

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

GENEOSCOPY, INC.,)
)
Petitioner,)
) Case No.
-vs-) IPR2024-01330
) U.S. Patent
EXACT SCIENCES CORPORATION,) 11,970,746
)
Patent Owner.)
_____)

The deposition of VADIM BACKMAN, Ph.D.,
called by the Petitioner for examination, pursuant to
notice and pursuant to the Federal Rules of Civil
Procedure for the United States District Courts
pertaining to the taking of depositions, taken before
Michelle A. Duzan, Certified Shorthand Reporter,
Registered Merit Reporter, and Certified Realtime
Reporter, at Polsinelli, P.C., 150 North Riverside
Plaza, Suite 3000, Chicago, Illinois, commencing at
the hour of 9:08 a.m. on the 7th day of August, A.D.,
2025.

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

FOLEY HOAG, LLP, By
MR. BRENDAN JONES, Ph.D.
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On behalf of the Petitioner;

QUINN EMANUEL URQUHART & SULLIVAN, LLP, By
MS. ANASTASIA FERNANDS
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On behalf of the Patent Owner;

ALSO PRESENT:

Ms. Alexandra Gorman, Esq., Exact Sciences,
Ms. Carly Conway, Exact Sciences (via Zoom),
Ms. Sarojini Adusumilli, Exact Sciences
(via Zoom).

* * * *

I N D E X

WITNESS DX CX RDX RCX

VADIM BACKMAN, Ph.D.

By Mr. Jones

4

E X H I B I T S

DEPOSITION EXHIBIT

MARKED FOR ID

Exhibit 1001	United States Patent	
	11,970,746	4
Exhibit 1004	Analysis of Promoter Methylation in	
	Stool: A Novel Method for the	
	Detection of Colorectal Cancer	86
Exhibit 1007	Kanakoa Patent	162
Exhibit 1023	Hoepffner paper	56
Exhibit 1080	Cologuard Physician Brochure	78
Exhibit 1081	Cologuard sDNA-based Colorectal	
	Cancer Screening Test Instructions	
	for Use	31
Exhibit 2001	Declaration of Vadim Backman,	
	Ph.D.	4
Exhibit 2002	CV Vadim Backman, Ph.D.	4
Exhibit 2044	Declaration of Vadim Backman,	
	Ph.D.	5
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(Exhibits not tendered for inclusion.)

1 (Witness duly sworn.)

2 VADIM BACKMAN, Ph.D.,

3 called as a witness herein, having been first duly
4 sworn, was examined and testified as follows:

5 DIRECT EXAMINATION

6 BY MR. JONES:

7 Q. Good morning, Dr. Backman.

8 A. Good morning.

9 Q. So just to -- for the record, I put
10 before you a bunch of things that -- I don't think
11 anything will be a surprise.

12 So the first document is Exhibit 1001,
13 which you'll recognize is the '746 patent that you
14 talk about in your declaration, right?

15 A. Uh-huh. Right.

16 Q. The second document is Exhibit 2001.

17 And do you recognize this as a
18 declaration you submitted in conjunction with the
19 preliminary patent owner response in
20 November 2024?

21 A. Correct. Yep.

22 Q. Then the next document is Exhibit 2002.

23 And do you recognize this as the CV
24 that's dated November 1st, 2024?

1 A. Right.

2 Q. Your CV, I should say.

3 A. My CV.

4 Q. And then the final document I put
5 before you is Exhibit 2044.

6 Do you -- it should be --

7 A. Somewhere here?

8 Q. No. Right next to you.

9 MS. FERNANDS: On the other side.

10 THE WITNESS: Right. Okay.

11 BY MR. JONES:

12 Q. And do you recognize Exhibit 2044 as
13 the declaration you submitted in support of the
14 patent owner's response in May of 2025?

15 A. Correct. Yeah.

16 Q. So, Dr. Backman, I know you've been
17 deposed at least once before.

18 A. Once.

19 Q. Have you been deposed any other time
20 other than the time when I deposed you earlier
21 this year?

22 A. No.

23 Q. So just as a reminder how depositions
24 work, I'll ask you a question, and you'll provide

1 the response. In between the question and the
2 response, your counsel may wish to offer an
3 objection. So it's important that we don't talk
4 over each other and that you pause a second before
5 you respond to give your opportunity -- your
6 counsel a chance to object.

7 Do you understand that?

8 A. I understand.

9 Q. So for this reason, it's very important
10 for you to wait until the question is complete
11 before answering.

12 A. I understand.

13 Q. We have no videographer. We are
14 relying on the court reporter today. So it's
15 especially important for you to answer verbally
16 rather -- so that -- because it's very hard for
17 her to record head nods and shakes and body
18 language or anything like that. So will you be
19 sure to answer questions verbally?

20 A. I understand.

21 Q. If I ask a question and you don't
22 understand the context, could you please ask me to
23 clarify?

24 A. I will.

1 Q. And I'll try and take a break every
2 hour or so. I set my timer to remind myself. If
3 for some reason you need to take a break before
4 then, just let me know, and we'll accommodate
5 that. The only restriction is that if there's a
6 question pending, I'll ask you to answer that
7 question before we take a break. Is that okay?

8 A. It's perfectly okay. One hour sounds
9 good.

10 Q. Is there any reason you can't give
11 complete and truthful answers today?

12 A. No, no -- no reason.

13 Q. And I see you brought materials with
14 you.

15 A. Correct. Yes.

16 Q. Could I just ask that you put your cell
17 phone on the floor or in a bag or give it to your
18 counsel or something just so it's not --

19 A. Right here.

20 Q. Thank you. Just so it's not
21 distracting.

22 So what document did you bring with
23 you?

24 A. This is a copy -- clean copy of my

1 declaration, which is the same thing you gave me,
2 I believe.

