim 1, and step (b)
10 recites "forming a plurality of cis-reactive cells
11 wherein a cis-reactive cell comprises at least two
12 interactors bound in proximity to one another by an
13 associated oligonucleotide formed from the association
14 between at least two nucleic acid moieties."

15 Do you see that part I just read there,
16 step (b)?

17 A Yes.

18 Q Do you have an understanding of what a
19 cis-reactive cell is in the '848 patent?

20 A Yes.

21 Q What is your understanding of a cis-reactive
22 cell?

23 A If I can look at my declaration again.

24 Found in paragraph 49 of my declaration. My
25 understanding is, as quoted from '848, "The plurality of

1 interactors is then 'permitted to interact and
2 equilibrate, creating a secondary library of
3 'cis-reactive cells' wherein each CRC consists of MOI,
4 molecules of interest, brought into proximity by the
5 affinity between their respective NAMS and co-localized
6 by the association of their respective NAMS,' nucleic
7 acid moeties.

8 Q Do agree that a cis-reactive cell of the '848
9 patent requires at least two interactors found in
10 proximity to one another by an associated
11 oligonucleotide?

12 A In the context of the '848 patent, that is my
13 understanding, that is correct.

14 Q And is that -- would that also be the
15 customary and ordinary meaning understood to a POSA in
16 2005?

17 A That would be the understanding as it applies
18 to the '848 patent to a POSA reading this disclosure,
19 that is correct. It may be different in different
20 fields.

21 Q All right. If you have still claim 1 in front
22 of you, if you take a look at step (d).

23 Step (d) of claim 11 recites "selecting all
24 cis-reactive cells exhibiting the detectable trace."

25 Do you see that?

1 A I do.

2 Q Do you agree that claim 1's selecting step
3 requires selecting all of the cis-reactive cells that
4 were formed in step (b) that exhibit detectable trace?

5 A Let me take a look at my declaration.

6 MR. PLATT: Objection to form.

7 THE WITNESS: Could you repeat the question
8 for me, please?

9 BY MR. HOLMAN:

10 Q Yeah. We'll go about it a different way.

11 So step (b) of claim 1 recites "forming a
12 plurality of cis-reactive cells," correct?

13 A It does say that, yes.

14 Q Okay. And then step (c) of claim 1 recites
15 "subjecting the plurality of cis-reactive cells to
16 conditions which stimulate desired functional
17 interactions having a detectable trace"; is that
18 correct?

19 A That is correct.

20 Q And then step (d) recites "selecting all
21 cis-reactive cells exhibiting the detectable trace"; is
22 that correct?

23 A Yes. That's what it reads.

24 Q Okay. So my question is: Do you agree that
25 step (d) requires selecting cis-reactive cells

1 exhibiting detectable trace, but the cis-reactive cells
2 were formed in step (b)?

3 MR. PLATT: Objection to form.

4 THE WITNESS: My answer can best be stated by
5 reciting lines -- excerpts from lines 41 through 55,
6 column 19 of the '848 patent, which states "the CRCs
7 which display functional interactions must be selected
8 for detection and/or analysis," and gives examples of
9 filters and other forms -- other methods.

10 So that would be my response and my opinion as
11 stated in my declaration.

12 BY MR. HOLMAN:

13 Q So do you agree that step (d) requires
14 selecting cis-reactive cells?

15 A Step (d) you said? D as in "dog"?

16 Q D as in "dog."

17 A Yeah.

18 Q Do you agree that step (d) requires selecting
19 cis-reactive cells?

20 MR. PLATT: Objection to form.

21 THE WITNESS: Well, my understanding as a
22 technical person, as we discussed before, of the legal
23 aspects here is that claim 1 says "the method
24 comprising." So with that language, it's not required
25 that all -- that be included in the methodology as

1 written.

2 BY MR. HOLMAN:

3 Q Is it your testimony that because the claim
4 says "comprising," steps A through E aren't necessarily
5 required to practice claim 1?

6 A You know what? I don't really know. That's a
7 legal matter, and I'm not an expert on that. All I can
8 say is what my -- what I read in my declaration. That's
9 the -- my answer to that question.

10 Q All right. Even the part you read to me in
11 column 19, let's take a look at that. That part you
12 read says that "the CRCs which display a functional
13 interactions must be selected for detection and/or
14 analysis." Right?

15 Did I read that correctly?

16 A Let me find it again real quickly.

17 Q This is column 19, line 41 -- beginning of
18 line 41.

19 So do you agree that step (d) of claim 1
20 requires selecting CRCs?

21 A If you hold on just a minute, there's another
22 part of the '848 disclosure which I must find that I
23 believe can answer that question appropriately.

24 Okay. My answer is no, not necessarily. It
25 depends on -- and if you look at claim 2, which is what

1 I was looking for, of the '848 patent, it says "wherein
2 selecting all cis-reactive cells exhibiting the
3 detectable trace is accomplished via selective
4 separation or selective detection of the cis-reactive
5 cells."

6 So no because of the clarification in claim 2.

7 Q Well, claim 2 still recites "selective
8 separation or selected detection of the cis-reactive
9 cells," does it not?

10 A It does. And it says "accomplished via
11 selective separation or selective detection."

12 Q And selective separation and selective
13 detection of what?

14 A The cis-reactive cells, as stated in claim 2.

15 Q So, based on that, going back to step 1(d),
16 claim 1(d), do you agree that claim 1(d) requires
17 selecting cis-reactive cells?

18 A With the understanding that selected can be
19 selective separation or selective detection is the way
20 I'd answer that.

21 Q Again, you said selective separation or
22 selective detection. You're implying of the
23 cis-reactive cell, correct?

24 A Correct.

25 MR. PLATT: David, we've been going a bit over

1 an hour. I'm not sure when a good breaking point would
2 be.

3 MR. HOLMAN: Yeah, we can take a break.
4 That's fine.

5 (Recess taken from 10:00 to 10:12 a.m.)

6 BY MR. HOLMAN:

7 Q Dr. Nelson, during the break, did you speak
8 with anyone about the substance of your testimony today?

9 A No.

10 Q If you could turn in your declaration to
11 page 112, paragraph 220, please.

12 A I'm there.

13 Q All right. Here in this section of your
14 declaration, you discuss a document called "Landegren."
15 And that is Exhibit 1004; is that correct?

16 A Yes.

17 Q All right. I'm going to give you a copy of
18 Landegren, Exhibit 1004.

19 Do you recognize this document, Dr. Nelson?

20 A Yes.

21 Q This is the same Landegren Exhibit 1004 that
22 you provided opinions on in your declaration, correct?

23 A That is correct.

24 Q Did you review Landegren before signing your
25 declaration?

1 A Yes.

2 Q Did you review the whole document of Landegren
3 before signing your declaration?

4 A Generally speaking, yes. Although, I don't
5 think I read it word for word, cover to cover. I didn't
6 study all the nucleotide sequences, et cetera. But
7 generally reviewed it.

8 Q When was the last time you reviewed Landegren
9 before today?

10 A Well, in regards to what I state in my
11 declaration, those small sections in the preparation for
12 this deposition. Read the whole document? That was
13 probably back in 2024.

14 Q When is the last time you generally reviewed
15 Landegren before today?

16 A Could you clarify that?

17 Do you mean generally reviewed cover to cover
18 or just specific segments of it?

19 Q We'll go with specific segments of it.

20 A Well, again, as cited in my declaration,
21 probably those sections had a -- reviewed the relevant
22 pieces of information that were cited in my declaration.

23 Q So, sitting here today, your testimony is that
24 you haven't reviewed the entirety of Landegren since
25 2024; is that right?

1 A I would say that's a fair statement.

2 Q In preparation for the deposition today, you
3 reviewed the portions of Landegren that you cite in your
4 declaration; is that right?

5 A That is the best of my recollection at the
6 moment, that is correct.

7 Q All right. If could you look on the first
8 page of Landegren, at the bottom of the page, there's a
9 section called "Abstract."

10 Do you see that?

11 A Yes, I do.

12 Q The first sentence of the abstract in
13 Landegren states that "The present invention relates to
14 sensitive, rapid and convenient assays for detection
15 and/or quantification of one or several analytes in
16 solution using so called proximity probes."

17 Do you see that?

18 A I do.

19 Q Do agree that Landegren teaches sensitive,
20 rapid and convenient assays for detection and/or
21 quantification of one or several analytes in solution
22 using proximity probes?

23 A Well, that's a subjective statement. Whether
24 they teach that or not, they claim the present invention
25 relates to this, as you just read. That's what I could

1 also say.

2 Q Are you unsure of whether Landegren teaches
3 sensitive, rapid and convenient assays for detection
4 and/or quantification of one or several analytes in
5 solution using proximity probes?

6 A Well, they -- as far as the extent of their
7 disclosure, everything that's in here, which I would
8 have to analyze specifically, teaches to the best of
9 their ability that statement -- to that statement.

10 Q The same section, the abstract, the last
11 sentence, Landegren recites "The present invention
12 relates to methods and kits for proximity probing and
13 are performed in solution without the need of a solid
14 phase."

15 Do you see that?

16 A I do.

17 Q Do you agree that Landegren teaches methods
18 and kits for proximity probing that are performed in
19 solution without the need of a solid phase?

20 A Give me a moment to glance through the
21 document again and to review my declaration.

22 So my answer is, reading from my disclosure,
23 paragraph 222 of my declaration, 222, paragraph 222,
24 "Landegren discloses 'sensitive, rapid and convenient
25 assays for detection and/or quantification of one or

1 more -- quantification of one or several analytes in
2 solution.'" "

3 So, without fully analyzing it again, to the
4 extent that it's disclosed in this document, they teach
5 just that. They teach "sensitive, rapid and convenient
6 assays for detection and/or quantification of one or
7 several analytes in solution."

8 Q Okay. And that language you're reading there
9 in your declaration comes from the first sentence of
10 Landegren's abstract, correct?

11 A That -- let me double-check.

12 Yes. And also column 4 or page 4, lines 29
13 through 31.

14 Q Okay. My question is -- relates to the last
15 sentence of the abstract.

16 Do you agree that Landegren teaches methods
17 and kits for proximity probing that are performed in
18 solution without the need for a solid phase?

19 A I would say that, within the scope of what's
20 disclosed in there in this document, that would be a
21 reasonably accurate statement, depending on all the
22 definitions of those terms.

23 Q Is it your understanding that Landegren
24 presents its solution phase methods as advantageous over
25 solid phase assays.

1 A All these questions I haven't really performed
2 the analysis that you're describing, I would need to go
3 back and -- that's separate from how I utilized that in
4 the current case in Grounds 3 and 4. Now we're getting
5 into territory where I would -- to give you a really
6 solid scientific answer, I would need to go back and
7 review that document as a separate analysis. I've just
8 not done that analysis.

9 Q You reviewed Landegren to prepare the opinions
10 in your declaration, correct?

11 A That is correct.

12 Q And you understand or you understood at the
13 time you prepared your declaration what Landegren's
14 disclosures would have conveyed to a POSA; is that
15 correct?

16 A In regards to how it applied to the case at
17 hand, I would say that is correct. And generally
18 speaking, that's also correct.

19 Q So did you only focus on the disclosures that
20 you cited in your declaration to prepare the opinions in
21 your declaration?

22 A Could you ask that question again, please?

23 Q Yeah. That wasn't a very good question. I
24 apologize.

25 In preparing the opinions in your declaration

1 with regard to Landegren, did you only focus on the
2 Landegren disclosures that you cite in your declaration?

3 A Anything that had a bearing on my opinion in
4 my declaration is in the exhibit list. And so this one
5 from Landegren is the one that is the only one that has
6 relevance to my opinions formed in my declaration,
7 unless there is another Landegren that I can't recall.
8 But this is the only Landegren that I can recall off the
9 top of my head.

10 Q Sitting here today, are you unable to say one
11 way or the other whether Landegren presents its solution
12 phase methods using proximity probes as advantageous
13 over solid phase assays?

14 A Again, I would need to do further analysis to
15 be able to truthfully and accurately answer that
16 question.

17 Q If you could turn to page 1 of Landegren.
18 There's a section entitled "Background of the
19 Invention."

20 Do you see that there?

21 A I do.

22 Q And the second paragraph there, there's a
23 sentence that begins "Assays that use a solid phase."

24 Do you see that paragraph?

25 A I do see that.

1 Q Landegren states "Assays that use a solid
2 phase require considerable time and effort for
3 analysis."

4 Do you see that full sentence there I just
5 read?

6 A I do.

7 Q Do you agree that Landegren teaches that solid
8 phase assays require considerable time and effort for
9 the analysis?

10 A They claim that in that sentence, as you just
11 read that. But it depends on circumstances.

12 Q Would you agree a person of ordinary skill in
13 the art reading Landegren would have understood
14 Landegren as stating some assays that use a solid phase
15 require considerable time and effort for analysis?

16 A They would understand that's what Landegren
17 stated, yes.

18 Q The second sentence of this paragraph states
19 "The binding of reagents and analytes to the surface is
20 a time consuming process and the washing steps must be
21 precisely and reproducibly controlled between samples to
22 give exact results."

23 Do you see that sentence?

24 A I do.

25 Q Would a person of ordinary skill in the art

1 reading Landegren have understood Landegren as teaching
2 that the binding of reagents and analytes to the surface
3 is a time consuming process?

4 A They would understand that that's what
5 Landegren stated. And a POSA would think that it was
6 dependent on the exact conditions and circumstances of a
7 test. So it just depends on what -- how that applies to
8 each particular situation. They would understand that
9 that's what Landegren stated.

10 Q Would a POSA have any reason to doubt what
11 Landegren is stating here?

12 A I can't presume what a person would doubt or
13 not doubt.

14 Q Well, given their skill and understanding in
15 the art, would a POSA reading Landegren have taken
16 Landegren's statements at face value?

17 A I think they -- a POSA would have said, "Well,
18 it depends on the exact conditions of the exact
19 experiment."

20 Q The last sentence of this paragraph states
21 "Solid phase assays are also more difficult to automate
22 than homogenous assays."

23 Do you see that?

24 A I do see that.

25 Q Would a POSA in 2005 have understood Landegren

1 as teaching that solid phase assays are more difficult
2 to automate than homogenous assays?

3 A I think they would understand that this is a
4 statement that they made.

5 Q Would they have any reason to doubt
6 Landegren's statements?

7 A I think a POSA would think that it would
8 depend on circumstances whether that would be true or
9 not. It would depend on context and exact conditions of
10 an assay.

11 Q Well, assuming the circumstances and
12 conditions of the assays are taught within Landegren,
13 would a POSA have any reason to doubt Landegren's
14 disclosures here?

15 A Could you repeat that question, please?

16 Q Well, you said that it's -- the POSA's
17 interpretation of the sentence in Landegren is context
18 dependent, correct?

19 A Correct.

20 Q And as part of the context, I think you
21 mentioned the conditions of the assay, correct?

22 A Correct.

23 Q So my question is, first, would a POSA have
24 considered the conditions of the assays in Landegren
25 when interpreting these statements in -- on page 1?

1 A I can't answer that. Each person reads an
2 article differently, and I do not know. Reading this
3 introduction, they would say, "Well, it depends on
4 context."

5 Q I'm asking you how a person of ordinary skill
6 in the art would have read this.

7 A Right. That was my answer is that a person of
8 ordinary skill in the art would read this and think,
9 "Well, it depends on circumstances." Then that's my
10 answer.

11 Q Okay. But my question is about the
12 circumstances.

13 The circumstances -- do you agree that the
14 circumstances are disclosed within Landegren, for
15 example, the experiments and disclosures of Landegren?

16 A Well, yes. I mean, what they disclose in
17 Landegren is disclosed in Landegren, that is correct,
18 these exact details.

19 Q Given those circumstances, is it fair to say
20 that a person of skill in the art would have accepted
21 Landegren's statements here on page 1 referring to solid
22 phase assays?

23 A I haven't really performed that analysis. I
24 would need to go back through it again with that
25 question in mind and do a full analysis of that. I've

1 just not done that. So I can't answer appropriately.

2 Q Did you review the experiments and disclosures
3 of Landegren in preparing your declaration?

4 A As I mentioned before, I went through it and
5 generally understood it, but I also have already gone on
6 record saying that I didn't read every single word and
7 every exact condition. So the depth of the analysis I
8 don't recall at this time because I -- what's disclosed
9 in my declaration is the detail that I extracted from
10 it.

11 Q On page 1 of Landegren, the next paragraph
12 states that "Assays that do not require a solid phase
13 and the associated washing steps have important
14 advantages."

15 Do you see that?

16 A I do.

17 Q Would a POSA reading Landegren in 2005 have
18 understood that assays that do not require a solid phase
19 and the associated washing steps have important
20 advantages?

