

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD:

BIO-RAD LABORATORIES, INC.,

PETITIONER,

-against-

Case No.:

IPR2024-01451

USA Patent No.

11,827,921 B2

CALIFORNIA INSTITUTE OF TECHNOLOGY,

PATENT OWNER.

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DATE: June 4, 2025

TIME: 9:00 A.M.

DEPOSITION OF EXPERT DR. CARL BATT,
held at Jones Day, 250 Vesey Street, New
York, New York, before Rivka Trop, a Notary
Public of the State of New York.

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A P P E A R A N C E S:

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JAIME D. CHOI, ESQ.

1 DR. C. BATT

2 C A R L B A T T, called as a witness,
3 having been first duly sworn by a Notary
4 Public of the State of New York, was
5 examined and testified as follows:

6 EXAMINATION BY

7 MR. GILL:

8 Q. Please state your name for the
9 record.

10 A. Dr. Carl Batt.

11 Q. What is your business address?

12 A. 351 Stocking Hall, Cornell
13 University, Ithaca, New York 14853.

14 Q. Good morning, Dr. Batt?

15 A. Good morning.

16 Q. My name is Eric Gill. I am one of
17 the lawyers representing Caltech in this IPR
18 involving the '921 patent. And we are here
19 to take your deposition in connection with
20 that IPR.

21 Do you understand that you are
22 under oath today?

23 A. I do.

24 Q. And that's the same oath that you
25 would take if you were testifying in a court

1 DR. C. BATT

2 of law?

3 A. I do.

4 Q. Have you any drugs or alcohol in
5 the last 24 hours that would impact your
6 ability to testify or recall?

7 A. I have not.

8 Q. Any medication that would --

9 A. No.

10 Q. Is there any reason you can't
11 testify and provide your best testimony
12 today?

13 A. No reason.

14 Q. Have you been deposed before?

15 A. I have.

16 Q. How many times?

17 A. I am going to guess probably ten
18 or twelve times.

19 Q. As an expert?

20 A. Correct.

21 Q. In all those 10 to 12 times?

22 A. Oh, yes, sorry, yes.

23 Q. Let's go over some ground rules
24 for your deposition. Just please wait until
25 I am done asking a question before you start

1 DR. C. BATT

2 answering. And I will do the same for your
3 answers before I ask the next question. And
4 if you don't understand any of my questions,
5 will you agree to let me know?

6 A. I will.

7 Q. Otherwise I am going to assume
8 that you understand the question, is that
9 fair?

10 A. Fair enough.

11 Q. If at any time during the
12 deposition something else occurs to you, you
13 want to go back and discuss one of your
14 previous answers, just let me know, we can
15 do that. And we will take breaks probably
16 every hour. But if you need a break before
17 then, just let me know, we will finish the
18 question we are on and take a break, okay?

19 A. Yes.

20 Q. And Bio-Rad's counsel may object
21 to some my questions today. But unless
22 there is a privilege or work product
23 objection, you have to answer the question,
24 okay?

25 A. Yes, that's okay.

1 DR. C. BATT

2 Q. And you have to answer the
3 questions verbally so the court reporter can
4 record them. You can't just shake your head
5 or nod or shrug your shoulders, okay?

6 A. Absolutely.

7 Q. Do you have any documents with
8 you?

9 A. I do not.

10 Q. Any notes?

11 A. No.

12 Q. Do you have any questions about
13 the deposition process at this point?

14 A. I do not.

15 Q. Is there any reason your
16 deposition should not go forward today?

17 A. None that I know of.

18 Q. This is a notice to take your
19 deposition today. Have you reviewed it?

20 A. I will. Okay.

21 Q. Do you understand you are here
22 today pursuant to this deposition notice?

23 A. Yes.

24 MR. GILL: And for the record,
25 this is paper 16 in the IPR.

1 DR. C. BATT

2 Q. Dr. Batt, I have just handed you
3 Exhibit 1002, which is your declaration,
4 correct?

5 A. It appears so.

6 Q. This is your declaration involving
7 the '921 patent, correct?

8 A. That is correct.

9 Q. And if you look down at the
10 bottom, there is a stamp that says Bio-Rad
11 Exhibit 1002, do you see that?

12 A. I do see that.

13 Q. I am going to call that the
14 stamped page number, is that okay?

15 A. Yes, that's acceptable.

16 Q. So if you go to stamped page 189?

17 A. I have it.

18 Q. That's your signature, correct?

19 A. That's an electronic version of my
20 signature, yes.

21 Q. Are there any errors or mistakes
22 in your declaration that you wish to
23 correct?

24 A. I haven't reviewed this copy, but
25 we could assume for the moment that this

1 DR. C. BATT

2 accurately reflects my declaration. So I
3 don't have any changes.

4 Q. Do you have any reason to believe
5 this is not the declaration that you signed
6 on September 16, 2024?

7 A. Well, I have been handed a copy of
8 something, and from you -- so let's just
9 assume under the assumption that this is
10 what I signed, this is what I signed.

11 Q. On the next page on stamped page
12 190 of your declaration is appendix A, do
13 you see that?

14 A. Correct, yes, I see that.

15 Q. And that's appendix A?

16 A. That is listed as appendix A,
17 correct.

18 Q. And this contains your CV?

19 A. Yes, that's correct, this is my
20 CV.

21 Q. And then if you flip to stamped
22 page 195, there is a list of peer review
23 publications starting on stamped page 195,
24 correct?

25 A. That is correct.

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2 Q. Are those articles that you
3 authored or co-authored?

4 A. Yes, again, assuming that this is
5 the same copy, yes, these are all papers
6 that I authored, contributed to, yes, yes.

7 Q. What did you do to prepare for
8 this deposition?

9 A. I reviewed my declaration,
10 reviewed some of the documents associated
11 with the matter at hand, I also consulted
12 with my attorney -- not my attorney, but the
13 attorney in this case.

14 Q. Mr. Walter?

15 A. That is correct.

16 Q. How many times did you meet with
17 Mr. Walter?

18 A. I would say a total of three or
19 four times.

20 Q. How much time did you spend
21 preparing?

22 A. By myself or with him?

23 Q. Total.

24 A. In total, including the
25 declaration preparation or when we --

1 DR. C. BATT

2 Q. No, after you submitted the
3 declaration?

4 A. After I submitted this, probably I
5 am going to guess ten to twelve hours.

6 Q. What documents did you review when
7 you were preparing for the deposition?

8 A. So as I stated before, I reviewed
9 my report, my declaration I should say and
10 some of the salient exhibits in the case.

11 Q. Describe the process of preparing
12 your declaration?

13 A. The declaration itself, so we are
14 talking about this document was prepared in
15 collaboration with Mr. Walter and myself and
16 basically was a back and forth of various
17 drafts in the declaration.

18 Q. How much time did you spend
19 preparing the declaration?

20 A. I would have to go back and look
21 at my records.

22 Q. Ballpark?

23 A. Ballpark I would say 20 to 30
24 hours, in that neighborhood.

25 Q. Was any portion of your

1 DR. C. BATT

2 declaration copied from other declarations
3 or documents?

4 A. Not that I know.

5 Q. So if you go to paragraph 29 of
6 your declaration, why did you write that
7 paragraph?

8 A. Are we talking about the one that
9 says, To the extent the following discussion
10 is similar to other declarations the ideas
11 contained are entirely my own and I agree
12 with the content therein?

13 Q. Yes.

14 A. Just to simply reflect the fact
15 that this particular narrative was my work
16 and the fact that I agree with the content
17 and the facts as presented.

18 Q. What materials did you consider
19 when preparing your declaration?

20 A. The materials that I considered,
21 well, I mean, you know, we have the sum
22 total of the knowledge that I carry in my
23 head, you know, the literature pertinent to
24 various subject matter here and other sorts
25 of documents, other sources of information.

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2 Q. Did you consider any documents
3 that you do not cite in your declaration?

4 A. Oh, absolutely, yes, absolutely.

5 Q. Like what?

6 A. You know, we are talking about
7 certain basic matters of PCR. As I look
8 through this TaqMan, other sorts of things,
9 they might not necessarily have been cited
10 to the original reference, but certainly
11 they are knowledge that is common in the
12 field.

13 Q. What is your hourly rate for this
14 matter?

15 A. My hourly rate is \$425 an hour.

16 Q. And how many hours have you billed
17 to Bio-Rad so far for this IPR?

18 A. Actually billed none.

19 Q. Invoiced?

20 A. So I operate through as a third
21 party involved here. So that's where things
22 are a little bit -- so I haven't billed at
23 all to this point. I have not invoiced at
24 all for this matter.

25 Q. Understood.

1 DR. C. BATT

2 And I want to go stamped page 210
3 of your declaration. And here you list nine
4 district court cases, and I think one ITC
5 case and one IPR where you testified,
6 correct?

7 A. Where I was deposed, yes.

8 Q. And that's an accurate list of
9 your cases where you were deposed or
10 testified?

11 A. To the best of my knowledge, yes.

12 Q. Have there been any cases since
13 you submitted your declaration?

14 A. No.

15 Q. Are there cases where you served
16 as an expert witness, but did not testify in
17 deposition or at a hearing or trial?

18 A. Probably.

19 Q. And then the last three cases on
20 your list, you were working on behalf of
21 Bio-Rad, correct?

22 A. That is correct.

23 Q. Those were the 10X Genomics, Silla
24 Technology and Dropworks matters, correct?

25 A. That is correct.

1 DR. C. BATT

2 Q. About how long has it been since
3 you acted as a testifying expert on behalf
4 of a company other than Bio-Rad?

5 A. Oh, other than Bio-Rad, I would
6 have to go back and look. That would be the
7 Novo case. And honestly I don't recall off
8 the top of my head when that occurred.

9 Q. Is it before COVID?

10 A. Yes, thank you.

11 Q. So the last case on your list
12 Bio-Rad Lab, Inc. v. Dropworks, that was an
13 IPR, correct?

14 A. That is correct.

15 Q. And that involved U.S. patent
16 number RE43,365, correct?

17 A. That is what is noted here, yes.

18 Q. We are going to talk about that
19 IPR a little bit?

20 MR. GILL: This one is going to be
21 Exhibit 2016.

22 (Whereupon, a Declaration was
23 marked Exhibit 2016 for identification
24 as of this date.)

25 Q. This is a declaration that you

1 DR. C. BATT

2 submitted in IPR styled IPR number
3 2021-00302, correct?

4 A. That is what it appears to be,
5 yes.

6 Q. Do you remember working on this
7 declaration?

8 A. This was three and a bit years
9 ago. I don't remember a whole lot of the
10 details.

11 Q. So just looking at the caption of
12 the IPR, it lists Dropworks, Inc. as
13 petitioner, correct?

14 A. That is what it says, yes.

15 Q. And then Lawrence Liveremore
16 National Security, LLC as the patent owner?

17 A. That is correct.

18 Q. But your list of cases says you
19 testified on behalf of Bio-Rad; is that
20 correct?

21 A. To the best of my recollection I
22 think that Bio-Rad might have licensed this
23 patent. Certainly I was not in direct
24 contact with Lawrence Liveremore.

25 Q. Could you go to paragraph 2 of

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2 this declaration?

3 A. Okay.

4 Q. Paragraph 2 is under the heading
5 of Qualifications and Experience, correct?

6 A. Correct.

7 Q. And paragraphs 2 through 4, and
8 there are a few more paragraphs, but I want
9 to focus on the first couple of paragraphs,
10 are part of your background and
11 qualifications as of September 2021,
12 correct?

13 A. Yes.

14 Q. And paragraph 5 describes your
15 practical experience with PCR as of the time
16 you submitted this declaration?

17 A. That is correct.

18 Q. And you talk about your
19 experience, your practical experience in PCR
20 and realtime PCR, do you see that?

21 A. I do.

22 Q. Have you had any additional
23 practical experience with PCR or realtime
24 PCR between September of 2021 when you
25 signed this declaration and September of

1 DR. C. BATT

2 2024 when you signed your declaration that
3 you submitted in this IPR?

4 A. Could you clarify what you mean by
5 practical experience?

6 Q. Yes, in paragraph 5 you say
7 practical use?

8 A. If we are talking about practice
9 use, since that time, no.

10 Q. Have you had any practical use of
11 PCR, realtime PCR since you signed your
12 declaration in this IPR, September of 2024?

13 A. Again, if we are talking about
14 practical use, then I interpret to have I
15 done hands-on experiments in that, the
16 answer is no.

17 Q. What is the different between PCR
18 and realtime PCR, if any?

19 A. So PCR, polymerase chain reaction,
20 is basically a method whereby you can
21 amplify a targeted DNA sequence with a
22 series of primers, enzyme, some nucleotides
23 and some other reagents. You are basically
24 amplifying that sequence, that target
25 sequence which is flanked by those two

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2 primers.

3 Realtime PCR is probably not an
4 exceptionally well defining term, but it is
5 meant to define where you are having a
6 quantitative measure of the process through
7 which you can then go back and quantify the
8 amount of initial template in a particular
9 sample. And you do so in realtime.

10 Q. So in paragraph 5 you talk about
11 an instrument you built in your lab for
12 performing realtime PCR, and that your group
13 had made use of microfluidic devices for
14 realtime PCR?

15 A. To clarify what it says, we have
16 used microfluidic devices for a variety of
17 applications including realtime molecular
18 analysis of various organisms. So at the
19 time we were both employing polymerase chain
20 reaction and something called ligase chain
21 reaction to do amplifications. So nominally
22 what you are saying is correct.

23 Q. You also talk about your research
24 labs in public and private practice, can you
25 explain what you mean by that?

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2 A. Can you point out specifically.

3 Q. It is in paragraph 5 in the second
4 sentence?

5 A. PCR and real time PCR are still
6 integral tools in my research lab in both
7 public and private practice.

8 I honestly don't recall the
9 context of that statement.

10 Q. And you say in particular, I and
11 others in my laboratory working at my
12 direction built an instrument in my
13 laboratory for performing realtime PCR for
14 research purposes, that's in paragraph 5,
15 correct?

16 A. That is correct.

17 Q. Which laboratory are you referring
18 to in this paragraph?

19 A. Well, it says my laboratory, so
20 that I would interpret to be my academic
21 laboratory.

22 Q. Where is that?

23 A. At Cornell University.

24 Q. Did your instrument that you built
25 that you are referencing here in paragraph

1 DR. C. BATT

2 5, did that perform PCR inside of droplets?

3 A. No, it did not.

4 Q. That instrument didn't perform
5 digital PCR, correct?

6 A. Within the context of digital PCR
7 occurring in droplets, no, it did not.

8 Q. How many analytes did the
9 instrument detect at once?

10 A. I don't recall. I am going to say
11 four or less given the technology at that
12 time. This was work that was conducted in
13 the early 2000s.

14 Q. Let's go back to your declaration
15 from this IPR Exhibit 1002. I want to talk
16 about again your publications which, again,
17 start on stamp paged 195.

18 Do any of the articles relate to
19 droplet-based PCR for detecting or measuring
20 polynucleotide analytes?

21 A. So to answer your question we did
22 not conduct research regarding that. What I
23 can't leave out is any mention of droplet
24 PCR in either the context of background
25 material for any of these papers or any of

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2 the reviews and any of the book chapters.

3 So I can't state that nowhere in any of
4 these 300 publications droplet PCR or
5 digital PCR is mentioned.

6 Q. But sitting here now, can you
7 identify any one of these papers that
8 discuss that topic?

9 A. No. I mean, no, in terms of I
10 can't identify them. I am not disputing
11 that someplace there may be some reference
12 to them.

13 Q. Do any of the articles listed here
14 discuss multiplex digital PCR?

15 A. Again, within the context of the
16 articles, I can't eliminate that
17 possibility. If you are talking about
18 multiplex digital as in droplet PCR, we did
19 not conduct any primary research in that
20 area.

21 Q. Do any of these articles relate to
22 labeling probes and detecting multiple
23 targets using fewer differently colored
24 fluorophores than the number of
25 polynucleotide analytes?

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2 MR. WALTER: Objection, vague.

3 A. Yes, can you give me a little bit
4 more. Let me preface this by saying that we
5 did do multiplex PCR with a variety of
6 different fluorophores, so a variety of
7 different colors, if you would. To sort of
8 categorically say we did or did not do, as
9 you state, where the number of targets
10 exceed the number of fluorophores, is that
11 what you are asking?

12 Q. Yes.

13 A. I can't state that for an absolute
14 fact and point to that article.

15 Q. Thanks. Let's go back to
16 paragraphs 5 through 7 of Exhibit 1002.

17 Paragraphs 5 through 7 describe
18 your background and qualifications as of
19 September of 2024, correct?

20 A. That is correct.

21 Q. Now, looking back at the
22 declaration from the Dropworks IPR, I want
23 to look at paragraph 5 of that IPR which was
24 Exhibit 2016?

25 A. Okay, but we are talking about the

1 DR. C. BATT

2 IPR from the Dropworks?

3 Q. Yes.

4 A. And what paragraph are we talking
5 about?

6 Q. Paragraph 5.

7 A. Okay.

8 Q. Actually, let's look at paragraphs
9 2 through 4 first?

10 A. In which document?

11 Q. The Dropworks.

12 So review paragraphs 2 through 4
13 in the Dropworks declaration, and then
14 review paragraphs 5 through 7 of Exhibit
15 1002, your declaration, this IPR?

16 A. And which in the current IPR, 5
17 through 7, you said?

18 Q. Correct.

19 A. Okay.

20 Q. So it is fair to say that those
21 paragraphs are similar, but may be updated
22 in your current declaration with dates and
23 so forth?

24 A. Yes, without spending a lot of
25 time going back and forth, it does appear

1 DR. C. BATT

2 that they are similar.

3 Q. Your current declaration doesn't
4 have a paragraph corresponding to paragraph
5 5 of the Dropworks declaration, correct, at
6 least not in the background and
7 qualification section of your current
8 declaration?

9 A. So paragraph A which starts off, I
10 have made practical use of polymerase chain
11 reaction, realtime PCR.

12 Q. I am referring to paragraph 5,
13 that's correct?

14 A. Yes, that paragraph appears in the
15 Dropworks IPR declaration, but not in the
16 current declaration, yes.

17 Q. Why didn't you include that
18 paragraph?

19 A. I honestly don't recall.

20 Q. You could set aside the Dropworks
21 for now.

22 Paragraph 5, your experience in
23 PCR, in realtime PCR did not involve digital
24 PCR, correct?

25 A. I believe I answered that

1 DR. C. BATT

2 previously. Well, so let's clarify, and
3 repeat the question one more time, please.

4 Q. Yes, your earlier experience in
5 PCR, realtime PCR did not involve digital
6 PCR?

7 A. So if what you are asking me at
8 the time when we first started doing
9 realtime PCR, which is mid '90s, digital PCR
10 didn't exist. And so we were some of the
11 pioneers in realtime PCR for a variety of
12 applications, instrument development.
13 Digital PCR was close to 15 years later.

14 Q. So is the answer yes?

15 A. What is the question again?

16 Q. Your early experience in PCR, your
17 experience in PCR, in realtime PCR did not
18 involve digital PCR?

19 A. So as a practical use the answer
20 is correct. As a body of knowledge I am
21 well familiar with digital PCR.

22 Q. To your knowledge, for any matters
23 in which you have acted as an expert
24 witness, has opposing party argued that you
25 were not qualified to offer expert

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2 testimony?

3 A. I was involved in a Daubert
4 proceeding, if I am remembering, and that
5 was a proceeding that was called by Richard
6 Posner in one case, I don't even remember
7 what it was. So I was questioned about my
8 qualifications in that particular case. And
9 I was ruled to be exceptionally qualified.
10 I was given praise by a rather
11 well-recognized judge.

12 Q. You don't remember which case that
13 was?

14 A. I don't, I don't.

15 Q. But that's the only case where
16 your qualifications were challenged that you
17 are aware of?

18 A. That I am aware of, yes.

19 Q. Let's talk about your educational
20 background.

21 And looking at your current
22 declaration stamped page 190, which is part
23 of your CV. You received your bachelor's in
24 1975 in microbiology from Kansas State; is
25 that correct?

1 DR. C. BATT

2 A. That is correct.

3 Q. Did you study PCR testing during
4 your bachelor's courses?

5 A. No. I was probably about ten
6 years too early.

7 Q. And you received your master's
8 degree in 1979 from Rutgers Department of
9 Food Science, correct?

10 A. That is correct.

11 Q. Did you take any courses about PCR
12 during your master's program?

13 A. That would have been prophetic,
14 but the answer is no.

15 Q. Did you write a master's thesis?

16 A. I did.

17 Q. Did your master's thesis involve
18 using PCR?

19 A. No.

20 Q. And you received your Ph.D. in
21 1981 from Rutgers Department of Food
22 Science, correct?

23 A. That is correct.

24 Q. You did not take any courses about
25 PCR during your Ph.D. program, correct?

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2 A. Not that I recall.

3 Q. Your Ph.D. thesis did not involve
4 analyzing polynucleotide sequences, correct?

5 A. Define what that means.

6 Q. You don't know what that means?

7 A. No, I am not sure what you are
8 referring to when you say analyzing
9 polynucleotide sequences. There is various
10 ways to interrupt that, right.

11 Q. Did you do it in any way of
12 interpreting it?

13 A. If what you are asking me did I
14 perform any experiments involving the
15 analysis of polynucleotide -- and you said
16 sequences; right?

17 Q. Correct.

18 A. Then let's just narrow that down
19 by saying did I do DNA sequencing, is that
20 the gist of your question?

21 Q. Sure.

22 A. The answer is no, that was not a
23 technology at the time.

24 Q. So your Ph.D. thesis did not
25 involve using PCR, correct?

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2 A. Absolutely not.

3 Q. According to, again, stamped page
4 190 of your declaration, you were a
5 post-doctoral research associate in the
6 Department of Nutrition and Food Science at
7 MIT from 1982 to 1984, correct?

8 A. That is correct.

9 Q. And your research associate
10 position did not involve PCR testing,
11 correct?

12 A. Again, correct, PCR was not a
13 technology at the time.

14 Q. And then in 1984 and 1985 you were
15 a research scientist at the department -- in
16 the Department of Applied Biological
17 Sciences at MIT, correct?

18 A. That is correct.

19 Q. And that work didn't involve PCR
20 testing, correct?

21 A. That is correct.

22 Q. When was PCR invented?

23 A. Define what you mean when, please.
24 So PCR was basically conceived by Kary
25 Mullis some time in the early 1980s. It was

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2 reduced to practice where it could be
3 practically used probably about 1985, 1986.
4 Reagents probably were not available until
5 maybe mid 1980s, late 1980s, something like
6 that.

7 Q. So after all the academic
8 experience listed in your CV; yes?

9 A. No. Because what it includes in
10 my academic experience is my position as an
11 assistant professor beginning in 1985. And
12 so to elaborate a little bit, we were
13 practicing polymerase chain reaction before
14 thermocyclers were actually commercially
15 available, which are machines that basically
16 alter temperatures to carry out polymerase
17 chain reaction.