3 Q. Okay. So it's a clean copy of your
4 second declaration submitted in this case?

5 A. In May.

6 Q. In May?

7 A. Yeah, May. Yeah, the May one.

8 Q. And it's completely clean; no
9 highlighting or --

10 A. It is, yes.

11 Q. -- notes?

12 A. It is.

13 Q. No notes.

14 And as far as you know, it's the --
15 identical to the copy that was submitted in the
16 IPR?

17 A. Correct.

18 Q. Okay. So feel free --

19 A. I --

20 Q. Since that's nicely bound rather than
21 stapled, feel free to use whichever version you
22 like.

23 A. I'll -- I'll figure it out which one to
24 use.

1 Q. So other than this IPR proceeding that
2 has to do with the '746 patent and the IPR
3 proceeding in which you were earlier deposed
4 having to do with the '781 proceeding, have you
5 served in a -- as an expert in any other legal
6 proceeding?

7 A. I -- I have started serving in a
8 completely different case, not related to this
9 matter. No deposition yet. Just as a consultant.

10 Q. Okay. And that additional matter, does
11 it involve any of the parties in --

12 A. No.

13 Q. -- this case?

14 A. No.

15 Q. And just at a really high level, what's
16 the technology that's relevant to that proceeding?

17 MS. FERNANDS: And I know you've said
18 at a really high level.

19 I just caution you, if it's not
20 public, to be very careful about how much you
21 disclose.

22 BY MR. JONES:

23 Q. Yeah. So if it's antibody technology,
24 say, Antibody technology. If it's diagnostics,

1 say, Diagnostics; at that level.

2 A. Tumor analysis.

3 Q. But not --

4 A. Not related to fecal matter, not
5 related to blood proteins or stool DNA or
6 colorectal cancer or any of the parties that are
7 involved in this case.

8 It's a very different industry. Very
9 different --

10 Q. Okay.

11 A. -- biology.

12 Q. And your engagement in that matter is
13 not yet public, as far as you know?

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

15 Q. Okay.

16 A. -- frankly what is public, what is not.
17 I presume that it's not.

18 Q. Okay. And you said you haven't been
19 deposed yet?

20 A. No.

21 Q. Have you provided any other kind of
22 testimony in that proceeding?

23 A. Mostly opinion, literature search.

24 Q. But you have only discussed this case

1 with --

2 A. With counsel.

3 Q. -- with counsel?

4 A. Yeah.

5 Q. So aside from the case we just
6 discussed involving tumor analysis, are you
7 currently engaged as an expert in any other legal
8 proceeding?

9 A. No.

10 Q. And am I correct in saying that you've
11 never before given testimony at trial or in a
12 hearing?

13 A. No.

14 Q. Aside from a deposition?

15 A. Aside from a deposition.

16 Q. Without revealing the substance of
17 conversation with counsel -- with -- of
18 conversations with counsel, what did you do
19 generally to prepare for this deposition?

20 A. Literature search, literature review.
21 I reviewed materials related to Dr. Whitney's
22 deposition -- depositions and board judgment. The
23 transcript of the trial. Declarations, obviously.
24 Dr. Whitney's declarations. And patent review, of

1 course.

2 Q. Did you meet with counsel in
3 preparation for this deposition, either in person
4 or remotely?

5 A. Yes, I did.

6 Q. About how many times did you meet with
7 counsel?

8 A. As a preparation for the deposition?

9 Q. Sorry. Let me clarify.
10 In preparation for this deposition
11 today, how many times did you meet with counsel?

12 A. Twice.

13 Q. About when were these meetings?

14 A. This week.

15 Q. Were they in person or remote?

16 A. In person.

17 Q. So which day this week was the first of
18 these meetings?

19 A. Tuesday and Wednesday.

20 Q. So the first meeting was Tuesday, and
21 the second meeting was Wednesday?

22 A. Correct.

23 Q. About how long did you meet on Tuesday?

24 A. Three and a half hours.

1 Q. Who was present at the meeting on
2 Tuesday?

3 A. Just the two of us.

4 Q. When you say the two of us, are you
5 referring --

6 A. To counsel.

7 Q. -- to Anastasia?

8 A. Right. Anastasia, yeah.

9 Q. And on Wednesday, about how long did
10 you meet?

11 A. About six and a half hours.

12 Q. And who was present at that meeting?

13 A. Anastasia and me. Plus there were a
14 couple of observers.

15 Q. Do you recall who the observers were?

16 A. Some of them are -- I was not familiar
17 with. I recognized one name. See if I can
18 remember the last name. Sandra.

19 Q. Haberny?

20 A. Yes. I believe she argued the case
21 during the trial. That's why I recognize the
22 name.

23 Q. Uh-huh. Do you know whether the other
24 person was an attorney for Quinn Emanuel?

1 A. I presume so.

2 Q. Have you discussed this IPR proceeding
3 with anyone other than counsel for Quinn Emanuel?

4 A. The -- so another person present
5 yesterday was counsel for Exact Sciences, again,
6 as an observer. We did not discuss the case per
7 se, but she was in the room.

8 Q. So other than counsel for Quinn Emanuel
9 and counsel for Exact Sciences, have you discussed
10 this case with --

11 A. No.

12 Q. -- anyone?

13 So if you look at Exhibit 2002, which
14 is your CV.

15 So you recognize Exhibit 2002 as your
16 CV, which was submitted in November of 2024?

17 A. I do.

18 Q. So the CV is dated November 1st, 2024?

19 A. (Nodding.)

20 Correct.

21 Q. Are there any substantive additions
22 that would be added to your CV if it were dated
23 for today?

24 A. They're mostly in the publication

1 section. We have -- we have published lately
2 quite a few new papers. I presume that the
3 funding section would be updated with new federal
4 funding.

5 And I see American BioOptics is listed
6 here. American BioOptics has been shut down as a
7 company. So it would not be, yeah, listed here.