21 A Again, I would say it was dependent on
22 context.

23 Q I'm asking you about, within the context of
24 Landegren, would a POSA have understood that
25 Landegren -- would a POSA have understood that Landegren

1 teaches that assays that do not require a solid phase
2 and the associated washing steps have important
3 advantages?

4 A I didn't analyze Landegren with that
5 particular question in mind. I'd have to perform that
6 analysis to be able to answer that appropriately.

7 Q Sitting here today, you're not able to answer
8 one way or the other how a POSA would have understood
9 this sentence; is that right?

10 A Well, I'm answering it, but it's -- it's
11 context dependent. And that's -- that's my answer.

12 Q Well, you're not able to speak to the context
13 of Landegren?

14 A No. I haven't doing that full analysis in
15 regards to this question.

16 Q All right. You can put Landegren aside for
17 now. I'm going to hand you a copy of the Kanan
18 reference that's Exhibit 1010.

19 Dr. Nelson, do you recognize this document?

20 A Yes, I do.

21 Q This is the Kanan reference that you provide
22 opinions on in your declaration, correct?

23 A Yes, it is.

24 Q Did you review Kanan in preparing the opinions
25 in your declaration?

1 A I did.

2 Q Did you review all of Kanan in preparing the
3 opinions in your declaration?

4 A I reviewed a majority of it. I probably
5 didn't not study every chemical compound, such as in
6 Figure 4 in chemical detail, but I reviewed the majority
7 of the document.

8 Q You understand the disclosures of Kanan; is
9 that fair?

10 A To the best of my ability, yes, I do.

11 Q All right. Let's turn to Figure 1 of Kanan.
12 It's on the second page, 546.

13 As part of your review of Kanan, did you
14 review Figure 1?

15 A Yes.

16 Q Did you understand Figure 1 in Kanan?

17 A To the best of my ability, yes.

18 Q Is it your understanding that Figure 1 of
19 Kanan discloses a general workflow of Kanan's methods?

20 A I would say that's a fair statement.

21 Q Figure 1a depicts two pools of substrates each
22 linked to an oligonucleotide; is that correct?

23 A That is -- I believe that is correct.

24 Q One pool is labeled "Pool A" and the other
25 pool is labeled "Pool B," right?

1 A That is correct.

2 Q Okay. What are the differences between Pool A
3 and Pool B here on Figure 1a?

4 A I don't know what you're looking for, other
5 than it's exactly spelled out in this figure. I mean,
6 everything is labeled. For example, Pool A has
7 A-labeled substrates and Pool B has B-labeled
8 substrates. It's -- I'm not sure if you want me to
9 recite every -- every label that's in this figure or
10 not, but it's pretty well laid out.

11 Q Pool B -- the oligonucleotides in Pool B do
12 not contain a separate coding region and annealing
13 region; is that correct?

14 A Could you define an annealing region?

15 Q Sure. So, if you look at Pool A, the
16 oligonucleotides in Pool A, Kanan labels in blue
17 annealing region and then in orange a coding region.

18 Do you see that?

19 A Yes.

20 Q And so, if we look at the oligonucleotides in
21 Pool B, Kanan labels it only with blue coding region.

22 Do you see that?

23 A I do see that.

24 Q Okay. So my question is, in Pool B, the
25 oligonucleotides do not have -- do not contain a

1 separate coding region and annealing region; is that
2 correct?

3 A I understand the question. Whereas they don't
4 contain distinct and separate coding regions and
5 annealing regions, that region serves the same purpose
6 of coding and annealing. And you'll see in my
7 declaration that we also cite Neri in combination with
8 Kanan who shows distinct coding and annealing regions,
9 which is the combination of those, which we cite as --
10 in my declaration.

11 Q Sure. I understand. And we'll talk about
12 Neri at some point today. Right now I'm just asking you
13 about Kanan's Figure 1a and trying to understand your
14 understanding of the differences between Pool B and
15 Pool A. And starting with the coding region in the
16 molecules.

17 A Uh-huh.

18 Q So is it fair to say that Pool B
19 oligonucleotides in Kanan are only labeled with coding
20 region for B while the Pool A oligonucleotides in Kanan
21 are labeled with an annealing region for B and a coding
22 region for A?

23 A My answer is the same. If I get the exact
24 wording right, I'm not sure. But Pool B has a coding
25 region, and coincident with that, rather than being a

1 separate annealing region, it also serves as an
2 annealing region.

3 Q All right. So, if you look on Kanan -- the
4 front page, 545, and in the second column on the right,
5 the second sentence, Kanan states "We covalently linked
6 each Pool B substrate to its corresponding
7 oligonucleotide by a linker containing a biotin group
8 and a disulfide bond." And it cites Figure 1b and
9 supplementary information.

10 Do you see that sentence there?

11 A Yes.

12 Q Would a POSA reading Kanan have understood
13 that the oligonucleotides in Pool B are linked to the B
14 substrate by a linker containing a biotin group and a
15 disulfide bond?

16 A As is depicted in the figure, Figure 1a, and
17 the supplemental information, they would understand that
18 that linkage configuration containing a biotin and a
19 disulfide bond, as depicted in Figure 1.

20 Q And then Figure 1b -- looking at Figure 1b, do
21 you agree that Figure 1b depicts the steps of Kanan's
22 workflow?

23 A In a very simplistic format, yes.

24 Q And beginning at the top left, Kanan's
25 workflow begins with mixing Pool A and Pool B together;

1 is that right?

2 A Uh-huh.

3 Q And then moving from left to right, the
4 mixture is incubated under a set of reaction conditions;
5 is that right?

6 A According to this figure, that is correct.

7 Q And the reaction conditions in Kanan produce
8 some combinations of A and B that form bonds and others
9 that do not form bonds; is that correct?

10 A To clarify, it's bonds between the substrates.
11 And they both form hydrogen bonds between the nucleic
12 acid strands. So with that clarification, then I would
13 agree with that statement.

14 Q Okay. Sure. So there's two types of bonds
15 going on there; is that what you're saying?

16 A At least two, yes.

17 Q Bonds between the substrates A and B, right?

18 A Uh-huh.

19 Q And then I think you mentioned hydrogen bonds
20 between the oligonucleotide portions; is that correct?

21 A Correct.

22 Q Okay. And are the hydrogen bonds between the
23 oligonucleotide portions in this figure -- are those
24 depicted by the vertical lines within the
25 oligonucleotide arms there?

1 A Well, they -- there's several vertical lines,
2 but the ones where the lines -- the two different
3 colored lines overlap and there's two different vertical
4 lines indicate the pairing of the base pairs, which I
5 generally refer to as hydrogen bonding. As I mentioned
6 before, there's more forces than just hydrogen bonding,
7 but where those have annealed to one another, that is
8 correct.

9 Q Would you say that's a standard way to present
10 or depict hybridized nucleic acid strands, showing these
11 vertical lines connecting?

12 A No, I would not. I mean, there's so many
13 different formats that are used to represent a duplex, I
14 could not call this a standard form.

15 Q Is it fair to say that a POSA would have
16 understood what this is depicting, that it's depicting
17 hybridized nucleic acid strands there?

18 A In my opinion, I would say that, yes.

19 Q Moving on in the figure, if we go down to the
20 next row, after the bond formation, there's a step of
21 cleaving the disulfide bond on Pool B
22 oligonucleotides; is that right?

23 A Uh-huh.

24 Q And then after this disulfide cleavage,
25 there's a selection of biotin molecules using

1 streptavidin-linked beads; is that right?

2 A Avidin, but that is correct.

3 Q Okay. So, after disulfide cleavage, there's a
4 selection of biotin molecules using avidin-linked
5 beads; is that right?

6 A From this figure, that appears to be what
7 they're depicting, yes.

8 Q All right. And by performing this avidin
9 affinity selection in Kanan, Kanan is selecting biotin
10 and anything that is bound to biotin; is that right?

11 A Well, when you say "selecting biotin," I'm not
12 sure that's an accurate term. But as depicted in this
13 figure, the complex that -- between B9 and A6, which was
14 formed -- which is a bond-forming combination, and all
15 other such bond-forming combinations would, through the
16 biotin, be linked to the avidin microspheres.

17 Q So what's being selected here in Kanan's
18 affinity selection step?

19 A Well, could you define "selected" in this
20 context, please.

21 Q Sure. If you could go to your declaration,
22 paragraph 122. Are you there?

23 A Yes.

24 Q And in your second sentence, you say "Kanan
25 discloses that after bond formation 'streptavidin

1 affinity selection of the resulting solution separates
2 biotinylated from non-biotinylated sequences.'" "

3 A I see that.

4 Q All right. So, using that definition of
5 "selection" that you have used here, what is Kanan
6 selecting in this streptavidin affinity selection?

7 A Well, I might point out that that's not my
8 definition of "selection." This is a quote from Kanan.

9 But what we can say is that the process is
10 depicted in the figure below that, which also comes from
11 their paper, that the bond-forming combinations are
12 collected onto the avidin spheres via the linkage with
13 biotin and B9, A5, and the oligonucleotide appended to
14 A5.

15 Q And in this Figure 1b from Kanan, which you
16 have copied here in paragraph 122 of your declaration,
17 what is the bond-forming combination that's been
18 selected?

19 A In this case, it's -- the bond forming is
20 between the substrates. And in this particular example,
21 it's substrate B9 and substrate A6 of this particular
22 combination. But again, it's the whole complex with --
23 and that's -- the bond-forming ones are the only
24 complexes that retain the biotin linkage all the way
25 through to the oligonucleotide on Pool A.

1 Q And the biotin here is linked to the B
2 substrate B9; is that right?

3 A Well, we covered that earlier in Figure 1a
4 where all Pool B -- all -- yeah, the Pool B components,
5 we have a substrate, a biotin disulfide bond, and an
6 oligonucleotide as their construct. So that's where the
7 biotin comes from.

8 Q And in the same figure, the oligonucleotide
9 strand that's depicted here, that is the oligonucleotide
10 from the Pool A library member still conjugated to
11 substrate A6; is that right?

12 A That is correct.

13 Q Okay. Now, after this affinity selection
14 method in Kanan, what happens next in this workflow
15 method here?

16 A Well, according to this figure, there's an
17 arrow to the right and there's a PCR amplification.

18 Q And then what does Kanan disclose after PCR
19 amplification? What's the next step after that?

20 A Well, reading back to you which -- what we can
21 all see in Figure 1 of the Kanan publication, the next
22 arrow says "Label with red preselection or green
23 post-selection fluorophore and hybridize to DNA
24 micro-array containing all possible coding plus
25 annealing sequences."

1 Q All right. Let's take a look at Kanan's
2 supplemental materials document, which is Exhibit 1013.

3 Dr. Nelson, do you recognize Exhibit 1013?

4 A Yes.

5 Q Did you review Exhibit 1013 in forming the
6 opinions in your declaration?

7 A Yes, I did. Although, I have to admit, I
8 didn't read every NMR result, for example, some of the
9 finer details.

10 Q When is the last time you reviewed
11 Exhibit 1013?

12 A The last time was in preparation for this --
13 within the last couple weeks, I've reviewed it as it
14 relates to my statements in my declaration.

15 Q All right. If you could turn to page 8 of
16 this document, please. Page numbers are at the top.

17 About a fourth of the way down or so, there's
18 a section header titled "Reaction Discovery Experiments
19 and Selection Procedure."

20 Do you see that header?

21 A I do.

22 Q Did you review this section of Exhibit 1013 in
23 preparing the opinions in your declaration?

24 A I did. But not every single chemical
25 component of their composition, for example. So enough

1 to understand generally what they did without knowing
2 the concentration of Tris, for example.

3 Q Did you review this section of 1013 to prepare
4 for today's deposition?

5 A Yes. But not the entire document.

6 Q So you reviewed this section of 1013, but you
7 did not review the entire Exhibit 1013?

8 A Oh, I'm sorry. I perhaps misunderstood the
9 question.

10 So could you repeat that preceding question?
11 I apologize. I think I misheard it.

12 Q Sure.

13 Did you review the section entitled "Reaction
14 Discovery Experiments and Selection Procedure" in
15 Exhibit 1013 to prepare for today's deposition?

16 A Gotcha. I did misunderstand the question. I
17 apologize. So let me look at this entire section, and
18 then I will answer you truthfully.

19 Q I'm asking do you recall if you reviewed it or
20 not?

21 A Well, I'm looking to remind myself the full
22 breadth of this section, because I had to look at the
23 other page. And I have to look at it again even -- I've
24 reviewed a lot of material in the last couple weeks, so
25 I need to look at it to make sure I give you the correct

1 answer.

2 Q I'm sure you reviewed a lot. I'm just asking
3 generally, if you recall, did you review these two
4 paragraphs and five bullet points to prepare for today's
5 deposition?

6 A I understand the question. I'm going to look
7 at it for a moment to be able to answer that question.

8 To the best of my recollection, I did not
9 specifically review these two paragraphs in, you know,
10 the last several days here preparing for the deposition.

11 Q I think you did say you reviewed these
12 paragraphs to prepare the opinions in your
13 declaration; is that correct?

14 A Correct.

15 Q Is it your understanding that this disclosure
16 in Exhibit 1013 provides a more detailed description of
17 Kanan's methods?

18 A Now, you're not referring to just these two
19 paragraphs but just the whole supplemental materials?

20 Q Yeah. We'll start with the whole supplemental
21 materials.

22 Is it your understanding that Exhibit 1013
23 provides more details -- a more detailed description of
24 the experiments that are disclosed in Kanan
25 Exhibit 1010?

1 A I would say that's a fair and accurate
2 statement.

3 Q All right. And in the section that we're
4 looking at on page 8, the second sentence there begins
5 with "Two picomoles of total pool A material, 2
6 picomoles of total pool B material, 8 picomoles of the
7 universal clamp, and 1.2 femtomoles of the biotinylated
8 internal standard were combined in buffer and allowed to
9 hybridize at 25 degrees Celsius for 30 minutes."
10 Do you see that sentence there?

11 A I do.

12 Q And is it your understanding that this
13 disclosure represents that first step we looked at in
14 Kanan where Pool A and Pool B are combined and allow the
15 oligonucleotides to hybridize?

16 A I haven't analyzed it to see that exact
17 linkage, so let me take a moment to look at it here
18 before answering.

19 I would say this appears to be a general
20 workflow that corresponds to the figure we've reviewed.
21 Whether they do every single experiment this way or not,
22 I could not tell you.

23 Q But you agree that it begins with, at bottom,
24 combining Pool A and Pool B into a mixture to allow them
25 to associate, correct?

1 A That appears to be correct.

2 Q And the next sentence there, Kanan states in
3 Exhibit 1013 "Reactions were initiated by adding 1
4 microliter of a solution containing the metal or
5 non-DNA-linked reagents."

6 Do you see that sentence there?

7 A I do.

8 Q And is it fair to say that this sentence is
9 referring to subjecting this mixture of Pool A and
10 Pool B to reaction conditions?

11 A Could you repeat that question, please?

12 Q Sure.

13 Is it fair to say that this sentence in
14 Exhibit 1013 that I just read to you is referring to
15 subjecting the mixture of Pool A and Pool B to a
16 specific set of reaction conditions?

17 A This states that after the hybridization event
18 that reactions are initiated with the solutions that --
19 yes, with an additional solution.

20 Q So just so I can understand for clarity, do
21 you agree that this is referring to subjecting the
22 mixture to a specific set of reaction conditions?

23 A It's referring if you're -- if you're meaning
24 it subjecting the reactions after the hybridization
25 event, which was in the first part of this paragraph,

1 then that appears to be correct.

2 Q Okay. And then there's a list of bullet
3 points there. Do you see that?

4 A I do.

5 Q And Exhibit 1013 states that the detailed
6 conditions for each experiment shown in Figure 2b are as
7 follows, and then there's a list of bullet points.

8 Do you see that there?

9 A I do see that.

10 Q Okay. And the next paragraph begins "After
11 the reaction times." Do you see that there?

12 A I do.

13 Q All right. And here, Exhibit 1013 states
14 "After the reaction times indicated above, the solution
15 was diluted with 20 microliters of H2O and passed
16 through a gel filtration microcentrifuge column
17 (Princeton Separations) to remove small molecule
18 reactants."

19 Did I read that correctly?

20 A Yes, you did.

21 Q All right. So here do you agree that Kanan is
22 disclosing in Exhibit 1013 that, after these reactions
23 have occurred, the solution is diluted with water and
24 passed through a gel filtration column to remove small
25 molecule reactants?