18 Q. When you say "we were," which
19 position in your CV were you talking about?

20 A. So we being some time in the
21 late -- I would have to go -- do you want a
22 specific year?

23 Q. Just what position in your CV?

24 A. Oh, when I was assistant
25 professor, sorry, yes. By the time I was

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2 assistant professor, probably within the
3 first year or two, we were attempting to
4 practice PCR.

5 Q. All right, then you have a section
6 called other experience in your CV, correct?

7 A. Correct.

8 Q. And I want to go and kind of
9 reverse chronological order here starting on
10 stamped page 191?

11 A. Okay.

12 Q. And starting in 1996 you were the
13 founder and direction of the Laboratory for
14 Molecular Typing at Cornell, correct?

15 A. That is correct.

16 Q. You worked there from 1996 to
17 2001?

18 A. Worked, so I was the director of
19 it.

20 Q. Director of it?

21 A. Basically it was a facility that
22 we established to carry out as it says here
23 molecular typing.

24 Q. Did that work involve digital PCR
25 testing?

1 DR. C. BATT

2 A. No, it did not.

3 Q. And from 1999 to 2016 you have
4 Agave Bio Systems, correct?

5 A. That is correct.

6 Q. Did that work cover digital PCR
7 testing?

8 A. I can't accurately answer that.
9 So I was the adviser for a company. And I
10 would have to review all the projects that
11 we carried out during that period of time to
12 actually tell you whether or not any of
13 those projects involved digital PCR.

14 Q. But you don't know if any of the
15 projects you worked on, the work that you
16 actually did involved digital PCR?

17 A. Define what you mean by actually
18 did.

19 Q. The work that you were doing?

20 A. So work meaning that I was a
21 science adviser. So if work means I sat on
22 a bench and conducted experiments, I didn't
23 do that at all in that position.

24 Q. Well, what you were doing as a
25 scientific adviser?

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2 A. I was advising.

3 Q. On what?

4 A. Science.

5 Q. What kind of science?

6 A. That company did all sorts of
7 different sciences.

8 Q. Did they do digital PCR?

9 A. I don't think so.

10 Q. From 1999 to 2004 you worked at
11 Nanobiotechnology Center at Cornell,
12 correct?

13 A. Again, I was the codirector.

14 Q. Sure, codirector?

15 A. At the same time I was running my
16 research lab at the same time I was the
17 science adviser for Agave Biosystems.

18 Q. What did you do as a codirector
19 for Cornell?

20 A. So the Nanobiotechnology Center at
21 Cornell University was a National Science
22 Foundation supported science and technology
23 center. It ran from 1999 to 2004 -- well,
24 actually it ran to 2010. Basically it was
25 about \$5 million a year of support. It

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2 supported probably 25 to 30 different
3 faculty. My role there, the cofounder and
4 codirector, was an administrative position
5 that basically involved overseeing some of
6 the research, but mainly the educational
7 components of that particular center.

8 Q. Did the educational components you
9 were overseeing include digital PCR?

10 A. No.

11 Q. Did the research you were
12 overseeing include digital PCR?

13 A. I can't answer that.

14 Q. Why not?

15 A. Because it was probably 25 faculty
16 across five institutions doing various
17 research. And I don't recall some 20 years
18 later exactly what every single project was
19 all about.

20 Q. From 2001 to 2004 you worked at
21 the Alliance for Nanomedical Technologies at
22 Cornell, correct?

23 A. Again, I was the founder of that.
24 I was the principal investigator for their
25 project leader. That particular involved

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2 \$3 million of New York State funding,
3 probably I want to say somewhere in the
4 neighborhood of around ten different faculty
5 doing research projects. Did any of those
6 involve digital PCR, is that what you are
7 asking?

8 Q. Yes.

9 A. And the answer is I can't give you
10 a clear answer on it.

11 Q. And then you went, you cofounded
12 Main Street Science in 2004; is that
13 correct?

14 A. That is correct.

15 Q. What was Main Street Science doing
16 at that time?

17 A. So Main Street Science as it says
18 was a non-for profit and basically was
19 involved taking some of the educational work
20 that we were doing at the National Science
21 Foundation supported Nanobiotechnology
22 Center, and sort of doing outreach for that
23 and developing materials for that.

24 Q. Did any of the work at Main Street
25 Science include digital PCR?

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2 A. No.

3 Q. And then from 2005 to 2009 you
4 worked for Illuminaria?

5 A. Again, I didn't work for
6 Illuminaria, I was the founder and president
7 of that small start-up.

8 Q. Did that start-up do digital PCR?

9 A. No, because, again, it is 2009.

10 Q. In your description of your
11 experience at Illuminaria, you say that the
12 company sought to commercialize microfluidic
13 technology, do you see that?

14 A. I do.

15 Q. What was that technology?

16 A. Let see, 20 years ago, that
17 particular technology was probably related
18 to either some mixing components or some
19 microfluidic focusing components that we had
20 received funding for through the SBIR
21 program.

22 Q. Then in 1999 going to 2011 you
23 were a director at Cornell in the Ludwig
24 Institute for Cancer Research Partnership;
25 is that correct?

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2 A. That is correct.

3 Q. What was your role as director in
4 that department?

5 A. So it wasn't a department. It was
6 an entity that was established as a
7 partnership between the Ludwig Institute for
8 Cancer Research and Cornell University. The
9 primary focus of that particular entity, if
10 you would, was to establish a good
11 manufacturing practices facility for
12 producing basically phase one clinical
13 materials for cancer trials.

14 Q. Did that entity focus on digital
15 PCR?

16 A. It did not.

17 Q. And then going onto stamped page
18 190, starting in 2000, going to the present,
19 you are a principal consultant at Stone
20 Fence Collaborative; is that correct?

21 A. That is correct.

22 Q. Does your consulting work include
23 digital PCR?

24 A. So that particular entity -- and
25 through that entity I do consulting -- I

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2 probably have over that period of time an
3 excess of 100 clients that I have done
4 pre-submission grant reviews for. Do any of
5 those involve digital PCR? I can't give you
6 a clear answer, and I wouldn't because it is
7 confidential.

8 Q. From 2010 to the present, you
9 served as an adjunct senior scientist at
10 MOTE Marine Laboratory in Florida; is that
11 correct?

12 A. That is correct.

13 Q. Did that work cover digital PCR?

14 A. Certainly not.

15 Q. From 2018 to 2024 you were the
16 managing partner of Salvatore BKLYN in
17 Brooklyn; is that correct?

18 A. Yes.

19 Q. Did that work cover digital PCR?

20 A. Certainly not.

21 Q. From 2020 to 2021 you were a food
22 safety expert at Ample Hills Creamery; is
23 that correct?

24 A. That's correct.

25 Q. Did that work cover digital PCR?

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2 A. That did not.

3 Q. And finally from 2021 to the
4 present you were a managing partner at
5 Empire Syrups; is that correct?

6 A. That is correct.

7 Q. Did that work cover digital PCR?

8 A. That did not.

9 Q. Okay, let's go back to paragraphs
10 5 through 7 of your declaration. Paragraph
11 5 says you are a professor of biology at
12 Cornell in the Department of Food Science,
13 correct?

14 A. So what it says is I am the
15 Liberty Hyde Bailey professor of biology.
16 And that is actually not entirely correct, I
17 am the Liberty Hyde Bailey professor, we
18 typically don't have subject matter
19 associated with that title. So of the five
20 Liberty Hyde Bailey professors, nobody has a
21 Liberty Hyde Bailey professor of X, Y or Z.

22 Q. So as a professor do you teach
23 courses?

24 A. I do.

25 Q. Do any of those courses include

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2 digital PCR?

3 A. Define what you mean include?

4 Q. Do you teach digital PCR in any of
5 your courses?

6 A. In the course of any one of those
7 courses the topic may come up. It is not a
8 focus -- I don't teach a course in digital
9 PCR.

10 Q. Paragraph 5 also says at the end
11 that your current research interests are a
12 fusion of biology and nanotechnology
13 focusing on important biomedical problems,
14 correct?

15 A. That is correct.

16 Q. Does that research include digital
17 PCR?

18 A. Define what you mean by research?

19 Q. Well, you said research interests,
20 so what does that mean?

21 A. So that means that I include in my
22 research interests my academic interests in
23 a subject matter that might not necessarily
24 be a topic that we are conducting in the
25 research laboratory.

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2 Q. Does the research that you are
3 conducting in the research laboratory
4 include digital PCR?

5 A. It does not.

6 Let me just finish by saying
7 again, you are sort of defining research as
8 something that perhaps I personally sit at a
9 bench and do, which I don't do. I have not
10 done that probably since I was an assistant
11 professor. So when I consider research and
12 my academic interests, I don't necessarily
13 restrict my knowledge to things that I sit
14 at a bench and do.

15 Q. In this matter you have offered
16 opinions that the '921 patent is allegedly
17 invalid as obvious, correct?

18 A. That is correct.

19 Q. And anticipated; is that correct?

20 A. Yes, that is correct as well.

21 Q. Do you understand that obviousness
22 is considered from the perspective of a
23 person of ordinary skill in the art?

24 A. Yes.

25 Q. And that's at the time of the

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2 claimed invention, correct?

3 A. That is correct.

4 Q. So I am going to refer to person
5 of ordinary skill in the art as POSITA or
6 P-O-S-I-T-A, are you comfortable with that?

7 A. I will be.

8 Q. If I say POSITA, I mean person of
9 ordinary skill in the art?

10 A. Sure, I can keep that one
11 straight.

12 Q. And then whenever we discuss a
13 POSITA, I am going to be referring to the
14 time of the '921 patent's priority date,
15 that's the relevant time frame, when I say
16 what a POSITA would have understood, is that
17 fair?

18 A. That's fair.

19 Q. Now, in paragraph 67 of your
20 declaration you propose a definition of a
21 POSITA in this matter, correct?

22 A. Give me a moment, starting in that
23 section of your declaration, not necessarily
24 paragraph 67, section Roman Numeral 7. So
25 Roman numeral 7 is person of ordinary skill

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2 in the art, POSITA, as you are calling it.

3 Q. And paragraph 67 includes your
4 opinion of basically what qualifications a
5 POSITA would have to have, correct?

6 A. That is correct.

7 Q. And then in paragraph 69 you list
8 a number of techniques that a POSITA would
9 have had to have a strong understanding
10 and/or experience with, correct?

11 A. That is correct.

12 Q. And there are a number of
13 techniques, correct?

14 A. So there is multiplex PCR,
15 fluorescence labeling, quantitative
16 detection, labeling, detecting and
17 quantitative PCR and digital PCR, correct.

18 MR. GILL: Why don't we take a
19 quick break.

20 (Whereupon, a short recess was
21 taken.)

22 Q. I want to go to stamped page 12 of
23 your declaration. You talked about legal
24 standards. That's section 4 of your
25 declaration, do you see that?

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2 A. Yes, I see that.

3 Q. Is this the legal standards you
4 relied on in forming your opinions in this
5 IPR?

6 A. So we are talking about a written
7 description support, the claim construction,
8 is that what you are referring to as the
9 legal standards?

10 Q. And then it goes on?

11 A. Anticipation, obviousness, I guess
12 that's the last section, is that what you
13 are asking me?

14 Q. Yes, are these the legal
15 principles you relied on?

16 A. Yes, these are.

17 Q. Did you rely on any other legal
18 principles to form your opinions?

19 A. You know, I have a general
20 knowledge of the subject matter. So I
21 wouldn't exclude that there might be
22 something sitting in my knowledge that might
23 have had an impact, but the answer is that I
24 mainly relied on these terms and the
25 description of those terms as described in

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2 section 4.

3 Q. If there were different legal
4 standards that applied, is it possible that
5 that would change your opinions?

6 MR. WALTER: Objection, vague.

7 A. Yes, sorry, I am not sure what
8 that question means.

9 Q. Well, if there were legal
10 principles that you left out?

11 A. I am not getting it, you are
12 asking me what legal principles did I leave
13 out that I might have considered -- I am a
14 little -- sorry, I am a little bit confused
15 by the question.

16 Q. Yes, if there were legal standards
17 that you didn't consider, that could change
18 your opinions, correct?

19 MR. WALTER: Objection, vague,
20 incomplete hypothetical, calls for
21 speculation.

22 A. Yes, within the context of some
23 legal principle or standard that you are not
24 telling me what it is, could it change my
25 mind and change my mind in terms of what I

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2 have written here?

3 Q. Yes, is that possible?

4 MR. WALTER: Objection, vague,
5 incomplete hypothetical, calls for
6 speculation.

7 A. Yes, I would say that anything is
8 possible. I will say anything is possible,
9 but I still have no clue as to what you are
10 really asking. So with that vague question,
11 my vague answer is the best I can do.

12 Q. Paragraph 17 contains the legal
13 principles you applied when interpreting the
14 meaning of the words in the '921 patent
15 claims, correct?

16 A. So you are asking me paragraph 17
17 which starts off with, I understand that in
18 determining whether a patent claim under IPR
19 review, that's what we are talking about?

20 Q. Yes, the words of the claims of
21 the patent are generally given their
22 ordinary and customary meaning?

23 A. Yes, so when I read this, further
24 on it says, I also understand the patent
25 claims are construed in the light of claimed

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2 language, the patent specification fiction
3 and the prosecution history. Yes, so these
4 are the principles or legal standards, I
5 guess you call them, that I included when I
6 was looking at the '921 patent and the claim
7 language in the '921 patent.

8 Q. Now, your invalidity opinions in
9 this IPR are based in part on Caltech's
10 infringement contentions, correct, the
11 infringement contentions from the parallel
12 litigation, correct?

13 A. Right, from the district court,
14 yes, yes, the ChromaCode cases, I sometimes
15 refer to it, yes.

16 Q. But section 4B on claim
17 construction doesn't say anything about the
18 legal standard for interpreting claims in an
19 IPR based on the patent owner's infringement
20 contentions in a parallel litigation,
21 correct?

22 A. What are you referring to, I am
23 sorry?

24 Q. The legal principals on claim
25 construction that you are relying on here?

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2 A. Yes, oh, sorry, now I understand
3 what your nomenclature means. 4B.

4 So please repeat your question.

5 Q. Yes, the legal principals you
6 relied on here for claim construction, they
7 don't say anything about relying on the
8 patent owner's infringement contentions,
9 correct?

10 A. If you give me a minute to read
11 it, I will reconfirm that.

12 So we are just dealing with what
13 is under claim construction, correct?

14 Q. Yes.

15 A. Give me a moment.

16 Q. Interpreting the claims?

17 A. So again, your question is whether
18 or not the parallel proceedings and
19 consideration of the parallel proceedings
20 are listed here as one of the things to be
21 considered?

22 Q. Correct.

23 A. It does not state that, it doesn't
24 exclude it. There is no statement here do
25 not include.

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2 Q. It doesn't mention it at all,
3 correct?

4 A. It does not mention that one
5 should include, yes.

6 Q. Do you know what the legal
7 standard is for interpreting claims in an
8 IPR based on the patent owner's infringement
9 contentions in a parallel litigation?

10 A. I do not have that information off
11 the top of my head.

12 Q. Let's go to paragraph 21. This is
13 section D on obviousness; right?

14 A. That is correct.

15 Q. And this is your understanding of
16 the legal standard for obviousness?

17 A. The paragraph 21 starts off with I
18 understand, so I will stand by that I
19 understand what is written here.

20 Q. Are you aware that if a proposed
21 modification changes the prior art's basic
22 principle of operation, this modification
23 fails to support a conclusion of
24 obviousness?

25 MR. WALTER: Objection, vague,

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2 incomplete hypothetical.

3 A. Yes, if you could give me a little
4 bit more definition as to what you are
5 asking me, that would be appreciated.

6 Q. Sure, it is just a legal standard?

7 A. Okay, repeat it one more time.

8 Q. If a proposed modification changes
9 the prior art's basic principle of
10 operation, that modification fails to
11 support a conclusion of obviousness, were
12 you aware of that?

13 MR. WALTER: Objection, vague,
14 incomplete hypothetical and also object
15 to the extent the question
16 mischaracterizes the law.

17 A. I am not sure I agree with that
18 statement. Because if I understand
19 correctly to simplify what you are saying is
20 that a prior art is modified, that it
21 doesn't necessarily constitute prior art?

22 Q. It depends on the modification?

23 A. Right, of course, it depends on
24 the modification. So one, if the legal
25 question is can one modify the prior art, I

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2 can only deal with those issues that I read
3 here and I understand here. And I don't
4 think that's necessarily covered under the
5 narrative that is provided here. If what
6 you are asking me is that any modification
7 to any prior art, assuming that it is okay,
8 somehow invalidates the invalidity argument,
9 I think is what you are asking me?

10 Q. Correct.

11 A. I can't answer that without
12 knowing what specific modification you are
13 talking about.

14 So let's parse this down two
15 different things. One is can one do that.
16 I am not an expert in that field. Two, does
17 that modification constitute in making the
18 invalidity argument invalid, which is a
19 terrible way to phrase it, I can't answer
20 that question, because I don't know what
21 that modification is.

22 Q. Let's go to the table of contents
23 of your declaration starting in Section 11,
24 the table of contents lists the invalidity
25 grounds that Bio-Rad is advancing in this

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2 IPR, correct?

3 A. So it is 11, ground 1, is that
4 what we are talking about?

5 Q. Yes.

6 A. It continues on to 12, ground 2,
7 13, ground 3, bear with me and then 14,
8 ground 4, is that what we are talking about?

9 Q. Yes. And ground 1 is the claims 1
10 through 10 and 13 through 19 are anticipated
11 by Larson, correct?

12 A. That is correct.

13 Q. And ground 2 is that claims 4, 7
14 and 14 through 19 are or would have been
15 obvious in view of Larson?

16 A. I am seeing claim 4, claim 6 and
17 claim 7 and then claims 14 through 19, claim
18 4, claim 6, the bottom of page 5.

19 Q. Stamped 5.

20 A. Yes.

21 Q. Okay, I am looking at the heading?

22 A. So you are correct that that's
23 what the heading says, but underneath it
24 includes also claim 6.

25 Q. Okay, fine. Ground 3 is claims 1

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2 through 10 and 12 through 19 would have been
3 obvious in view of Larson and Saxonov?

4 A. So again, claim 1, 2 through 10,
5 12, 13, 14, 15 through 18, 19 are all under
6 claim 3. And that's obviousness, as
7 considered with both Larson and Saxonov, the
8 combination, right.

9 Q. And ground 4 is claim 11 would
10 have been obvious in view of Larson, Saxonov
11 and Silverbrook, correct?

12 A. Claim 11, correct.

13 Q. So you are not asserting an
14 invalidity ground that claim 1 of the '921
15 patent would have been obvious in view of
16 Larson alone, correct?

17 A. So claim 1 with just Larson is a
18 claim of anticipation. And then ground 2
19 doesn't apply to claim 1 -- I am sorry,
20 ground 3 is Larson and Saxonov, again,
21 addressing claim 1. And the final one is
22 claim 11 which is a combination of Larson
23 Saxonov and Silverbrook.

24 Q. So you are not attacking claim 1
25 based on obviousness based on Larson alone;

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2 is that correct?

3 A. That is correct.

4 Q. And you are not asserting
5 invalidity an invalidity ground that claims
6 2, 3 or 5 or 8 through 13 would have been
7 obvious in view of Larson allow?

8 A. Correct, give me that one time.

9 Q. Claim 2, 3, 5 and 8 through 13?

10 A. That is correct.

11 Q. Let's go to paragraph 36.

12 A. That's a paragraph that starts out
13 with polymerase chain reaction PCR as a
14 method?

15 Q. Yes, it is in the technology
16 background.

17 A. Got it.

18 Q. In paragraph 36 through 39, you
19 are discussing the background on multiplex
20 PCR amplification, correct?

21 A. Yes, it includes a general
22 background on the polymerase chain reaction,
23 and then the last paragraph addresses
24 multiplex PCR.

25 Q. And paragraph 39 you say, at least

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2 of 2012 such multiplex PCR and its use was
3 well-known in the art, do you see that?

4 A. I do.

5 Q. You don't cite any documents to
6 support that opinion, correct?

7 A. That opinion meaning that as of
8 2012 --

9 Q. Multiplex PCR was well-known?

10 A. I am not sure what reference you
11 would find that would say something like
12 that, that is well-known in the art. There
13 is no arbiter of well-known in the art for
14 any scientific term. It is not like there
15 is a body of experts that say, oh, yes, that
16 is well-known in the art. I would say that
17 it is my opinion that as of 2012 multiplex
18 PCR was well-known, yes.

19 Q. And also in paragraph 39 you say,
20 Multiplex PCR provides numerous advantages
21 including being faster, less expensive and
22 more convenient than doing separate PCRs for
23 each target, correct?

24 A. I would say as a broad statement
25 that is correct.

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2 Q. And you don't cite any documents
3 to support that statement, correct?

4 A. No, this is, again, as was
5 well-known in the art, my opinion.

6 Q. Paragraph 47, if you want to flip
7 there, is meant to provide a background on
8 digital PCR or dPCR, correct?

9 A. Give me a moment while I take a
10 look at it. The answer is yes, that's a
11 very brief and nominal description of what
12 digital PCR is.

13 Q. And in the second sentence of
14 paragraph 47, the second sentence, Unlike
15 the comparative nature, you say, dPCR relies
16 on highly dilute samples that are divided
17 into partitions such as droplets, correct?

18 A. That is what it says, yes,
19 correct.

20 Q. What did you mean here by "highly
21 dilute samples"?

22 A. So digital PCR is a process
23 through which you are taking a sample, a
24 sample volume and then partitioning that
25 into smaller compartments, let's call them

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2 drops or droplets, wherein the goal is to
3 dilute the sample out to reduce the
4 concentration of targets in those droplets.

5 So highly dilute I think it is a
6 relative term, it depends upon the
7 concentration in the original sample volume.

8 Q. And then in the second sentence
9 you say specifically a sample is subjected
10 to limiting dilution prior to qPCR, correct?

11 A. That is what it says.

12 Q. Are you talking about digital PCR
13 in that sentence or qPCR?

14 A. No, we are talking about digital
15 PCR. In other words, if the sample which is
16 being subjected to digital PCR is diluted
17 limiting dilution, and then on that those
18 individual, let's say, droplets for the time
19 being, those are subjected to qPCR. So you
20 quantitate the fluorescence signal in each
21 individual droplet.

22 Q. What did you mean by limiting
23 dilution?

24 A. So limiting dilution is a
25 relatively standard term used across both

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2 PCR -- it is used in a wide variety of
3 techniques, whereby you are taking a sample
4 and then you are diluting that sample to the
5 point where in limiting dilutions you have a
6 preponderance, but not an exclusivity of
7 somewhere around one target per partition or
8 let's just say per droplet. So that's
9 limiting dilution. It is a technique you
10 use for monoclonal antibodies, it is used in
11 certain type of assays, it is used in
12 standard biological testing, where the goal
13 is to have a test that you conduct on a
14 partition of a larger sample that will give
15 you essentially a 1 or zero result.