8 Let me see what else.

9 Everything else seems to be fairly well
10 updated.

11 Q. So your current position in the --
12 is -- is the same as it was in November of 2024?

13 A. Correct.

14 Q. And your professional experience, with
15 the exception of American BioOptics, no longer
16 being a present employer --

17 A. Correct.

18 Q. -- is accurate?

19 A. Yes, it is.

20 Q. The new papers that you've published
21 since November 2024, were any of them in the field
22 of fecal colorectal cancer diagnostic tests?

23 A. No.

24 Q. And any funding updates from -- since

1 November 2024, would any of them be for work done
2 in the field of fecal colorectal cancer
3 diagnostics?

4 A. No, no.

5 Q. Okay. You can put your CV aside. And
6 I direct your attention to Exhibit 2001, which is
7 your declaration submitted in November of 2024.

8 Do you see that?

9 A. I do.

10 Q. If you can turn to page 85 of the
11 declaration, which is the very last page.

12 That's your signature on this page?

13 A. Yes, it is.

14 Q. And did you write this declaration?

15 A. I did with -- with help of counsel.

16 Q. Did you review this declaration
17 carefully before signing it?

18 A. I always do.

19 Q. Okay. I know this was back in November
20 of 2024 when you submitted this declaration.

21 But do you recall approximately how
22 much time you spent preparing this declaration?

23 A. If you -- if you include hours reading
24 materials, literature -- doing literature

1 research, writing, reviewing, probably around a
2 hundred hours.

3 Q. Okay. Turning your attention to
4 Exhibit 2024 -- sorry. Scratch that.
5 Exhibit 2044.

6 Do you recognize this exhibit as the
7 second declaration you submitted in this case?

8 A. Right. I do.

9 Q. And just for brevity, I'll call this
10 the second declaration.

11 And most of my questions --

12 A. Sure.

13 Q. -- if I'm referring to your
14 declaration, I'll be referring to this
15 declaration, so we're on the same page.

16 Can you turn to page 120 of this
17 declaration?

18 A. I see my signature on it.

19 Q. Yeah. That's your signature on the
20 page?

21 A. Correct.

22 Q. And you also wrote this declaration?

23 A. I did.

24 Q. And this was also written with the

1 assistance of counsel?

2 A. Correct.

3 Q. And you reviewed this declaration
4 carefully before signing it?

5 A. I did.

6 Q. Do you recall how much -- about how
7 much time you spent working on this declaration?

8 A. So some aspects -- some parts of this
9 declaration -- quite a few of them were either
10 very similar or identical to the -- declaration
11 No. 1. So if we count hours spent on --
12 additional hours spent on declaration 2, I would
13 say maybe 50 hours.

14 Q. So between --

15 A. Maybe a little more.

16 Q. So between the preparation of
17 Exhibit 1 -- I mean, Exhibit 2001 and
18 Exhibit 2044, you'd estimate you'd spent 150 hours
19 or maybe a little more in total?

20 A. Sounds about right, yeah.

21 Q. Can you turn to paragraph 11 of your
22 declaration?

23 A. Declaration No. 2, right?

24 Q. Declaration No. 2, yes.

1 You see you list a series of documents
2 that you reviewed in conjunction with this
3 declaration?

4 A. I do.

5 Q. Is this a complete list of documents
6 that you relied on in preparing this declaration?

7 A. Let me -- let me review it again.

8 I mean, clearly, this list does not
9 include all the scientific papers that -- or
10 patents that I relied on or read.

11 I -- the list is pretty complete. I --
12 maybe I'm missing it here. I do not see the --
13 the -- the board judgment listed or the transcript
14 of -- of the trial, which I also reviewed.

15 Q. Do you recall that the -- the --

16 A. But I do not remember the date when I
17 reviewed them. So it might have been reviewed
18 after the completion -- after signing this
19 declaration --

20 Q. Okay.

21 A. -- which is likely, which is probably
22 why it's not listed here.

23 Q. Okay. With the possible exception of
24 the hearing transcript and the judgment -- the

1 final written decision in the '781 IPR, is it --
2 am I correct in saying that you cannot identify as
3 you sit here any specific document upon which you
4 relied in preparing your declaration that would
5 not be within the category -- the list provided in
6 paragraph 11?

7 A. Correct.

8 Q. Okay. So in paragraph 11 on page 5 of
9 your declaration -- for the purpose of your
10 declaration, I'm going to refer to the page that
11 you have in the center bottom of your -- of your
12 declaration rather than the page in the Bates
13 stamp --

14 A. Right.

15 Q. -- because there's a discrepancy.

16 But on page 5, you reference U.S.
17 Patent No. 11,634,781, right?

18 A. I see that.

19 Q. And then you have parentheses next to
20 it, IPR 2024-00459?

21 A. Correct.

22 Q. This is -- the IPR 2024-00459 is the
23 IPR -- other IPR proceeding upon which you've
24 provided expert declaration, correct?

1 A. Correct.

2 Q. And in that IPR proceeding, you
3 submitted two declarations, right?

4 And when I say in that IPR, I mean the
5 IPR proceeding associated with the '781 -- sorry.
6 Let me just start over.

7 In the IPR proceeding associated with
8 the '781 patent, which is 2024-00459, you
9 submitted two declarations, right?

10 A. Correct.

11 Q. And in those declarations, you opined
12 on -- that the claims of the '781 patent were
13 rendered obvious by Lenhard, Vilkin, and
14 Itzkowitz?

15 MS. FERNANDS: Objection to the form.

16 BY MR. JONES:

17 Q. Actually, let me just change that
18 question.

19 In the second declaration you submitted
20 in the '781 IPR proceeding, you opined that the
21 claims of the '781 patent were not rendered
22 obvious by Lenhard, Vilkin, and Itzkowitz, right?

23 A. Not rendered, right.

24 I believe the first time you said

1 rendered?

2 Q. Yes.

3 A. Yeah. Not rendered.

4 Q. So just to clarify the record, in that
5 declaration with -- in conjunction with the '781
6 patent, you offered the opinion that the claims
7 were not rendered obvious by Lenhard, Vilkin, and
8 Itzkowitz, right?