1 A Since that's exactly what they stated, then I
2 would have to agree that that's what they did.

3 Q And that next sentence goes on. It says "To
4 the eluant was added 150 microliters of a 0.1 molar
5 aqueous solution of" -- and there's a long chemical
6 name -- "in 1.0 molar sodium phosphate, pH 8.0 to effect
7 disulfide cleavage."

8 Do you see that sentence there?

9 A I do.

10 Q All right. So here in this sentence that I
11 just read, do you agree that Kanan discloses that, after
12 removing the small molecule reactants, they hybridized
13 Pool A and Pool B pairs that were subjected to this
14 disulfide cleavage?

15 A Hybridized and further reacted, according to
16 the bullet points up above. And then the subsequent
17 step is the disulfide cleavage. According to this
18 protocol, that is correct.

19 Q Right. So the Pool A and B are hybridized
20 together. There's a reaction conditions. There's a gel
21 filtration step. And then now Kanan says to perform
22 this disulfide cleavage step; is that right?

23 A That is correct, from what they've written
24 here, yeah.

25 Q Correct so far?

1 A Yeah.

2 Q Moving on to the next sentence, Kanan states
3 "After one hour at 25 degrees Celsius, this solution was
4 added to a 20 picomole binding-capacity aliquot of
5 streptavidin-linked magnetic particles (Roche
6 Biosciences) suspended in 300 microliters of 0.1 molar
7 sodium chloride, 10 millimolar Tris, 1 millimolar EDTA,
8 pH 7.5 ('loading buffer')."

9 Did I read that right?

10 A Yes, you did.

11 Q Okay. So this sentence -- do you agree that
12 Kanan in Exhibit 13 is disclosing, after the disulfide
13 cleavage step, this mixture is put through Kanan's
14 streptavidin selection process?

15 A That appears to be correct, according to this
16 particular experiment.

17 Q Okay. And then the next sentence after the
18 streptavidin selection states -- sorry. Forget the next
19 sentence. Go towards the end. The last sentence of
20 the -- of this paragraph states that "This solution was
21 used directly in PCR reactions for micro-array
22 analysis."

23 Do you see that in the last sentence?

24 A I do see that.

25 Q So here, this is sort of the last step from

1 Kanan's Figure 1b that we were looking at, do you agree
2 that Kanan is disclosing, after putting the molecules
3 through these steps above, that the solution is used in
4 PCR reactions for micro-array analysis?

5 A Well, if the steps include those ones we
6 skipped over, which we didn't talk about specifically --
7 I'm assuming that's what you meant -- then the answer is
8 that's correct, from their disclosure here.

9 Q Let's go back and look at these steps, spend a
10 little time making sure I understand your understanding
11 of these.

12 After the solution is added to the
13 streptavidin-linked magnetic particles, Kanan states in
14 Exhibit 1013 "The supernatant was removed after 15
15 minutes," right?

16 Do you see that?

17 A I do.

18 Q And then Kanan says "The particles were rinsed
19 once with 200 microliters H2O and once with 200
20 microliters of sodium chloride Tris EDTA, pH 7.5," and
21 in parens "washing buffer."

22 Do you see that?

23 A I do.

24 Q Do you agree there's a water rinse step --
25 this begins with a water rinse step?

1 A What was the question?

2 Q Do you agree that this process disclosed in
3 Kanan begins with a water rinse step?

4 A I do.

5 Q And then there's another wash with this sodium
6 chloride Tris EDTA mixture?

7 A Another rinse, that's correct, yes.

8 Q Do you have an understanding of what EDTA is?

9 A Yes.

10 Q What is EDTA?

11 A It's a chelating agent.

12 Q What is a chelating agent?

13 A A chelating agent is a molecule which binds
14 various other compounds, typically metal ions.

15 Q What is the purpose of including a chelating
16 agent like EDTA in this step?

17 A Well, I -- you know, I don't know exactly why
18 they did it. Generally, a POSA would understand that
19 it's typically included in solutions of DNA because that
20 will bind metal ions that might catalyze nucleases and
21 helps to protect the DNA from being degraded.

22 Just this is off topic and just the best of my
23 knowledge as a POSA, but -- nothing to do with my
24 opinion about this reference, but that would be my
25 speculation as to why they included it.

1 Q And in your opinion, is that what a POSA would
2 have understood?

3 A I think that's a generally fair statement.
4 Again, it could have -- they could have had different
5 opinions, even POSAs skilled in the art at the time. I
6 can't predict for everyone but generally speaking.

7 Q Is it your opinion that there are different
8 POSAs, different individual POSAs?

9 A No. All I'm saying is that a POSA -- all
10 POSAs would have said "Well it's situation, context
11 dependent." And you're asking me what they would assume
12 in reading this art, and I would assume a POSA would
13 think, "Well, EDTA is a standard solution put into
14 solutions containing DNA."

15 Q Okay. So, after this washing buffer step,
16 Kanan Exhibit 1013 goes on, states that "The particles
17 were then resuspended in 20 microliters of 95 percent
18 formamide-5 percent 10 millimolars EDTA and incubated
19 65 degrees Celsius for 10 minutes."

20 Do you see that?

21 A I do.

22 Q All right. What is the consequence of putting
23 the particles through this formamide EDTA mixture?

24 A Well, clearly, from what they say next, "15
25 microliters of this eluant." So it's to elute the

1 complex off of the beads.

2 Q When you say "the complex," you're referring
3 to the complex that was selected in the streptavidin
4 affinity selection above we were looking at?

5 A I was referring to this figure in the Kanan
6 reference, which is also in paragraph 122 of my
7 declaration which shows the binding of the avidin beads
8 with biotin, the sulfide relinkage to B9, A5, and the
9 oligonucleotide. So that's the complex to which I
10 refer.

11 Q After the eluant, you refer to that sentence
12 that begins "15 microliters of this eluant."

13 Do you see that sentence there?

14 A Uh-huh.

15 Q The eluent is diluted in water and then added
16 to a fresh aliquot of streptavidin particles suspended
17 in 50 microliters of loading buffer.

18 Do you see that there?

19 A I do see that.

20 Q And then after that step, there's, I guess --
21 does Kanan in Exhibit 1013 disclose that that's
22 incubated for 15 minutes; is that right?

23 A I do see that, yes.

24 Q And then it says "The supernatant was removed
25 and the particles were rinsed with H2O and washing

1 buffer as above"; is that right?

2 A Yes.

3 Q Is it your understanding there's another water
4 rinse step here? Is that right?

5 A That is correct.

6 Q And then there's a washing buffer step as
7 well?

8 A That's what I read here, yes.

9 Q Okay. And then the particles are resuspended
10 again in 15 microliters of 95 percent
11 formamide-5 percent 10 millimolars EDTA and incubated at
12 90 degrees Celsius for 10 minutes.

13 Is that, again, to elute the complexes off of
14 the beads?

15 A That appears to be correct.

16 Q All right. And then the final step is that
17 the eluant -- 10 microliters of the eluant is diluted in
18 35 microliters of water and passed through gel
19 filtration spin-column; is that right?

20 A Yes.

21 Q And then we saw this last sentence already,
22 that the final solution is used directly in the PCR
23 reactions for micro-array. Is that correct?

24 A Yes.

25 Q All right. Let's turn back to your

1 declaration. And I want to look at your figure that you
2 have on page 62.

3 Are you there?

4 A Yes.

5 Q What is depicted in your figure here on
6 page 62 of your declaration?

7 A Yes. Let me take a few moments to orient
8 myself.

9 Q I'll withdraw that question, Dr. Nelson.
10 If you look in paragraph 114 of your
11 declaration, the last sentence there, you state "Below I
12 have included a figure I have created to represent the
13 library members in Kanan with the additional elements of
14 Neri."

15 Do you see that there?

16 A Yes, I do.

17 Q So is it your testimony that this figure
18 represents the library members of Kanan with additional
19 elements of Neri?

20 A Since that's stated right there, yes, it is.

21 Q Did you create this figure?

22 A I created the technical details of this.

23 Q Did you create this figure?

24 A Actually making the figure, I did not use the
25 program to make this figure and colorize it.

1 Q This figure is not disclosed in Kanan,
2 correct?

3 A That is correct.

4 Q This figure is not disclosed in Neri, correct?

5 A That is correct.

6 Q All right.

7 MR. PLATT: David, we've been going a bit over
8 an hour. Good time for a break?

9 MR. HOLMAN: Yeah. We can take a break.
10 That's fine.

11 (Recess taken from 11:17 to 11:32 a.m.)

12 BY MR. HOLMAN:

13 Q Dr. Nelson, during the break, did you speak
14 with anyone about the substance of your testimony today?

15 A I did not.

16 Q All right. We're looking at your figure,
17 page 62 of your declaration.

18 A Yes.

19 Q Do you still have that in front of you?

20 A Uh-huh.

21 Q And you stated there in paragraph 114 that
22 this figure represents the library members of Kanan with
23 additional elements of Neri, right?

24 A It's created to represent the vision of that,
25 that's correct.

1 Q Okay. And in the figure here, Pool A and
2 Pool B library members both have a region colored in
3 purple that you've labeled as "Self-assembly sequence to
4 B" and "Self-assembly sequence to A."

5 Do you see that?

6 A Yes, I do.

7 Q And these self-assembly sequences, does that
8 come from the Neri reference?

9 A Well, it's all laid out in the declaration.

10 Q Well, let me ask you this:

11 The self-assembly sequences here in this
12 figure that you provide hybridize to -- would you call
13 those universal hybridization sequences where all -- any
14 member of Pool A can hybridize to any member of Pool B?

15 A That is what I state in my declaration, that
16 that is -- those are -- allows for the association of --
17 between all of the elements of the two different pools.
18 So that is what they represent.

19 Q And going back to that sentence in
20 paragraph 114 when you say this -- you created this
21 figure to represent the library members of Kanan with
22 the additional elements of Neri, when you say
23 "additional elements of Neri," are you referring to the
24 elements from Neri's embodiment depicted in Neri's
25 Figure 5?

1 A Do I have Neri in front of me?

2 Q Sure. We can give you a copy of Neri.

3 All right. We've just given you a copy of
4 Neri, Exhibit 1011.

5 A Uh-huh.

6 Q And the question is in reference to Neri's
7 Figure 5.

8 So, when you state in your declaration that
9 you've included, quote, "additional elements of Neri" in
10 paragraph 114, do these additional elements come from
11 Neri's Figure 5?

12 A I'm going to take a few minutes to review my
13 declaration to see exactly what I said about that.
14 There are several pages which talk about answer to that
15 question.

16 Q Well, if it helps, I'll direct you to your
17 declaration, paragraph 96. And in that paragraph, you
18 provide a labeled version of Neri's Figure 5.

19 A So I would say that self-assembly sequences
20 come from the overall teaching of Neri that we combine
21 with Kanan, as I disclose in my declaration. Figure 5
22 is one representation of one of their modes in their
23 disclosure.

24 Q Okay. So self-assembly sequence is present in
25 Figure 5 of Neri but also in other embodiments of

1 Neri; is that right?

2 A I'm going to double-check to make sure that
3 that is an accurate statement.

4 Self-assembly sequence are certainly disclosed
5 throughout Neri, including in other figures.

6 Q Okay. Going back to your figure on page 62 of
7 your declaration, on Pool B, to the left of
8 "Self-assembly sequence to A," there's a red-colored
9 region labeled as a "D-spacer."

10 Do you see that?

11 A Yes, I do see that.

12 Q And does that D-spacer element -- does that
13 also come from Neri?

14 A That is something -- a feature that was also
15 disclosed in Neri.

16 Q And is that feature in Neri's Figure 5?

17 A That feature is disclosed in Figure 5 of Neri.

18 Q And on the same Pool B molecule, you have to
19 the -- on the right where the B substrate, B1, is linked
20 to the oligonucleotide, there's a biotin and a disulfide
21 bond there. So is that -- let me ask you this first:
22 Is that a linker containing biotin and disulfide bond?

23 A Well, I can read to you exactly how it's
24 disclosed in the Kanan supplemental materials. This
25 would be the most accurate.

1 Q We don't need to read Kanan. Basically, what
2 I want to understand is does this linker design with the
3 biotin and disulfide bond, does that come from the Kanan
4 reference?

5 A As we discussed previously, that is one of the
6 features of the Kanan art.

7 Q All right. If you can turn to the next page
8 of your declaration, there's another figure on page 63.

9 A I see it.

10 Q Did you create this figure?

11 A I was responsible for the technical content
12 thereof.

13 Q Did you create this figure?

14 A I did not drive the software program to make
15 the actual figure in the computer.

16 Q This figure is not disclosed in Kanan,
17 correct?

18 MR. PLATT: Objection to form.

19 BY MR. HOLMAN:

20 Q Is this figure disclosed in Kanan?

21 A This figure represents what I say in the
22 sentence right above the figure "I have created the
23 below figure to represent a cis-reactive cell formed by
24 interactors from pool A and pool B library members in
25 Kanan combined with the additional elements of Neri."

1 So these components appear in one form or the
2 other in both -- in Kanan and Neri, as stated here.

3 Q Okay. This figure is not disclosed in Kanan
4 alone.

5 Do you agree with that?

6 A The exact representation of this figure is not
7 disclosed, but the features are disclosed within Kanan
8 and Neri.

9 Q Is it your opinion that this figure represents
10 what a POSA would have generated by combining these
11 modified pool A and pool B library members from a
12 combination of Kanan and Neri?

13 A This represents a figure to represent -- this
14 figure represents the combination of Kanan and Neri, as
15 we discussed, and a POSA would have been able to
16 generate a similar concept and figure as well.

17 Q And the POSA, in your opinion, would have used
18 these -- the pool A and pool B library members that you
19 depict on page 62 and when combining them produce the
20 complex you present on page 63. Is that a reasonable
21 understanding there?

22 A Could you repeat the exact question, please?

23 Q Sure.

24 Is it your opinion that a POSA would have used
25 the library A -- the library members pool A and pool B

1 that you depict on page 62 of your declaration and when
2 combining them produce this complex that you present on
3 page 63 of your declaration?

4 A I would say a more accurate statement would be
5 a POSA would have understood the concepts of Kanan and
6 Neri and the motivation to combine those. And whether
7 they depicted them exactly this way or not, they would
8 have understood that the result is to have what is
9 depicted in one format the figure on page 63.

10 Q And this figure on page 63 also possesses the
11 biotin and disulfide linker between substrate B9 and its
12 oligonucleotide; is that correct?

13 A Yes, that is correct.

14 Q And the other substrate in this figure is
15 A6; is that right?

16 A That is what the figure represents, correct.

17 Q Okay. Now, in this figure, the purple region
18 that you've labeled "association elements" here, are you
19 depicting that this region is hybridized between the two
20 nucleic acid strands?

21 A That is what this figure represents.

22 Q And is that hybridization depicted here by the
23 vertical lines coming down from one of the DNA strands
24 and vertical lines going up from the other DNA strand?

25 A That is how the duplex is represented in this

1 figure, that is correct.

2 Q What do these vertical lines represent?

3 A In this figure, they represent the base
4 pairing between strands of the nucleic acid. Roughly
5 depict.

6 Q So, if there's vertical lines from one strand
7 connected to the other strand, that represents base
8 pairing between the two nucleic acid strands?

9 A It represents in a rough way the bonding
10 between those strands, which is via base pairing and
11 other forces that we talked about earlier.

12 Q Sure. Sure. Understood.

13 Okay. And then if we move to the left of this
14 purple base paired region, there is a -- the d-spacer,
15 the red d-spacer region and then a blue region.

16 Do you see that segment?

17 A Yes, I do.

18 Q And in this region, is it fair to say that
19 there is no hybridization between the two strands?

20 A I would say that, according to the disclosure
21 of Neri, what they use for their d-spacer, there would
22 not be any conventional Watson-Crick base pairing
23 between those two strands in this particular depicted
24 configuration.

25 Q Why is there no Watson-Crick base pairing

1 between the two strands in this section?

2 A Yes. Let me -- give me just a moment to look
3 at my declaration so I can use -- recite the correct
4 answer.

5 As I state on page 57 of my disclosure,
6 paragraph 105, just above the last -- the second-to-last
7 sentence before the figure in the -- halfway down there,
8 "The d-spacer is 'a small segment . . . composed of a
9 phosphodiester backbone without bases.'"

10 So the d-spacer does not have bases, and
11 that's nucleotide bases, and that's why it does not form
12 classic Watson-Crick base pairing with an opposing
13 strand.

14 Q And so your figure to depict that there is no
15 hybridization here between the d-spacer and this blue
16 piece, you only include vertical lines coming from the
17 blue piece; is that right?