16 Q. One or zero analyte in each
17 droplet?

18 A. That's the interpretation. I
19 mean, it is basically you are doing in this
20 particular case, it is a qPCR, so you are
21 looking at a response from that qPCR. Let's
22 just say it is fluorescence for right now,
23 and you are doing something like a TaqMan
24 reaction, whereby the fluorescence signal
25 that you are you getting is above the

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2 background and you would call that sample
3 positive. Because it is referred to as
4 digital PCR, it is frequently annotated with
5 1 and 0 to sort of reflect that digital
6 nature of the outcome.

7 Q. Got you. Limiting dilution, what
8 portion of droplets are empty?

9 A. That's hard to say. It is based
10 on the Poisson distribution, which is this
11 technique that is close to 200 years old,
12 right, Poisson French mathematician or
13 something like that, whereby he estimated
14 how much, when you dilute something down and
15 you have a certain mean. Let's just say you
16 are targeting one, so the mean is one, there
17 is a mathematical probability of something
18 containing 1 or something containing 2 or 3
19 or 4, 5, going on to infinity.

20 So Poisson distribution basically
21 reflects the probability of any particular
22 number of events happening. So I think your
23 question was how many would have -- what was
24 your question, sorry?

25 Q. Yes, what proportion of droplets

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2 would have zero?

3 A. So zero, so now you are looking at
4 the other end, right. Since we are dealing
5 with finite entities, we can't have point 1
6 or point 5, it has to be 1 or 0. And that's
7 hard to say, it depends on the distribution
8 itself. It depends on a variety of things.
9 So the answer to that is that is a question
10 that cannot be necessarily answered in
11 certain of an absolute sense.

12 Q. Okay, but some droplets would be
13 empty?

14 A. Certainly some droplets would be
15 empty, that is correct.

16 Q. And some droplets would contain
17 exactly one of the target analyte, correct?

18 A. That is correct. And some -- in
19 some absolutely finite small probability may
20 have a billion, that's just you can't
21 really --

22 Q. A billion analytes?

23 A. A billion, yes, it is not,
24 basically that Poisson curves asymptotically
25 reaches zero. But it never reaches zero.

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2 So in terms of probability, right. Sorry, I
3 am gesturing and that's not going to show
4 up. But you understand what I mean, in the
5 tail of that when you go from 1 -- is this
6 going to work, am I allowed to do this? As
7 you go from 1 to a billion, let's just say,
8 that curve reaches zero, but doesn't hit
9 zero.

10 Q. I understand. So is it fair to
11 say that most droplets under a limiting
12 dilution would be either empty or contain
13 one analyte?

14 A. That's hard to say, that would be
15 the goal under a limiting dilution. But
16 again, there is basically limiting dilutions
17 and terminal dilutions. So terminal
18 dilutions you are really trying to push that
19 mean down to zero. So by virtue of doing
20 that the probability of having zero is
21 higher than one. And go on as that tail end
22 of that curve is concerned, under limiting
23 dilutions you are trying to have at least
24 one there.

25 But again, you can't answer with

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2 absolute certainty, without knowing exactly
3 what the mean is, determining how many have
4 zero, how many have one, how many have, you
5 know, whatever.

6 Q. So I think what you said is that
7 in limiting dilution the goal is to have one
8 analyte?

9 A. The goal is to have the
10 preponderance of one analyte.

11 Q. And in terminal dissolution is the
12 goal to have zero analytes as a
13 preponderance?

14 A. That is correct.

15 Q. So terminal dilution is an even
16 more dilute regime than limiting dilution,
17 correct?

18 A. All things being equal that is
19 correct.

20 Q. Is it fair to say that it is very
21 rare to have a droplet that contains two
22 analytes in terminal dilution?

23 A. I am not sure what you mean by
24 rare, right. So not understanding what rare
25 is as a frequency -- if you are talking

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2 relatively, relatively then yes, terminal
3 dilutions would have more preponderance of
4 empty zero droplets as opposed to a limiting
5 dilution. But there is no, there is no
6 bright line demarcation between limiting and
7 terminal. Those are relative terms, and
8 those are goals that you try to achieve.
9 And it depends upon specifically what you
10 are trying to do, what that analysis is all
11 about.

12 Again, we are talking about
13 analytical techniques that range from sort
14 of standard microbiology to very complicated
15 systems where your analytical technique is
16 best or most efficient or most accurate when
17 you have a limiting or terminal number of
18 analytes in in the droplet.

19 Q. In paragraph 47 you indicate that
20 the Poisson distribution is an example of a
21 statistical technique, correct?

22 A. That is correct.

23 Q. Are there other statistical
24 techniques that you had in mind as when you
25 wrote this you said such as the Poisson

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2 distribution?

3 A. I think that such as was meant to
4 not exclude other things, but certainly the
5 Poisson distribution is a predominant
6 mathematical approach to doing these types
7 of dilutions. I shouldn't say doing them,
8 because it is basically a theoretical
9 analysis of the likelihood of a certain
10 number of analytes in a particular partition
11 or droplet.

12 Q. What other statistical techniques
13 would apply?

14 A. I don't have that information off
15 the top of my head. I am well familiar with
16 Poisson, and that is sufficient for what I
17 want to do.

18 Q. Why does digital PCR rely on
19 highly dilute samples?

20 A. So basically, okay, so a little
21 bit of historical context, when quantitative
22 or qPCR was first coming to practice let's
23 just say, there are limitations to that
24 technique because of competition between
25 primers and targets and also between

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2 products and primers. So the notion was
3 that at relatively low starting template
4 numbers, the system was much more efficient,
5 much more predictable. So the dynamic range
6 of any given assay was sort of limited by
7 that unpredictability, depending upon the
8 number of targets that were present. So in
9 digital PCR basically the notion was that
10 what you did was take your original sample
11 volume, divide that up into smaller, smaller
12 bites, if you will, smaller aliquots, if you
13 would, and analyze those individual aliquots
14 such that the results of an individual
15 aliquot droplet was much more accurate
16 reflecting what the initial number of
17 targets were in the sample.

18 Q. Paragraph 47 you also refer to an
19 image for the workflow for performing dPCR,
20 correct?

21 A. So we are talking about figure
22 2.7?

23 Q. Yes.

24 A. And that would be Exhibit 1038, I
25 assume, I am just reading what the

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2 annotation is here.

3 Q. Yes, that's the citation you
4 provide, correct?

5 A. Correct, what was your question
6 again?

7 Q. You say it is a workflow for
8 performing dPCR using Bio-Rad's droplet
9 based products; is that correct?

10 A. That is correct.

11 Q. Which Bio-Rad product is shown
12 here?

13 A. So basically there are -- well,
14 what do you mean by product?

15 Q. Well, you said products, droplet
16 based products?

17 A. Products. So I would consider the
18 products to be inclusive of what is shown in
19 A, B, C and D. A is simply, you know, the
20 reagents that are required for carrying out
21 this image. B is a droplet generator, so
22 that's actually what takes the original
23 sample volume and then divides that into
24 these droplets. Right, and that's shown
25 through that -- we have no visuals -- so

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2 that's shown in column B, if you would.

3 Column C is a standard
4 thermocycler, which basically carries out
5 the PCR amplification. So it goes through
6 thermocycling the reagents which are in A,
7 in each individual droplet, are collectively
8 amplified to give you end products, in this
9 particular case fluorescence.

10 And then finally in D is a reader,
11 so it is an instrument that will actually
12 read individual droplets and determine the
13 fluorescence intensity at different
14 wavelengths for each individual droplet.

15 And then finally at the bottom of
16 D, that column is a chromatogram, if you
17 would, or histogram of what the outcomes
18 look like. And you could barely see it, but
19 there are clusters which are represented as
20 different colors that represent the droplets
21 that have different colors. And I am going
22 to guess, because it is way too small to
23 see, maybe different intensities.

24 Q. And column B, it mentions the
25 QX200 for droplet generation, do you see

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2 that?

3 A. I am seeing QX00 -- oh, sorry,
4 give me that one time, column B?

5 Q. Yes.

6 A. Sorry I misunderstood you. I
7 thought you said column D. Column B, yes,
8 is this instrument called the QX200.

9 Q. That's a droplet generator?

10 A. That's a machine that will take
11 your original sample volume with your
12 reagents in there and generate droplets.

13 Q. And then column D is references
14 QX00, which product does that refer to?

15 A. I am assuming that refers to the
16 digital droplet reader.

17 Q. Could that be the QX200?

18 A. No, no. Those are certainly two
19 different instruments. QX200 is simply
20 there to generate droplets, the QX00 is what
21 reads the droplets.

22 Q. Step D, you said that's a droplet
23 reader, correct?

24 A. That is correct.

25 Q. And step D states fluorescence

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2 detection in each droplet using multiple
3 channels?

4 A. Where are you reading that from?

5 Q. That's the third step?

6 A. Oh, I see, sorry. Fluorescence
7 detection in each droplet using multiple
8 channels, that is correct.

9 Q. And I think you said the bottom
10 step of column D includes a chromatogram?

11 A. There is various terms that you
12 could use to refer to this chromatogram,
13 histogram, scatter plaque. It is
14 representing, you know -- so you can't see
15 it, right, because it is too small to be
16 representative. But each of those blobs of
17 color represent an individual droplet,
18 represents a collection of individual
19 droplets. So if you peer very closely you
20 will see little dots there, and those little
21 dots represent droplets that have either one
22 of a couple of different wavelengths, and
23 also they record the intensity of that
24 fluorescence.

25 Q. Is this plot here, is that

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2 something that is visualized using Bio-Rad's
3 software?

4 A. Yes.

5 Q. And I think you said the different
6 color regions, you can call them clusters?

7 A. Well, I am just saying that, you
8 know, if you are looking, for example, on
9 the top, right portion of that last little
10 graph there, there are a bunch of -- there
11 is a blob of, you know, I would say the
12 color is okra. And that blob of okra
13 represents individual droplets, so many
14 individual droplets.

15 Q. What does the black or dark-gray
16 cluster in the bottom, left of that plot
17 represent?

18 A. I am going to guess that's is
19 negative. So some estimate of those that do
20 not have any fluorescence.

21 Q. And is the blue cluster, is that a
22 cluster that is positive for an analyte?

23 A. That would be my interpretation of
24 it, yes.

25 Q. Would that be a single positive

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2 cluster?

3 MR. WALTER: Objection, calls for
4 speculation.

5 A. Can I ask what you mean by single
6 positive?

7 Q. Yes, it has one analyte in it?

8 A. I can't answer.

9 Q. How did you learn how to read this
10 type of plot?

11 A. A scatter plot?

12 Q. Yes.

13 A. I want to say when I was in
14 undergraduate. It is basically a
15 two-dimensional plot. It is a plot that is
16 used to look at two different things at the
17 same time. And what we are talking about is
18 discrete events that have no relationship to
19 one another. So in other words, it is not
20 something you draw a line through or put a
21 bar code bar or column graph. So it is
22 basically, it is again, you can't
23 individually resolve one drop at a time.
24 But this is a common, common technique used
25 to, again, analyze different events across

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2 two dimensions that each individual dot, if
3 you would, or analyte outcome, if you would.

4 You could say this is a plot of, I don't
5 know, height versus weight in the average
6 person or something like that. The answer
7 to your question is maybe not in high
8 school, but certainly when I was in
9 undergraduate, this is a common graphical
10 technique.

11 Q. But you were not reading graphs
12 that show the results of PCR tests in high
13 school or college, correct?

14 A. No.

15 Q. Let's look at step C or column C?

16 A. Yes.

17 Q. If you look at the caption down
18 below, figure 2.7 it says for column C
19 droplets with green were designated as
20 positive reaction and gray color as
21 negative, correct?

22 A. Oh, I see, you are reading in the
23 figure legend itself?

24 Q. Yes.

25 A. Green, gray, negative, yes,

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2 correct.

3 Q. So it says green is positive, and
4 those are droplets with an analyte, correct?

5 A. Those are droplets with a positive
6 reaction. The interpretation would be, and
7 it is probably easier with positive than it
8 is for negative, would be that that has one
9 or more analytes in it.

10 Q. And then the gray droplets, those
11 are the negative droplets, and it is meant
12 to indicate that there is no analyte in
13 those droplets, correct?

14 A. Not necessarily. It is for
15 whatever reason. So when you are doing
16 these, when you are doing droplet PCR,
17 basically your assumption is that both
18 analyte, reagents, primers, probe,
19 everything gets distributed, right. And it
20 is a pretty good assumption, but it is not
21 an absolute assumption. So all we are
22 saying here is that the reaction here for
23 anything that is gray is a reaction that did
24 not work, right. And the most likely
25 argument for that is that there was not an

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2 analyte molecule or target molecule, let's
3 call it a target molecule in that particular
4 droplet.

5 Q. And in this figure 2.7, is PCR
6 amplification performed in each of the
7 droplets individually?

8 A. What do you mean individually?

9 Q. Like each droplet has a separate
10 PCR reaction?

11 A. No -- well, again, define what you
12 mean by PCR reaction?

13 Q. You don't know what that means?

14 A. No, I am not sure what you mean.

15 Q. An amplification?

16 A. So in other words, so again, this
17 may be a difference in our relative
18 terminology here, so these are done in bulk,
19 right, so there is a tube sitting there with
20 droplets in there. Inside of each droplet
21 are primer, probe, other reagents, DNA
22 preliminaries and maybe or maybe not a
23 target molecule. Right, so the PCR reaction
24 which occurs in bulk in that tube occurs in
25 each of those individual droplets. And, you

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2 know, the point is, and I don't know what
3 the probability of this actually is, at any
4 point in time when you have a target
5 molecule and those reagents, again, it is an
6 exceptionally rare event, outside of a
7 droplet, but in the solution, that would
8 also amplify.

9 Q. And column B shows you automated
10 droplet generation by QX200, correct?

11 A. That is correct.

12 Q. And you said that's a droplet
13 generator?

14 A. That is what it says, yes, it says
15 automatic droplet generator.

16 Q. Step B also shown samples
17 separated into 20,000 droplets, correct?

18 A. Yes.

19 Q. And there are nine droplets shown
20 where it says that in column B?

21 A. This artistic rendition shows nine
22 representative droplets.

23 Q. And it is pretty small, but the
24 green line within those droplets, it says
25 target of interest, do you see that?

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2 A. Oh, God, you are pressuring my
3 69-year-old eyes. It says target of
4 interest, and then it says background DNA.

5 Q. Which is the blue line, right?

6 A. That appears to be what is going
7 on there.

8 Q. And then some of the droplets
9 include one, two or three pieces of
10 background DNA, correct, the nine droplets
11 that are shown there?

12 A. So, again, this is an artistic
13 representation, right, this is not a
14 statistical analysis of the 20,000 drops
15 that one in 11 percent would be one thing.
16 This is just a representation to show you a
17 limited range of the possibilities.

18 So with that in mind, if I am
19 looking at this thing, I see some background
20 DNA, the top, let's call it number 1, top
21 left is -- correct me if I am wrong, it
22 looks like there is one background?

23 Q. Yes.

24 A. The second one is maybe one target
25 and one background, the third one is three

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2 background, the fourth one, so second row,
3 column 1, is three targets. And then --
4 anyways, so.

5 Q. So the droplets that contain a
6 target of interest, if the PCR is successful
7 or accurate, those would be positive
8 droplets, correct?

9 A. So in theory, and I would not say
10 every single one, but yes, in theory, the
11 goal is where there is a target of interest
12 as referred to here, those primers and
13 probes specifically against that target of
14 interest would generate a green fluorescence
15 signal.

16 Q. And that would be the same as the
17 green droplets shown in step C, correct?

18 A. That is correct.

19 Q. Which cluster in step D in the
20 plot would those droplets correspond to?

21 A. I am not able to answer that,
22 because I am not sure -- I didn't draw that
23 last -- I didn't draw this figure, right. I
24 assembled this figure, but I didn't draw
25 individual components of this figure, so I

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2 am not exactly sure what the artistic
3 translation of -- because obviously there is
4 more than one color in that last scattergram
5 or chromatogram. But I am not sure exactly
6 whether the simplistic answer would be that
7 the green dots or green droplets refer to
8 the green cluster in the lower right hand.
9 But there is clearly an artistic
10 representation here, because nowhere -- and
11 I called this okra, I apologize, nowhere
12 here is okra accounted for in the color
13 scheme.

14 Q. Okay. And then going back to step
15 B, the nine droplets we were talking about,
16 one of them contains neither target of
17 interest or background DNA, correct?

18 A. So yes, in column 3, of the nine
19 droplets column 3, row 2, it appears as
20 though that particular droplet is empty, or
21 doesn't contain -- I shouldn't say empty, it
22 doesn't contain a target of interest or
23 background DNA.

24 Q. So if the PCR is accurate, that
25 droplet would be negative, correct?

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2 A. So, you know, there is various
3 reasons why you get fluorescence
4 amplification with qPCR. And sometimes in
5 the early stages of any assay development,
6 PCR primers will generate spontaneous, let's
7 just call it, false positive signals. So
8 assuming that this represents a final,
9 optimized working assay, that is correct.
10 But in the development of that assay, there
11 is certainly a possibility that even an
12 empty droplet -- obviously this is something
13 you go back through, you optimize, you
14 improve on the primers and you improve on
15 the probes and you try to eliminate those.

16 So again, assuming this represents
17 an assay that works and works well, then
18 yes. The negative, the empty droplets
19 should not generate any color whatsoever,
20 again, let's just leave it at that.

21 Q. And going back to column A, here
22 in figure 2.7, the caption says, These are
23 the ddPCR reaction mixtures that are
24 prepared, ddPCR reaction mixture, correct?

25 A. That is correct.

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2 Q. And the mixture is prepared in
3 tubes?

4 A. You could prepare them in a
5 variety of vessels. In this particular case
6 what we are looking at is micro-centrifuge
7 or what we call Eppendorf tubes. So yes,
8 these would be -- assuming, if this was a
9 commercial product, that would be part of a
10 kit. And those represent the important
11 components of a kit that you would use to
12 carry out digital PCR.

13 Q. And the kit includes a template,
14 primers, probes and ddPCR reaction mix; is
15 that correct?

16 A. That's typically what you see in a
17 product or in a kit, yes, you would keep
18 these all separate, because they are all
19 prepared separately. You have various
20 probes, various primers and your template is
21 what you are starting off with. You know,
22 generically the ddPCR mix is probably pretty
23 uniform across that, but you want to be able
24 to swap in difference probes, different
25 primers.

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2 Q. Basically you mix in different
3 primers with different probes and you get
4 the ddPCR reaction mix; is that correct?

5 A. That is correct, yes. What is not
6 illustrated here, now that you pointed out,
7 there are other reagents. So it is not just
8 templates, primers and probes, but you
9 require DNA preliminaries, you require
10 magnesium, you require other sorts of
11 components, which are, again, as part of
12 that kit, it would be one of the things in
13 that series of tubes.

14 Q. And then do you know if the kit is
15 a Bio-Rad kit?

16 A. Well, this is a Bio-Rad figure.
17 So my assumption is that their system is
18 primarily designed to work with -- I can
19 imagine where an individual might generate
20 some of this. And certainly, again, if it
21 is kit specific for a given analyte, that is
22 one thing, if I am as a researcher
23 developing my own type of assay, I would
24 probably come to the laboratory with one or
25 more of those components that I assembled

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2 myself. But again, it is part of what I
3 would call a kit, which is basically the
4 various things we need to do PCR reactions.

5 Q. So when preparing, when mixing
6 these things together in step A, would the
7 user control the concentration of the
8 components to obtain what is referred to in
9 column C as low concentration, medium
10 concentration or high concentration?

11 MR. WALTER: Objection, vague,
12 incomplete hypothetical.

13 A. Yes, so the answer is that where
14 you are seeing low concentration, medium
15 concentration or high concentration, my
16 interpretation of this figure or what it is
17 trying to present is what the initial
18 concentration of template is in the original
19 sample volume. Again, it depends on where
20 you are. If you are a researcher using
21 digital PCR to develop a new assay, you
22 would be optimizing probes, primers, all
23 these sorts of different elements to get a
24 robust assay, right, one that was accurate
25 and gave the anticipated results.

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2 Now if I am then buying a kit,
3 let's just say from Bio-Rad, whatever kit,
4 then the expectation is that all of those
5 components in column A are already
6 determined, and I am looking at a recipe
7 that will tell me exactly what to do.

8 Q. Under what circumstances would the
9 recipe result in low concentration?

10 A. Well, the concentration depends
11 upon the initial concentration of target
12 molecules, target of interest as it is
13 called here, in the original sample volume.

14 So there is two ways to view that,
15 one is that I have no idea, right. And
16 there is a certain dynamic range in these
17 assays. So you don't have to hit a specific
18 concentration. The assay has a certain
19 dynamic range that allows you to look at
20 concentrations, let's say from -- I am just
21 making this up and not giving you units --
22 let's say ten to a thousand, and I don't
23 know where I am in that, because it is an
24 unknown sample. That particular case, you
25 know, I wouldn't necessarily know it, maybe

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2 I would have to go back, based upon the
3 results, to further dilute the sample,
4 because I have no empirical way of
5 determining the initial target of interest
6 concentration of my sample through something
7 other than doing the assay itself. So I may
8 wind up with a result in column D that may
9 be beyond the dynamic range, and I have to
10 go back and further dilute the original
11 sample.

12 And again, that's, you know, it
13 depends upon the sample itself. And it also
14 depends on what I am trying to accomplish,
15 right. If I am just simply trying to ask
16 the question, does this sample have anything
17 in there, right, versus does this sample
18 have between a thousand and ten thousand, as
19 sort of an arbitrary range.

20 Q. So here in column C, the low
21 concentration, in the low concentration the
22 proportion of multianalyte droplets to the
23 total number of droplets would be very low,
24 correct?

25 A. So if what you are saying is that

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2 in low concentrations, again, with the
3 Poisson distribution in mind, there is a
4 probability of having more than one, is it
5 lower, yes, the answer is yes.

6 Q. And in the medium concentration,
7 the probability of a multi-target molecule
8 droplet is higher than it is at the low
9 concentration; is that correct?

10 A. That is correct. The Poisson
11 distribution is based on the mean number of
12 let's just say targets of interest in a
13 droplet as an example. So that's the mean
14 number. So obviously as the mean goes up,
15 then the probability of those having more
16 than one goes up.

17 Q. And it goes up for high
18 concentration even further; is that correct?

19 A. That would be a simplistic, but
20 relatively accurate interpretation.

21 Q. Is it fair to say that the high
22 concentration scenario here would be
23 significantly more concentrated than would
24 occur under limiting dilution?

25 A. Could you repeat that, I am not

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2 sure what you are asking.