9 A. Correct. Not obvious.

10 Q. And also, in that declaration, you
11 opined that the claims of the '781 patent were not
12 rendered obvious by Shuber and Vilkin, right?

13 A. Correct.

14 Q. And you've since read the final written
15 description -- I'm sorry. Scratch that.

16 You've since read the final written
17 decision from that IPR proceeding?

18 A. I did.

19 Q. So you're aware that in the final
20 written decision for that IPR proceeding, the PTAB
21 determined all the claims of the '781 patent to be
22 obvious?

23 A. That's what I read, yes. I'm aware of
24 the decision.

1 Q. Okay. Turn to paragraph 13 of your
2 declaration.

3 A. I'm on it.

4 Q. So in this paragraph you say you were
5 asked to provide your opinion as to whether the
6 claims of the '746 patent would have been obvious
7 to a person of ordinary skill in the art as of
8 February 3, 2009, correct?

9 A. Correct.

10 Q. Are you aware that Exact Sciences
11 disclaimed claims 1 and 2 of the '746 patent last
12 year?

13 A. Disclaim- -- that they disclaimed?

14 Q. Yes.

15 A. Yes, I was aware of that.

16 Q. So the validity of claims 1 and 2 of
17 the '746 patent is no longer at issue in this IPR
18 proceeding?

19 A. I understand that.

20 Q. Did Exact's disclaimer of claims 1 and
21 2 of the '746 patent factor in any way into the
22 analysis you set forth in your declaration?

23 A. It did not because I express my opinion
24 regardless -- as my personal opinion -- my

1 professional opinion regardless of the outcome of
2 the other legal proceedings.

3 Q. What do you mean by the outcome
4 regardless of the other legal proceedings?

5 A. My -- my job and my task has been
6 focused on scientific analysis of aspects such as
7 obviousness and validity of claims. That's what I
8 based my judgment and analysis on.

9 I did not consider other opinions in
10 the analysis.

11 Q. So for your analysis, you didn't
12 consider Exact's disclaimers of claims 1 and 2 of
13 the '746 patent?

14 MS. FERNANDS: Objection.

15 THE WITNESS: I -- I was aware of that.
16 That was not part of the analysis that I had
17 to do.

18 BY MR. JONES:

19 Q. So Exact's disclaimer of claims 1 and 2
20 of the '746 patent didn't factor into your
21 analysis you set forth in your declaration?

22 A. It --

23 MS. FERNANDS: Objection.

24 THE WITNESS: Correct. It did not.

1 BY MR. JONES:

2 Q. If you turn your attention to
3 Exhibit 1001 of the '746 patent -- sorry,
4 Exhibit 1001, which is the '746 patent. And I
5 direct your attention to the claims, which are on
6 page 27 as the document is Bates stamped.

7 I should clarify, they begin on
8 page 27.

9 A. Right. I -- I -- I'm on it.

10 Q. So as we discussed, claims 1 and 2 here
11 of this patent have been disclaimed by Exact and
12 are not at issue in this IPR proceeding any
13 longer, right?

14 A. Correct.

15 Q. Okay. So if you look at claim 3, is it
16 your understanding that claim 3 requires
17 separation of a stool sample by a subject at home?

18 A. I -- I believe claim 3 does depend or
19 does require a stool sample to be separated.

20 Q. By a patient at home?

21 A. Into two portions. And this is done at
22 home even though, as far as I can tell, at home is
23 not mentioned in claim 3 itself, but it relies on
24 claim 1. It's an independent claim of claim 1,

1 and claim 1 does say home.

2 Q. So what you're referring to is on
3 page 28, right after subsection ii, there's a
4 clause, wherein the pair of portions are obtained
5 by the method of claim 1?

6 A. Correct. Wherein the pair of portions
7 are obtained by the method of claim 1. The "pair
8 of portions" refers to the items a(i) and a(ii) of
9 claim 3 by the method of claim 1. Claim 1 says at
10 home.

11 Q. Is it your understanding that based on
12 this clause, claim 3 requires the practice of
13 claim 1?

14 MS. FERNANDS: Objection.

15 THE WITNESS: I will say so. I do have
16 to state a disclaimer that I'm not a lawyer.
17 But as far as I can tell, yes, it requires
18 practice claim 1.

19 BY MR. JONES:

20 Q. Uh-huh. Are you aware of how
21 product-by-process limitations are interpreted
22 when conducting an obviousness analysis?

23 A. I believe so.

24 Q. What's your understanding of how

1 product-by-process limitations are interpreted
2 when conducting an obviousness analysis?

3 MS. FERNANDS: Objection.

4 THE WITNESS: Are you specifically
5 referring to independent claims or --

6 BY MR. JONES:

7 Q. Do -- do you understand when I say --
8 when I use the term "product-by-process
9 limitation"?

10 A. Why don't you elaborate, and then I can
11 elaborate on that.

12 Q. I'll -- I'll elaborate one step -- one
13 step at a time -- the first step, just to help me.

14 Are you familiar with the term
15 "product-by-process limitation" in its legal
16 context?

17 A. I would not be able to give a legally
18 correct definition.

19 Q. Okay. So if a claim limitation defines
20 composition based on the method through which
21 it -- the process through which it was obtained,
22 would you recognize that as a product-by-process
23 limitation?

24 MS. FERNANDS: Objection.

1 THE WITNESS: Yes.

2 BY MR. JONES:

3 Q. Do you know when such a limitation is
4 present in a claim, whether the process needs to
5 be performed in the prior art in order to render
6 the claim anticipated?

7 MS. FERNANDS: Objection.

8 THE WITNESS: Do you mind repeating the
9 question?

10 BY MR. JONES:

11 Q. In such a product-by-process
12 limitation, do you know whether, for a claim to be
13 obvious, the performance of the actual process
14 needs to have been performed in the prior art?