18 A That is the correct assessment of the
19 depiction in this figure.

20 Q Okay. All right. So moving in your
21 declaration to a few pages over on page 67, you have
22 another figure there.

23 A Yes.

24 Q Do you see that?

25 A I do.

1 Q And did you create this figure, Dr. Nelson?

2 A Same basic answer. I was responsible for the
3 technical details of this figure.

4 Q Did you create the figure?

5 A I was not responsible for driving the software
6 program to actually make the electronic version of this
7 figure.

8 Q And does this figure represent what the
9 bond-forming pair of A and B substrates would look like
10 after subjecting these molecules in Kanan's reaction
11 conditions?

12 A This is a depiction to represent one such pair
13 of a bond-forming combination, in this case, B9 and A6.

14 Q And the bond between B9 and A6, is that
15 represented by the green line between the two?

16 A That's correct. Yes, that is green. I have
17 to admit, I have a little bit of a red/green color
18 blindness so I have to look carefully.

19 Yes, that is the green line.

20 Q The line between B9 and A6?

21 A Thank you, yes.

22 Q Whatever color it may be. It looks green to
23 me.

24 A Yes. It is green.

25 Q Okay. And in your opinion, that bond between

1 B9 and A6, or the B substrate and A substrate,
2 represents a detectable trace, as defined in the '848
3 patent; is that right?

4 A I did not represent that in my declaration, so
5 no. I would have to -- I would like to look at my
6 declaration just so I can read you and recite exactly
7 what I stated about the detectable trace to answer that
8 more accurately.

9 Q So sitting here today, is it your testimony
10 that the bond between B9 and A6 is not a detectable
11 trace according to the '848 patent?

12 A I'm going to review my declaration for just a
13 little bit.

14 Okay. I would like to answer my question by
15 reciting paragraph 119 in my declaration.

16 "Kanan teaches subjecting the CRCs, such as
17 those generated from the combination of Kanan and Neri,
18 to conditions that stimulate a desired functional
19 interaction with a detectable trace. Kanan teaches each
20 pool B substrate is linked 'to its corresponding
21 oligonucleotide by a linker containing a biotin group
22 and a disulfide bond. After incubations under a set of
23 chosen reaction conditions, followed by cleavage of the
24 disulfide bonds, only pool A sequences encoding bond
25 formation between pool A and pool B substrate remain

1 covalently linked to biotin.'"

2 Continuing, "A POSA would have understood that
3 the bond forming -- the bond formation between
4 substrate A and B (i.e., the addition of substrate B to
5 A) would be the functional interaction between the
6 substrates. Further, a POSA would have had understood
7 that the bond formation between a pool A substrate and
8 pool B substrate covalently linked to biotin would be
9 the detectable trace, as only the bond-forming pairs
10 contain the biotin that is subsequently selected using
11 streptavidin or avidin for analysis." And so "A POSA
12 would understand that the CRCs made from Kanan and Neri,
13 consisting of interactors of any A1 through N,"
14 subscript, "within a B1 through M," subscript, "would be
15 subjected to conditions that stimulate a desired
16 functional interaction having a detectable trace as
17 shown," in the figure we're discussing.

18 So that's my answer.

19 Q So the detectable trace, in your opinion, is
20 the bond formation between a pool A substrate and a
21 pool B substrate covalently linked to biotin; is that
22 fair?

23 A That's -- the biotin is the detectable trace
24 in this case because that's linked to the -- well, I
25 just read it. So my answer is what I just read.

1 Q Okay. And so, in this figure here, the pool B
2 member, B9 in this case, contains the same linker we saw
3 earlier with the biotin and the disulfide bond, correct?

4 A That is correct.

5 Q And as you were reading from your declaration
6 in paragraph 19, is it your opinion that a POSA would
7 have subjected this molecule to these same steps in
8 Kanan as far as a the disulfide cleavage and then the
9 streptavidin affinity selection process?

10 A Just one point. I think you said
11 paragraph 19.

12 Q Sorry. I misspoke if I did. I meant
13 paragraph 119.

14 A And I wasn't sure if heard you correctly, so
15 just to make sure it was correct on the record.

16 So now sorry for my interruption, but I want
17 to make sure. Could you please repeat your question.

18 Q Sure.

19 So is it your opinion that a POSA combining
20 Kanan and Neri in this way that you've depicted here in
21 the figure would have subjected this complex to the
22 procedures that you outline in paragraph 119 in Kanan
23 where there's a disulfide cleavage step and a selection
24 with the streptavidin affinity process?

25 A I believe what I said in the last part of

1 paragraph 119, yes, it is my opinion that a POSA would
2 have understood that the bond formation would be the
3 functional interaction and that would have also
4 understood that only those covalently linked to the
5 biotin would be the detectable trace, as only the
6 bond-forming pairs contain the biotin that is
7 subsequently selected for streptavidin analysis, and
8 that yes, I would -- they would -- my opinion is a POSA
9 would have understood that the disulfide cleavage step,
10 as disclosed in Kanan, would still be part of that
11 process.

12 Q Let's talk about your discussion of the
13 selection step. This is in your declaration beginning
14 paragraph 121. So I think we're on the same page as
15 your figure here.

16 A Okay.

17 Q And this section of your declaration,
18 paragraphs 121 to 124, this is where you discuss the
19 step (d) selection step of the '848 patent in relation
20 to Kanan and Neri; is that correct?

21 A This is it step (d) of the '848 patent.
22 That's where I discuss it, yes.

23 Q And then on page 68 of your declaration,
24 paragraph 122, you have a figure there at the bottom of
25 the page.

1 Do you see that figure?

2 A I do.

3 Q And that figure is from Kanan's Figure 1b; is
4 that right?

5 A That is correct.

6 Q All right. And then in that paragraph 122 --
7 I think we were looking at this disclosure earlier --
8 you state "Kanan discloses that after bond formation
9 'streptavidin affinity selection of the resulting
10 solution separates biotinylated from non-biotinylated
11 sequences.'"

12 Did I read that correctly?

13 A You did read that correctly.

14 Q And that quoted language comes from Kanan,
15 right? That's Exhibit 1010 that you've cited there; is
16 that right?

17 A That is correct.

18 Q Is it your opinion that a POSA combining Kanan
19 and Neri in the way that you've presented it here would
20 have followed Kanan's teachings in Figure 1b that you
21 have copied here on page 68?

22 A It is my opinion that a POSA would have viewed
23 the steps in Kanan, as depicted in this figure at the
24 bottom of page 68, as part of one of the methods they
25 could follow to achieve their desired goals.

1 Q But the methods include -- did you describe
2 any other methods in your declaration that a POSA would
3 have followed?

4 A That's a very broad question.
5 Do you mean in my entire declaration or any
6 other methods of anything that I could have described?

7 Q Well, I'm just trying to understand the
8 process that you've laid out here in your declaration
9 where we were looking at this figure on page 67 of your
10 dec, right? You have this complex, B9 and A6.

11 A Yeah.

12 Q You recall looking at that.

13 And then is that figure -- or that complex, as
14 you've explained in paragraph 122, is it your opinion
15 that that complex goes through this process depicted in
16 Kanan's Figure 1b?

17 A It's my opinion that a POSA would have seen
18 that as one possible method to use in application to
19 their desired outcome, whatever that might be.

20 Q You agree that in all of your figures
21 representing a combination of Kanan and Neri, you
22 portray it as following or as including Kanan's methods
23 of disulfide cleavage followed by the streptavidin
24 affinity selection process; is that correct?

25 A Well, all the figures don't depict that exact

1 step.

2 Q Fair enough. That was a poorly worded
3 question.

4 Your figures showing the combination of Kanan
5 and Neri depict the pool B molecules, including the
6 linker with a biotin and a disulfide bond, correct?

7 A Again, I don't know if all the figures do
8 that, but certainly the one on page 67 we've been
9 discussing show that component.

10 Q Okay. And based on that design that you've
11 presented, is it your opinion that a POSA would have
12 processed that complex through Kanan's workflow that
13 involves the disulfide cleavage and then this
14 streptavidin affinity selection process depicted in
15 Figure 1b?

16 A It is my opinion that a POSA would have seen
17 it as obvious that that would be one method that they
18 could follow, the method of Kanan and cleavage of the
19 disulfide to achieve the goals of their particular
20 experiment, depending on what that experiment was.

21 Q All right. Do you still have the Neri
22 reference?

23 A Yes, I do.

24 Q Exhibit 1011. Let's take a look at that one.
25 Earlier we were looking at Figure 5.

1 Let me ask this: Did you review the Neri
2 reference in forming the opinions in your declaration?

3 A I did.

4 Q Did you review all of Neri in forming the
5 opinions of your declaration?

6 A I reviewed a good portion of it. I would say
7 that I didn't necessary read every dependent claim or
8 study the sequences in Example 1, for example. But I
9 studied the Neri reference in relation to how it applied
10 to formulate my opinion in my declaration.

11 Q Let's turn to Neri paragraph 60. It's on
12 page 20 if you're using the page numbers at the bottom.

13 A Okay. Got it.

14 Q Sorry. Not paragraph 60. Paragraph 59.
15 Begins on the bottom of page 19.

16 A Okay. I'm there.

17 Q Apologies. Read paragraph 59 to refresh your
18 recollection and let me know when you're done, please.

19 A All right.

20 Okay. I'm done reading it.

21 Q The last sentence of that paragraph refers to
22 biopanning procedures used with antibody phage
23 libraries.

24 Do you see that?

25 A I do.

1 Q Do you have an understanding of what Neri is
2 referring to when Neri states "biopanning procedures"?

3 A Could you repeat the question, please?

4 Q Do you understand what biopanning procedures
5 are that Neri is referring to here?

6 A I haven't performed that analysis in my
7 preparation of this declaration, so I would have to
8 really review that more carefully to say that I was
9 fully aware of what that meant.

10 Q Do you have a general understanding of what
11 biopanning is?

12 A I really would have to do that analysis to
13 even get a general understanding of what he means -- of
14 what they're referring to here.

15 Q Sitting here today, you're not able to tell me
16 what "biopanning" means?

17 A I would want to perform an analysis separate
18 from what we're discussing here in the current
19 declaration to be able to form that answer.

20 Q All right. Let's look at paragraph 84 of Neri
21 that's on page 22, using the page numbers at the bottom.

22 A I have it.

23 Q Go ahead and take a look at that paragraph,
24 refresh your recollection, please.

25 A All right.

1 Okay.

2 Q All right. So, in paragraph 84 of Neri
3 there's a sentence that begins "In this respect,
4 ESACHEL."

5 Do you see that?

6 A I do.

7 Q Neri states "In this respect, ESACHEL
8 biopanning experiments are analogous to biopanning
9 experiments which can be performed with phage libraries
10 and/or ribosome display libraries, for which an
11 extensive literature and several experimental protocols
12 are available."

13 Do you see that sentence I just read there?

14 A I do.

15 Q Do you understand or do you have an
16 understanding of what ESACHEL biopanning experiments
17 are?

18 A I did not perform that analysis in regards to
19 preparation for the case at hand here, so I would have
20 to do that analysis to really understand that
21 terminology.

22 Q You reviewed Neri to prepare your opinions in
23 your declaration, did you not?

24 A I reviewed it. But as I mentioned, I didn't
25 review every single detail of every single word.

1 Q And this is a section -- paragraph 83 is a
2 section header entitled "Biopanning Experiments."

3 Do you see that?

4 A I do.

5 Q But your testimony today is that you're not
6 able to tell me what "biopanning" means in Neri?

7 A I have not formed analysis of that. I wasn't
8 looking for that. And I would say that I could not
9 respond to that question without performing that
10 analysis.

11 Q Let's look at paragraph 30 of Neri, please.

12 A Found it.

13 Q In the first sentence here in paragraph 30,
14 Neri states "After biopanning, oligonucleotides of
15 sublibrary B remain stably annealed to oligonucleotides
16 of sublibrary A, and can work as primers for a DNA
17 polymerase reaction on the template A."

18 Do you see that there?

19 A I do.

20 Q And do you have an understanding of what Neri
21 is referring to when Neri says "after biopanning" here
22 in paragraph 30?

23 A I have not performed an analysis of
24 biopanning, and I would need to do that to be able to
25 accurately answer that statement.

1 Q So, putting aside the process of biopanning,
2 is it fair to say that the steps here disclosed in
3 paragraph 30 begin with, again, after biopanning, the
4 sublibrary B oligos annealing with the sublibrary A
5 oligos?

6 A Could you repeat that question, please?

7 Q Strike that. Let me rephrase the question.

8 Let's go back to paragraph 84. That's on
9 page 22 again.

10 A Okay. I'm there.

11 Q All right. And the first sentence refers to
12 this acronym again, "ESACHEL."

13 Do you see that?

14 A Yes, I do.

15 Q Do you know what that is?

16 A Well, that's their technology. I'd have to
17 remember exactly what that acronym stands for, but yes.

18 Q If you look on the first page of the title of
19 Neri. Could you read that out loud for the record.

20 A "Encoded Self-Assembling Chemical Libraries.

21 Q And is that what "ESACHEL" stands for?

22 A According to their disclosure, yes.

23 Q Let's go back to paragraph 84.

24 And I just want to understand your
25 understanding of the steps here.

1 This is a section that refers to "biopanning
2 experiments," correct? Do you see that there?

3 A I do see that.

4 Q That's in paragraph 3.

5 And the first sentence says that "The use of
6 ESACHEL for the identification of specific binders
7 relies on the incubation of ESACHEL components with the
8 target molecule (e.g., a protein of pharmacological
9 interest), followed by the physical separation of the
10 resulting complex from the ESACHEL components which have
11 not bound to the target."

12 Okay. Did I read that correctly?

13 A Yes.

14 Q All right. So let's break this down.

15 What are the steps outlined in this first
16 sentence here in paragraph 84?

17 A I can't provide any more than the exact words
18 that you just read. So I can read it again if you'd
19 like.

20 Q So you're not able to tell me what the steps
21 are in this first sentence of paragraph 84?

22 A I can recite to you exactly what they wrote
23 here.

24 Q All right. Do you agree that the steps
25 follow -- the first step is incubating the ESACHEL

1 components with the target molecule?

2 A I'm reading the same words as you. So for
3 this one disclosure, that's apparently one method that
4 they disclose.

5 Q And then, after that, it's followed by the
6 physical separation of the resulting complex from
7 components which have not bound to the target; is that
8 right?

9 A Those are the same words that I read.

10 Q And then Neri says "In this respect, ESACHEL
11 biopanning experiments are analogous to the biopanning
12 experiments which can be performed with phage libraries
13 or ribosome display libraries," right?

14 Do you see that sentence there?

15 A I see that sentence.

16 Q Do you agree that this process that's outlined
17 here in paragraph 84 is the process of biopanning in
18 Neri?

19 A I have not performed the analysis to
20 understand exactly what they mean in this paragraph. I
21 would have to perform an independent analysis. It's not
22 part of my analysis for my declaration.

23 Q So you're not sure? You're not able to tell
24 me one way or the other what the process -- what Neri's
25 biopanning process is?

1 A As I stated for the biopanning, I would have
2 to do a -- I didn't do that analysis.

3 Q Is it fair to say you didn't analyze Neri's
4 methods of biopanning disclosed in this reference?

5 A I would say I did not analyze the references
6 that they make to biopanning.

7 Q All right. In your declaration,
8 paragraph 1 -- let's look at paragraph 177, please.

9 A Okay.

10 Q And here you refer to false negative. And in
11 particular, I'm looking at the second sentence here.
12 You refer to "false negatives produced by errors in the
13 polymerization step."

14 Do you see that there?

15 A I do.

16 Q And then same paragraph at the end, last
17 sentence that's on the next page, you again refer to
18 false negatives based on errors in the polymerization.

19 Do you see that reference there? Very last
20 sentence of paragraph 177.

21 A Yes. I see that sentence.

22 Q Okay. What -- when you say "polymerization
23 step," what polymerization step are you referring to?

24 A Yes. I will find that in the declaration so I
25 can tell you accurately.

1 On page 94.

2 Q Of your declaration?

3 A Of my declaration. Thank you. Sorry.

4 It's at the end of paragraph 181, which starts
5 on page 93. But there's a figure there. And then one
6 of the configurations in Neri, shown on the left there,
7 there is a step shown on the right middle that has an
8 arrow down and has "DNA Polymerase." And you can see
9 from the diagram right below that arrow down with "DNA
10 Polymerase" next to it, there's an extension step that
11 fills in that single-stranded portion of the construct.
12 That's the DNA polymerase step in this example to which
13 I refer.

14 Q And is it your opinion that that
15 polymerization step can produce errors that result in
16 false negatives?

17 A It's well known in the art that polymerases
18 can make mistakes. So that is one potential source of
19 errors that can lead to false negatives.