3 Q. Yes, which of the scenarios, low
4 concentration, medium concentration and high
5 concentration, which of those corresponds to
6 limiting dilution?

7 A. So limiting dilution, again, is
8 where your target goal is to have an average
9 of 1 per droplet, right. So I am not sure
10 what you are asking. And again, you may
11 carry out limiting dilutions or you may
12 carry out terminal dilutions depending on
13 how you set up the instrument in column B.

14 Q. But can you tell from column C
15 which scenario is limiting dilution?

16 A. So my assumption here is that this
17 process and this mechanism is set up for,
18 and I don't know off the top of my head
19 whether it is set something up for limiting
20 dilution or terminal dilution. But there is
21 no reason to believe that you would suddenly
22 say, oh, I want to do limiting dilution for
23 this one, I want to do terminal dilution for
24 this one, that the low, medium and high
25 concentrations represents a difference in

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2 the type of dilution you are doing.

3 It is more based upon outcome,
4 what the goal of the assay to do -- what the
5 goal of the assay is.

6 MR. GILL: I think it has been
7 about an hour, why don't we take a
8 quick break.

9 (Whereupon, a short recess was
10 taken.)

11 Q. Here you go, sir. Dr. Batt, I
12 have handed you Exhibit 1017 from the IPR.
13 This is the Larson patent publication; is
14 that correct?

15 A. That is correct.

16 Q. And this is the Larson publication
17 that's part of your declaration?

18 A. That is correct.

19 Q. Throughout your declaration you
20 describe Larson as forming sample droplets;
21 is that correct?

22 A. Yes.

23 Q. And you describe Larson as
24 performing dPCR in droplets to generate
25 amplified products; is that correct?

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2 A. You do you want to refer to a
3 specific passage in my declaration.

4 Q. Sure, so for example, paragraph
5 78.

6 A. Sorry, can you repeat your
7 characterization -- sorry, your question?

8 Q. You describe Larson as performing
9 dPCR in droplets to generate amplified
10 products; is that correct?

11 A. So I don't see the phrase "dPCR"
12 used. What I see is Larson discloses
13 forming sample droplets where some of the
14 droplets contain zero.

15 But as far as your using the word
16 "digital" in that paragraph, I am not seeing
17 correct me if I am wrong, the word
18 "digital."

19 Q. Yes, but it describes PCR,
20 correct?

21 A. So the word "PCR" is used, and
22 yes, it does describe using PCR.

23 Q. A droplet generating amplified
24 products and droplets, it is the last
25 paragraph of 78?

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2 A. So PCR is then conducted within
3 the merged droplets to generate amplified
4 products, that's what it says.

5 Q. Then if we go to paragraph 44 of
6 Larson.

7 A. Okay, I have paragraph 44.

8 Q. Larson teaches performing PCR
9 reactions in aqueous droplets that are
10 separated from each other by oil; is that
11 correct?

12 A. It says, In the preferred
13 embodiment of the invention digital PCR is
14 performed in aqueous droplets separated by
15 oil, your question was is that what it says,
16 and that's what it says.

17 Q. Okay. Paragraph 44 of Larson also
18 talks about reaction compartmentalization
19 for dPCR?

20 A. The last sentence, is that what
21 you are referring to?

22 Q. Yes.

23 A. Yes, reaction compartmentalization
24 for dPCR.

25 Q. And are droplets a form of

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2 reaction compartmentalization for dPCR?

3 A. Okay, digital or droplet, digital,
4 okay.

5 Q. So the question was are droplets a
6 form of reaction compartmentalization for
7 dPCR or digital PCR?

8 A. Yes.

9 Q. Are the droplets used in dPCR
10 important to Larson's invention?

11 MR. WALTER: Objection, vague.

12 A. Yes. Can you give me a little
13 more clarification by what you mean by
14 important?

15 Q. It means the focus of the
16 reference, correct?

17 A. Well, in the claim language the
18 term "microdroplet" is used repeatedly. And
19 so it is part of the claim language. So is
20 it important, I would say yes.

21 Q. Larson teaches collections of
22 droplets, correct?

23 A. Can you give me a specific?

24 Q. Sure, we could look at figures 2
25 and 3, for example?

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2 A. So figure 2 is with a portion of
3 the droplet generator, and what was the
4 other figure you are asking me about?

5 Q. 3.

6 A. So 3, so 3C is actually part of
7 the analysis system, right.

8 Q. It shows droplets in figure 3,
9 right?

10 A. So the question is are the little
11 piecer here droplets?

12 Q. Yes.

13 A. That's your question?

14 Q. Yes.

15 A. Yes, they are.

16 Q. So Larson teaches collections of
17 droplets; is that correct?

18 A. What do you mean by collections?

19 Q. Just a number of droplets?

20 A. You are analyzing a number of
21 droplets, that's correct.

22 Q. And in Larson is it true that PCR
23 reactions are individually performed in each
24 of those droplets?

25 A. In other words, do the droplets

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2 segregate a PCR in one droplet from a PCR in
3 a second droplet?

4 Q. Correct.

5 A. Yes.

6 Q. And in each of those droplets, as
7 a result of the PCR, amplicons are
8 generated; is that correct?

9 A. Again, it depends on what is in
10 the droplet.

11 Q. If there is a target molecule?

12 A. If there is a target of interest,
13 if there are primers there, so if you are
14 asking, you used the specific word
15 "amplicon," right?

16 Q. Yes.

17 A. So the amplicon is simply the
18 product of the reaction doesn't necessary
19 mean it is fluorescence. So you are asking
20 me simply is an amplicon, is a PCR
21 amplification product produced in a droplet,
22 yes, provided it has a target of interest,
23 provide it has primers, provided it has DNA
24 preliminaries and a couple of other
25 associated factors.

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2 Q. Is it fair to say that using
3 fluorescent probes during PCR generates a
4 signal?

5 A. Not necessarily.

6 Q. Why not?

7 A. Well, again, in most cases the
8 fluorescent signal is generated based upon a
9 reaction called TaqMan. So the probes in
10 and of themselves don't necessarily have
11 fluorescence associated with them. And in
12 TaqMan PCR, if you would, the probe has a
13 quencher and fluorophore, and those are
14 released.

15 So in most of these figures this
16 is shown in a rather simplistic manner. But
17 the fluorescence is typically only generated
18 when the PCR process continues and the
19 amplicon, to use your phrase, is generated.

20 Q. Does that generate a signal?

21 A. Yes, if the droplet contains a
22 fluorescently labeled probe and the target
23 there is specific for that fluorescently
24 labeled probe, then, yes, it would.

25 Q. And would that signal in Larson be

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2 individually obtained from each of the
3 droplets?

4 A. Again, it depends upon if there is
5 a target there.

6 Q. But if there is, then it would,
7 right?

8 A. The probability is high, you know.
9 Would any individual droplet out of a
10 million fail for a variety of other reasons?
11 For example, the droplet might lyse, might
12 sort of release its contents, it might
13 through some rare events not have any
14 primers there, it might be not have any
15 probe there.

16 Q. So figure 3C, if we look at figure
17 3C of Larson, it shows a laser emitted, and
18 the laser goes through a droplet and then
19 comes out the other side of the three
20 arrows, do you see that?

21 A. So figure 3C is basically a flow
22 fluorimeter. So what you are doing is on
23 the left-hand side these are all these
24 droplets piling up, it flows through that
25 little junction there, and the droplets are

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2 separated, then the laser excites at a
3 particular wavelength. And then if there is
4 a fluorescent molecule there, a fluorophore,
5 then you get an emitted light, so you
6 excite, you get an emitted light at a
7 specific wavelength. And there is a little
8 bit of scattering, which is what those three
9 arrows is meant to portray. And then the
10 thing that looks like a little eyeball is a
11 detector and detects the fluorescence.

12 Q. For each droplet, correct?

13 A. If the system is working properly,
14 yes, it should. Non other words, as
15 demonstrated in figure 3C, you are basically
16 separating those droplets out into
17 individual entities with a little bit of
18 space between them, then yes, that flow
19 fluorimeter should detect individual
20 droplets.

21 Q. Each droplet constitutes its own
22 PCR reaction volume; is that correct?

23 A. I am not sure what you mean by
24 individual PCR reaction volume. I would say
25 each individual droplet is an individual

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2 droplet.

3 Q. In which PCR reaction occurs; is
4 that correct?

5 A. So the PCR reaction, again, it
6 could in theory occur outside the droplet.
7 There is nothing specific about it that the
8 droplet is there to basically contain the
9 reaction products and the fluorescence, so
10 it stays there as opposed to diffusing away.
11 The answer to your question is yes, inside
12 that droplet PCR is occurring.

13 Q. And each droplet is its own
14 individual volume, right?

15 A. I don't understand what you mean
16 by volume. Each droplet --

17 Q. Is a volume of liquid?

18 A. So in each droplet there are
19 contents. Those contents obviously have a
20 specific volume. But I am not sure what you
21 mean by your term, because it doesn't
22 intuitively make sense to me.

23 Q. The contents of each droplet are
24 in an aqueous solution that is separated
25 from the other droplets by oil; is that

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2 correct?

3 A. So let's clarify what the droplets
4 actually are. So the droplets have a
5 surrounding -- so the droplets, it is not
6 simply an oil in water -- I am sorry, a
7 water in oil, let me clarify that, it is not
8 simply a droplet of water. It is surrounded
9 by a variety of different polymers that help
10 retain the integrity of the droplet itself.

11 Q. To keep them separate?

12 A. To keep them -- it is not so much
13 separate, because it doesn't necessarily --
14 the oil is what keeps them separate. But
15 the polymers that form the surface of the
16 droplet itself are what keeps the droplet,
17 the integrity of the droplet.

18 In other words, if you want to
19 think about soap bubbles, right, so soap
20 bubbles really, a bubble of air in air,
21 well, the bubble itself is a component of
22 soap, and that's what forms the bubble. So
23 you can think of an analogous thing, that
24 there is a molecule that forms the surface
25 of that droplet and keeps that droplet

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2 intact.

3 Q. Let's go back to your declaration,
4 paragraph 187. And at this point in your
5 declaration you are discussing Larson's
6 teaching regarding limiting dilution,
7 correct?

8 A. So it starts off by additionally
9 Larson teaches a Poisson distribution of
10 analytics, and later on it goes to talk
11 about limiting dilution.

12 Q. And in limiting dilution,
13 according to Larson's summary, some
14 reactions contain zero DNA molecules, some
15 contain one molecule and frequently some
16 contain multiple molecules following the
17 Poisson distribution, right?

18 A. Where specifically? Are you
19 paraphrasing?

20 Q. You quoted a block of Larson from
21 paragraph 6, it is in paragraph 187 of your
22 declaration?

23 A. Okay, I got that. Sorry, what was
24 your question again?

25 Q. It is okay. I want to actually go

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2 back to what we were talking about before
3 regarding droplets and droplets being
4 separate from each other I think is what I
5 was asking just a minute ago?

6 A. Sure.

7 Q. Would you interpret Larson as
8 teaching performing PCR in a larger single
9 sample volume that is partitioned into
10 droplets after the PCR takes place?

11 MR. WALTER: Objection, vague.

12 A. If you want to point to something
13 specific in Larson that you want me to
14 respond to.

15 Q. No, just overall?

16 MR. WALTER: Same objection.

17 A. Sorry, I am --

18 Q. Would you interpret Larson as
19 teaching performing PCR in a larger volume
20 that is then partitioned into droplets after
21 the PCR takes place?

22 MR. WALTER: Objection, vague.

23 A. So in Larson you are basically
24 starting off with a larger sample volume,
25 you are forming droplets from that larger

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2 sample volume, you are then as an aggregate
3 taking those droplets and analyzing those.

4 Q. And doing PCR on each droplet?

5 A. Yes, so what I mean by analyzing
6 is again doing polymerase chain reaction
7 with a fluorescence outcome or fluorescence
8 output, yes.

9 Q. So in paragraph 187 of your
10 declaration you talk about the Poisson
11 distribution and Larson's teachings
12 regarding limiting dilution and terminal
13 dilution, do you see that?

14 A. The term terminal dilution is used
15 and the term limiting dilution is also used.

16 Q. And Larson teaches that at
17 terminal dilution the vast majority of
18 reactions contain either 1 or zero target
19 DNA molecules, correct?

20 A. Correct, that is what it says and
21 that is what I wrote.

22 Q. The way that Larson uses limiting
23 and terminal dilution, is that consistent
24 with how a person of ordinary skill in the
25 art would understand those terms?

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2 A. So those are sort of common terms.
3 The question is, and it is exemplified here,
4 what do you mean by vast majority. So it is
5 basically a degree of dilution whereby the
6 terminal dilution is the vast majority,
7 paraphrased that, and limited dilution said
8 some reactions. So you know, obviously
9 neither the "vast majority" nor "some" has
10 an absolute quantitative interpretation.

11 Q. But in terms of the qualitative,
12 is that how a POSITA would have understood?

13 A. Yes.

14 Q. And again, in paragraph 187 under
15 the block quote, you say Larson also
16 specifically teaches using its assays at
17 limiting dilution and you cite to Larson
18 paragraph 45, correct?

19 A. That is correct.

20 Q. Let's look at paragraph 45 of
21 Larson. Starting off Larson says, Methods
22 of the invention for multiplexing dPCR
23 assays promise greater plexity the number of
24 simultaneous reactions than possible with
25 existing --

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2 A. I am sorry, you are reading, am I
3 missing something? It is 45. Oh, I see,
4 sorry.

5 Q. Promise greater plexity than the
6 number of the simultaneous reactions than
7 possibly with existing qPCR or dPCR
8 techniques, correct?

9 A. Correct, that's what it says.

10 Q. And when Larson talks about
11 increasing plexity in paragraph 45, what he
12 means is increasing the number of
13 simultaneous reactions is that correct?

14 A. "Plexity" is not a term that I
15 frequently, if ever, encounter. But I would
16 say that that's a reasonable, in other
17 words, what Larson is trying to teach and
18 what this method is trying to accomplish is
19 looking at a greater degree of target
20 molecules.

21 Q. And Larson in paragraph 45 goes on
22 and he says it, but I think he is referring
23 to the invention is based on the singular
24 nature of amplifications at terminal or
25 limiting dilution that arises because most

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2 often only a single target allele is ever
3 present in one droplet even when multiple
4 primers/probes targeting different alleles
5 are present, correct?

6 A. That is what it says.

7 Q. Alleles is A-L-L-E-L-E, correct?

8 A. As the spelling, yes, sir.

9 Q. Then in paragraph 45 says that
10 this alleviates the complications that
11 otherwise plague simultaneous competing
12 reactions, correct?

13 A. That is what it says.

14 Q. And when that sentence says
15 "this," it is talking about the previous
16 sentence, correct?

17 A. Well, it is talking about the
18 invention and the approach propose of the
19 invention and doing either terminal or
20 limiting dilutions.

21 Q. Larson alleviates the
22 complications of simultaneous reactions by
23 having only a single target allele per
24 droplet, correct?

25 A. Yes, so the problem in PCR in

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2 general is that when you have multiple
3 events going on, they obviously, not they
4 obviously, but they can compete for one
5 another and the products of those reactions.
6 So the more simplistic, the lower the number
7 of targets you have in a sample, the less
8 likely it is that those competing reactions
9 would cause problems.

10 Q. That's what Larson teaches, right?

11 A. Yes. And it goes on, there is a
12 curious term here using such as varying
13 arrival times. That has to do in PCR
14 reactions, if you are measuring
15 fluorescence, there is a lag phase. And
16 then at some point, after a number of
17 cycles, it goes into an exponential phase.
18 So that's I think what he meant by this
19 varying arrival time. So the fluorescence
20 basically starts to increase above a
21 threshold. In sort of the old-schooled
22 quantitative PCR that number of cycles, what
23 he is calling the arrival time, was
24 basically used as a means of quantifying the
25 number of the initial target molecules. The

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2 greater the number of target molecules, the
3 earlier the reaction occurred or the lower
4 the number of cycles it required to get
5 above that threshold. So that's what he is
6 talking about.

7 Q. In for example, paragraph 7 of
8 Larson, Larson it is the second sentence,
9 Larson says the invention provides a droplet
10 that contains a nucleic acid template,
11 correct?

12 A. I am sorry, you said paragraph 7?

13 Q. The second sentence?

14 A. In one aspect.

15 Q. Yes, in one aspect the invention
16 provides a droplet that contains a single
17 nucleic acid template, correct?

18 A. Yes, that is what it says.

19 Q. And in paragraph 8 the first
20 sentence says the ability to amplify and
21 detect single nucleic acids in droplets
22 enables digital PCR, correct?

23 A. That is what it says, yes.

24 Q. And then about halfway down the
25 paragraph on page 1 of Larson, there is a

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2 sentence that starts on the right-hand side
3 of the column, even though, do you see that?

4 A. Yes, even though the number of
5 PCRs.

6 Q. Yes, Larson says there is only one
7 template molecule per droplet, correct?

8 A. Well, I think that's an
9 aspirational statement.

10 Q. That's what Larson was trying to
11 do?

12 A. Well, correct. It doesn't mean
13 that every droplet has to contain just one
14 template, right. That's the aspirational
15 goal. In a perfect world you would
16 mysteriously be able to accomplish that when
17 you are doing either limited or terminal
18 dilutions. In terminal dilutions you are
19 further diluting it out, you have zero to 1,
20 in limiting dilutions the predominance is 1.
21 So this is an aspirational statement that
22 says you should have just one. But it
23 doesn't mean that the PCR reaction doesn't
24 occur if you have more than one. It
25 certainly doesn't occur if you have less

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2 than one, meaning zero.

3 And you know, this statement about
4 primer pairs is sort of obvious, the
5 concentration of primer pairs is always
6 there in excess of 1, actually, far in
7 excess of 1. So in other words, the whole
8 reaction is not limited by anything other
9 than the number of template molecules or
10 whether a template molecule is there or not.

11 Q. Okay, I want to look at paragraph
12 19 of Larson.

13 The first sentence describes
14 implementations of Larson's invention,
15 right, the first sentence of paragraph 19?

16 A. Give me a second. So 19 you are
17 saying. Okay, go ahead.

18 Q. So Larson says, its method is for
19 compartmentalizing a first fluid into
20 portions, each portion containing a single
21 target nucleic acid, correct?

22 A. That is the aspirational
23 statement, yes.

24 Q. That's what Larson was trying to
25 do?

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2 A. That's an aspirational statement,
3 yes.

4 Q. Let's go to paragraph 188 of your
5 declaration, in this paragraph you are
6 suggesting that paragraph 121 and figure 9,
7 9C of Larson disclosed how Larson's assays
8 work, quote, to detect multiple analytes in
9 a single droplet, correct?

10 A. So I am seeing specifically in
11 figure the 9 of Larson, give me a second
12 here. So figure 9 is basically a series of
13 four figures, right, A, B, C and D discloses
14 using two probes, P1.

15 Q. I am really just talking about
16 paragraph 188 of your declaration?

17 A. That's what I am reading. It says
18 Larson discloses an assay of two probes, P1
19 and P3, so figure 9A, and they have
20 different intensities, correct.

21 Q. And you cite paragraph 121 as
22 well?

23 A. And I cite paragraph 121 as well.
24 So bear with me.

25 So paragraph 121 describes what is

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2 going on in figure 9 and it describes -- so
3 paragraph 121 is basically a text narrative
4 that describes figure 9A, B, C and D.

5 Q. Sure. And that's the paragraph
6 you cite to support your statement that
7 Larson discloses detecting multiple analytes
8 in a single droplet, in paragraph 121 of 188
9 of your declaration, correct?

10 A. So figure 9A, B, C and D describe
11 the process for how you lay out the
12 different probes, how you laser interrogate
13 the different droplets, how you analyze the
14 fluorescence intensity of those different
15 droplets and finally a histogram or
16 chromatogram of basically the results, yes.

17 So the answer to your question is
18 does what I have written in 118 describe
19 this figure 9A and paragraph 121, yes.

20 Q. So in paragraph 188 you say that
21 in figure 9 the second sentence, in figure 9
22 Larson discloses an assay using two probes,
23 P1 and P3, labeled with the same color
24 labels, but of different intensity, correct?

25 A. That is correct.

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2 Q. And you state that in figure 9
3 Larson discloses probe P2 as labeled with a
4 different color label, correct?

5 A. Yes, yes.

6 Q. Let's go to paragraph 121 of
7 Larson. And on page 13 towards the end of
8 the paragraph, on page 13 of Larson it says,
9 Microdroplets containing target sequence 1
10 or 3 emit fluorescence of color 1 at two
11 different intensities, correct?

12 A. Correct.

13 Q. And it says microdroplets
14 containing target sequence 2 emit
15 fluorescence of color 2, correct?

16 A. That is what it says, correct.

17 Q. So here Larson refers to
18 microdroplets containing target 1 or target
19 2, correct?

20 A. I am not sure I understand what
21 you are asking. You know, I would have
22 to -- if you give me a moment, but I don't
23 necessarily think it specifically talks
24 about -- no, sorry, you are right. So
25 microdroplets containing target 1 or target

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2 3, but what was your question?

3 Q. I said 1 or 2, I meant 1 or 3, it
4 is 1 or 3, correct?

5 A. So it says microdroplets
6 containing target sequence 1 or 3.

7 Q. That's what I was asking?

8 A. Emit fluorescence, yes.

9 Q. And then Larson separately refers
10 to droplets containing target 2, correct?

11 A. Correct.

12 Q. And then the last sentence of
13 paragraph 121 Larson states the number of
14 microdroplets containing target 1, 2 or 3 is
15 shown by histogram in panel D, correct?

16 A. That is correct.

17 Q. Here Larson refers to
18 microdroplets containing target 1, target 2
19 or target 3, correct?

20 A. Correct.

21 Q. Larson doesn't say any of the
22 microdroplets contain target 1, 2 and 3,
23 correct?

24 A. No. I think, first of all, Larson
25 doesn't know what is in the droplet, right.

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2 He doesn't have this separate analytical
3 eye. What he is recording is the
4 fluorescence. So the outcome is the
5 fluorescence, that's what he is reporting
6 on, that's what he is plotting on histogram
7 9D.

8 Q. And the fluorescence is either
9 target 1 or target 2 or target 3, correct?

10 A. Well, you know, first of all, a
11 histogram, and this is a bad copy of it,
12 right, so let's just appreciate that for the
13 moment. But it doesn't say what is going on
14 in every single droplet. Right, you can't
15 say there is not a droplet -- so, okay,
16 figure 9, this histogram, this chromatogram
17 is basically plotting the fluorescence
18 intensity from two different fluorophores,
19 one is called VIC, the other one is called
20 FAM. So what you can visually see here are
21 clusters of droplets. So for example, the
22 one that is somewhere around 25 on the FAM,
23 140 or so on the VIC is one particular
24 outcome. On the FAM side, again, you have
25 droplets. So that's where the clusters are.