15 MS. FERNANDS: Objection.

16 THE WITNESS: With the caveat that I
17 am -- I'm not a lawyer, so I would be a
18 little hesitant of saying -- agreeing or
19 disagreeing with this on the basis that it
20 would be hard for me to evaluate at this
21 point every single word in the statement and
22 make sure that it's correct. Conceptually
23 that does sound correct.

24 BY MR. JONES:

1 Q. Was the law governing how to interpret
2 product-by-process limitations something you
3 considered when performing the opinions set forth
4 in your declaration -- your second declaration?

5 MS. FERNANDS: Objection.

6 THE WITNESS: As far as the -- the
7 essence is concerned -- essence related to
8 obviousness and related to prior art, from
9 the scientific perspective, the answer would
10 be yes.

11 I did not review any laws related
12 to that. I did not read any precedents or
13 any legal literature related to the
14 considerations.

15 BY MR. JONES:

16 Q. So you're not familiar with the concept
17 that a product-by-process element can be met even
18 if the process itself wouldn't have been obvious
19 in the prior art?

20 MS. FERNANDS: Objection.

21 THE WITNESS: I'm sorry. Could you
22 repeat the last part? Even if -- so the
23 obviousness would not be met or would be met?

24 BY MR. JONES:

1 Q. Let me re- --

2 A. Okay.

3 Q. Let me repeat the question.

4 You're not familiar with the legal
5 principle that a product-by-process element could
6 be met by a product that is produced by a process
7 that's different from the one that's defined in
8 the claim?

9 MS. FERNANDS: Objection.

10 THE WITNESS: I would have to say that
11 I -- I'm not -- I'm not fully familiar with
12 this -- with the -- with all -- with the
13 intricacies -- potential intricacies of
14 the -- of the laws regarding product --

15 BY MR. JONES:

16 Q. Okay.

17 A. -- product by practice.

18 Q. So is it your understanding that
19 claim 3 requires that the method of processing the
20 fecal sample to be performed without freezing?

21 A. I -- I -- I believe so.

22 Q. Are you aware whether Exact Sciences
23 freezes their fecal sample once it's received at
24 the laboratory?

1 A. I cannot comment on -- on the aspects
2 of sample processing after received by
3 Exact Sciences. What I can say is that the
4 freshly collected sample at home by a patient is
5 not -- is not frozen at home.

6 Q. So I'm providing you with Exhibit 1081.
7 I only have three copies of this one.

8 Do you recognize this exhibit?

9 A. I do.

10 Q. And this exhibit is Cologuard
11 sDNA-Based Colorectal Cancer -- Cancer Screening
12 Test Instructions for Use?

13 A. Correct.

14 Q. Can you turn to page 16 of the
15 document?

16 And you'll see there's a section called
17 Preparation of Stool Homogenate for DNA Testing?

18 A. I do.

19 Q. So at a high level, what's -- are
20 you -- do you know what this process is?

21 A. I do.

22 Q. So what is this process?

23 A. So the section you are referring to,
24 it's -- I believe we're looking at preparation of

1 stool homogenate for DNA testing. Describes the
2 first series of steps in a fairly -- at least
3 conceptually typical DNA-capture procedure.

4 One of the -- so this section refers to
5 what happens after the -- the sample is received
6 in the lab. The first step is frequently to
7 homogenize the sample. And this section describes
8 steps to validate or invalidate the sample; that
9 includes weighing the sample and then using a
10 mixer equipment to homogenize it, followed by what
11 I believe is described in the following sections
12 where DNA is tested -- where the sample is tested
13 for DNA.

14 There are, of course, steps related to
15 barcoding labels and other similar steps, and
16 before the -- before the analysis, the homogenate
17 is frozen -- and I can check the temperature --
18 minus 15 degrees centigrade.

19 Q. Okay. So Step 9 in this process is a
20 step in which the sample is frozen, right?

21 A. That is correct.

22 Q. And then at the top of page 20, under
23 Step 1(a) of preparing the sample for DNA capture,
24 it says, Place the frozen samples in racks to

1 allow air to circulate around the tubes. Leave
2 the racks of frozen samples at 2 to 8 degrees
3 Celsius for at least 13 hours but no more than
4 80 hours until use. Right?

5 A. 1(a)?

6 Q. Yes.

7 A. I see that.

8 Q. So in this step, the frozen samples are
9 presumably thawed, right?

10 A. I believe so.

11 Q. And you offer an opinion in your
12 declaration that performance of the Cologuard
13 assay practices claim 3 of the '746 patent, right?

14 A. I believe so.

15 Q. So is it your understanding that
16 claim 3 does not preclude freezing of the sample
17 once it's obtained at a laboratory?

18 A. It does not preclude freezing in the
19 laboratory.

20 Q. Is it your understanding that the only
21 preclusion on freezing is for the steps performed
22 in claim 1 of the '746 patent?

23 MS. FERNANDS: Objection.

24 THE WITNESS: I agree that claim 3

1 relies on claim 1, and claim 1 talks about
2 freezing freshly collected fecal samples.
3 This limitation refers to -- in my opinion,
4 it refers to freezing of freshly collected
5 fecal samples well after their collection.

6 BY MR. JONES:

7 Q. But not after they're sent to the
8 laboratory?

9 MS. FERNANDS: Objection.

10 THE WITNESS: I do not believe that
11 freezing in the laboratory is limitation,
12 according to claim 1.

13 BY MR. JONES:

14 Q. And you also don't believe that
15 freezing in the laboratory is a limitation of
16 claim 3; is that true?

17 MS. FERNANDS: Objection.

18 THE WITNESS: You're asking if I
19 believe that it is a limitation? Do you mind
20 repeating the question?

21 BY MR. JONES:

22 Q. I said -- asked the opposite. I was
23 just clarifying.

24 A. Uh-huh.

1 Q. You said you don't believe freezing in
2 the laboratory is a limitation of claim 1.

3 I just wanted to clarify, you also
4 don't believe that freezing in the laboratory is a
5 limitation of claim 3 of the '746 patent; is that
6 right?