20 Q How do polymerases create errors?

21 A Well, that's somewhat -- that's very much
22 beyond the scope of what's in my declaration here. But
23 just generally, in any situation, not related to the
24 declaration, they incorporate the wrong base once in a
25 while. Just polymerases. That's kind of common

1 knowledge.

2 Q How would a POSA have mitigated dealing with
3 polymerase errors -- potential polymerase errors?

4 A Well, again, that's beyond the scope of my
5 declaration. And I can't -- I'd have to do an analysis
6 to see all the methods that they use to reduce
7 polymerase errors. But one motivating factor would be
8 to not do a polymerization. That would be one method
9 that a POSA would be aware of.

10 Q Right. So, for example, I think you provide
11 some testimony that a POSA would have been motivated to
12 do a ligation method from the Famulok reference; is that
13 right?

14 A That's what we started with, correct? What
15 paragraph was that in?

16 Q That was paragraph 177.

17 A I'd like to turn back to that paragraph.

18 The first two sentences say that. So my
19 opinion is "A POSA would have had understood that it
20 would have been obvious to use a method of ligation of
21 the oligonucleotides as taught in Famulok to ligate
22 together the ends of the DNA oligonucleotides of the
23 paired substrates in Kanan. A POSA would have been
24 motivated to reduce false negatives produced by errors
25 in the polymerization step--for example, matched pairs

1 not being properly encoded during polymerization."

2 So that's my opinion.

3 Q Is it your opinion that, given the risk of
4 polymerase errors, a POSA would not have pursued Neri's
5 polymerase step depicted in Figure 5?

6 A That does not reflect my opinion, no.

7 I would need to do a further analysis to be
8 able to fully bottom on that. But that does not reflect
9 my opinion.

10 Q Well, you provide the opinion that a POSA
11 would have been motivated to perform a ligation step to
12 avoid this polymerization step, correct?

13 A I state that they would have been motivated,
14 relying -- based on the potential need. It depends on
15 the context. If they were having, depending on the
16 application, any kind of issues with errors produced by
17 polymerization, they would be motivated to combine the
18 teaching of Kanan and Neri with Famulok for ligation,
19 and in other circumstance they might not. So it's
20 dependent on the context in their particular
21 experimental conditions.

22 Q Is it fair to say that a POSA would have had
23 the skills and resources to deal with any polymerase
24 errors from this method?

25 A That question is vague, and it's difficult to

1 answer that.

2 Could you restate that perhaps in a different
3 way?

4 Q Sure.

5 I mean, so a person of skill in the art has an
6 advanced degree, such as a Ph.D. in chemistry, molecular
7 biology, biochemistry or related field and at least two
8 years of experience in industry and/or laboratory
9 experience relating to small molecules and proteins and
10 would have been familiar with nucleic acid chemistry and
11 conventional hybridization techniques.

12 Do you agree with that characterization of a
13 person skilled in the art?

14 A If that's what you read directly -- I wasn't
15 reading with you -- then that captures my opinion.

16 Q Okay. And given that background and skill set
17 of a POSA, is it your opinion that a POSA would have
18 been able to overcome any polymerase errors associated
19 with Neri's Figure 5?

20 A Well, again, the term "overcome" is vague
21 because it depends. It depends on the context. It
22 depends on if there was a problem, the degree of the
23 problem, and what the objective of their experiment was.

24 But a POSA would have understood that
25 polymerization errors occur. They would have understood

1 that not doing polymerization would be one possible
2 method to avoid those issues and that Famulok, which
3 was -- would have -- the ligation method of Famulok
4 combined with Kanan and Neri would have presented an
5 obvious alternative to them.

6 Q Going back to Neri -- do you still have Neri
7 in front of you?

8 A I've got to grab it here.
9 Yes.

10 Q And on page 18, paragraph 29.

11 A Okay. Got it.

12 Q That refers to Figure 5 of Neri.
13 Do you see that?

14 A Yes.

15 Q And that's the same figure that you refer to
16 in your declaration that we were looking at, on page 94
17 of your declaration; is that right?

18 A Yes. Let me confirm that.

19 Yes. That is correct.

20 Q Is it your understanding that paragraph 29 of
21 Neri describes what's depicted in Figure 5?

22 A I'll have to read that sentence or that
23 paragraph first, and then I can respond.

24 I would say paragraph 29 generally depicts
25 what's in Figure 5.

1 Q Okay. And then moving to the next paragraph,
2 30 -- we looked at this earlier -- Neri says "After
3 biopanning, the oligonucleotides of sublibrary B remain
4 stably annealed to the oligonucleotides of sublibrary A
5 and can work as primers for a DNA polymerase reaction on
6 the template A."

7 Do you see that first sentence there?

8 A I do.

9 Q Now is that DNA polymerase reaction there, is
10 that the polymerization that you're referring to in your
11 declaration?

12 A The -- I'm sorry. One moment.

13 That appears to be correct. It's not clear
14 from this paragraph 30 that they're referring to the
15 exact representation in Figure 5, but it's likely that
16 that is the case.

17 Q And this step, this DNA polymerase reaction in
18 paragraph 30, Neri says that this takes place after the
19 biopanning method; is that right?

20 A That's what -- I mean, I read the same words
21 as you. That's what Neri says in paragraph 30. So, if
22 we're just reading that, that is an accurate reading of
23 that paragraph.

24 MR. HOLMAN: Let's take a break. Go off the
25 record.

1 (Recess taken from 12:33 to 1:19 p.m.)

2 BY MR. HOLMAN:

3 Q Dr. Nelson, welcome back.

4 A Thank you.

5 Q During the lunch break, did you speak to
6 anyone about the substance of your testimony today?

7 A I did not.

8 Q Do you still have a copy of the '848 patent in
9 your materials there?

10 A Let me find it.

11 Q Exhibit 1001.

12 A Yes, I have it.

13 Q Okay. Let's take a look at the claims,
14 claim 16. It's on page 33, if you're looking at the
15 bottom page numbers.

16 A Okay.

17 Q Claim 16 depends from claim 1, correct?

18 A Yes.

19 Q Do you have an understanding what it means to
20 be a dependent claim?

21 A Yes.

22 Q What is your understanding of a dependent
23 claim?

24 A It's dependent on, in this case, the one
25 independent claim. So that entire claim, claim 1 in

1 this case, is in play. It stands. And this is just
2 with all of those conditions, in addition, it's the
3 method of that's recited in claim 1, wherein the
4 association which they recite in claim 1 is via
5 ligation.

6 Q So is it your understanding that claim 16
7 requires all the elements of claim 1 in addition to
8 specifying that the association is via ligation?

9 A Let me make sure I have it an accurate answer.
10 I'm going to briefly review claim 1.

11 That is my understanding.

12 Q All right. If you can -- in your declaration,
13 let's take a look at page 90 --

14 A Okay.

15 Q -- where you discuss claim 16.

16 A I'm there.

17 Q You're faster than I am.

18 All right. So, in your declaration, page 90
19 is where you begin your discussion of claim 16 in the
20 context of Neri, Kanan and Famulok, correct?

21 A Correct.

22 Q All right. And Famulok is -- you introduce it
23 here in paragraph 175. That's Exhibit 1012.

24 Do you see that there, last sentence there?

25 A Yes.

1 Q I'm going to give you a copy of Famulok. I
2 don't know if I'm pronouncing it correctly, but that's
3 how we've been saying it.

4 All right. This is Exhibit 1012, the Famulok
5 reference.

6 Do you recognize this document?

7 A It looks a little different.

8 Q You said it looks a little different.

9 How does it look a little different?

10 A It's just two-sided and more colors. I just
11 wanted to make sure it was the correct document.

12 Yes. I believe this is the one.

13 Q Okay. And you reviewed this document in
14 preparing the opinions in your declaration, correct?

15 A I reviewed parts of it as it was relevant to
16 the -- my argument here.

17 Q Which parts of it did you review?

18 A Those related to ligation.

19 Q And you didn't review other parts of the
20 document?

21 A I did not read every word of this document,
22 no, I did not.

23 Q When was the last time reviewed Famulok before
24 today?

25 A Other than the citation in the figure in my

1 declaration, probably in 2024.

2 Q So my question is, when was the last time you
3 reviewed Famulok before today?

4 A Before today, yes.

5 Q Yes.

6 And you said other than your citation and the
7 figure in your declaration?

8 A Yes. So what I meant by that was, other than
9 reviewing what I've recited regarding Famulok in my
10 declaration, the last time I picked up this document and
11 reviewed it was in 2024.

12 Q Okay. Understood.

13 Is it your opinion that Famulok is a research
14 paper?

15 A Yes. I would say that my opinion is that this
16 is a research paper.

17 Q Does Famulok report the author's original
18 research?

19 A I would have to review it again to recall the
20 answer to that question. So I will take a look now.

21 Scanning this and then also to my
22 recollection, the article by Famulok refers to the
23 article by Fredriksson, which is citation No. 1, as well
24 as other articles. So I would say it's a combination of
25 reviewing some of the Fredriksson work as well as

1 discussion by the author themselves, Michael Famulok.

2 Q So does Famulok report Famulok's original
3 research?

4 A I would have to look at it even more carefully
5 to see if there is any of Famulok's research involved.
6 I would have to look at it more closely to answer that
7 truthfully.

8 Q And you pointed me to this reference on the
9 front page referring to the Fredriksson, et al.?

10 A I actually pointed you to reference No. 1 on
11 the back page. Reference 1, Fredriksson.

12 Q Sure. I was looking on the front page, the
13 second column where they say -- Famulok says "In this
14 issue, Fredriksson, et al. describe a new method,
15 proximity ligation"?

16 A Yes.

17 Q And that's reference No. 1?

18 A So yes. One and the same. Yes, we do
19 understand the same thing.

20 Q Okay. So let's see. So Fredriksson is
21 reference No. 1.

22 Are you familiar with this Fredriksson
23 reference?

24 A I would have to look at this exact address, as
25 it were, of the reference to see if this is one that I'm

1 familiar with or not. I certainly recognize the name.
2 I would have to look at that a little more deeply.

3 Q In your declaration, if you could look at
4 paragraph 32. There's a citation there to Exhibit 1020,
5 Fredriksson 2002.

6 Do you see that?

7 A Let's see. Page 32 you said?

8 Q Paragraph 32. Page 12.

9 A Yes. So, again, just to make sure this is the
10 correct Fredriksson article, I know we had cited
11 Fredriksson, and I know the year is the same, but I
12 would have to look at all the details. I believe that's
13 correct, but I can't verify that.

14 Q All right. Let me give you a copy of
15 Exhibit 1020.

16 A Okay.

17 Q Do you recognize this Exhibit 1020?

18 A Yes.

19 Q Is this the same Fredriksson article that you
20 cited in your declaration as Exhibit 1020, paragraph 32?

21 A Yes.

22 Q And is it your understanding that this is the
23 same Fredriksson 2002 that's referenced in the Famulok
24 paper?

25 A Yes.

1 Q In your opinion, Dr. Nelson, what does Famulok
2 disclose that is not disclosed in Fredriksson?

3 A I would have to -- I have not done that
4 exercise. I'd have to read both articles again word for
5 word to be able to answer that. I cannot say that
6 without doing the proper research.

7 Q Can you -- sitting here today, can you tell me
8 what's different between disclosures of Famulok and
9 Fredriksson?

10 A I would need to do a further analysis to be
11 able to tell you what's different between them.

12 Q Are there technical aspects disclosed in
13 Famulok that are not disclosed in Fredriksson?

14 A I would have to do a further analysis to be
15 able to answer that question.

16 Q Are there experiments disclosed in Famulok
17 that are not disclosed in Fredriksson?

18 A I would have to do a further analysis to be
19 able to answer that question.

20 Q Are you aware if there is any data disclosed
21 in Famulok that's not disclosed in Fredriksson?

22 A I would have to do a further analysis to be
23 able to answer that question.

24 Q Did you review Fredriksson in preparing your
25 declaration?

1 A I did.

2 Q Did you review all of Fredriksson in preparing
3 your declaration?

4 A I did not read every single word, but I
5 reviewed it in enough detail to support my opinion in my
6 declaration.

7 Q But sitting here today, you're not able to
8 tell me what the differences are in the disclosures
9 between Famulok and Fredriksson; is that right?

10 A I would have to do a further analysis to be
11 able to tell you the differences.

12 Q Do you still have the '848 patent available
13 there?

14 A I do.

15 Q In the '848 patent on the front page, the
16 left-hand column, there's a section entitled "References
17 Cited" marked as section 56.

18 Do you see that?

19 A Yes.

20 Q Do you have an understanding what this means
21 on a patent where it says "References Cited" and it
22 provides a list of references?

23 A These are references that -- my understanding
24 is that these are references that the patent applicant
25 included or cited in the patent application.

1 Q So it's your understanding this is essentially
2 like a bibliography of references that are cited in the
3 patent application?

4 A Again, my understanding would have to be
5 refreshed and reviewed. I believe that is -- I believe
6 that's my understanding as well, that these are
7 references cited in the patent application.

8 Q And is it -- do you understand that -- strike
9 that.

10 Is it your understanding that the patent
11 examiner considered these references that are listed
12 under the "References Cited" during examination of the
13 application that led to the '848 patent?

14 A That is outside of my expertise, and I do not
15 know whether that examiner, if they examined all of
16 these or not.

17 Q On the left-hand column under this "References
18 Cited" list, there's a subheader titled "Other
19 Publications."

20 Do you see that?

21 A Yes, I do.

22 Q And at the bottom there, there's a reference
23 to Fredriksson, a Fredriksson 2002 paper.

24 Do you see that?

25 A I do see that.

1 Q And is that the same Fredriksson 2002 that we
2 were looking at as Exhibit 1020?

3 A That appears to be correct.

4 Q And that's the same Fredriksson 2002 that's
5 discussed in the commentary of Famulok, correct?

6 A That is cited as reference 1. To that degree,
7 yes.

8 Q Okay. On the Fredriksson paper, Exhibit 1020,
9 do you understand that Fredriksson refers to something
10 called a "connector oligonucleotide." Strike that.

11 I'll direct your attention to -- if you look
12 on the front page in the right-hand column, there's a
13 "Results" header.

14 Do you see that?

15 A Yes, I do.

16 Q And the second paragraph there, there's a
17 sentence that begins with -- referring to the connector
18 oligonucleotide.

19 Do you see that?

20 A Yes.

21 Q Do you have an understanding of what the
22 connector oligonucleotide is in Fredriksson?

23 A Yes, I do.

24 Q What is the connector oligonucleotide in
25 Fredriksson?

1 A An answer would come from my reading of the
2 figure legend from Figure 1 on page 474 of Fredriksson,
3 picking it up in the middle: Comma, "sequence
4 extensions to be joined by ligation upon hybridization
5 to a common connector oligonucleotide are shown in blue
6 (A1) and red (A2)."

7 Q If you look at Famulok, Figure 1, there's also
8 a reference to "connector oligonucleotide" there; is
9 that correct?

10 A Yes.

11 Q Is that the same molecule you refer to as a
12 "splint oligonucleotide" in your declaration?

13 A Could you refer to me in my declaration where
14 I use "splint" so I can answer that question correctly?

15 Q Your declaration, paragraph 176, you state
16 "Famulok teaches associating the oligonucleotide
17 extensions of the aptamers by hybridizing the end of the
18 two oligonucleotides to a third 'connector' or 'splint
19 'oligonucleotide and then ligating the ends together
20 using DNA ligase."

21 Do you see that?

22 A I do see that.

23 Q So, having refreshed your recollection, is the
24 connector oligonucleotide you're referring to -- strike
25 that.

1 Having refreshed your recollection, is the
2 connector oligonucleotide disclosed in Famulok's
3 Figure 1 what you're referring to as a splint
4 oligonucleotide here?

5 A What I'm referring to is the general concept
6 of using an oligonucleotide, as shown in Famulok, which
7 they call a "connector" and referring to that as the
8 connector as generally described in Famulok, an
9 oligonucleotide shown as configured there, or another
10 term would be "splint oligonucleotide" and then ligating
11 the ends together. So it's just two general terms for
12 this concept that was disclosed in Famulok in this case.

13 Q So is it your opinion that the term "split
14 oligonucleotide" and "connector oligonucleotide" are
15 synonymous in this context?

16 A It depends.

17 In this context, they are similar. Whether
18 they would have the exact same meanings for different
19 ones, it's hard to say. It depends on the exact
20 context. But here in my paragraph 176, I'm giving two
21 names for this concept of an oligonucleotide.

22 Q And is that concept of a connector or a splint
23 oligonucleotide the same concept that's disclosed in
24 Fredriksson where you referred to Figure 1, for example?