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2 It doesn't mean that there is not a droplet
3 somewhere, because the instrument will not
4 or this result, this histogram will not
5 necessarily portray every single droplet.

6 Q. Right, it only portrays droplets
7 with one target in figure 9D?

8 A. No, all I can see here from this
9 histogram are those clusters of droplets.
10 There may be a droplet floating around at
11 250, let's say a FAM, let's pick up what
12 appears to be a blank level, 125 on the FAM,
13 125 on the VIC, right, it looks pretty blank
14 to me, does that mean there is no droplets
15 there? I don't know.

16 Q. You don't know?

17 A. No, you don't know, right, because
18 the analysis of the original sample volume
19 is dependent upon these clusters.

20 Q. Right, and those clusters, Larson
21 explains, he says, Four populations of
22 droplets with target 1, with target 2, with
23 target 3 and without any of the three
24 targets, that's what he says, correct?

25 A. Right. And the operative word

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2 there is "populations." He doesn't say
3 droplets.

4 Q. Populations of droplets?

5 A. Populations, right.

6 And the interpretation of
7 populations, let me just clarify, are these
8 clusters.

9 Q. Okay?

10 A. So he is not accounting for --
11 what you can see here is not every single
12 droplet.

13 Q. And in paragraph 121, the last
14 sentence, Larson doesn't say anything about
15 microdroplets containing targets 1, 2 and 3,
16 does he?

17 A. Containing all three of them, is
18 that what you are asking?

19 Q. He doesn't say that, correct?

20 A. He doesn't account for those, he
21 doesn't say that per se. It doesn't mean
22 that they don't exist.

23 Q. I am just asking what he says in
24 this paragraph?

25 A. Sure.

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2 Q. And you doesn't say that any
3 droplets contain targets 1 and 2, correct?

4 A. He doesn't say that they don't
5 exist. You know, again, he is referring to
6 these populations, not necessarily every
7 single microdroplet.

8 Q. And he doesn't say anything about
9 microdroplets containing targets 1 and 3,
10 correct?

11 A. Again, I will come back and repeat
12 what I just said, it doesn't mean that they
13 don't exist. He is simply focusing, as you
14 do in these analyses, focusing in on the
15 populations of those particular singular
16 events. But it doesn't mean that there
17 isn't droplets that contain 1, 2 and 3, 1
18 and 2, 1 and 3, 2 and 3.

19 Q. But you can't tell from figure 9D
20 whether those droplets exist?

21 A. So I do not have powerful enough
22 eyes to look at this histogram and find
23 individual droplets.

24 Q. And Larson doesn't mention it in
25 paragraph 121, correct?

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2 A. Again, because he is focusing in
3 on populations of droplets. It doesn't mean
4 that they don't exist.

5 Q. But Larson doesn't say anything
6 about more than the four populations, he
7 only mentions the four, target 1, target 2
8 or target 3 or no targets, correct, four
9 populations?

10 A. Because he is talking about
11 populations, yes. But again, let me
12 emphasize that it doesn't mean that droplets
13 do not exist in targets 1 and 3, 2 and 3 or
14 1 and 2 or any combinations thereof.

15 Q. Let's go to paragraph 82 of your
16 declaration. And here again you are talking
17 about Larson, and you have a big block quote
18 to paragraph 139 of Larson, correct?

19 A. Correct.

20 Q. And in that quotation that you
21 included, among other things, it says,
22 Single droplets might contain four different
23 probes for measuring four different targets,
24 correct?

25 A. Are you paraphrasing?

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2 Q. It is the first sentence.

3 A. For example, a single droplet
4 might contain four different probes
5 measuring four different targets, that is
6 correct.

7 Q. And then the third sentence of
8 that quotation says, The corresponding
9 targets are T1, T2, T3, and T4 for A1, A2 B1
10 and B2?

11 A. That is the coding scheme,
12 correct.

13 Q. Those are probes?

14 A. No, no.

15 Q. Colors?

16 A. You know, I am not sure what his
17 reason for translating these things are.
18 Maybe it has to do with some reference to
19 some other figure. The targets he is just
20 calling T1, T2, T3 and T4. And let's just
21 argue that I think in this particular case
22 he is talking about alleles, so there is two
23 pairs of alleles. The first pair is A1 and
24 A2, and the second pair is B1 and B2. I
25 think that's what he is referring to.

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2 Q. It is a combination of color
3 intensity, correct?

4 A. Yes, as it says above there, there
5 are two colors and two intensities.

6 Q. And then in the next sentence it
7 says, If a droplet shows an increase in
8 fluoresce, in color A the droplet therefore
9 contained either targets T1 or T2, correct?

10 A. Yes, that's a bad phrasing, but
11 that's what it says.

12 Q. So again, he says either/or,
13 correct?

14 A. Because the operative word is
15 increase. He is not talking about the
16 intensity of that increase. Because T1 and
17 T2 have the same color, right. So if either
18 T1 or T2 was there, the fluorescence would
19 increase, but obviously they would increase
20 differently because they have two different
21 intensities.

22 So the increase in fluorescence
23 would not be the same for target 1 as it is
24 for target 2.

25 Q. So it would be different whether

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2 you have target 1 or whether you have target
3 2?

4 A. Right, that's the second dimension
5 in the invention, which is dimension number
6 1 is fluorescence wavelength, color. And
7 dimension number two is the intensity of
8 that color. So that's how you get four
9 analytes from two colors.

10 Q. Either analyte T1, analyte T2,
11 analyte T3 or analyte T4, correct?

12 A. So in other words, again, in this
13 particular iteration color A, which
14 corresponds to probes that correspond to T1
15 and T2, have one color and two different
16 intensities, the T3 and T4 have another
17 color, two different intensities.

18 Q. So for T3 if there is an increase
19 in fluorescence in color B, the droplet
20 contained either target T3 or target T4,
21 correct?

22 A. Again, just simply, yes, the
23 fluorescence would increase, but you have a
24 diagnostic on that increase.

25 Q. That shows whether you have either

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2 target 3 or target T4, correct?

3 A. Or B1 or B2, yes.

4 So again, you are basically doing
5 four targets with two colors.

6 Q. You are determining whether any
7 one of those four targets is present,
8 correct?

9 A. That is correct. And again, it is
10 expandable, because there are more than two
11 colors, it is expandable, because there are
12 more than two intensities.

13 Q. Paragraph 139 of Larson doesn't
14 say anything about multiple targets being
15 present in a single droplet, does it?

16 A. You said 139?

17 Q. Yes.

18 A. And your question was does it say
19 anything about multiple targets?

20 Q. Per droplet?

21 A. Okay, your question again, sorry?
22 You are asking me whether or not Larson says
23 that a droplet might have more than one
24 target?

25 Q. Whether paragraph 39 talks about

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2 detecting multiple targets in a single
3 droplet, it doesn't, does it?

4 A. So the text that is in paragraph
5 139 does not refer to multiple targets
6 within a single droplet. It doesn't exclude
7 it. It just didn't consider it in that
8 particular paragraph.

9 Q. Let's go to paragraph 140 of
10 Larson.

11 A. Okay.

12 Q. Now you cite paragraph 140 a
13 number of times in your declaration; is that
14 correct?

15 A. I will accept that.

16 Q. So for example in paragraph 130 of
17 your declaration you discuss paragraph 140
18 of Larson, correct?

19 A. Give me a moment, please.
20 Paragraph 130, I am referring to paragraph
21 140, 141. Yes, the answer is that I do
22 refer to paragraph 140 of Larson and in
23 paragraph 129 of my declaration.

24 Q. And down at the bottom of stamped
25 page 80 in paragraph 130 of your

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2 declaration, you say, Larson discloses
3 conducting the digital PCR assay in
4 paragraph 140, under conditions of terminal
5 dilution where the probability of a single
6 target molecule in droplets is much greater
7 than and overwhelms that of multiple
8 targets, correct?

9 A. The answer is yes, that's what it
10 says.

11 Q. So you agree, paragraph 140 of
12 Larson teaches digital PCR under terminal
13 dilution, correct?

14 A. So I will agree that paragraph
15 130 -- I am sorry, you are referring to
16 paragraph 130 here or paragraph 140 there?

17 Q. Paragraph 140 of Larson teaches
18 digital PCR under terminal dilution,
19 correct?

20 A. Unless I am missing something, the
21 term "terminal dilution" does not exist. I
22 apologize if I am missing something, but I
23 don't see that phrase there. I also don't
24 see the phrases you referred to as digital
25 PCR.

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2 Q. Oh, let me clarify, in your
3 declaration, in paragraph 130 you say,
4 Larson discloses conducting the digital PCR
5 assay in paragraph 140, I think you are
6 referring to Larson, under conditions of
7 terminal dilution?

8 A. That is what I said, yes.

9 Q. Do you agree with that?

10 A. Do I agree that -- but then we go
11 on to say that -- so 140 to be accurate does
12 not say terminal dilution. The implication
13 is that it does by virtue of describing the
14 targets in that. I might have miss -- yes,
15 I think the problem is that the phrase
16 "terminal dilution" pops up in 141. So
17 there may be a slight, slight
18 mischaracterization of specifically what --
19 so in paragraph 141 of Larson it does talk
20 about under conditions of terminal
21 dilutions.

22 Q. And he is referring to the above
23 three methods?

24 A. Yes, it is contiguous.

25 Q. Which includes paragraph 140,

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2 correct?

3 A. Correct.

4 Q. So you agree then under the
5 conditions of terminal dilutions Larson, you
6 agree under the conditions of terminal
7 dilutions in Larson, the probability of
8 single target droplets overwhelms the
9 probability of multiple target droplets,
10 correct?

11 A. Yes, you know, I use the word
12 "overwhelms." I am not entirely happy with
13 the choice of that word. But I will stand
14 by it. Because overwhelms doesn't -- you
15 know, so again, limiting dilutions are where
16 the preponderance is one, but it could be
17 more than one. Terminal dilution is where
18 the preponderance is zero or one. Exactly
19 what is going on in any individual droplet
20 is a statistical probability. Again, you
21 could have a droplet that has a billion
22 targets in it. It is not statistically
23 impossible.

24 Q. You cite paragraph 140 of Larson
25 over 50 separate times in your declaration,

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2 does that sound accurate?

3 A. I will accept your analysis, I
4 don't know that.

5 Q. Would you say paragraph 140 of
6 Larson is a key disclosure for your opinions
7 in this matter?

8 A. I would say that I refer back to
9 140 you said how many times?

10 Q. I think we counted over 50?

11 A. Okay, over 50 times, yes, I would
12 say it has a significance in my arguments.

13 Q. Paragraph 140 discusses
14 identifying three targets, correct, talking
15 about Larson?

16 A. Correct, it talks about targets
17 one, two and three, but it is exemplary, it
18 is not exclusive.

19 Q. And it discusses three different
20 scenarios of colors and intensities when any
21 one of the targets is present, correct?

22 A. Correct, it utilizes two colors
23 with one color and two intensities, the
24 second color, one intensity. But again, it
25 is exemplary, it is not exclusive.

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2 Q. And Larson discloses that under
3 conditions of terminal dilution the
4 detectable signal generated for each
5 potential analyte is distinct and readily
6 distinguishable, correct?

7 A. Are you reading directly from a
8 specific?

9 Q. I am talking about paragraph 130
10 of your declaration.

11 A. Paragraph 130.

12 Q. The end of the paragraph?

13 A. Correct, that's what it says, yes.

14 Q. Going back to paragraph 140 of
15 Larson, paragraph 140 of Larson doesn't
16 discuss detecting multiple targets in a
17 single droplet, correct?

18 A. Its focus is -- yes, you are
19 correct as far as its focus, it doesn't
20 exclude detecting more than one target. And
21 it would happen, because again, in either
22 terminal or limiting dilutions those
23 reactions occur, those results are there.
24 So it is not like there is some magical
25 exclusionary process in Larson or in

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2 anything that has to do with digital PCR
3 that eliminates any possibility that there
4 are more than one target there and that the
5 results reflect more than one target.

6 Q. And Larson doesn't discuss that in
7 paragraph 140, correct?

8 A. No, these are aspirational
9 statements of a perfect world where again,
10 you are doing dilutions and everything only
11 has one target.

12 Q. And Larson explains there are
13 advantages to having only one target
14 molecule per droplet; is that correct?

15 A. So there are advantages to having
16 one copy of one target, right. So let's
17 clarify that. You can have more than one
18 target, and there is no intrinsic problem
19 associated with that, except that the
20 outcomes are a little bit -- the outcomes
21 are sort of not singular.

22 Q. Let's go to paragraph 100 of
23 Larson, and paragraph 99.

24 And paragraph 100 says these
25 issues are avoided in droplet-based PCR

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2 because there is only one template molecule
3 per droplet, correct?

4 A. That is what it says, yes.

5 Q. And these issues refers to
6 problems when you have multiple template
7 molecules in a droplet, correct?

8 A. Define what you mean by multiple
9 template molecules?

10 Q. Well, Larson in paragraph 99 says,
11 is talking about traditional PCR both
12 alleles are present in the reaction mix?

13 A. Correct.

14 Q. And he says basically that the
15 allele with the highest efficiency will be
16 overrepresented, correct?

17 A. Correct, in bulk, yes.

18 Q. And then there can be variances in
19 the sequence to which the PCR primers
20 hybridize?

21 A. Correct, this is in general the
22 problem with bulk PCR is the fact that
23 should you have -- let's put some
24 percentages on this, just bear with me. and
25 let's just talk about the probe. If you

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2 have a probe that has two potential target
3 sequences, one of which binds 50 percent of
4 the time, the other one binds 100 percent of
5 the time, in equal amounts, yes, you could
6 tell the difference. But if you had a
7 thousand-fold excess of the one that binds
8 only with 50 percent of the time, that will
9 wash out or will compete for the probes that
10 you might not see the one that binds
11 100 percent of the time, if that makes
12 sense.

13 Q. And those are issues that Larson
14 avoids by having only one template molecule
15 per droplet, that's what he says in
16 paragraph 100, correct?

17 A. So if you are looking at that
18 phrase that says these issues are avoided in
19 droplet PCR, that is correct. And it says
20 there is only one. In other words, you
21 can't exclude only one a priori, but that
22 would be your aspiration.

23 Q. That's how Larson sought to avoid
24 the issues of having multiple alleles,
25 right?

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2 A. Yes, digital PCR in general,
3 Larson being an example of that, that is the
4 goal of digital PCR.

5 MR. GILL: I don't know how long
6 we have been on the record since the
7 last break.

8 (Luncheon recess taken.)

9 Q. Dr. Batt, did you discuss your
10 testimony with Mr. Walter at all during the
11 break?

12 A. No.

13 Q. I want to talk about paragraph 163
14 of your declaration. Are you there?

15 A. I am.

16 Q. In paragraph 163 in the second
17 sentence you say, basically you say Larson
18 seeks to avoid overlap between signals for
19 droplet populations containing two different
20 target analytes, correct?

21 A. I am seeing, if I am reading it
22 right, it says for example, Larson discloses
23 adjusting, that's the sentence you refer to?

24 Q. Yes.

25 A. I see that, yes.

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2 Q. Do you mean to say Larson seeks to
3 avoid overlap between different droplets
4 that each contain a single different
5 analyte?

6 A. Seeks to avoid, sorry, one more
7 time?

8 Q. Do you mean to say that Larson
9 seeks to avoid overlap between different
10 droplets that each contain a single
11 different analyte?

12 A. So I think what Larson is doing is
13 just simply expanding the dimension of the
14 assay by not just including the fluorescence
15 wavelength, but also including the
16 intensity.

17 Q. To avoid overlap?

18 A. You know, yes, these are my words,
19 I used the word overlap. But I think you
20 are basically, again, you are improving
21 resolution between different targets by not
22 just wavelength, but also intensity.

23 Q. So when you say droplet
24 populations containing two different target
25 analytes, are you referring to like two

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2 different populations that contain two
3 different target analytes?

4 A. No, so what it is referring to
5 here, it says here, it says droplet
6 populations, not two different droplet -- in
7 other words, you have a sample volume, you
8 have a sample volume and in that sample
9 volume are two different target analytes,
10 and you want to tell the difference between
11 A1 and A2 as an example. This dimension
12 allows you to do that.

13 Q. So you want to tell the difference
14 between a droplet that contains A1 and a
15 droplet that contains A2?

16 A. No, you want -- yes, empirically
17 that's the end result. But what you want to
18 determine is does my sample have A1 and/or
19 A2 or A1 and A2.

20 Q. So you are allowing for a
21 possibility that a droplet contains multiple
22 analytes in that statement?

23 A. Well, so again, when you are doing
24 limited or terminal dilutions, you can't
25 exclude that possibility as a statistical

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2 probability.

3 Q. And then you cite paragraph 35 of
4 Larson and paragraphs 146 and 150 of Larson,
5 correct?

6 A. That is what it says here, yes.

7 Q. And figure 15 of Larson?

8 A. That is what it says here, yes.

9 Q. Now, paragraph 35 of Larson
10 doesn't say anything about multiple analytes
11 in a droplet, correct?

12 A. Give me a moment to read paragraph
13 35 again.

14 Q. So figure 15 has nine different --

15 A. Okay, yes, sorry, the question one
16 more time?

17 Q. Paragraph 35 doesn't say anything
18 about multianalyte droplets, correct?

19 A. Well, again, so paragraph 35 is a
20 text description of figure 15, right. And
21 again, as with the previous histogram or
22 chromatogram, it doesn't represent every
23 single droplet. It represents these
24 clusters or these populations of droplets.
25 So does it say anything about multiple

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2 droplets or droplets containing multiple
3 analytes as a matter of describing the
4 figure? It doesn't. Do droplets with
5 multiple analytes exist in this population?
6 I would say there is a high probability of
7 that.

8 Q. But they are not labeled in figure
9 15, correct?

10 A. Again, the focus of this
11 particular figure is looking at those
12 populations. It doesn't list every one of
13 the 20, 30, 50,000 droplets that is in that
14 population that they analyzed.

15 Q. Yes, the multianalyte droplets are
16 not labeled in figure 15, correct?

17 A. There is no labeled population of
18 multianalyte droplets. It doesn't mean that
19 they don't exist.

20 Q. In paragraph 163 of your
21 declaration you also cite to paragraphs 146
22 and 150 of Larson, do you see that?

23 A. Yes, I see that.

24 Q. Now, paragraph 146 of Larson
25 doesn't say anything about droplets with

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2 multiple targets. Correct?

3 A. So it says, it says, for example,
4 samples were one at a 0.06 occupancy per
5 target. So this is a fairly dilute. Does
6 it mean that there aren't any that have
7 multiple targets in that? No, absolutely
8 not. It is not stated in there, because
9 again, it is not -- Larson is not spending
10 time talking about, you know, every
11 statistical probability in a Poisson
12 distribution. And the likelihood is that at
13 a certain frequency they do exist.

14 Because, for example, it says six
15 populations were clearly evident. By
16 clearly evident he is attempting to identify
17 populations that represent, you know, one of
18 the analytes that they are trying to analyze
19 for. It doesn't mean every droplet is
20 accounted for.

21 Q. I want to go to paragraph 188 of
22 your declaration. We talked about this
23 paragraph earlier, you a cite paragraph 121
24 of Larson and figure 9C of Larson, correct?

25 A. That is what is written here, yes.

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2 Q. And paragraph 121?

3 A. Of Larson.

4 Q. Of Larson. Larson's operating
5 under conditions of limiting or terminal
6 dilution, correct?

7 A. It states here that microdroplets
8 are made of diluted solution of template of
9 either conditions of limiting or terminal
10 dilution.

11 Q. And paragraph 121 describes Larson
12 figure 9 as well, correct?

13 A. Yes, it refers back to figure 9.

14 Q. And let's go to figure 9.

15 Figure 9C on the right-hand side
16 of Larson's page shows one peak with
17 intensity 2, correct?

18 A. So Larson 9C right panel shows a
19 peak, yes, it is labeled intensity 2.

20 Q. That peak corresponds to a droplet
21 containing just target 2, correct?

22 A. If I accept -- I don't recall off
23 the top of my head the translation between
24 intensity 2 and target 2. But if that's
25 what you are stating, I am willing to accept

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2 that.

3 Q. What do the other smaller peaks in
4 figure 9C on the right-hand side indicate?

5 A. So basically, first of all, this
6 is a representation of some data. The data
7 is being gathered from that device that is
8 sort of pictorially shown in the center. It
9 is a flow fluorimeter whereby individual
10 droplets are passing through. And again,
11 this is a stylized representation of what
12 the data would look like. So all of those
13 little peaks shown there both before and
14 after on the right-hand panel of intensity 2
15 represents individual droplets that do not
16 have an intensity, a fluorescence intensity
17 above the threshold.

18 Q. And looking at paragraph 121
19 Larson says microdroplets containing
20 sequence 2 emit fluorescence of color 2, do
21 you see that, it is in the bottom part of
22 the paragraph?

23 A. So yes, that's what I guess, but
24 yes, intensity 2, color 2, intensity 2
25 droplets, sequence 2, yes.

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2 Q. And then the left-hand plot in
3 figure 9C shows one large peak, a relatively
4 large peak with intensity 1, correct?

5 A. So not necessarily. You know, I
6 think this is again, a representation of the
7 data. You know, this could be interpreted,
8 and it is not, two intensities at the
9 same -- but it is marking -- let me rephrase
10 that.

11 The peak is marking intensity
12 number 1. It is also indicating where
13 intensity number 3 would lie. It is not
14 a -- yes, where intensity number 3 would
15 lie.

16 Q. And there is one peak that goes up
17 to intensity 1?

18 A. Right. So the interpretation of
19 this particular panel on the left-hand side
20 is that there is one droplet exhibiting
21 intensity number 1 indicating target number
22 1. And that if there was a droplet
23 indicating or having intensity number 3, it
24 would show up where that line is for
25 intensity number 3.

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2 Q. For target 3, correct?

3 A. For target 3 for intensity 3.

4 Q. Dr. Batt, we are talking about
5 figure 9C of Larson. And remind me, did you
6 say that the smaller peaks represent
7 droplets where no analyte was detected?

8 A. So the smaller peaks in both the
9 left and the right panel represent droplets
10 that have no significant fluorescence.
11 Again, it doesn't necessarily mean there is
12 no analyte there. There is no amplification
13 or fluorescents above a threshold.

14 Q. So it might have an analyte, but
15 it depends on various factors whether the
16 fluorescence rises to the level of intensity
17 3 or intensity 1?

18 A. Right, right. So you know, first
19 of all, all of these droplets have a certain
20 degree of fluorescence associated with them.
21 That where you are seeing a peak that arises
22 above let's say point 1 on this scale, you
23 are basically measuring that. So that's
24 why, you know, it doesn't mean the
25 fluorescence, and obviously with the data,

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2 it doesn't mean the fluorescence in a
3 droplet is zero. But it indicates more than
4 like there is no analyte. But again, if for
5 some absolutely some bizarre situation,
6 there is no primers in there, there is no
7 DNA polymerase in there, there is no probe
8 in there, it is not necessarily impossible.