7 A. Correct. Yeah. Correct.

8 Q. And if you turn -- so I'm about to
9 switch to a different line of questioning that'll
10 take a little while. It's 50 -- we're at
11 54 minutes.

12 Would you prefer to go like an hour and
13 20, or do you want to take a break now? I'm
14 happy --

15 A. An hour and 20 is good.

16 Q. Okay.

17 MR. JONES: Is that okay with you?

18 MS. FERNANDS: Yeah, absolutely.

19 MR. JONES: I can do it either way. I
20 just don't want to do five minutes of this --

21 MS. FERNANDS: Sure.

22 MR. JONES: -- and then have to cut
23 off.

24 BY MR. JONES:

1 Q. Okay. If you turn to paragraph 46 on
2 page 12 of your second declaration.

3 I'm sorry. It is not page 12. Sorry.
4 On -- it's page 21. It was a typo. I inverted
5 it.

6 A. Uh-huh.

7 Q. So paragraph 46 on page 21 of your
8 second declaration.

9 A. I see it.

10 Q. On this page is the start of Section 4
11 of your declaration titled Overview of the '746
12 Patent.

13 Do you see that?

14 A. I see that.

15 Q. And about halfway -- or the last
16 sentence, it's part of a quote in this paragraph.

17 You say, The invention is based upon a
18 combination of tests for detecting proteins and
19 epigenetic modification -- sorry. Let me start
20 that...

21 The sentence says, The invention is
22 based upon a combination of tests for detecting
23 proteins and epigenetic modification markers,
24 respectively, in the same fecal sample shown for

1 the first time herein to provide a particularly
2 useful overall test.

3 Do you see that?

4 A. I see that.

5 Q. Do you agree with this sentence?

6 A. I do.

7 Q. The '78- -- sorry. The '746 patent
8 disclosure does not disclose any buffers that were
9 not already known in the art, does it?

10 A. I don't think so.

11 Q. So it does not disclose any new buffers
12 for preserving DNA, does it?

13 MS. FERNANDS: Objection.

14 THE WITNESS: It -- it does not.

15 BY MR. JONES:

16 Q. And it does not preserve -- disclose
17 any new buffers for preserving blood proteins,
18 does it?

19 MS. FERNANDS: Objection.

20 THE WITNESS: It doesn't.

21 BY MR. JONES:

22 Q. And it doesn't disclose any new buffers
23 for preserving RNA, does it?

24 MS. FERNANDS: Objection.

1 THE WITNESS: It doesn't.

2 BY MR. JONES:

3 Q. So if you go to claim 12 of the '746
4 patent, which is on page 28, final page.

5 A. I see claim 12.

6 Q. Yeah. This claim reads, The method of
7 claim 4 wherein determining expression from the
8 human gene comprises measuring an amount of RNA
9 expressed from the human gene.

10 Do you see that?

11 A. I see that.

12 Q. So this claim relates to measuring an
13 amount of RNA in a fecal sample, doesn't it?

14 A. Yes.

15 Q. Your declaration doesn't provide an
16 opinion that Cologuard practices claim 12, does
17 it?

18 A. I do not -- I did not provide opinion
19 on Exact Sciences' product practicing RNA
20 detection.

21 Q. Are you aware of whether
22 Exact Sciences' Cologuard product practices RNA
23 detection?

24 A. I do know that the Cologuard product

1 tests for DNA, including a couple of methylation
2 markers and several KRAS markers as far as the
3 nucleic acids are concerned.

4 Based on the publicly available
5 materials that I reviewed, RNA is not part of the
6 diagnostic prediction rule as Cologuard is
7 practiced today. Obviously, I cannot comment on
8 any research and development that they might be
9 doing or have done in the past.

10 Q. So my question -- okay. Let me take a
11 step back.

12 So you provide an opinion that the
13 Cologuard product -- use of -- sorry. Scratch
14 that.

15 You provided an opinion in your
16 declaration that use of the Cologuard product
17 practices claim 3 of the '746 patent --

18 A. It does.

19 Q. -- right?

20 You don't have an opinion that the
21 Cologuard product practices claim 12 of the '746
22 patent, do you?

23 A. I do not.

24 Q. When practicing claim 12 of the '746

1 patent, would an RNA stabilizing buffer be used to
2 preserve the RNA in the stool sample prior to
3 testing?

4 MS. FERNANDS: Objection.

5 THE WITNESS: Do you mind repeating the
6 question?

7 BY MR. JONES:

8 Q. When practicing claim 12 of the '746
9 patent, would an RNA stabilizing buffer be used to
10 preserve the RNA in the stool sample prior to
11 testing?

12 MS. FERNANDS: Objection, outside the
13 scope of the opinions.

14 THE WITNESS: Yes, an RNA buffer, which
15 is a type of nucleic acid buffer, would be
16 used or would have to be used.

17 BY MR. JONES:

18 Q. And as we mentioned, the '746 patent
19 doesn't disclose any new buffers for preserving
20 RNA in stool samples, does it?

21 MS. FERNANDS: Objection.

22 THE WITNESS: It does not. The -- you
23 know, both DNA and RNA buffers are implied in
24 the claims of the -- of the patent. They are

1 not specifically mentioned, and no new
2 buffers or no new formulations are explicitly
3 claimed in the claims, but they are clearly
4 implied.

5 BY MR. JONES:

6 Q. So to practice claim 12 of the '746
7 patent in 2009, a person of ordinary skill in the
8 art would have had to use buffers already known in
9 the art, right?

10 MS. FERNANDS: Objection, outside the
11 scope.

12 THE WITNESS: They would have to use
13 a -- an appropriate buffer.

14 BY MR. JONES:

15 Q. That was already -- a buffer that was
16 already known in the art?

17 MS. FERNANDS: Outside the scope.

18 THE WITNESS: They -- they wouldn't use
19 buffers stated in the claims because no new
20 specific buffer is mentioned in the claims.