25 A Well, I would say, in general terms, not

1 speaking to exactly my opinion in the declaration as it
2 applies to this case, but the concept shown in Figure 1
3 of what's called the "connector oligonucleotide" there
4 is a similar concept of what appears in Figure 1 of
5 Famulok, in general terms.

6 Q And would that have been understood by a POSA
7 in 2005?

8 A What I state is that a POSA would have
9 understood the concept of using a connector
10 oligonucleotide, or whatever a preferred vernacular
11 would be, as disclosed in Famulok at the time of the
12 invention.

13 Q But do you agree that Famulok's disclosure is
14 in reference to Fredriksson's connector oligonucleotide?

15 A I believe what we've agreed to is that Famulok
16 cites Fredriksson. And I'd have to do a -- in that
17 Figure 1 in Fredriksson and Figure 1 in Famulok show a
18 similar connector oligonucleotide.

19 But after that, to answer the question, I'd
20 have to do a more -- a deeper analysis to understand
21 what a POSA might believe at that point.

22 Q If you look in Famulok on the front page on
23 the right-hand column, the first full paragraph begins
24 "Fredriksson, et al. do not use."

25 Do you see that sentence there?

1 A I do.

2 Q Is it your understanding that this paragraph
3 is discussing the methods of Fredriksson?

4 A Well, since you asked about the paragraph, I
5 will need to read the paragraph to refresh my memory.
6 And I'll do that now.

7 From my reading at this time of this
8 paragraph, it appears as though Famulok is referencing
9 the Fredriksson article in this case -- Fredriksson
10 et al. in this case.

11 Q All right. And about halfway down the same
12 disclosure here in Famulok, Famulok states -- there's a
13 sentence that says "Binding of the aptamer pair."

14 Do you see that sentence there?

15 A I do.

16 Q Famulok states "Binding of aptamer pair brings
17 the ends of the oligonucleotide extensions into close
18 spatial proximity (Figure 1A) so that a 'splint'
19 oligonucleotide can hybridize to both ends, which are
20 subsequently ligated together by T4 DNA ligase."

21 Do you see that sentence I just read there?

22 A Yes, I do.

23 Q And is it fair to say that this description in
24 Famulok is referring to Fredriksson's method of using a
25 splint oligo or a connector oligo?

1 A Well, since we just spoke about how Famulok
2 appears to be studying the Fredriksson reference in this
3 paragraph, it appears as though they are referencing
4 that method of an oligo and ligation in Fredriksson.

5 Q All right. Let's go back to your declaration
6 and the same discussion of claim 16. If I could direct
7 your attention to paragraph 177.

8 A Okay.

9 Q We looked at this language earlier about the
10 errors produced by a polymerization step.

11 Do you recall that discussion earlier today?

12 A I do.

13 Q So is it your opinion that a POSA would have
14 been motivated to combine the teachings of Kanan, Neri
15 and Famulok to avoid a polymerization step in the
16 workflow?

17 A My opinion, as best stated here -- I'll recite
18 my exact opinion, which is starting at the beginning of
19 paragraph 177: "A POSA would have understood that it
20 would have been obvious to use the method of ligation of
21 the oligonucleotides as taught in Famulok to ligate
22 together the ends of the DNA oligonucleotides of the
23 paired substrates in Kanan. A POSA would have been
24 motivated to reduce false negatives produced by errors
25 in the polymerization step."

1 So that's my opinion that's what would have
2 been obvious to a POSA.

3 Q So are you saying that the motivation is to
4 avoid the polymerization step and replace it with a
5 ligation, as taught in Famulok?

6 A A POSA would have known that using ligation
7 instead of polymerization, as the last complete sentence
8 on page 91 states, as an alternative instead of
9 polymerization. To that degree, that is correct.

10 Q Okay. And on the next paragraph, 178 of your
11 declaration, you refer to Neri's Figure 7.

12 Do you see that?

13 A Yes.

14 Q Do you still have the Neri reference
15 available?

16 A I do. Okay. I've got it.

17 Q So is it your opinion that a POSA, combining
18 the teachings of Kanan, Neri, and Famulok, would have
19 used Neri's embodiment shown in Figure 7?

20 A My view -- my opinion is, seeing Figure 7 of
21 Neri along with the other things we've been discussing
22 that have been -- would have been obvious to a POSA at
23 the time of the invention, that would have increased
24 their expectation of success because that design would
25 avail itself to using the ligation method as generally

1 described in Famulok. Whether they used that exact
2 design or not would be up to the POSA and it would
3 depend on their particular application.

4 Q That's the figure you referred to in your
5 discussion in paragraph 178, right?

6 A It is.

7 Q And according to your testimony, you point to
8 that figure as an example of an interactor that contains
9 an overhang region; is that right?

10 A That is -- let's see. Let me see the exact.
11 Yes, an overhang region is disclosed in paragraph 178,
12 that is correct.

13 Q And according to your testimony here, that
14 overhang region in Neri's Figure 7 can be ligated
15 together using the method in Famulok of the splint
16 oligonucleotide; is that right?

17 A That is what I state here, yes.

18 Q So, looking at Neri's Figure 7, do you have an
19 understanding of the workflow that's depicted here in
20 Neri's Figure 7?

21 A I'll review it again quickly.

22 Yes, I do.

23 Q All right. And so how does this workflow
24 begin? What is your understanding about how this
25 workflow begins? In other words, the beginning of this

1 workflow starts with this structure of A and B from the
2 A and B library members.

3 Do you see that on the left?

4 A Yes, I do.

5 Q How does that structure come to be in this
6 workflow?

7 A Well, let's go back and read through the
8 disclosure.

9 Q I'll ask you a different question. I'll
10 withdraw that one.

11 A Okay.

12 Q Is it your understanding that the molecules P
13 and Q in this Figure 7 interact with each other?

14 A That is a different subject than the ligation,
15 but we can go back and discuss this further. But I'd
16 have to go back to the disclosure to read the words out
17 of the Neri disclosure.

18 Q Do you have an understanding how library
19 member A and library member B are held together here in
20 Figure 7?

21 A When you say -- could you elaborate on what
22 you mean by "held together"?

23 Q Are -- does this figure depict library
24 member A and library member B bound together?

25 A Oh, I see, the library member A and B.

1 This figure depicts hybridization of those two
2 black lines.

3 Q Is the hybridization -- that's depicted by the
4 horizontal lines which are going down; is that right?
5 Looks like they're dotted dashed lines connecting the
6 two; is that right?

7 A Again, to answer this question appropriately
8 and truthfully, I would want to go back and see the
9 exact figure description to give you an exact answer to
10 that. I can do that if you like.

11 Q Sure. Let's take a look at paragraph 32 of
12 Neri.

13 A Uh-huh.

14 Q It's on page 18.

15 A Yep.

16 Q Do you see that there?

17 A Yes, I do.

18 Q It begins "A PCR-based method for ESACHEL
19 deconvolution. Sublibraries A and B form a
20 heteroduplex."

21 Do you see that part there?

22 A I do.

23 Q So how are -- what does Neri mean when Neri
24 says "sublibraries A and B form a heteroduplex"?

25 A Again, it goes back to this -- the entire

1 disclosure of Neri, which we've discussed already.

2 I need to go back further to give you the
3 details of that. I'm going to go to my declaration and
4 pull up the discussion in there. I think that would be
5 the wisest way to proceed.

6 Okay. So, if you look at paragraph 75 of my
7 declaration, the method of Neri is generally described.
8 And it says "Neri teaches 'self-assembling libraries of
9 organic molecules (typically forming dimers, trimers or
10 tetramers), in which the organic molecules are linked to
11 an oligonucleotide which mediates the self-assembly of
12 the library and/or provides a code associated to each
13 binding moiety.'"

14 And further, in that the third sentence, "Neri
15 relates to 'chemical compounds, comprising an
16 oligonucleotide moiety linked to an oligomerization
17 domain mediating homo or hetero dimerization,
18 trimerization at the tetramerization."

19 So it's with this method, taking individual
20 libraries, and those mediate, in this case,
21 dimerization. And it's hetero. So a heteroduplex is
22 two strands of, in this case, A and B oligonucleotides.

23 Q And those two strands A and B oligonucleotides
24 in Figure 7 are hybridized together here? Is that
25 what's depicted in the figure?

1 A That is to the best of my recollection at this
2 time, yes.

3 Q And is it your understanding that's what you
4 refer to as the self-assembly sequence of Neri?

5 A There's more to it than that. There are other
6 segments of that oligonucleotide. Figure 7, I'd have to
7 deconvolute that more carefully to see what that black
8 line comprises, if it's the self-assembly sequence or
9 the self-assembly sequence and more.

10 Q I see. But you agree that the black line --
11 the heavy black line in Figure 7, at minimum, is
12 depicting hybridization of the two strands?

13 A To the best of my ability now, without more
14 fully looking at it, that is the best understanding I
15 have at this moment.

16 Q Is it fair to say that a POSA would have that
17 understanding as well, a POSA reading Neri?

18 A That is correct. That is my opinion, that
19 they would have that understanding as well.

20 Q So, looking back, going through the steps in
21 Figure 7 in Neri, after forming this heteroduplex of A
22 and B, what happens next?

23 A Are you referring back to paragraph 32 now?

24 Q I'm just looking at Figure 7.

25 A Figure 7. Okay.

1 According to paragraph 32, which is the figure
2 legend for Figure 7, it says "pairs of primers allow the
3 PCR amplification of the two strands, yielding PCR
4 products whose sequence can be identified using standard
5 methods." So that's what's depicted in Figure 7.

6 Q You referred to the -- you said "pairs of
7 primers allow the PCR amplification of the two strands."
8 That's depicted there where it says "2 PCRs" -- is that
9 right? -- in the figure?

10 A That is the PCRs depicted in the figure above
11 where it says "2 PCRs." And I'd have to look further
12 whether the "2 PCRs" mean two aliquots are the same PCR
13 or if they're just different PCR reactions but the same
14 components. I don't recall that level of detail.

15 Q What happens after this PCR reaction here in
16 the work flow Figure 7?

17 A Well, without knowing the exact details, they
18 go on to use -- as they describe in paragraph 32, they
19 go on to sequencing using standard methods.

20 So my assumption is they're depicting very
21 generally a method they use to perform the sequencing
22 analysis.

23 Q So is it your opinion that a POSA combining
24 Kanan, Neri and Famulok would have further modified this
25 embodiment in Neri, Figure 7, to ligate the ends A and B

1 with the -- using a splint oligonucleotide technique of
2 Famulok?

3 A Hold on momentarily, please.

4 I believe, looking at Figure 7, this left
5 diagram, the one at the top left with the "p" and "q" at
6 the top, that a POSA would have been motivated to
7 combine the teachings of Kanan and Neri with the
8 teachings of Famulok because the splint oligonucleotide
9 discussed in Famulok would create a DNA strand that does
10 not rely on polymerization to encode the anti-codon of
11 the shorter library member, and so forth.

12 And continuing in 178, paragraph 178, "A POSA
13 would have a reasonable expectation of success in
14 combining the Kanan, Neri and Famulok because Neri
15 teaches how to design interactors that contain an
16 overhang region."

17 So combining those so you can make an
18 overhang, it would have been obvious to a POSA to
19 combine Kanan, Neri and Famulok to ligate the ends of
20 such a structure or one to their -- that fit their
21 experimental outcome better.

22 Q So when you're referring to interactors that
23 contain an overhang region, you're referring to that
24 structure in Figure 7 at the top of that; is that right?

25 A I'm referring to -- I didn't say "interactor."

1 I just said that overhanging regions of the
2 ends that are shown in Figure 7. That's what I'm
3 referring to.

4 Q You used the term "interactors" in your
5 declaration?

6 A Yeah, you're right. Okay. Thank you. I
7 correct myself.

8 So, just reading it, yeah, a reasonable
9 expectation of success combining Kanan, Neri, and
10 Famulok. Because Neri teaches how to design interactors
11 that contain an overhang region.

12 So that's what -- that is correct. That is my
13 view, that they show that type of structure in Figure 7.

14 Q So just one more time so it's clear.

15 When you refer to interactors that contain an
16 overhang region in paragraph 178, you're referring to
17 this example in Figure 7, the structure that's shown in
18 Figure 7?

19 A That's what's cited there in my opinion. So
20 see that as an example, that is correct.

21 Q Okay.

22 A They show that.

23 Q Okay. And then -- how does the -- strike
24 that.

25 Let's go through the steps here with the

1 ligation modification. So for the ligation
2 modification, is it fair to say that the first step is
3 to form the interactors that contain an overhang region
4 that we see here in Figure 7?

5 A All I'm stating in this section, which is
6 dependent claim 16, is focused on the ligation step.
7 All the other things have been covered -- all the other
8 aspects have been covered in the declaration before
9 that.

10 All I'm saying is that a POSA would have
11 understood from Famulok and combining what I've already
12 discussed about Neri and Kanan that they could ligate
13 the ends of a structure, for example, shown in Figure 7,
14 using a method such as disclosed by Famulok to ligate
15 those ends. That's the extent of what I'm saying in
16 this section.

17 Q Understood.

18 And after this ligation event occurs to ligate
19 the ends of this molecule, is it your opinion that the
20 rest of the workflow follows that of taught in Kanan?

21 A Of what now? The rest of the workflow
22 follows?

23 Q Is it your opinion that the rest of the
24 workflow follows what's taught in Kanan?

25 A Gotcha.

1 Not necessarily. It depends on what a POSA
2 would be -- how they would be -- what the goals of their
3 experiment were and what their objective was at that
4 point. So that, again, would be within the skill set of
5 the POSA to decide exactly how to finish that
6 experiment.

7 Q Does the structure for this ligation
8 embodiment still include a linker with a biotin and a
9 disulfide bond, as taught in Kanan?

10 A Now we're going to combining -- this is Neri.
11 So the structure isn't Kanan. So we'd have to go back
12 to that diagram.

13 I would like to look at my declaration again
14 to look for a figure that I have in mind.

15 So, in one embodiment, if there were
16 single-stranded tails, as depicted in Neri, and combined
17 with Kanan, in that one working example, a POSA could
18 envision using the biotin -- the sulfide on the biotin
19 connected to the substrate. It's generally depicted in
20 the figure above paragraph 120 of my declaration.

21 Q Sorry. Which paragraph are you referring to?

22 A 120 of my declaration.

23 Q So is it your opinion that in this
24 combination -- because the figure in paragraph 120 or
25 just above paragraph 120, you include the d-spacer

1 aspect from Neri's Figure 5, correct?

2 A Correct, in this diagram.

3 Q So is it your opinion that in the ligation
4 embodiment that you're discussing for claim 16, that
5 that embodiment would also include the d-spacer element?

6 A That would be one configuration that a POSA
7 could envision and make, depending on the needs of their
8 experiment and the goals thereof.

9 Q And you said that that would also include, as
10 you depict here in the figure, the linker for the B
11 library containing biotin and disulfide bond, correct?

12 A To be clear, what I said was that was one
13 possible configuration they could use. To that degree,
14 that is correct.

15 Q But you don't refer to any other
16 configurations in your discussion of claim 16, do you?

17 A I do not. As far as I -- let's see. You know
18 what? I'm going to hold off on that and strike that.

19 Let me go back and read 16, and I'll make sure
20 that I'm correct about that.

21 What I state is I give that figure as an
22 example of how ligation can work, not stating that
23 that's the method -- exact structure that has to be
24 used. Just showing that a POSA would have combined this
25 art with a reasonable expectation of success, for

1 example, using this structure. It doesn't say that that
2 is a required structure to use.

3 Q But the rationale for pointing to the
4 structure is because of the overhang of A and B; is that
5 right?

6 A The motivation of using this as an example is
7 through other -- yes, because of that overhang, to show
8 that it's -- definitely has a reasonable expectation of
9 success in combining Kanan, Neri and Famulok with the
10 ligation method disclosed in Famulok.

11 Q And one embodiment that you're telling me
12 today that a POSA would have envisioned is using this
13 overhang design in Figure 7 but also including the
14 d-spacer element of Figure 5 from Neri, as you've
15 depicted in your declaration just above
16 paragraph 120; is that right?

17 A If the POSA were combining Kanan, Neri and
18 Famulok, that is my suggestion of one possible
19 configuration that they might select to use the ligation
20 method.

21 Q Okay. And looking at your figure here just
22 above paragraph 120 of your declaration, for the
23 ligation embodiment, what portion of the
24 oligonucleotides are going to be ligated using the
25 splint oligo method of Famulok?