9 Q. But kind of the way Larson
10 describes it is that if it contains target
11 1, 2 or 3 the intensity will be intensity 1,
12 2 or 3?

13 A. That is correct.

14 Q. Figure 9C, would you say it is
15 consistent with terminal dilution?

16 A. I can't answer that.

17 Q. Why not?

18 A. Because I am seeing, maybe, you
19 know, I don't know how many of those little
20 peaks there are. Let's just say there is 20
21 little peaks and one big peak. So I am
22 looking at .0001 percent of the population.

23 Q. Had the peaks, the intensity 1 and
24 the intensity 2 peaks, those aren't
25 multianalyte droplets, correct?

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2 A. What do you mean by multianalyte?

3 Q. Like two different targets.

4 A. So does the intensity in peak 2 --
5 no, because what you are -- so what you are,
6 you know, in panel on the left-hand side and
7 panel on the right-hand side, you are
8 interrogating droplets for one wavelength
9 and another wavelength, right, you are not
10 doing them simultaneously.

11 Q. You mean between the left and the
12 right?

13 A. Correct, correct. So all I can
14 say about -- let's just deal with the panel
15 on the right-hand side, fluorescence channel
16 2, is that there is one droplet there that
17 has at least one target 2 in it.

18 Q. Right?

19 A. Because I am interrogating that
20 droplet for that fluorescence.

21 Q. Let's go to paragraph 189 of your
22 declaration. Are you talking about in
23 paragraph 189 scattered plots for Larson's
24 assays, is that what you are talking about,
25 these assays?

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2 A. So 189, yes, let's say that I am
3 referring to an example, figure 9C, I am
4 sorry, 9D, sorry.

5 Q. 9D?

6 A. Yes.

7 Q. Of Larson?

8 A. Of Larson.

9 Q. And you say the scattered plots
10 for these assays and the droplets used in
11 those assays would have included the
12 combined signals for every combination of
13 the analyte targets as present in the single
14 sample solution, correct?

15 A. That is correct, that's what it
16 says.

17 Q. Which portion of Larson are you
18 relying on when making that statement?

19 A. Well, you know, I mean as an
20 example, the portion in Larson I am
21 referring to is figure 9D, as an example,
22 where, you know, in figure 9D I am looking
23 at in this particular case droplets that
24 have target 1, droplets that have target 2,
25 droplets that have target 3.

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2 So the scatter plot shown below in
3 figure 9D, also listed as a histogram, also
4 a chromatogram, basically shows you those
5 three populations as well as the population
6 of droplets that don't have any of those,
7 that don't show any fluorescence.

8 Q. And then figure 9D doesn't show
9 any other populations of droplets, correct?

10 A. Well, it depends on, you know
11 again, what we are talking about here is a
12 term "populations," which is an aggregate of
13 those droplets or those assay responses for
14 given droplets that we are noting as being
15 visible. It doesn't mean, would a
16 population of three droplets represent a
17 population, I don't necessarily know that.
18 In this particular case they are simply
19 trying to show those significant populations
20 that are the result of target 1, target 2 or
21 target 3.

22 Q. Now, none of Larson scatter plots
23 show any clusters with more than one target
24 molecule, correct?

25 A. I am not sure what you mean by

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2 doesn't show. Again, this is a Poisson
3 distribution, from a statistical point of
4 view those will exist, right. There is no
5 way to say they are zero. In a Poisson
6 distribution you can't say anything is zero
7 as far as a probability is concerned, right.
8 So if you are asking me are there any
9 droplets, for example, in figure 9D that
10 have more than one target in there, the
11 probability is that they exist. Now, in
12 Larson, his primary concern is looking for
13 target 1, 2 and 3 as individual targets, but
14 it doesn't mean that there aren't any
15 droplets that have more than one target in
16 there.

17 Q. Can you identify a single droplet
18 in any of Larson's figures that includes
19 more than one analyte?

20 A. I will say that there is a
21 statistical probability that those exist.

22 Q. But you can't identify one in the
23 figures, correct?

24 A. You are asking me to identify a
25 xerox copy of a xerox copy of some primary

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2 data. Do they exist, yes. Can I identify
3 them, yes. Someplace on this plot are
4 droplets that have more than one target in
5 them.

6 Q. In Larson?

7 A. In Larson. The statistical
8 probabilities argues that they have to
9 exist, it can't be zero.

10 Q. Larson didn't label any of those
11 droplets, correct?

12 A. He didn't, because that wasn't the
13 focus of what he was trying to show here.

14 Q. And he didn't describe any of
15 those droplets in the figures, did he?

16 A. No, but he talks about -- you
17 know, he does talk about multiple occupancy
18 in various points of the patent and does
19 discuss them. And again, I will say on a
20 statistical basis those droplets exist.

21 Q. In paragraph 190 of your
22 declaration, you have a couple of different
23 plots, the first one is a chromatogram from
24 Exhibit 1012, which is I believe patent
25 owner's infringement contentions, does that

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2 sound right?

3 A. I don't have an instantaneous
4 recollection of what exhibit number belongs
5 to what exhibit. So I will take your word
6 that that's what 1012 is.

7 Q. It says, Patent owner contends the
8 chromatogram plotting all intensity clusters
9 of the analytes infringe this claim, and
10 then you have the chromatogram there, right.
11 So you are referring to some argument that
12 Caltech made regarding infringement of the
13 '921 patent?

14 A. Some infringement of the patent
15 owner, some infringement of the '921 patent,
16 sorry, now I am catching up.

17 Yes, that appears to be what this
18 is.

19 Q. What is shown in that
20 chromatogram?

21 A. So if I am reading this correctly,
22 it is channel 1 amplitude and channel 2
23 amplitude. So what I am seeing is eight,
24 eight populations, clusters of different
25 colors or different fluorophores and

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2 different fluorescence and different
3 intensities. So it is similar to Larson's
4 histograms, yes, in fact, it is similar to
5 figure 15 which lines below.

6 Q. Do you know if any of the clusters
7 in the color chromatogram include multiple
8 analyte droplets?

9 A. Again, from a statistical basis
10 there is a probability that those exist.
11 Can I point to any? And this is, I will
12 give you this as a much better
13 representation than the black and white ones
14 below. So this suggests that there are
15 different droplets that stray from the
16 populations. Exactly what those have in
17 them is impossible to say from this kind of
18 figure.

19 Q. If we assume that the chromatogram
20 is displaying droplets that have potentially
21 any of three different analytes?

22 A. Where are you getting three from?

23 Q. I am just asking you to assume?

24 A. Oh, so now we are taking this
25 figure and saying that there are three

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2 analytes there?

3 Q. Yes.

4 A. Okay.

5 Q. Then that figure would though
6 multianalyte droplets, correct?

7 A. You have to understand there is a
8 visualization issue, can I find droplets
9 that have multiple analytes in there versus
10 do they exist on a statistical basis. So
11 the answer is more the latter than the
12 former, that on a statistical basis those
13 droplets exist, right, their probability is
14 not zero. Again, you are saying there are
15 three analytes there, I am not sure what is
16 going on because I am seeing at least eight
17 populations. But I am saying from a
18 statistical basis there are droplets
19 containing multiple analytes in this sample
20 volume.

21 Q. Three analytes in all possible
22 combinations would give eight clusters,
23 correct?

24 A. Sure.

25 Q. So if this chromatogram showing

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2 different combinations of three analytes, it
3 would include clusters that are double
4 positives and triple positive?

5 A. Again, I am trying to understand
6 what you mean by clusters and versus what I
7 am seeing here.

8 Q. The different colors, are they
9 clusters?

10 A. We called them populations
11 previously. We could call them clusters
12 now, that's okay.

13 Q. And if there are three analytes
14 being analyzed in this chromatogram, each
15 cluster represents a combination of those
16 three analytes?

17 A. Well, again, I don't have Exhibit
18 1012 sitting in front of me, so I don't
19 particularly recall the nature of this
20 particular chromatogram. So I could imagine
21 where this chromatogram is, as you say,
22 eight different, and maybe it is three
23 colors and a couple of intensities. I mean,
24 the argument is that they are different
25 colors.

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2 Q. You show figure 15 of Larson
3 further down on that page, correct?

4 A. So yes.

5 Q. And that figure has two different
6 plots?

7 A. Correct.

8 Q. The left-hand plot shows clusters
9 or populations before optimization of probe
10 concentrations; is that correct?

11 A. Yes, it talks about iterations.

12 Q. Then the right-hand side of figure
13 15 of Larson shows populations after
14 optimization of the probe are iterations of
15 probe concentrations; is that correct?

16 A. Correct.

17 Q. So the location of 5G population
18 shifted as a result of the optimization; is
19 that correct?

20 A. Which one are you referring to?

21 Q. 5G.

22 A. Yes, I will accept that as an
23 explanation.

24 Q. And the location of 88G also
25 shifted, correct?

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2 A. 88G, yes, correct.

3 Q. And for example, the location E1a
4 shifted as well, correct?

5 A. It looks like E1a -- you know, the
6 thing you have to keep in mind is that the
7 scale, the number, you know, the figure left
8 goes from 0 to 100, or figure 2, or the one
9 on the right goes from 0 to 140, on the
10 bottom is goes from 20 to 160 on the left
11 and on the right-hand side it goes from 20
12 to 1 to 200, are you following me?

13 Q. Yes.

14 A. So the exact sort of positions,
15 you cannot take one figure and overlay with
16 the other.

17 Q. But E1a --

18 A. It sort of nominally looks like
19 E1a is in the mid 70s, and E1a here looks
20 like it is the high 80s. Yes, I will accept
21 that.

22 Q. In the plot on the right-hand side
23 the clusters can be distinguished from each
24 other, correct?

25 A. They can be distinguished better

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2 than it certainly is on the left-hand side.

3 Q. And in the right-hand plot, the
4 clusters are non-degenerate; is that
5 correct?

6 A. So this notion of degenerate
7 versus nondegenerate as it applies to this,
8 I would prefer to use that the difference
9 between the nine targets here and the
10 control, the resolution is much better.

11 Q. So you can tell each cluster is
12 different, is that what you mean?

13 A. You can tell them apart, like I
14 said, resolution is much better.

15 Q. So basically Larson is shifting
16 the positions of the different clusters
17 going from left to right to allow for easier
18 or better resolution as you said?

19 A. Larson is approving the assay to
20 make that discrimination between those nine
21 targets much easier or much better
22 resolution.

23 Q. In the left-hand side, you could
24 tell the different clusters apart from each
25 other, correct?

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2 A. You know, if they weren't labeled
3 and you sort of had to do this, I would say
4 I would be much happier analyzing the
5 results on the right-hand side than on the
6 left-hand side.

7 Q. But you would be able to do it on
8 the left-hand side, right?

9 A. Well, you know --

10 MR. WALTER: Hold on, objection,
11 incomplete hypothetical, vague.

12 Q. I am just saying looking at the
13 figure?

14 A. So let me --

15 MR. WALTER: Objection, incomplete
16 hypothetical, vague.

17 A. Let me give you my answer, all
18 right. My answer is that if I was
19 developing an assay, and I saw the results
20 on the left-hand panel, I would try to make
21 it better, you know, period. You know, it
22 is the nature of the business.

23 Q. But looking at the left-hand side
24 you could distinguish those clusters from
25 each other, correct?

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2 MR. WALTER: Objection, vague,
3 incomplete hypothetical.

4 A. Again, what you are looking at is
5 essentially one sample volume. Now, if I
6 was presented with ten of these things and I
7 was asked identify exactly which ones
8 have -- for example, I mean, let's just
9 say -- I would say the most problematic one
10 is 81. Yes, it is not as clear on the
11 right-hand side, I am sorry, the label, if I
12 am looking at, say, cluster 815A, are you
13 following me --

14 Q. Yes.

15 A. -- versus the negative cluster,
16 there is sort of not much separation there,
17 right. And again, this is one example of
18 one sample, right. If I am looking on the
19 right-hand side after optimization, 815A,
20 sorry, at least on my copy the one is kind
21 of squished, is much, much more clearly
22 resolved than the negatives. So if you are
23 asking me which one am I happier in, which
24 one do I have a higher degree of confidence
25 in, it is clearly the optimized assay on the

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2 right-hand side.

3 Q. I am just asking whether you could
4 distinguish them on the left-hand side?

5 MR. WALTER: Objection, calls for
6 speculation, incomplete hypothetical.

7 A. I wouldn't as a practicing
8 scientist make that determination unless I
9 couldn't make the assay better. But clearly
10 I can, so.

11 Let me give you an example, I am
12 going to take my driving test, we have done
13 all done this before, we have all looked at
14 these eye charts. There comes a time when
15 you can probably figure out what that next
16 line is, but you would probably be not very
17 comfortable doing that. This is the same
18 sort of thing. The left-hand side is the
19 eye chart without my glasses on, the
20 right-hand side is the eye chart with my
21 glasses on.

22 Now if you are asking me do I want
23 to drive with my or without my glasses on, I
24 think I would probably wear my glasses.

25 Q. Every result that is on the

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2 left-hand side of figure 15 is present on
3 the right-hand side of figure 15 as well,
4 correct?

5 A. What do you mean by result?

6 Q. Cluster.

7 A. Again, you know, I mean, it
8 appears to be based upon the labels. Again, we
9 are being presented with a figure here that
10 has labels on them. All right, we are not
11 being presented with let's just say the raw
12 data or the unannotated data. And if I was
13 sitting there on the left-hand side going,
14 yes, I think there are, you know, basically
15 nine additional spots, I would be a little
16 bit less confident than looking at the ones
17 on the right-hand side where I could clearly
18 distinguish nine, ten, if you include the
19 control.

20 Q. Figure 15 whether you talk about
21 the left-hand side or right-hand side shows
22 nine different populations, correct?

23 A. There are nine clusters labeled on
24 the left-hand side. Again, this is a
25 reproduction of what was the original data,

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2 and I am sure that it was labeled based upon
3 the original data.

4 Q. And the nine clusters, each of
5 those represents a droplet with a single
6 analyte present, correct?

7 A. Again, you can't exclude that in
8 any one of those clusters there isn't a
9 droplet that has two analytes in there,
10 depending upon what exactly those analytes
11 are.

12 Q. But Larson only labeled each
13 cluster with one analyte, correct?

14 A. Yes, the presentation of the
15 figure itself is one that they have
16 identified nine clusters in each one.

17 Q. And each one is labeled with a
18 single analyte, correct?

19 A. Yes, yes.

20 It doesn't mean that every droplet
21 has just one of those analytes. It means
22 that in those clusters that predominant
23 analyte is that single analyte as
24 identified.

25 Q. Are you basing that on something

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2 that Larson teaches?

3 A. I am basing that on looking at
4 these figures.

5 Q. What in the figure shows that?

6 A. Shows what?

7 Q. That any of these clusters have
8 droplets with more than one analyte.

9 A. Again, it is a statistical
10 argument.

11 Q. If I have nine different analytes,
12 how many populations would result from
13 combining those analytes and different
14 droplets in different ways?

15 A. You mean in different
16 combinations, it is nine factorial.
17 Apologies I don't know that number off the
18 top of my head, multiply it out.

19 Q. And would you consider in Larson
20 each of those combinations to be a
21 legitimate result?

22 A. What do you mean by legitimate?

23 Q. Legitimate, like a valid
24 combination of analytes that could result
25 statistically?

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2 A. So again, understand that these
3 sorts of analyses is not an analysis of a
4 single droplet, right. It is not saying a
5 single droplet this is what is going on. It
6 is looking at the population of droplets
7 that is formed from that single sample
8 volume and looking at that population on a
9 whole and then doing statistical analyses of
10 the predominant outcomes, right. So that's
11 what you are seeing here, those clusters are
12 the predominant outcomes. It doesn't mean
13 that any other outcome does not exist.

14 So if you are asking me what is
15 the probability of -- and again, you could
16 do the math, you could calculate it based
17 upon Poisson distribution. But even that's
18 sort of an estimate, because these things
19 don't segregate in complete independence.

20 Q. If Larson were to show all the
21 populations that result from any combination
22 of nine analytes, that would be 512
23 populations, correct?

24 A. Okay, so somebody did the math,
25 yes. That's 9 factorial.

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2 Q. Two to the ninth?

3 A. Right, so it is nine factorial.

4 Q. Let's go to paragraph 291 of your
5 declaration?

6 A. Okay.

7 Q. And here you are talking about
8 that same figure, figure 15?

9 A. Correct.

10 Q. And in the last sentence of
11 paragraph 291 you say that Larson's figure
12 15, POSA or POSITA would have understood
13 that iteration to constitute enumerating
14 every legitimate result that can be
15 obtained?

16 A. So it says POSITA would have
17 understood to constitute.

18 So the iteration is referring to
19 the figure on the left, to constitute
20 enumerating every legitimate result that be
21 obtained from said coding scheme required by
22 the claimant, yes.

23 Q. And that's every result that is
24 present on the scatter plot, right?

25 A. Well, it depends on what you mean

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2 by result. I would argue that in this
3 particular case the analysis is looking at
4 the clusters or the populations, not
5 necessarily every single droplet.

6 Q. And then this in paragraph 292,
7 you say that this iteration, or you call it
8 an optimization process, going from left to
9 right in figure 15, you say that's
10 functionally no different than eliminating
11 an analyte code that is degenerate to remove
12 the degeneracy, correct?

13 A. Correct, that's what I have
14 stated.

15 Q. That's because as you say the
16 optimized analyte codes are necessarily
17 eliminated and subsequently replaced to
18 eliminate degeneracy, correct?

19 A. Correct. So in this particular
20 case by degeneracy, it is an outcome that is
21 not associated with a single result or a
22 single conclusion.

23 Q. Claim 4 of the '921, that's what
24 you are discussing here in this section of
25 your declaration, correct?

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2 A. Yes.

3 Q. Claim 4 recites eliminating at
4 least one potential analyte code from said
5 coding scheme to eliminate degeneracy,
6 correct?

7 A. That is correct.

8 Q. And your opinion is that figure 15
9 discloses that limitation; is that correct?

10 A. So figure 15 discloses a process
11 through which you are removing a degeneracy
12 in a result through a process.

13 Q. By eliminating codes?

14 A. Yes. Without going back through,
15 and I am not sure that the patent explains
16 precisely what these three iterations mean,
17 but presumably there was something that was
18 done between the assay on the left-hand side
19 and the assay on the right-hand side to
20 eliminate those problematic events that
21 result in a lower resolution, a lower
22 accuracy result.

23 Q. You point to figure 15 of Larson
24 as rendering other claims with the '921
25 patent obvious, correct?

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2 A. If you give me specific citations,
3 I am happy to review those.

4 Q. Yes, so for example in paragraph
5 208 of your declaration, you talk about, you
6 say Larson teaching formulating coding
7 schemes in assays that are inherently
8 non-degenerate?

9 A. Yes.

10 Q. You talk about fine-tuning
11 intensities, using multiple fluorophores,
12 each analyte is inherently non-degenerate,
13 and then you cite figure 15 of Larson?

14 A. I am seeing figure 9.

15 Q. It says figures 9, 12B, 15?

16 A. Oh, sorry, you are correct. So
17 the answer is yes.

18 I mean, again, I don't know off
19 the top of my head, I am not sure if it is
20 described in Larson to any great technical
21 detail as to what those iterations were.
22 But you can certainly imagine where, for
23 example, intensities were changed or
24 fluorophores, something that they did.
25 There is some clue, right, there is some

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2 clue in Larson when you look at, for
3 example, when you look at 88A -- no, that's
4 about the same. Let's use that example, it
5 is probably something that wasn't
6 necessarily done, I would say the position
7 of 88A in the panel on the left and the
8 panel on the right are more or less the
9 same. And then you even cited ones that
10 seemed to have shifted a lot. That shift is
11 likely an intensity issue. It might also
12 be, although it is doubtful, a change in
13 fluorophore. But it is probably more of an
14 intensity issue or some other tweaking of
15 those probes, so that the intensity of the
16 clusters is more resolved from the intensity
17 of other clusters giving you a much clearer
18 resolution of those nine different analytes.

19 So that's a long answer to yes, I
20 believe that that's described in figure 15.

21 Q. So I think what you are saying is
22 using the optimization of figure 15, you can
23 get an assay that is inherently
24 nondegenerate, is that what you are saying?

25 A. You could get an assay that is

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2 less degenerate. And what is described here
3 is good practice, good scientific practice.

4 Q. Because figure 15 of Larson
5 doesn't show any multianalyte clusters, it
6 couldn't show how to optimize the
7 intensities of any multianalyte clusters
8 either, correct?

9 A. I disagree with that first portion
10 of the statement. I am not saying -- you
11 are saying that this doesn't represent any
12 multianalyte clusters. I am saying on a
13 statistical basis they exist.

14 Q. You just can't see them?

15 A. I just can't see them. I mean, if
16 you are sitting in front of this as raw
17 data, you could probably tease those out.
18 But again, as presented, you can exclude,
19 and statistically you certainly can exclude
20 that event.

21 And you know, part of the
22 ambiguity in the left-hand side of the
23 figure versus the right-hand side may be
24 somewhat addressing a variety of issues
25 including multianalytes.

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2 Q. Let's flip to paragraph 321 of
3 your declaration. In paragraph 321 you say,
4 Larson expressly teaches that its methods
5 accommodate multiple occupancy situations,
6 i.e., when an individual droplet contains
7 multiple droplets, right?

8 A. Uh-huh.

9 Q. Did you mean multiple analytes?

10 A. Well, it says multiple droplets.
11 Basically there is two reasons why you might
12 have more than one analyte in a droplet.
13 One is just pure statistics. There are
14 other things that there are times in this
15 process that droplets will merge, even
16 though we sort of describe these things as a
17 very discrete, very singular entities, they
18 do tend to merge at times. So I think that
19 statement could reflect either multiple
20 analytes, or again, multiple droplets is not
21 incorrect.

22 Q. So when two droplets merge, one
23 droplet includes or contains another
24 droplet?

25 A. It is not like Moby Dick kind of

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2 stuff. They basically merge, they form one
3 droplet.

4 Q. Okay. And in paragraph 321, you
5 cite to paragraphs 129 and 141 of Larson,
6 correct?

7 A. That is correct.

8 Q. Let's look at paragraph 129 of
9 Larson.

10 Paragraph 129 teaches when you
11 increase the number of targets you are
12 trying to detect, you should increase
13 dilution, correct?

14 A. Correct.

15 Q. And that is because Larson teaches
16 with multiple analytes in a single droplet
17 there is an issue with unintended cross
18 reactivity between analytes, correct?

19 A. Where are you picking up the
20 phrase cross reactivity?

21 Q. It is in the second sentence of
22 paragraph 129.

23 A. I am with you, what is your
24 question again?

25 Q. Larson says you increase dilution

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2 when you have higher degrees of
3 multiplexing, and one reason for that is you
4 want to reduce cross reactivity that is
5 unintended; is that correct?