21 How they would develop the buffer
22 exactly, I believe that's outside of the
23 scope of the -- of this -- of this patent.
24 Practically, they would -- they -- they would

1 use a buffer that was available, known in
2 prior art, designed their own, mix existing
3 components. They -- they would certainly
4 have to use a buffer.

5 BY MR. JONES:

6 Q. Were buffers for preserving RNA known
7 in the art in 2009?

8 MS. FERNANDS: Objection. This is also
9 outside the scope.

10 THE WITNESS: There were -- there were
11 buffers that would preserve RNA.

12 BY MR. JONES:

13 Q. So if you look at claim 13 of the '746
14 patent.

15 A. I see claim 13.

16 Q. This claim relates to measuring an
17 amount of RNA in a fecal sample using RT-PCR,
18 right?

19 A. Correct.

20 Q. You also do not provide an opinion in
21 your declaration that Cologuard practices this
22 claim, do you?

23 A. I do not provide an opinion.

24 MR. JONES: Okay. We can take a break

1 now. I only had to go five minutes past.

2 (Whereupon, a break was taken,
3 after which the following
4 proceedings were had:)

5 BY MR. JONES:

6 Q. Okay. If you can turn to page 22 of
7 your second declaration.

8 A. I am on it.

9 Q. Okay. So you have a section here
10 titled Level of Ordinary Skill in the Art.

11 Do you see that?

12 A. I do.

13 Q. And if you look at paragraph 51, you
14 give your understanding of Geneoscopy's proposed
15 definition of a person skilled in the art in this
16 IPR.

17 Do you see that?

18 A. I do.

19 Q. And this is the opinion -- this is a
20 definition of one skilled in the art that was
21 provided by Dr. Whitney in this IPR, right?

22 A. Correct.

23 Q. Dr. Whitney's definition states that a
24 person skilled in the art would have at least five

1 years of experience -- let me scratch that.

2 Dr. Whitney's definition states that,
3 among other things, a person of skill in the art
4 would have at least five years of experience
5 designing and performing diagnostic assays on
6 fecal samples, right?

7 A. Correct.

8 Q. Okay. If you go to paragraph 54 of
9 your declaration.

10 In this paragraph, you provide your own
11 definition for a person of ordinary skill in the
12 art, right?

13 A. I believe so.

14 Q. And you say in this paragraph that,
15 among other things, a person of ordinary skill in
16 the art would have one to two years of experience
17 in the processing and analysis of biological
18 samples, including fecal samples, right?

19 A. Right.

20 Q. In this definition, what do you mean by
21 the processing and analysis of biological samples?

22 A. This could include a number of things,
23 including preservation of biological samples such
24 as fecal samples for molecular analysis or blood

1 protein analysis, nucleic acid testing,
2 sequencing. Could be a variety of things.

3 Q. Your definition doesn't require a
4 person with skill in the art to have any
5 experience designing the diagnostic assays on
6 fecal sample, does it?

7 A. I think in some way. It just depends
8 on what -- how we define designing assays. In
9 the -- in the strict sense of what designing an
10 assay may mean. Among most complete sense, I
11 would say no, that would be too specialized -- too
12 of a specialized skill.

13 Q. So would your definition be met by a
14 doctor who had spent a year running FIT assays
15 using a commercial kit?

16 MS. FERNANDS: Objection.

17 THE WITNESS: I don't think that would
18 be somebody who's fully skilled in the art.
19 If all they do is run commercially
20 available -- as a new example, right. All
21 they do is, they run commercially available
22 assays, that would not be somebody who is
23 fully skilled in the art.

24 BY MR. JONES:

1 Q. So in addition -- what additional
2 experience would be required by that person in
3 order to make them qualified as a person of skill
4 in the art under your definition?

5 A. They would have to do some sort of
6 analysis of the samples or the results. I think
7 the distinction is, if I understood correctly your
8 example, it's somebody who runs a commercially
9 available premade assay. The assay returns the
10 result.

11 So there is no -- there is no
12 intellectual step that is involved from that
13 person. In your example, the person is a
14 technician that happens to be -- to have a
15 doctoral degree.

16 That would not be a person of ordinary
17 skill in the art in this case. If, on the other
18 hand, the work involves analysis, as it says here,
19 processing an analysis -- an analysis step, I
20 think that would qualify.

21 Q. What do you mean by an analysis step?

22 A. Analysis of data. For example,
23 biomarker data. If it -- following your example,
24 let's take a physician has, let's say, two years

1 of experience running -- again, following your
2 example -- fecal samples, the result -- using a
3 commercially available kit and the kit returns --
4 the output of a kit -- of the kit is the DNA
5 methylation data, or RNA sequencing data, the
6 person would use this data and analyze this data
7 to arrive to a certain -- to certain conclusions,
8 whether those are research conclusions or
9 diagnostic conclusions.

10 That would be an example of analysis.

11 Somebody -- again, following on your
12 example, you know, degree -- doctoral degree of
13 medicine, two years of experience running --
14 running samples but they experiment and think
15 through what kind of buffer, for example, they
16 would use to preserve the samples better in order
17 to get the output that they want, using a
18 commercially available kit, that would be an
19 example of analysis.

20 There are many other examples.

21 I think, in essence, what -- what I'm
22 trying to convey here, so we don't get bogged down
23 in -- in words, is that somebody who
24 understands -- can understand what it takes to do

1 this kind of biological sample processing,
2 understand what kind of steps are involved and how
3 the data can be -- what kind of data can be
4 generated and how it can be used for diagnostics.
5 This is an essential aspect of somebody who is --
6 who is skillful in the art.

7 Q. So under your definition, the person of
8 skill in the art wouldn't have to have any
9 experience in actually designing the assay as is
10 being used as long as there's some analysis of the
11 output of the assay involved?