1 A In this hypothetical example and using
2 combining it with Neri showing two overhangs, there
3 would be an additional segment of the A molecule that's
4 already got a small overhang. It might be extended. It
5 might not be. And that those two ends could be ligated
6 using a connector or a split to the oligonucleotide as
7 one potential embodiment.

8 Q And in that embodiment, the oligonucleotides
9 are still connected by the association elements that you
10 have here in purple; is that right?

11 A In that embodiment, that would be a feature
12 that could indeed be included.

13 Q Well, it appears like it is included in
14 this --

15 A Yes. In this exemplary embodiment, it would
16 be included.

17 Q And same with Figure 7, the structure of the
18 overhang, there's an assembly sequence there connecting
19 the two oligos for ligation?

20 A Well, we already covered that. That, you
21 know, would comprise, as disclosed by Neri,
22 self-association elements. Those black lines would --
23 they would comprise that region.

24 Q In your declaration, if you could please turn
25 to page 118. This section of your declaration you're

1 discussing the Baez and Landegren combination; is that
2 right?

3 A When you say "this section," do you mean this
4 paragraph?

5 Q Yeah. This paragraph. Yeah, we'll start with
6 that. So paragraph 234.

7 A 234. Okay.

8 Q You begin -- you're discussing the claim 1
9 step (a) in the context of the Baez and Landegren
10 combination; is that right?

11 A Well, actually, it cites only Baez right
12 here -- Baez -- in paragraph 234.

13 Q I stand corrected. Let's look at
14 paragraph 237. This paragraph, you address the
15 Landegren reference, correct?

16 A Yes. Landegren is in this paragraph.

17 Q And in the second sentence of this paragraph,
18 you state "Landegren teaches that the nucleic acid
19 coupled to the proximity probe (i.e. conjugate) has a
20 sequence identification element or a 'tag.'"

21 Did I read that statement correctly?

22 A Yes, you did.

23 Q And after that statement, you cite Landegren
24 Exhibit 1004, page 11.

25 Do you see that?

1 A Yes.

2 Q Do you still have the Landegren reference in
3 your stack there?

4 A I do. Let me find it.

5 Q Let's take a look at Landegren. It's
6 Exhibit 1004.

7 A Okay. I have it.

8 Q And in your declaration, you cited page 11.
9 So let's turn to page 11 in Landegren.

10 A Okay.

11 Q All right. What disclosure on page 11 are you
12 relying on when you refer to Landegren's tag in your
13 declaration, paragraph 237?

14 A Yes. Just for 100 percent clarity, is this
15 Landegren? I don't have that list of references. I'm
16 pretty sure of this, but this is WO 01/61037.

17 Q Correct.

18 A Okay.

19 Q Exhibit 1004, the same document you cite in
20 paragraph 237 of your declaration.

21 A Yes. I just was clarifying, making sure.

22 Okay. I refer to the Figure 14 legend where
23 it refers to sequence identification tags. And
24 Figure 14 is shown on page 6 of the application or the
25 figure -- the drawings of the patent application.

1 Q And the sequence identification tags,
2 that's -- the tags are "ID:A" and "ID:B" -- is that
3 right? -- in Figure 14?

4 A Yes. That is correct.

5 Q Okay. And then in your declaration,
6 paragraph 238, you discuss -- the first sentence you
7 discuss -- or you mention the sequence identification
8 tags of Landegren.

9 Do you see that?

10 A Yes.

11 Q So is it your opinion that the disclosure of
12 tags in Landegren in reference to Figure 14 of Landegren
13 meets the identification sequence element of claim 1,
14 step (a), of the '848 patent?

15 A Well, I haven't done the analysis of my
16 opinion of mapping these parameters to the claims. This
17 is based on my Grounds 3 and 4, as stated earlier,
18 that -- so paragraph 210 of my declaration. This is
19 based on the following: "For my analysis in this
20 declaration related to Grounds 3 and 4, I have relied on
21 the Patent Owner's positions provided in its complaint,
22 infringement chart, and opposition to Alamar's motion to
23 dismiss and apply those positions to how a POSA would
24 have understood the claims as if Patent Owner's
25 positions were correct at the time of the application.

1 For clarity, my analysis for Grounds 3 and 4 do not
2 reflect my opinion on what a POA's ordinary
3 understanding of the scope of the '848 Patent but
4 instead applies the scope used by the Patent Owner in
5 the co-pending district court litigation against
6 Petitioner."

7 So that's a different exercise for me to
8 comment on how I would map these to the '848 claims.

9 This is based on what a POA would have
10 understood based on the paragraph that I just read.

11 Q Are you relying on Landegren's disclosure of
12 tags in Figure 14, or the discussion of Figure 14 on
13 page 11 of Landegren, to meet the sequence
14 identification element -- excuse me, identification
15 sequence element of claim 1, step (a)?

16 A I am simply saying that applying the Patent
17 Owner's position, it would have been obvious to a POA
18 to use the sequence element tags of Landegren. That's
19 all I'm saying.

20 Q But you don't cite anything from Baez
21 regarding identification of sequence elements, do you?
22 You're referring to Landegren here, correct?

23 A What it says, yeah. It says to add the
24 sequence identification tags of Landegren to the nucleic
25 acid labels of Baez.

1 Q And those sequence identification tags in
2 Landegren are the ones you referred to on page 11 in
3 your reference to Landegren's Figure 14, correct?

4 A That's an example from this literature that
5 was available to a POSA at the time of the application.

6 Q Okay. Thanks.

7 All right. On page -- in your declaration, if
8 you could turn to page 122, where you continue to
9 discuss the claim elements in the context of Baez and
10 Landegren, there's a header there or subheader where you
11 address claim 1 step (b).

12 Do you see that there?

13 A On page 122?

14 Q Page 122 of your declaration.

15 A Unless I misheard you, which is possible, I
16 don't see it. A (b)?

17 Q Well, it's -- there's a "C" in parentheses?

18 A Oh, step (b).

19 Q But then it talks about step (b).

20 A Got it. Yes.

21 Q All right. So this header is where you
22 discuss claim 1, step (b) in the context of the Baez and
23 Landegren combination; is that correct?

24 A Yes.

25 Q Okay. And in your header there, you have the

1 language from claim 1(b) and it says that -- it recites
2 that "the associated oligonucleotides" -- this is
3 towards the end -- "the associated oligonucleotides
4 comprise at least two identification elements derived
5 from the at least two nucleic acid moieties."

6 Do you see that?

7 A I do see that.

8 Q And in this discussion, further down,
9 paragraph 244 -- this is the same section -- you state
10 "Further, as shown above (paragraphs 237 and 238), the
11 nucleic acid labels comprise a unique identification
12 sequence."

13 Do you see that there?

14 A I do see that.

15 Q So here, are you referring to the same tags
16 from Landegren that we were discussing earlier when we
17 were looking at paragraph 237 and 238?

18 A I'm going to read paragraph 237 and 238 again
19 to confirm.

20 I'll read to you, as an answer to the
21 question, the last sentence -- the last two sentences in
22 paragraph 238. "The strategies employed in Landegren
23 such as use of unique identifier sequences allow for the
24 selection of only true positives. Thus, a POSA would
25 have been motivated to combine Baez with Landegren as a

1 way to reduce background signal."

2 So based on the Patent Owner's position, a
3 POSA would have been motivated to combine them using the
4 strategy of Landegren with unique identifier sequences
5 with the teaching in Baez.

6 Q That didn't quite answer my question.

7 My question is, on your statement in
8 paragraph 244, when you state "The nucleic acid labels
9 comprise a unique identification sequence," are you
10 referring to the tags disclosed in Landegren on page 11?

11 A Right. So I believe I answered -- did address
12 the question.

13 My answer, saying it in a different way, is
14 that your literal words, "the tags," of Landegren --
15 doesn't have to be the literal tags, as shown in
16 Figure 14 of Landegren -- is the strategies of using a
17 unique identification sequence that could be combined
18 with Baez that I referred to in paragraph 244.

19 Q Okay. I'm just trying to understand if
20 there's any other disclosures in Landegren I should be
21 looking at for disclosures of these unique
22 identification sequence tags.

23 A Understood. As far as --

24 Q Because you don't really -- I'm sorry.

25 A Go ahead.

1 Q Because you don't cite Landegren here in
2 paragraph 244, so I just want to understand what you're
3 referring to in paragraph 244.

4 A I see.

5 Q If it's the same disclosure in Landegren we've
6 already looked at or if there is something else.

7 A Now I understand more fully.

8 So, as far as this answer refers to
9 paragraphs 237 and 238, that is what it's referring to,
10 which also does cite the strategies in Landegren.

11 Q Okay.

12 MR. PLATT: David, we've been going about an
13 hour and 15 minutes or so. Good spot or?

14 MR. HOLMAN: Yes. We can take a break now.

15 MR. PLATT: Okay.

16 (Recess taken from 2:32 to 2:58 p.m.)

17 BY MR. HOLMAN:

18 Q Okay. Dr. Nelson, did you speak to anyone
19 during the break about the substance of your testimony
20 today?

21 A I did not.

22 Q Before the break, we were looking at your
23 declaration in your discussion about the Landegren and
24 Baez combination, and one of the paragraphs we looked at
25 was paragraph 244 of your declaration. If we could turn

1 back to that paragraph, please.

2 A Sure.

3 Q In paragraph 244, the second sentence, you
4 state "Thus, a POSA would have understood that the
5 nucleic acid labels within the ASA would contain the two
6 identification sequences, one from each label."

7 Do you see that --

8 A I do.

9 Q -- statement?

10 And again, are you referring to Landegren's
11 sequence tags when you refer to the identification
12 sequences in each label?

13 A Well, as I referred before, I'm relying on the
14 teachings from Landegren to combine with Baez to produce
15 specific examples. But that's the teaching that I'm
16 applying to this, the Landegren.

17 Q Landegren's teaching of the tags?

18 A Correct.

19 Q Okay. Great.

20 All right. If you could, in your declaration
21 turn a couple pages to paragraph or page 127.

22 And at the top of the page, you have a header.
23 The header is labeled (e), but it refers to step (d).

24 Do you see that?

25 A Yes, I do.

1 Q All right. And this is in reference to
2 claim 1, step (d) the selecting step; is that correct?

3 A Yes.

4 Q And in this section, you're discussing the
5 '848 patent's claim 1 step (d) in the context of the
6 Baez and Landegren combination; is that right?

7 A I would like to go back one, to the previous
8 question, where it's pointing back to claim 1. Step (d)
9 is -- I answered too quickly. I'm referring to
10 selecting all cis-reactive cells exhibiting the
11 detectable trace. That's what this section refers to.
12 So that's a minor clarification, but that's the
13 clarification.

14 And now, if you could repeat the last
15 question, I'd appreciate it.

16 Q Sure. Thanks for clarifying --

17 A Sure.

18 Q -- your previous answer.

19 Just generally, this section of your
20 declaration begins -- on this page 127, you're
21 addressing claim 1, step (d) in the context of the Baez
22 and Landegren combination; is that correct?

23 A I would have to look to make sure in this
24 section what I've relied on. And so far, refreshing my
25 memory, I only see reference to Baez and not the

1 combination of Baez and Landegren.

2 Q So this section only discusses Baez; is that
3 what you're saying?

4 A That is what I'm saying.

5 Q Okay. In paragraph 252, same page, you state
6 that Baez -- first sentence here -- "Baez discloses that
7 the ASAs can be selected using affinity purification."
8 And that "This involves detecting the ASA 'through the
9 linker oligonucleotide itself.'"

10 Do you see that statement there?

11 A I do see that.

12 Q And then you go on and you say "In one
13 example, the linker oligonucleotide is 'engineered to
14 contain a label such as biotin'"; is that right?

15 Did I read that right?

16 A Yes, you did read that right.

17 Q Okay.

18 A Just to clarify, you omitted the quotations,
19 because that's a direct -- the "engineered to contain a
20 label such as biotin" is a direct quotation from Baez.

21 Q Okay. Right. That's from the quote from Baez
22 at column 17, lines 53 to 54; is that right?

23 A Correct.

24 Q And then the last sentence here on this page,
25 you state that "Once the linker is bound in the ASA, the

1 incorporation of biotinylated bases provides means of
2 isolating the ASA from the solution onto an immobilized
3 streptavidin or avidin"; is that correct?

4 A I see that sentence, yes.

5 Q And would a POSA in 2005 understand what
6 mobilized streptavidin or avidin is?

7 A It is my opinion that they would have
8 understood that.

9 Q What would -- what would a POSA's
10 understanding of an immobilized streptavidin or avidin
11 be?

12 A My opinion is the understanding at that time
13 would be either streptavidin or avidin is somehow
14 affixed to a solid support.

15 Q Is that -- when you say "affixed to a solid
16 support," can you clarify what you mean by a solid
17 support?

18 A A solid support is a physical structure other
19 than having streptavidin or avidin in solution. For
20 example, a microsphere is one example.

21 Q If something is affixed to a solid support,
22 would that be the same as a solid phase substrate?

23 A I would have to look at the context of solid
24 phase substrate. It would depend completely on context.
25 So I can't say that because I would have to see

1 someplace where that was . . .

2 Q Could that be another way of referring to a
3 solid support, calling it solid phase?

4 A It depends. I would have to see the context.
5 I can't answer that unless I see the context.

6 Q What are some other examples of solid support?
7 You gave an example of microsphere.

8 Are there any other examples of solid support
9 that you can think of?

10 MR. PLATT: Objection to form.

11 THE WITNESS: A solid support in? Could you
12 provide more detail of what context you mean?

13 BY MR. HOLMAN:

14 Q Sure. You mentioned that the understanding of
15 immobilized streptavidin or avidin is that it's somehow
16 affixed to a solid support.

17 A Okay.

18 Q So my question is, what are some examples of
19 solid support that the immobilized streptavidin or
20 avidin would be affixed to?

21 A Well, let's go to Baez and see what they use
22 there, and that would be an example.

23 I don't think we've produced Baez yet. 1003.

24 Q Sitting here today, are you able to provide
25 any examples of a solid support beyond microsphere?

1 A I'd prefer -- I don't want to go beyond the --
2 my declaration. Because my opinions are written here.
3 So I'd just as soon -- use what they use, and that would
4 be the most relevant context.

5 Q You're not able to say any examples of what a
6 solid -- strike that.

7 Sitting here today, are you able to provide me
8 any examples of what a POSA would have understood a
9 solid support to be in the context of immobilized
10 streptavidin or avidin?

11 A Well, I've provided a good example in a
12 microsphere.

13 Q Can you provide any other examples?

14 A I'd prefer to go to the teaching of Baez to
15 see what they suggest.

16 Q Okay. Let's take a look at Baez.

17 All right. We've given you a copy of Baez,
18 Exhibit 1003.

19 Do you recognize that, Dr. Nelson?

20 A I do.

21 Q And I believe in your declaration, you cited
22 Exhibit 1003, Baez, column 17. Let's take a look at
23 that. It's on page 19.

24 A Yes. I see that.

25 Q And if you look in column 17, line 31 -- it's

1 the end of that paragraph -- Baez states "These can be
2 detected directly on the solid-phase support."

3 Do you see that?

4 A I'm looking for it.

5 Could you tell me again exactly where that is?

6 Q Sure. So column 17. Left-hand column.

7 A Yep.

8 Q And if you go down to around line 30 or 31.

9 A Okay.

10 Q The last sentence of that paragraph there,
11 Baez refers to "solid-phase support."

12 A Yes. Okay. I see that.

13 Q And then a little -- few sentences above that,
14 Baez discusses immobilized streptavidin or avidin.

15 A Yes.

16 Q Do you see that there?

17 A Uh-huh.

18 Q So would a POA understand that Baez's
19 disclosure of immobilized streptavidin or avidin here is
20 an assay performed on the solid-phase support?

21 A Well, the way I read this is, when Baez says
22 "These can be detected directly on the solid-phase
23 support," it follows the sentence "The amplified
24 sequences may also contain signal-generating labeled
25 bases, such as fluorescein or digoxigenin."

1 And so it doesn't directly state that the
2 streptavidin immobilized is the same as solid support.
3 But in the reading of Baez, a POSA might understand that
4 a solid phase -- it doesn't say that directly.

5 All it says about solid-phase support is that
6 it's amplified sequences containing signal-generating
7 labeled bases can be detected directly on the
8 solid-phase support. Not completely clear.

9 Q Is it your opinion that Baez is not very
10 clear?

11 A No. The reference to solid-phase support,
12 it's not clear whether that is the same as the
13 immobilized streptavidin or avidin they refer to in the
14 section above, the sentence above.

15 Q Do you agree that Baez's disclosure of
16 immobilized streptavidin or avidin is a disclosure of
17 the streptavidin or avidin being affixed to a solid
18 support?