6 A. That is correct, yes. But it does
7 gone on to say droplets would be double
8 resulting in at least as high or higher than
9 the -- so it does account for multiple
10 occupancy. It does talk about the outcomes.
11 It does say for a simple duplex system the
12 contribution for each probe could be
13 recovered.

14 Q. And then right after that he says
15 higher degrees of multiplexing would require
16 greater dilution, correct?

17 A. Correct. But again, it is not
18 excluding the possibility nor saying that
19 the possibility of droplets containing
20 multiple analytes is a lethal event.

21 Q. But without greater dilution, he
22 mentions that you would get errors that
23 would be too high, correct?

24 A. Certainly you would get more
25 errors. If you had a hundred target

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2 molecules in a droplet, that would be more
3 problematic than two or three. But
4 certainly two or three would be less
5 problematic. As it states here, it talks
6 about for each probe being recovered, in
7 other words, that you could analyze the
8 results, because they will occur, of
9 droplets that have more than one analyte in
10 them.

11 But begun, you strive to avoid
12 those. You don't statistically eliminate
13 those. The statistical probability of those
14 occurring, when you have a much higher
15 concentration of analyte in your original
16 sample volume would be greater.

17 Q. You strive to avoid that by
18 increasing dilution, correct?

19 A. Sure. But again, by dilution you
20 are not eliminating that possibility that
21 there are droplets that have multiple
22 analytes in them. And he talks about how to
23 resolve this.

24 Q. Going back to paragraph 321 of
25 your declaration, you also cite paragraph

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2 141 of Larson, correct?

3 A. Right.

4 Q. And you cite paragraph 141 as well
5 as paragraph 129 to say that Larson's
6 methods accommodate multiple occupancy,
7 correct?

8 A. Correct.

9 Q. But paragraph 141 doesn't say how
10 the complications that come from multiple
11 occupancy are accommodated, correct?

12 A. Well, it talks about the outcomes.
13 And then in the last sentence of this it
14 says, however, methods of the invention can
15 accommodate these complications arising from
16 multiple occupancy.

17 Q. It doesn't say how to do that,
18 though, does it?

19 A. It doesn't say it there. It
20 certainly contemplates that there are
21 methodologies available to do that.

22 Q. In paragraph 333 and 334 of your
23 declaration you discuss figure 9 of Larson,
24 do you see that?

25 A. I do.

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2 Q. And at the bottom of paragraph 334
3 on stamped page 163, you say figure 9C
4 explains and shows the intensity of the
5 signals, which allows for the
6 differentiation between the signals,
7 correct?

8 A. That is what it says, yes.

9 Q. And is it your position that
10 figure 9C shows how to accommodate the
11 complications that arise from multiple
12 occupancy?

13 A. I am sorry, what was that question
14 again?

15 Q. Does figure 9C show how Larson
16 accommodates the complications that arise
17 from multiple occupancy?

18 A. In and of itself figure 9C does
19 not show that. It shows basically two
20 chromatograms with plots and a piece of
21 instrumentation.

22 MR. GILL: Why don't we take a
23 break.

24 (Whereupon, a short recess was
25 taken.)

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2 Q. Let's go to paragraph 337 of your
3 declaration. You say in the second
4 sentence, that POSA would have had a
5 reasonable expectation of success in
6 handling multiple occupancy in a single
7 droplet because Larson explicitly discusses
8 this eventuality when using Poisson
9 distribution of DNA, correct?

10 A. Correct, that is what it says.

11 Q. Now, you don't cite any evidence
12 for that statement, do you?

13 A. For the statement of what Larson
14 discusses or the utility of the Poisson
15 distribution?

16 Q. The reasonable expectation of
17 success, you don't cite any documents or
18 evidence to support that, do you?

19 A. Well, it says here that Larson.
20 So Larson meaning the Larson prior art, I am
21 not sure what -- Larson is Larson, Larson is
22 that citation.

23 Q. So you are relying on Larson for
24 that?

25 A. I am relying on Larson for the

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2 benefits arose from that. But I agree with
3 that, because the Poisson distribution,
4 which is well-known in the field, accounts
5 for these issues. And again, as I have
6 stated before, you know, the statistical
7 probability of multiple occupancy is
8 inherent in the Poisson distribution. It is
9 the probability that is the underlying value
10 of the Poisson distribution.

11 Q. And talking about Poisson
12 distribution, let's go to paragraph 96 of
13 Larson?

14 A. Okay.

15 Q. Paragraph 96 Larson uses the term
16 "occupancy" to describe the average number
17 of target molecules per droplet, correct?

18 A. Correct.

19 Q. And in paragraph 129 of Larson he
20 gives the example of 10 percent occupancy,
21 do you see that?

22 A. For instance a 10 percent
23 occupancy, is that what you are referring
24 to?

25 Q. Yes.

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2 A. I see that.

3 Q. So in that instance only
4 10 percent of droplets would have analytes;
5 is that correct, on average?

6 A. Yes.

7 Q. And Larson states that a
8 10 percent occupancy in a duplex reaction,
9 in that situation 1 percent of the droplets
10 would have multiple analytes; is that
11 correct?

12 A. Yes. This is an extreme example,
13 but yes.

14 Q. And Larson states here that the
15 probability of one probe overlapping any of
16 the other three probes in a four plex
17 reaction is about 3 percent, correct, at
18 1 percent occupancy?

19 A. I see that.

20 Q. And Larson calls one probe
21 overlapping any of the other three probes an
22 error; is that correct?

23 A. He does call it an error, yes.

24 Q. And with 1 percent occupancy, the
25 error may be too high, that's what Larson

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2 says, correct?

3 A. It says the error may be too high
4 for some applications.

5 Q. And then Larson teaches that there
6 is a need for larger dilution to avoid this
7 type of error, correct?

8 A. Right, so if you are in a
9 situation where that error is something you
10 can't accommodate for, is too high or
11 whatever you deem it to be unacceptable,
12 then yes, that error would go down, because
13 the occupancy rate would go down and then
14 hence the double occupancy rate would go
15 down.

16 Q. Let's go to paragraph 338 of your
17 declaration. You state that the ability to
18 acquire data, not from just a fraction of
19 the droplets, but from all droplets in the
20 experiment would be extremely cost
21 effective, do you see that? It is at the
22 bottom of the page?

23 A. Yes, I am trying to remember the
24 contents of that statement. Yes, I see that
25 that's what it says.

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2 Q. Now, you don't cite any evidence
3 in support of that statement, do you?

4 A. You know, first of all, extremely
5 cost effective is not a very definitive
6 comment. And certainly logic would dictate
7 that as you increase the number of droplets
8 that you are looking at, right, acquired
9 data not just from a fraction of droplets,
10 but from all droplets would be extremely
11 cost effective. Right, I wrote these words,
12 but again, I am not -- there is no meaning
13 here beyond, you know, a relatively
14 straightforward conclusion that it would be
15 cost effective to look at all the droplets
16 in the experiment. I am not sure I can give
17 you a number what exactly I mean 10 percent
18 savings, 20 percent savings.

19 Q. In this paragraph are you
20 referring to keeping the number of multiple
21 analyte droplets the same, but just
22 acquiring data from them?

23 A. I believe so, yes.

24 Q. Are you referring to the cost
25 savings of having fewer empty droplets?

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2 A. Well, just simply that the empty
3 droplets don't represent any data points
4 that are useful. So therefore the more
5 empty droplets you have, the more, you know,
6 droplets you are analyzing without any
7 significant outcome.

8 Q. So are you saying reducing the
9 number of empty droplets results in cost
10 savings, is that what you are saying?

11 A. Well, I am saying that in an
12 empirical sense, all things being equal,
13 when you are analyzing empty droplets, you
14 are not collecting useful data.

15 Q. Are you proposing to modify Larson
16 to increase the concentration of analytes to
17 reduce the number of empty droplets?

18 A. I am sorry, what exactly are you
19 asking me, proposing to?

20 Q. Modify Larson?

21 A. Modify in what way?

22 Q. To increase the concentration of
23 analytes in your obviousness opinion?

24 A. Oh, okay, so am I proposing to
25 modify Larson to increase the number of --

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2 Q. To increase the concentration of
3 analytes?

4 A. I am not sure that I understand
5 the question. I am not sure where you are
6 deriving my desire to increase the
7 concentration.

8 Q. Yes, in paragraph 338?

9 A. Okay.

10 Q. At the bottom of stamped page 165?

11 A. At the bottom of page 338?

12 Q. Stamped page 165?

13 A. I am sorry, you are right, okay.

14 Q. You say, Additionally by allowing
15 more DNA into each droplet, the dilution
16 factor for the sample decreases.

17 So are you talking about
18 increasing the concentration in Larson's
19 assays?

20 A. Are you talking about increasing
21 the concentration? I wouldn't be
22 increasing, I would be reducing the
23 dilution, right. I don't have the means to
24 increase the concentration -- I mean, I
25 could concentrate the samples. I am not

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2 sure. It does say the dilution factor for
3 the sample decreases, so that meaning that
4 the amount of dilution that I carry out is
5 less.

6 Q. Does that increase the occurrence
7 of multianalyte droplets?

8 A. Yes. That would be nominally, as
9 we talked about previously, that 10 percent
10 number.

11 Q. Does that also decrease the number
12 of empty droplets?

13 A. Yes.

14 Q. And looking again at paragraph 338
15 of your declaration, in the first sentence
16 you say, Limiting an experiment to only the
17 single target droplets severely impacts the
18 total data collected in that experiment,
19 correct?

20 A. Correct.

21 Q. And you don't cite any evidence
22 for that statement, correct?

23 A. Any evidence for the statement of
24 logic?

25 Q. Correct.

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2 A. No. I mean, it is -- you know, in
3 other words, as you look at only single
4 targets, yes, I stand by that statement as
5 something that one of ordinary skill in the
6 art would understand without citation,
7 without the need for citation.

8 Q. And also in paragraph 338 you
9 state that Larson's assays were quite costly
10 to set up and run because many reagents are
11 required, correct?

12 A. Yes, I can't instantaneously
13 transport myself to that period of time to
14 remember how much things cost. I think that
15 the general rule of thumb is that
16 everything, despite inflation, everything
17 related to these sorts of analyses have
18 decreased.

19 Q. You cite to paragraph 68 of Larson
20 for that statement?

21 A. Let's go back and take a look at
22 that. I mean, that's what I have gotten.
23 Yes, 68, there is not an explicit cost. But
24 I would say in general reagents cost money.
25 Therefore the more information you are

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2 getting out of a population of droplets with
3 the same amount of DNA nucleotides, et
4 cetera, the more cost effective that would
5 be.

6 Q. And going back what you said about
7 allowing more DNA into each droplet and
8 decreasing the dilution factor, you said
9 this means less sample exists and machine
10 run time is less; is that correct?

11 A. Yes, I would say as a general rule
12 that's correct.

13 Q. And you cite to paragraph 96 of
14 Larson for that. It is at the end of
15 paragraph 338.

16 A. Well, again, it is talking about
17 occupancy. And again, there is a cost
18 associated with any type of reagents or any
19 type of assay performance, that obviously
20 the more information you got out of an
21 assay, the better off you would be.

22 Q. Larson didn't say anything about
23 machine run time in that paragraph, did he?

24 A. Not in paragraph 96.

25 Q. Paragraph 96 doesn't talk about

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2 decreasing the amount of sample, correct?

3 A. Specifically in 96, no.

4 Q. Now we touched on this before, but
5 Larson describes several downsides of
6 detecting multiple analytes in a droplet; is
7 that correct?

8 A. As a general statement, yes.

9 Q. And that includes bias from
10 allele-specific PCR; is that correct?

11 A. That is correct, yes.

12 Q. And the downsides also include
13 bias from competition between different
14 amplicons; is that correct?

15 A. If you want to point to some
16 specific statement in Larson.

17 Q. Yes, it is paragraph 101.

18 A. Again, your question?

19 Q. One of the downsides Larson
20 describes with detecting multiple analytes
21 in a droplet is bias from competition
22 between different amplicons, correct?

23 A. It states specifically these
24 result in varying yields between
25 different -- I am sorry, these results in

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2 varying yields between competing amplicon
3 which can result in a non-uniform amplicon
4 yield. So in other words, yes, there is
5 competition. I am not sure if this states
6 it exactly the way you phrased it.

7 Q. It is a complexity, correct?

8 A. Yes, it is a consideration.

9 Q. In paragraph 129 of Larson, Larson
10 describes another challenge as the
11 possibility of cross reactivity, correct?

12 A. Yes, I don't like the word "cross
13 reactivity," but yes.

14 Q. And Larson in paragraph 129
15 describes the downside of an error that
16 results from overlapping probes, correct?

17 A. Yes, it does speak to overlapping,
18 yes.

19 Q. Your proposed modification of
20 Larson doesn't address any of these concerns
21 about multiple analyte droplets, correct?

22 A. Exactly what are you referring to
23 by my modification of Larson?

24 Q. Handling multiple occupancy?

25 A. Where are you referring to, what

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2 paragraph?

3 Q. Paragraph 337 through 338 of your
4 declaration, decreasing dilution factor?

5 A. So where I say a POSA would have
6 reasonable expectation, you are saying that
7 converts to a modification?

8 Q. Yes.

9 A. Well, I disagree with that
10 statement. It doesn't require modification,
11 it says a reasonable expectation. In other
12 words, the way I would read it that a POSA
13 or POSITA, as you want to refer to them,
14 would have the ability to understand Larson
15 as it exists without, as you phrase it,
16 modification. I am not sure what you are
17 modifying.

18 Q. When discussing the reasonable
19 expectation of success, you don't discuss
20 any of the downsides that Larson teaches
21 with respect to detecting multiple analytes
22 in a droplet, correct?

23 A. Is that my responsibility? I am
24 saying, as I said here, a POSA would have a
25 reasonable expectation of success,

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2 reasonable, not perfect. And your
3 expectation is that I am going to sit here
4 and discuss why it is not going to work, is
5 that what you are asking me to do?

6 Q. You didn't account for any of the
7 reasons why it might not work, correct?

8 A. Right, because the overwhelming
9 thing is that it would work. That's a
10 reasonable expectation. With somebody
11 reading this of ordinary skill in the art,
12 they may say it might not work, it might
13 work, but they are going to come away from
14 this with a reasonable expectation of
15 success.

16 Q. Now, Dr. Batt, I have handed you
17 Exhibit 1001 from this IPR, it is the '921
18 patent, do you have that?

19 A. I do.

20 Q. I want to look at claim 14 of the
21 '921 patent.

22 Claim 14 is directed to a kit,
23 correct?

24 A. It does say a kit for detecting
25 the presence or absence of at least M

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2 analytes by generating a single cumulative
3 measurement, yes, a kit.

4 Q. So claim 1 requires that the kit
5 detects M analytes by generating a single
6 cumulative measurement, correct?

7 A. Correct.

8 Q. Let's go to your declaration
9 stamped page 117.

10 Now, you don't describe anything
11 in Larson that generates a single cumulative
12 measurement, do you?

13 A. I am not sure what you mean by
14 that.

15 Q. In paragraph 218, you talk about
16 Larson?

17 A. Okay.

18 Q. What do you cite here in Larson
19 that shows a single cumulative measurement?

20 A. Oh, I see, so you are using -- let
21 me catch up here to see. I am generating a
22 single cumulative measurement. So I would
23 interpret Larson as providing data results
24 and outcome that is cumulative, meaning that
25 in Larson the scatter plots represent a

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2 cumulative measurement, single cumulative
3 measurement, which is the way that those
4 results are being analyzed. So I think that
5 the clusters, populations of a specific
6 wavelength and a specific intensity and the
7 amount, the size of that population and the
8 number of droplets in that population is a
9 measurement.

10 Q. Going back to the '921 patent, the
11 '921 patent is directed to multiplex
12 detection of analytes in a single sample
13 volume; is that correct?

14 A. Yes.

15 Q. And in the abstract of the '921
16 patent it states, This disclosure provides
17 methods, systems, compositions and kits
18 wherein multiple analytes may be detected in
19 a single sample volume by acquiring a
20 cumulative measurement, correct?

21 A. Well, it says by acquiring
22 cumulative measurement or measurements.

23 Q. Correct?

24 A. Okay.

25 Q. And the summary of the invention,

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2 I am looking at column 1, line 53 states
3 that -- let me know when you are there?

4 A. Okay, column 1, line 53, you said?

5 Q. It also refers to detecting
6 analytes in a single sample volume, correct?

7 A. Column 1, line 53. I am not
8 seeing, unless we are talking about column
9 1, line 53, and you are saying a single.

10 Q. 53 to 56?

11 A. Oh, sorry, okay, now I got you.
12 In any combination of presence in a single
13 sample volume without immobilization,
14 separation, mass spectrometry or melting
15 curve analysis, that's what you are
16 referring to?

17 Q. In a single sample volume,
18 correct.

19 A. Yes, sorry, sorry, yes, yes, in a
20 single sample volume.

21 Q. And the '921 patent provides
22 methods that allow multiplexing in a
23 droplet, correct?

24 A. If you can point.

25 Q. We can look at column 36, line 64

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2 to 67?

3 A. It says in a droplet. You said I
4 think in a single droplet.

5 Q. Oh, did I say single? It allows
6 multiplexing in a droplet, correct?

7 A. In a droplet or in a dynamic
8 array, is that what we are talking about?

9 Q. Yes.

10 A. Okay. That's what it says, it
11 doesn't say in a single droplet. It says in
12 a droplet.

13 Q. Okay. The claims of the '921
14 patent require more than detecting a number
15 of targets that exceeds the number of
16 available colors, correct?

17 MR. WALTER: Objection, vague.

18 A. Right.

19 So the claim language, is that the
20 best way to address that?

21 Q. Yes.

22 A. Okay, so the claim language, let's
23 just take claim number 1, is detecting the
24 presence or absence of each of at least M
25 analytes so where we are restricting to --

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2 oh, later on in the third paragraph it does
3 say, let me read the entire thing, Wherein
4 said assay is capable of unambiguously
5 detecting the presence or absence of each of
6 said at least M analytes in any combination
7 of presence or absence in a single sample
8 volume based on detection of said F
9 wavelength components where M is greater
10 than F, right, that's the crux of your
11 question?

12 Q. Yes.

13 A. So to simplify it, it simply says
14 the number of analytes is less than the
15 number of wavelengths that you are using.

16 Q. And the analytes have to be in a
17 single sample volume, correct?

18 A. Well, that would be the goal, yes,
19 correct.

20 Q. And the last element of claim one
21 says that the analytes are amplified in the
22 single sample volume, correct?

23 A. Correct, that's what it says.

24 Q. What does that mean to you?

25 A. Well, you know, the first part is

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2 relatively simple, in other words, if the
3 number of analytes you are looking at is
4 less than the number of wavelengths that you
5 are using.

6 Q. More than?

7 A. I am sorry, correct, more than,
8 the number of analytes you are looking at is
9 more than the number of wavelengths that you
10 are looking at. And the second part has to
11 do with the single sample volume.

12 Okay, so that's what the words
13 say, yes.

14 Q. So the amplification occurs in the
15 single sample volume from which you are
16 detecting M analytes, correct?

17 A. Correct.

18 Q. Would you consider a collection of
19 droplets to be the same as a single sample
20 volume?

21 A. I would say that you could have a
22 collection of droplets from a single sample
23 volume.

24 Q. That's created --

25 A. You are going backwards, I think.

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2 Q. That's created from partitioning
3 the volume?

4 A. So you have a single sample volume
5 and you are partitioning against your
6 droplets.

7 Q. There is a section in your
8 declaration, looking at paragraph 55, and
9 you are discussing an encoding scheme for
10 the '921 patent, do you see that?

11 A. I do.

12 Q. And that coding scheme that you
13 are discussing is nondegenerate by design,
14 correct?

15 A. So in this particular coding
16 scheme there are no ambiguities where any
17 result in a color or intensity gives rise to
18 more than one analyte, yes.

19 Q. And then in paragraphs 59 to 62 of
20 your declaration, you describe an encoding
21 scheme from the '921 patent where degenerate
22 codes are eliminated to make the encoding
23 scheme nondegenerate, correct?

24 A. Yes.

25 Q. And looking at paragraph 62 of

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2 your declaration, you state certain
3 combinations of analytes are absent some
4 modification to the scheme necessarily
5 degenerate, correct?

6 A. We are referring to table 4,
7 which -- is table 4 easily accessible in
8 this or should we go to the '921 patent?

9 Q. Go to the '921.

10 A. So table 4, which is column 14,
11 right, has in it some degenerate results.

12 Q. And one example of that would be
13 the code 3111; is that correct?

14 A. Correct.

15 Q. And table 4 is the decoding
16 matrix, correct?

17 A. Well, it is what it is called,
18 yes, yes.

19 Q. So table 4 is the decoding matrix,
20 table 3 is the encoding table; is that fair?

21 MR. WALTER: Objection, vague.

22 A. Well, I will accept that, because
23 that's what it says, right. It says table
24 3, encoding, table 4, decoding.

25 Q. And in table 3 analyte A is

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2 encoded with a value of 1 in the blue
3 channel, zero in the green channel, zero in
4 the yellow channel and one in the red
5 channel, correct?

6 A. Well, it is because of the control
7 that is in there, yes, the control is in
8 every analyte.

9 Q. And we could call the code for
10 analyte A 1001 for short; is that okay?

11 A. Yes, I am sorry, go ahead, yes.

12 Q. And if you look at the next column
13 for analyte?

14 A. Hang on a minute, let me just back
15 up and say table 3, sorry I misread it,
16 table 3 separates the control, which is the
17 top line, which has a blue channel versus A
18 which has -- yes, which has blue and red.

19 Q. So A had the code 1001, correct?

20 A. Right.

21 Q. And F had the code 1110, correct?

22 A. 1110, correct.

23 Q. And C has the code 1100, correct?

24 A. Yes.

25 Q. And D has the code 1011, correct?

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2 A. Correct.

3 Q. And the control analyte P is
4 always present, correct?

5 A. That is an internal control added
6 to every reaction.

7 Q. And the code for P is 1000,
8 correct?

9 A. Correct.

10 Q. Now looking at table 4, the right
11 most column of table 4 lists the analytes
12 present for a given cumulative assay
13 results, correct?

14 A. Correct.

15 Q. So when you say in paragraph 62 of
16 your declaration that the presence of
17 analytes A and F gives the same cumulative
18 signal measurement as the presence of
19 analytes C and D, this corresponds to the
20 row of table 4 at column 14, line 56 of the
21 '921; is that correct?

22 A. Well, it is not only E and F and C
23 and D, but also B and E.

24 Q. Yes.

25 A. So those are all degenerate.

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2 Q. They all have the same cumulative
3 signal measurement as each other?

4 A. They would all have the same
5 outcome, yes.

6 Q. And that outcome is 3111, correct?

7 A. Correct.

8 Q. So I think what you said is that
9 those three combinations of analytes with
10 the code 3111 are degenerate, right?