19 A Well, I would say it's a reasonable assumption
20 that an immobilized streptavidin could be called as
21 affixing to a solid-phase support. It depends on the
22 particular application. But that is feasible.

23 Q Would that have been feasible to a POSA in
24 2005?

25 A Do what now?

1 Q Would that have been feasible to a POSA in
2 2005?

3 A Yes. Immobilized avidin or streptavidin was
4 feasible to a POSA in 2005.

5 Q All right. Can you look through your pile and
6 see if you can find the Kanan supplemental information
7 document. That's Exhibit 1013.

8 A Okay. I have it.

9 Q All right. Let's turn back to page 8 of the
10 supplemental materials.

11 A Okay. I'm there.

12 Q Earlier today we went through the bottom
13 paragraph of this page step by step.

14 Do you remember discussing that earlier today?

15 A Yes, I do.

16 Q Okay. The second sentence in this paragraph
17 begins with "To the eluant."

18 Do you see that?

19 A I do see that.

20 Q All right. And it refers to the -- it says
21 "To the eluant was added" this aqueous solution of --
22 and there's a long chemical name -- "in sodium
23 phosphate, pH 8 to effect disulfide cleavage."

24 Do you know what this long chemical compound
25 or chemical name is?

1 A I would have to study that to determine
2 exactly what compound that is.

3 Q Okay. And it reads -- it says
4 "tris(2-carboxyethyl)phospine hydrocholoride."

5 Did I read that correctly?

6 A Yes.

7 Q And are you able to tell me what
8 tris(2-carboxyethyl)phospine hydrocholoride is?

9 A Not off the top of my head. I would have to
10 research that.

11 Q Do you have an understanding of why this
12 tris(2-carboxyethyl)phospine hydrocholoride in sodium
13 phosphate is able to effect disulfide cleavage?

14 A Again, the mechanism of that particular
15 reagent to effect disulfide cleavage I'd have to
16 research to understand it more thor- -- to understand
17 it.

18 Q Do you know if tris(2-carboxyethyl)phospine
19 hydrocholoride is a reducing agent?

20 A I would have to research that further.

21 Q So do you know if it's a reducing agent?

22 A I don't know off the top of my head, no.

23 Q Sitting here today, do you have any
24 understanding of the purpose of including -- or the
25 purpose of adding a solution of

1 tris(2-carboxyethyl)phospine hydrochloride to the eluant
2 in this step?

3 A Well, they stated it in that sentence. It
4 says "to effect disulfide cleavage."

5 Q And you're not sure how this compound effects
6 disulfide cleavage; is that right?

7 A Other than to effect cleavage, I would have to
8 study the chemical to understand the mechanism.

9 Q Do you know if reducing agents can cleave
10 disulfide bonds?

11 A To the best of my recollection, there have to
12 be specific conditions included. But that is in the
13 realm of possibility that they could do that, yes,
14 reducing agents. But again, that's the best of my
15 recollection. I haven't looked at that for quite some
16 time, the chemistry thereof.

17 Q What are examples of reducing agents that can
18 effect disulfide cleavage?

19 A Again, I haven't considered that issue for a
20 very long time, and I'd really have to do some research
21 on that.

22 Q Sitting here today, you're not able to provide
23 me examples of reducing agents that could effect
24 disulfide cleavage?

25 A Not off the top of my head.

1 Q I'll direct your attention in your declaration
2 to page 5 of your section entitled "Relevant Legal
3 Standards."

4 A Okay.

5 Q This section which spans paragraphs 16 through
6 22 -- in this section, you provide your understanding of
7 the legal standard for obviousness?

8 A Uh-huh.

9 Q Are you familiar with the term "objective
10 indicia of non-obviousness"?

11 A Could you repeat that term, please?

12 Q Objective indicia of non-obviousness.

13 A I must admit, I am not.

14 Q Are you familiar with the term "secondary
15 considerations of non-obviousness"?

16 A Vaguely familiar with it.

17 Q What's your understanding of "secondary
18 considerations of non-obviousness"?

19 A Only from the context of what it sounds like.
20 There's other variables that to be considered in some --
21 something in life, not even necessarily related to this.
22 But that's about as far as I can get. I don't really
23 know what it means in a legal sense in a patent
24 obviousness case.

25 MR. HOLMAN: All right. Let's take a break,

1 go off the record.

2 (Recess taken from 3:22 to 3:31 p.m.)

3 BY MR. HOLMAN:

4 Q Dr. Nelson, during the break, did you have any
5 conversations with anyone about the substance of your
6 testimony today?

7 A I did not.

8 MR. HOLMAN: All right. We have no further
9 questions for you.

10 Subject to any redirect, we'll pass the
11 witness.

12 MR. PLATT: We'll have to take a short break.

13 (Recess taken from 3:32 to 3:51 p.m.)

14

15 EXAMINATION

16 BY MR. PLATT:

17 Q So Dr. Nelson, I have a few follow-up
18 questions for you. And if you could turn to your
19 declaration, Exhibit 1005, and turn to page 62 and let
20 me know when you're there.

21 A Okay. I'm there.

22 Q Now, you recall that Dr. Holman asked you some
23 questions about the figure that's shown here on page 62?

24 A Yes, I do.

25 Q And Dr. Holman asked you to confirm that Kanan

1 did not disclose that figure.

2 Do you recall that?

3 A I do recall that.

4 Q And he also asked you to confirm that Neri did
5 not disclose this figure.

6 Do you recall that?

7 A I do recall that.

8 Q What did you mean when you responded to
9 Dr. Holman's questions about that?

10 MR. HOLMAN: Objection. Form.

11 THE WITNESS: Still answer?

12 MR. PLATT: Yes, you can answer.

13 THE WITNESS: What I meant by that was that
14 these exact representations were not a screenshot pulled
15 from either Kanan or Neri, but they represent what would
16 have been obvious to a POSA in regards to the
17 combination of Kanan and Neri to produce these
18 structures shown here.

19 BY MR. PLATT:

20 Q Is it your opinion that Kanan and Neri
21 disclose what's shown in the figure shown on page 62?

22 A Yes.

23 Q Now, looking at the figure on page 62, what
24 are the small lines there that are shown off the bigger
25 line that shows the DNA strand?

1 A Those represent the bases of the DNA.

2 Q Now, do you see in the pool B illustration at
3 the bottom of the figure in red they're showing a
4 d-spacer.

5 Do you see that?

6 A Yes, I see that.

7 Q Now, you previously testified earlier today
8 that the d-spacer doesn't have any bases; is that
9 correct?

10 A That is correct.

11 Q So are there any corrections to the figure on
12 page 62 that you notice?

13 A Yes. Those have lines -- those small vertical
14 lines representing bases, and those should not be there.

15 Q And which specific vertical lines? Which
16 portion of the pool B diagram are you referring to?

17 A The red d-spacer segment.

18 Q So that should not have small little lines on
19 it?

20 A That is correct.

21 Q If you could turn to page 63.

22 A Okay.

23 Q And can you explain what's shown here on the
24 figure on page 63 relating to the d-spacer.

25 A Yes. That d-spacer is shown, again, as a red

1 line. And in this case, there are no vertical -- small
2 vertical lines, which is the correct rendering.

3 Q Do you notice any other corrections that you
4 would make to the figure shown on page 63?

5 A Yes. Just to the left of the red line, the
6 continuation of the red line, there is a black line, the
7 lower part, and that has no vertical little lines. And
8 those should be there. There should be small vertical
9 lines on that black segment at the bottom next to the
10 red d-spacer.

11 Q And would that be consistent with the figure
12 on page 62 with respect to the black line after the
13 d-spacer?

14 A Yes.

15 MR. HOLMAN: Objection. Form. Foundation.

16 THE WITNESS: Yes. Because you'll see those
17 vertical lines are on that black segment in the figure
18 on page 62.

19 BY MR. PLATT:

20 Q And that would be in between the d-spacer and
21 the coding region for pool B?

22 A Yes. That is correct.

23 Q And if you could turn to page 67.

24 My question for you is, are there any
25 corrections that you would make to the figure shown here

1 on page 67?

2 A Yes. The black line that's the continuation
3 of the red line to the left of it has no vertical lines,
4 and those should be there.

5 Q Okay. Thank you, Dr. Nelson. I have no
6 further questions for you.

7 A You're welcome.

8 MR. HOLMAN: All right. Let's take a break.

9 (Recess taken from 3:57 to 4:08)

10

11 FURTHER EXAMINATION

12 BY MR. HOLMAN:

13 Q During the redirect, you were asked about a
14 figure in your declaration -- a few different figures,
15 but one of them being on page 63 of your declaration.

16 A Okay.

17 Q Could you turn it that figure, please?

18 A Yes.

19 Okay.

20 Q And as you explained during the redirect, you
21 stated that this black region of the DNA strands to the
22 left of the d-spacer should be shown as depicting
23 vertical lines on both strands showing hybridization in
24 that black region; is that correct?

25 A Well, it should show a black line, vertical

1 lines representing bases, but I would have to -- it
2 would depend on a particular user's design whether those
3 two sections were complementary or not. So it wouldn't
4 necessarily represent hybridization. It may or may not.
5 Depends on context.

6 Q So the correction you want to make to the
7 figure is that the strand on the bottom should have
8 vertical lines representing bases?

9 A Correct. Which can be either hybridized or
10 not hybridized, depending on the particular design that
11 one would use.

12 Q What's the design that a POSA would have
13 chosen here as you presented in your declaration?

14 A Well, I would have to research a little bit
15 more to determine if those sections were hybridized or
16 not hybridized. And it depends on the particular
17 application. So I would say, for this figure, the
18 vertical lines would represent bases, and it would --
19 and for this particular figure, it would represent
20 hybridization.

21 Q And if the -- this particular figure
22 represents hybridization, is that hybridization of the
23 same sequences for every combination of pool A and
24 pool B strands?

25 A No. That's why I was saying that, depending

1 on what the user wanted those segments to be, they could
2 be complementary or not complementary. But they would
3 not be the same as these.

4 I would have to research that a little bit
5 more to completely think through this particular segment
6 to give you really a better answer.

7 Q Did you not think through this when you were
8 preparing this figure for declaration?

9 A Yes, I did. I would just have to just recall
10 the exact -- the exact details of that. I don't -- I
11 just can't -- as I'm talking through it, I would have to
12 review that just a little bit to refresh my memory on
13 what that comprised.

14 Q Is it your testimony that your analysis is
15 incomplete today?

16 A No. It's just that, in making this erratum,
17 that question came to mind. And I would have to review
18 just to see whether those two segments were
19 complementary or not. And they could be represented --
20 well, it would depend on the circumstance.

21 Q Well, I'm asking you about the circumstance
22 where you prepared this figure. You're telling me today
23 that you're correcting it or you'd like to correct to
24 show bases on the bottom strand, correct?

25 A Correct.

1 Q And so then my question is: Is that -- in
2 that design, which you're now correcting, are those
3 strands complementary such that they're hybridized
4 together in the black region? And if you're not sure,
5 you can say you're not sure.

6 A Yeah.

7 MR. PLATT: Objection to form.

8 THE WITNESS: I'm just trying to recall exact
9 details. I apologize for the delay.

10 May I look at another reference real quickly?

11 BY MR. HOLMAN:

12 Q Sure.

13 What reference are you looking at?

14 A The Kanan supplemental material.

15 Okay. Yes. Okay. I recall now.

16 So yes, looking back at the Kanan supplemental
17 material, Figure S1, I do recall now, and those should
18 be hybridized. The vertical lines should be there, and
19 they should be hybridized.

20 Q And you're basing that on Kanan's Figure S1?

21 A Correct.

22 Q All right. So, in this design that you have
23 in figure -- or on page 63, where the black region is
24 hybridized, are the sequences in the strand B and
25 strand A the same sequence such that any member of

1 pool A can hybridize to any member of pool B at this
2 black region?

3 A Those are primer binding sites. So those
4 would be -- they're referred to as the primer binding
5 site. And those are constant. So those would be the
6 same for all pool members.

7 Q Okay. Couple more questions.

8 If you turn to page 67.

9 A Okay.

10 Q The figure you have there.

11 And you were asked some questions about this
12 figure during the redirect.

13 Do you recall that?

14 A Uh-huh.

15 Q And similar to the figure we were previously
16 looking at, I believe you testified that the black
17 region to the left of the d-spacer should, again, show
18 vertical lines on both strands representing bases; is
19 that correct?

20 A Correct.

21 Q And based on your previous answer where you
22 were referring to Kanan's Figure S1, is it your opinion
23 that this region also should be hybridized?

24 A In this diagram, yes.

25 Q Okay. And that -- sorry?

1 A And recall too that I mentioned earlier in my
2 testimony and these questions that that's a design
3 element that's up to the user too. This is one option
4 of how this can be done.

5 Q Okay.

6 A It represents the combination of Kanan and
7 Neri.

8 Q Is it your opinion that this hybridization
9 that should be depicted in this figure, according to
10 you, is the same hybridization for all of pool A and
11 pool B because they're primer binding sites?

12 A In this example, yes.

13 Q In your declaration, do you provide any
14 alternative options on this design without hybridization
15 in this black region to the left of the d-spacer?

16 A Could you repeat that, please?

17 Q In your declaration, where you're discussing
18 these figures, do you provide any alternative options
19 without hybridization in this black region to the left
20 of the d-spacer?

21 A I do not, to the best of my recollection.

22 MR. HOLMAN: Okay. Thank you. We have no
23 further questions. Thank you for your time.

24 THE WITNESS: You're welcome. Thank you.

25 (TIME NOTED: 4:19 P.M.)

REPORTER'S CERTIFICATION

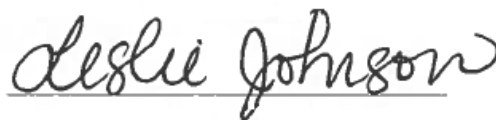
I, Leslie Johnson, a Certified Shorthand
Reporter of the State of California, do hereby certify:

That the foregoing proceedings were taken
before me at the time and place herein set forth; that
any witnesses in the foregoing proceedings, prior to
testifying, were administered an oath; that a record of
the proceedings was made by me using machine shorthand
which was thereafter transcribed under my direction;
that the foregoing transcript is a true record of the
testimony given.

Further, that if the foregoing pertains to
the original transcript of a deposition in a Federal
Case, before completion of the proceedings, review
of the transcript [] was [] was not requested.
I further certify I am neither financially interested in
the action nor a relative or employee of any attorney or
any party to this action.

IN WITNESS WHEREOF, I have this date
subscribed my name.

Dated: June 4, 2025

A handwritten signature in cursive script that reads "Leslie Johnson". The signature is written in dark ink and is positioned above the printed name "LESLIE JOHNSON".

LESLIE JOHNSON

CSR No. 11451, RPR, CCRR

1 Norman C. Nelson , Ph.D.

2
3 June 4, 2025

4 RE: Alamar Biosciences Inc v. Olink IPR

5 6/3/2025, Norman C. Nelson , Ph.D. (#7406576)

6 The above-referenced transcript is available for
7 review.

8 Within the applicable timeframe, the witness should
9 read the testimony to verify its accuracy. If there are
10 any changes, the witness should note those with the
11 reason, on the attached Errata Sheet.

12 The witness should sign the Acknowledgment of
13 Deponent and Errata and return to the deposing attorney.
14 Copies should be sent to all counsel, and to Veritext at
15 litsup-ga@veritext.com

16 Return completed errata within 30 days from
17 receipt of testimony.

18 If the witness fails to do so within the time
19 allotted, the transcript may be used as if signed.

20
21
22 Yours,

23 Veritext Legal Solutions
24
25

Alamar Biosciences Inc v. Olink IPR

Norman C. Nelson , Ph.D. (#7406576)

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Norman C. Nelson , Ph.D.

Date

Alamar Biosciences Inc v. Olink IPR

Norman C. Nelson , Ph.D. (#7406576)

ACKNOWLEDGEMENT OF DEPONENT

I, Norman C. Nelson , Ph.D., do hereby declare that I have read the foregoing transcript, I have made any corrections, additions, or changes I deemed necessary as noted above to be appended hereto, and that the same is a true, correct and complete transcript of the testimony given by me.

Norman C. Nelson , Ph.D.

Date

*If notary is required

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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.

DISCLAIMER: THE FOREGOING FEDERAL PROCEDURE RULES ARE PROVIDED FOR INFORMATIONAL PURPOSES ONLY.

THE ABOVE RULES ARE CURRENT AS OF APRIL 1, 2019. PLEASE REFER TO THE APPLICABLE FEDERAL RULES OF CIVIL PROCEDURE FOR UP-TO-DATE INFORMATION.

VERITEXT LEGAL SOLUTIONS

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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