11 A. Well, by virtue of the fact if you
12 can't tell if it is AF, CD or BE, yes, they
13 are degenerate.

14 Q. So going back to your declaration,
15 the last sentence of paragraph 62 states
16 that to address these potentially degenerate
17 signals where the signals are ambiguous, the
18 '921 patent suggests nothing more than
19 ignoring one or more analytes, correct?

20 A. Correct.

21 Q. And that's by the '921 says those
22 analytes are removed from the coding scheme?

23 A. So in some cases as described
24 below, and I am reading from the '921,
25 column 14, line 35, it says, again, starting

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2 over again, In some cases as described below
3 one or more analytes may be removed from the
4 coding scheme, table 3, in order to reduce
5 or eliminate degeneracy.

6 Q. Right, and that's consistent with
7 the end of paragraph 62 in your declaration,
8 right?

9 A. Correct.

10 Q. So by removing an analyte from the
11 coding scheme, does that mean the analyte
12 cannot be detected?

13 A. That means that it can't
14 unambiguously be detected. It can be
15 detected, but it is degenerate, so you
16 really don't know, you can't say whether it
17 is AF, CD or BE, but you would certainly say
18 that it is not DG, for example.

19 Q. So do you mean here that the '921
20 patent suggests just ignoring analytes AB,
21 CD, E and F?

22 A. Well, I will read you statement
23 that is provided here, which is curious. It
24 says, In some cases as described below one
25 or more analytes may be removed from the

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2 coding scheme.

3 It doesn't give specific citations
4 to, in this particular case with 3111, which
5 could be AF, CD or BE, you should eliminate
6 those, but it does say that one or more
7 analytes may be removed from the coding
8 scheme in order to reduce or eliminate
9 degeneracy.

10 Q. And you are saying that the '921
11 patent suggests just ignoring those
12 analytes, correct?

13 A. It says may be removed.

14 Q. But you say in your declaration,
15 the '921 patent suggests nothing more than
16 ignoring one or more analytes, that's what
17 you say?

18 A. Sure, I have gone further than
19 just saying removing to ignoring. I have
20 substituted the word "ignoring" to removing.

21 Q. Have you reviewed table 6 of the
22 '921 patent?

23 A. Have I cited it in my report?

24 Q. I don't know.

25 A. Well, if you tell me where I cited

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2 it, I will be happy to review it.

3 Q. Did you review all of the '921
4 patent when you prepared your declaration?

5 A. I read through it. Do I have a
6 recall of every table in it? Not
7 necessarily. Do I have an opinion? If I
8 have an opinion, I would have stated it
9 here.

10 Q. You don't talk about table 6 I
11 don't think in your declaration.

12 But let's look at table 6, do you
13 see where the right most column of table 6
14 says that analyte D is eliminated from the
15 coding scheme to eliminate degeneracy?

16 A. So if I am interpreting this
17 correctly, under tier 1 we are eliminating
18 D, is that right?

19 Q. It is kind of grayed out and
20 crossed out?

21 A. So presumably here we are
22 eliminating analyte D in tier 1, eliminate
23 from the coding scheme to eliminate
24 degeneracy. So we are no longer looking at
25 analyte D. Within the same tier, analyte F

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2 we have decided to eliminate. And again, it
3 is eliminated from the coding scheme to
4 eliminate degeneracy.

5 Q. And also analytes K, M, R and T
6 are eliminated as well, correct?

7 A. Yes, we will all accept that that
8 grayed out thing is --

9 Q. Well, that's what it says next to
10 it?

11 A. Well, it says eliminate. Anyway,
12 I think it is okay, we could certainly say
13 that D, F, J, M, R and T are all eliminated
14 from the coding scheme.

15 Q. So that's six codes that are
16 eliminated, correct?

17 A. One, two, three, four, five, six,
18 correct.

19 Q. Does this mean to you that those
20 analytes, D, F, K, M, R and T are ignored?

21 MR. WALTER: Objection, vague
22 incomplete hypothetical.

23 A. Again, it is eliminated meaning
24 that it is eliminated from what we are
25 calling here the encoding scheme. So

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2 presumably in their logic they are
3 eliminating it from it being part of the
4 original makeup of the coding, encoding
5 scheme. My interpretation of this unless
6 you are willing to accept, and Let's just
7 say it is the same, forgive me if I am
8 making an error, but it is the same as table
9 4, that, you know, there are certain
10 situations where either I am not going to
11 look at that analyte or when I do get a
12 positive result, the equivalent of whatever
13 D is, I can't read that, that I am going to
14 accept that result of being ambiguous, that
15 I am not going to know -- certain things I
16 can eliminate, but certain things I can't
17 eliminate.

18 Q. What are D, F, K, M, R and T, are
19 those analytes?

20 MR. WALTER: Objection, vague.

21 A. Well, it says analyte at the top
22 of the column, so that would be my
23 conclusion.

24 Q. And those letters are labeling a
25 code, correct?

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2 A. Those letters, what letters are
3 you referring to?

4 Q. A B, C, D, et cetera.

5 A. Yes, look, this is a theoretical
6 encoding, decoding scheme that doesn't
7 necessarily refer to anything specific. A,
8 it is not a specific target, it is a.

9 Q. Would it be fair to say that even
10 those some codes in table 6 are eliminated
11 or lined through, there are 15 codes that
12 remain.

13 If you flip the page?

14 A. Thank you, there it is, okay. 15.

15 Q. And is it fair to say that each of
16 those 15 codes could be used with an
17 arbitrary analyte?

18 MR. WALTER: Objection, calls for
19 speculation, incomplete hypothetical.

20 A. What do you mean by arbitrary
21 analyte?

22 Q. Like any analyte?

23 MR. WALTER: Same objection.

24 A. Any analyte, you mean that like
25 rock, paper, scissors, gene targets?

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2 Q. In a target molecule?

3 A. So, you know, again, I am
4 restricting this to what this covers, which
5 is DNA analysis, right. So let's just say
6 it is DNA, it is alleles, it is gene
7 targets. Then in theory, yes. But I am
8 going to stop.

9 Q. Would you say that unambiguously
10 detecting 15 analytes in a single droplet is
11 a high degree of multiplexing?

12 MR. WALTER: Objection, vague.

13 A. Yes, it is a relative question. I
14 would say that Larson lays the foundation
15 for doing 15, doing as many as you can slice
16 the intensities by, assuming that there is
17 only four or five fluorophores that
18 practically work.

19 So assuming within the context of
20 I think they have eight intensities that
21 they have suggested in the '921 patent, so
22 certainly, yes, Larson could do that. And
23 so therefore you could do that in a single
24 sample volume.

25 Q. Let's look at figure 2 of the '921

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2 patent.

3 Figure 2 is showing different PCR
4 targets, correct?

5 A. Correct.

6 Q. And looking at figure 2, if a
7 droplet contained dengue tuberculous, P17
8 malaria and herpes plus the control
9 template, the droplet would contain those
10 molecules before performing PCR, correct?

11 A. It depends. I mean, it sounds
12 like you are asking to describe one of these
13 template molecules in a single droplet.

14 Q. Well, all of them?

15 A. All of them. It depends.
16 Obviously when you are doing these
17 experiments, you are putting these into
18 droplets, and how they segregate themselves,
19 they don't all say one go here, one go here,
20 one go here. So ideally you want that to
21 happen. But you don't necessarily guarantee
22 that every droplet had all of these.

23 Not to correct you it is dengue.

24 Q. The coding scheme shown in Exhibit
25 2 is capable of identifying any combination

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2 of those PCR targets, plus control; is that
3 correct?

4 A. Yes.

5 Q. And for a measurement to be
6 non-degenerate, the code for the combination
7 of analytes that is being measured must be
8 unique; is that correct?

9 A. Right, it needs to be
10 non-degenerate. In other words, the result
11 that you see needs to unambiguously point to
12 or indicate the presence of a given target.

13 Q. And the code for that combination
14 would be different than the codes for any
15 other combinations of analytes, correct, if
16 it is nondegenerate?

17 A. Well, that's the way you would
18 design it, yes.

19 Q. Going back to, if we talk about a
20 single analyte per droplet regime, detecting
21 each of those analytes individually in its
22 own droplet, non-degenerately, would require
23 only a code that uniquely corresponds to a
24 single analyte, correct?

25 A. So if you had only one analyte, if

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2 you are only testing for one thing, you
3 would only need one probe to test for that
4 one thing, is that what you are asking?

5 Q. No, I am asking something
6 different. I am asking for if you are
7 operating in terminal dilution, such that
8 the overwhelming proportion of droplets are
9 either empty or only contain a single
10 analyte?

11 A. Okay.

12 Q. You would only require the same
13 number of codes as analytes; is that
14 correct?

15 MR. WALTER: Objection, incomplete
16 hypothetical, vague.

17 A. Yes, I mean -- no, okay, I am
18 going to leave it at no, because you know
19 again, if you have more than one analyte,
20 but you have more than one probe, you don't
21 necessarily have to segregate that, you
22 don't necessarily have to have one target in
23 one droplet.

24 Q. But if you could assume one target
25 per droplet, the encoding for that, for that

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2 assay would be simpler than the coding we
3 were just discussing in the '921 patent,
4 correct?

5 MR. WALTER: Objection, vague,
6 incomplete hypothetical.

7 A. Yes, in other words, you somehow
8 segregate it out. Let's say you had two
9 analytes and somehow you segregate it out,
10 so you only had one of the two in every
11 droplet, is that what you are saying?

12 Q. Yes.

13 A. So if you somehow had that
14 mysterious capability?

15 Q. Yes.

16 A. If you had that magical power, I
17 am not sure how you get to that that point,
18 but that's what you are asking? If the
19 probes were independent it wouldn't
20 necessarily matter, because you would get
21 two signals, two different colors, two
22 different intensities and you would be able
23 to resolve it.

24 But again, I am going to challenge
25 you to come up with a scheme whereby you can

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2 dilute this sample such that you segregate
3 out one and two in some independent fashion.

4 MR. GILL: Okay, let's go off the
5 record and take a break.

6 (Whereupon, a short recess was
7 taken.)

8 MR. GILL: We are going to pass
9 the witness.

10 MR. WALTER: Then we will need a
11 little break ourselves. Give me about
12 ten, fifteen minutes and we will come
13 back.

14 (Whereupon, a short recess was
15 taken.)

16 EXAMINATION BY

17 MR. WALTER:

18 Q. Dr. Batt, I have a few follow-up
19 questions from your direct examination.

20 Do you recall during the morning
21 portion of your deposition, you were asked
22 if you had any opinions as to whether
23 certain claims of the '921 patent were
24 obvious in view of Larson alone?

25 A. I do.

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2 Q. And I think you were asked,
3 although I don't recall perfectly if your
4 opinions were solely based on Larson and
5 Saxonov together?

6 A. Right.

7 Q. And again, I think you said your
8 opinions were not based on Larson alone, do
9 you recall that?

10 A. I recall I was asked if there was
11 anything about Larson that rendered the
12 claims obvious, and I answered that, no,
13 which was not correct at the time.

14 Q. Do you have opinions as to whether
15 any of the claims of the '921 patent are
16 obvious in view of Larson alone?

17 A. Yes, I do. And they were in my
18 report. I sort of misremembered them
19 because they were put under a header that
20 talked about Larson and Saxonov. But if we
21 turn to paragraph 331, there is a section
22 that talks about Larson alone rendering
23 obvious unambiguously detecting multiple
24 targets in a single droplet.

25 Q. Now, in connection with those

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2 opinions, you rely upon figure 9?

3 A. Correct.

4 Q. Of Larson?

5 A. Correct.

6 Q. In particular you rely upon Larson
7 to render obvious unambiguously detecting
8 multiple targets in a single droplet, do you
9 see that on paragraph 331, it is the header
10 there?

11 A. I do, yes.

12 Q. Can you briefly describe how
13 Larson alone would render obvious
14 unambiguously detecting multiple targets in
15 a single droplet based on figure 9?

16 A. So figure 9 has several components
17 to it. And we can turn to the one version
18 of it, it is in paragraph 331.

19 So there is two elements that I
20 want to sort of clarify. The first one is
21 figure 9A, which clearly shows multiple
22 targets. And these targets on a single
23 molecule would then segregate into a single
24 droplet and therefore could be detected
25 through Larson.

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2 The specific nature of figure 9C,
3 which is basically this fluorometry plot.
4 This data in and of itself doesn't show
5 specifically that that particular droplet,
6 either in the panel to the left or the panel
7 to the right, shows multiple occupancy. But
8 the technique displayed here clearly
9 indicates how you could account for multiple
10 occupancy.

11 And so for example, if you are
12 looking at the figure on the left-hand side,
13 the panel on the left-hand side 9C, you
14 basically have -- and we talked about this
15 in the context of this particular figure,
16 you have one peak showing up, which has an
17 intensity of 1, right.

18 It also indicates here that if you
19 had one peak, but it is not shown here,
20 there is no peak here that corresponds to
21 intensity number 3. But if you had both
22 target 1 and target 3, so therefore
23 intensity 1 and intensity 2, you would see
24 that as an intensity of somewhere around .6
25 or thereabouts.

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2 So specifically what I was saying
3 was that this data, this piece of data in
4 and of itself doesn't show multiple
5 occupancy, but the approach definitely does
6 show multiple occupancy. So for example, if
7 then you want to say, well, suppose you had
8 target 1 and target 2, you would actually
9 have a combination of these two
10 fluorescences shown in the left-hand panel
11 and right-hand panel at the same droplet.

12 Q. Now I want to follow up on one
13 specific question. I think you were asked a
14 question along the line does figure 9C show
15 how to deal with multiple occupancy, and you
16 said something along the lines of not in and
17 of itself, do you recall that testimony?

18 A. I do.

19 Q. What were you intending to say
20 there?

21 A. Well, what I was intending to say
22 is this data, in other words, this specific
23 plot here showing one peak for intensity 1
24 doesn't inherently show that there is a
25 droplet here with multiple occupancy. But

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2 the method itself clearly does show a
3 capability of doing that.

4 Q. One other topic that came up
5 during your cross-examination was the
6 question of whether Larson discloses or
7 contemplates the detection of multiple
8 targets in the same droplet. There were a
9 number of questions along those lines, do
10 you recall that testimony?

11 A. I do.

12 Q. What is your opinion as to whether
13 Larson contemplates detection of multiple
14 targets in the same droplet?

15 A. So the simplest sort of pictorial
16 is figure 22 in Larson itself. And there is
17 two components to this, right, there is a
18 component that shows the location of two
19 loci. And in those two loci one contains
20 either allele A or allele A prime, the other
21 one contains allele B or allele B prime.
22 And so in this particular figure it shows
23 them being contiguous or at least on the
24 same molecule. So therefore, again, they
25 would tend to segregate based upon their

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2 ability to occupy a single droplet.

3 So you have two targets in the
4 same droplet. And then when you are looking
5 at the scatter plot which shows no template
6 AB, A prime B, A prime, B prime and AB
7 prime, basically shows you that you could
8 detect the presence of both loci in the same
9 droplet.

10 Q. Take a look at paragraph 18 of
11 Larson?

12 A. Okay.

13 Q. What is being described in
14 paragraph 18? And if you need a moment to
15 review it, that is fine.

16 A. Yes, give me a second.

17 So in the middle of paragraph 18
18 it specifically says, a detection of two or
19 more variants in a single droplet that
20 contains a single intact nucleic acid. So
21 it is nominally referring to as exemplified
22 in figure 22, where you have two alleles on
23 the same molecule they would segregate into
24 a single droplet. And then it goes on to
25 further say the presence of two or more

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2 markers in the same droplet, more than one
3 target in the same droplet can be identified
4 by such methods as the presence of dyes and
5 multiple colors or intensities or the
6 increase in the intensity of a single dye.
7 So in other words, that you can either look
8 at two colors or two intensities within a
9 single droplet.

10 Q. During your cross-examination, you
11 were asked a lot of questions about
12 potential cross reactivity that happens when
13 you have two PCRs in the same droplet taking
14 place, do you recall those questions?

15 A. I do.

16 Q. Now, in this discussion that
17 appears in paragraph 18 of Larson, how many
18 PCRs would be taking place in the same
19 droplet?

20 A. Well, this issue of cross
21 reactivity is one of primer and probe
22 design. So there are certain things that
23 are inherent within sequences, but you could
24 typically get around it by judiciously a
25 voiding those things in the design of either

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2 the primers and/or the probe. So you can
3 get around this cross reactivity issue. And
4 you could detect multiple copies or multiple
5 target analytes in a single molecule by,
6 again, judiciously selecting primers and
7 probes so there is none of this cross
8 reactivity. And then on top of that by
9 using specific colors and specific
10 intensities, again, you could multiplex your
11 way towards more than one target in a
12 droplet.

13 Q. Now, in this scenario that is
14 posited in paragraph 18, how many PCRs would
15 be taking place at the same time in a single
16 droplet?

17 A. Well, it says two or more, so the
18 answer is two or more.

19 Q. Now, based on this disclosure in
20 paragraph 18 of Larson, how would a person
21 of ordinary skill in the art interpret
22 Larson's discussions about potential
23 problems when you have to do more than one
24 PCR in a single droplet?

25 A. So remember that, you know, 10

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2 years, 15 years before Larson, multiplex PCR
3 wasn't well-practiced. So the basic nature
4 of how do you design primers, probes to get
5 around those issues of what are referred to
6 as cross reactivity. But competing between
7 or competition between primers and between
8 probes was a well-known process, a software
9 that will basically eliminate things like
10 what we call primer dimers, for example. So
11 that was all well-known in the art.

12 Now, what Larson advances is how
13 do you get past four or five colors by the
14 inclusion of intensity. But then you fall
15 back on the previous knowledge of how do you
16 design primers that don't cross react or how
17 do you design probes that don't interfere
18 with each other.

19 Q. Now, to what extent does the '921
20 patent discuss these methods for addressing
21 problems like primer dimers and cross
22 reactivity?

23 A. Off the top of my head I didn't
24 see a lot of discussion.

25 Q. Let's take a look at paragraphs

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2 108 to 113 of Larson. Take a moment to
3 review, let me know when you are ready.

4 A. So 108 through 113 basically
5 describes an assay that looks at five
6 different targets, TERT, RNaseP, Ela, SMN1,
7 and SMN2. And these are five different
8 targets. And they have two different dyes
9 at different intensities. So these are all
10 mixed with reagents, and it goes on to talk
11 about six clusters which is what is in one
12 of the previous figures.

13 Do you want me to find that?

14 Q. If it is helpful for you.

15 A. Well, it is in one of the figures,
16 it is in one of scatter plots that talked
17 about these different targets.

18 And so the last sentence in
19 paragraph 117 says that the number of
20 droplets each having one or more selected
21 from TERT, RNaseP, Ela, SMN1 and SMN2 can be
22 determined from the scatter plot. So it
23 talks about droplets and the inevitable
24 consequence of having droplets that have
25 more than one of those sequences. And can

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2 be determined.

3 Now the scatter plot that is here
4 identifies those clusters that have just
5 one. But as described here, there are
6 methods of looking for clusters that have
7 more than one.

8 Q. So just a very simple question,
9 how, if at all, does the disclosure of 108
10 to 113 of Larson support your opinion that
11 in fact Larson does contemplate detection of
12 multiple targets in the same droplet?

13 A. Well, it speaks to that in the
14 last sentence. It also sort of relies on
15 what, again, a person of ordinary skill in
16 the art would know how to de-convolute these
17 scatter plots, and look not just for single
18 signals, but look for multiple signals.

19 Q. Finally, one just final follow-up
20 question, there were a lot of questions
21 asked by terminal dilution and limiting
22 dilution. Just to recap, how, if at all,
23 does the patent's discussion of terminal and
24 limiting dilution support your opinion,
25 again, that Larson does contemplate

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2 detection of multiple targets in the same
3 droplet?

4 MR. GILL: Objection, vague.

5 A. So we somehow segregated terminal
6 and limiting dilution, like somehow you do
7 them differently, right, it just has to do
8 with the degree to which you dilute the
9 sample. If you took a sample and continued
10 to dilute, at one point you would stop and
11 say that is limiting dilution. And if I go
12 down to further dilutions of that sample, I
13 would wind up with terminal dilution. So
14 the methodology is not different. What is
15 different is in limiting dilution you have a
16 preponderance of one, and in terminal
17 dilution you have a preponderance of zero,
18 right. It is just how far you dilute the
19 sample, that's it. There is nothing
20 magically different, you don't do the
21 process much differently.

22 The reason why those two terms
23 exist is because of the subsequent nature of
24 what you want to try to accomplish, right.
25 And in certain cases you can't have more

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2 than one, but in this particular case you
3 will have more than one. And Larson teaches
4 how to deal with that inevitability. So if
5 I was practicing Larson, I would do a less
6 dilute sample so I could look at multiple
7 occupancies, because I had the capabilities
8 of doing it.

9 MR. WALTER: Thank you, I don't
10 have any more questions.

11 BY MR. GILL

12 Q. Larson doesn't teach doing a less
13 dilute sample to look at multiple occupancy,
14 does he?

15 A. No, but it is an inevitability.
16 He doesn't teach to an absolute degree what
17 the targeted dilution should be. And again,
18 you have the capabilities of looking at
19 single occupancy, you have the capabilities
20 of looking at multiple occupancies.

21 MR. GILL: We are going to take a
22 quick break. I might have one or two
23 more questions. We will go off the
24 record.

25 (Whereupon, a short recess was

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2 taken.)

3 MR. GILL: No further questions at
4 this time.

5 MR. WALTER: Okay.

6 THE COURT REPORTER: Would you
7 like a copy of the transcript?

8 MR. GILL: Rough, three-day
9 expedite.

10 MR. WALTER: Rough, and regular.

11 (Whereupon, at 4:40 P.M., the
12 Examination of this witness was
13 concluded.)

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DR. C. BATT
D E C L A R A T I O N

I hereby certify that having been first
duly sworn to testify to the truth, I gave
the above testimony.

I FURTHER CERTIFY that the foregoing
transcript is a true and correct transcript
of the testimony given by me at the time and
place specified hereinbefore.

Subscribed and sworn to before me
this ____ day of _____ 20__.

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1 DR. C. BATT
2 C E R T I F I C A T E
3

4 STATE OF NEW YORK)
 : SS.:
5 COUNTY OF QUEENS)
6

7 I, RIVKA TROP, a Notary Public for and
8 within the State of New York, do hereby
9 certify:

10 That the witness whose examination is
11 hereinbefore set forth was duly sworn and
12 that such examination is a true record of
13 the testimony given by that witness.

14 I further certify that I am not related
15 to any of the parties to this action by
16 blood or by marriage and that I am in no way
17 interested in the outcome of this matter.

18 IN WITNESS WHEREOF, I have hereunto set
19 my hand this 4th day of June, 2025.
20
21
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23 
RIVKA TROP
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