12 A. Well, that's what I was trying to say.
13 There are different aspects of -- there are
14 multiple aspects of -- of designing an assay,
15 including protocol how to collect the sample; how
16 to preserve it better; what kind of buffer to use
17 or maybe design a buffer itself; how to, let's
18 say, extract molecular information such as DNA;
19 new technology versus standard commercially
20 available molecular techniques; what kind of data
21 you want to get out of it; how to process the
22 data; how to calibrate the data; how to convert
23 this data into diagnostic algorithm.

24 All these steps and many others are

1 part of designing an assay. None of them
2 exclusively is the designing an assay step. So
3 most people do not perform or study every one of
4 these steps, so it would be highly unlikely to
5 somebody who -- or have a person of -- require a
6 person of ordinary skill in the art to have
7 experience in every one of the steps. That's --
8 but all of them are aspects of designing an assay.

9 Q. So the fact that there are all of these
10 steps involved in designing an assay that you just
11 described in your answer, how does that relate to
12 your opinion with respect to the definition of one
13 of ordinary skill in the art?

14 A. That is -- that is included in -- in
15 the kind of education the person should have,
16 which is doctoral degree in the fields we
17 mentioned, medicine, chemistry, biochemistry,
18 biology, and the aspects of working or designing
19 the assay is processing an analysis.

20 Let me just, again, maybe make a
21 distinction here. When -- when I say processing
22 an analysis, I do not mean a technician who does
23 nothing but follows an existing protocol without
24 understanding what this assay does. That's not

1 processing an analysis that I meant. And I
2 apologize if it's not clearly stated in -- in
3 English.

4 Q. Okay. Would the processing and
5 analysis of biological samples need to include
6 molecular diagnostics processes?

7 A. It's -- it's an example, for sure.

8 Q. So if a doctor had experience examining
9 for -- fecal samples for parasites, would that
10 come -- fall within the purview of processing an
11 analysis of biological samples, including fecal
12 samples, from your definition?

13 MS. FERNANDS: Objection.

14 THE WITNESS: Parasites are -- or
15 molecular analysis of parasites is clearly
16 very, very different from a mammalian/human
17 DNA that have very significant biological
18 differences.

19 I would have to say that,
20 frankly, when I was writing this, I did not
21 think of parasites, so you're actually asking
22 a good question. I -- I would say that in
23 this particular case, the answer would
24 depend. It depends. Somebody with a --

1 let's say, Ph.D. in any of these fields or
2 M.D. and experience in working with, for
3 example, parasites could certainly learn and
4 acquire understanding of what it takes to
5 work with human samples.

6 I see no reason why they wouldn't
7 be able to do it. It does not mean that --
8 without additional understanding that the
9 person would -- would be fully versed in,
10 let's say, human DNA.

11 BY MR. JONES:

12 Q. So before that person who worked with
13 looking at parasites, did -- had experience and
14 learned how to work with human DNA in fecal
15 samples, would that person be a person of skill in
16 the art by your definition at that stage, or is it
17 only after they learned and had experience working
18 with the human samples?

19 A. I think they would be -- yeah, I think
20 they would be skilled in the art.

21 Q. So a person with no experience in
22 analyzing human DNA in fecal samples and only had
23 experience looking at parasites would be a person
24 of ordinary skill in the art under your

1 definition?

2 A. I thought what you said that if they --
3 if that person who studies parasites, if they --
4 in addition to their experience, if they learn
5 about --

6 Q. Oh, sorry. I --

7 A. -- human DNA --

8 Q. My question might not have been clear.

9 I meant that person who studied
10 parasites, who hadn't undergone additional
11 learning and experience with human DNA in fecal
12 samples, that person you wouldn't consider a
13 person of ordinary skill in the art under your
14 definition?

15 A. If I interpret your question
16 literally -- you said somebody who studied
17 parasites would not be -- would not be -- would
18 not be a person of ordinary skill in the art
19 because studying parasites implies studying
20 infectious diseases, studying a very different
21 organism. So taken literally, the answer would be
22 no.

23 Q. So in your mind, a person of skill in
24 the art would have had experience analyzing fecal

1 samples for human DNA?

2 MS. FERNANDS: Objection.

3 THE WITNESS: I would think that they
4 should have a familiarity with human DNA,
5 correct.

6 BY MR. JONES:

7 Q. And analyzing fecal samples for human
8 DNA?

9 MS. FERNANDS: Objection.

10 THE WITNESS: Yes.

11 BY MR. JONES:

12 Q. So if you turn to paragraph 33 on
13 page 13 of your second declaration.

14 A. I see it.

15 Q. So in this paragraph, you state that,
16 Colorectal cancer screening tests are applied to
17 healthy people where the risk of disease is
18 relatively low.

19 Do you see that?

20 A. I see that. It's a quote.

21 Q. Yes.

22 A. Uh-huh.

23 Q. Colorectal cancer screening tests are
24 also applied to people at high risk for colorectal

1 cancer; isn't that right?

2 A. That is correct.

3 Q. You'd agree with me that prior to 2009,
4 one type of fecal colorectal screening test being
5 used were guaiac FOBT tests?

6 A. Correct.

7 Q. If I call them gFOBT tests, you'll
8 know --

9 A. gFOBT is good, yeah. Some say guaiac.
10 gFOBT is good.

11 Q. Okay. So gFOBT tests typically involve
12 scooping up a part of a fecal sample with a
13 spatula and smearing it on a card. Is that
14 consistent with your understanding?

15 A. Yes.

16 Q. And often the patient for gFOBT tests
17 will actually smear three parts of a fecal sample
18 onto a card?

19 A. Yes.

20 Q. For at least some tests, this process
21 would have to be repeated on three different fecal
22 samples over three days, right?

23 A. Correct.

24 Q. So you'll agree with me that gFOBT

1 tests require substantial fecal manipulation by
2 the patient?

3 MS. FERNANDS: Objection.

4 THE WITNESS: I would not opine on the
5 word "substantial" because I think to
6 different people it may mean different
7 things. But it certainly requires
8 manipulation. It's probably substantial to
9 me if I were the one doing that.

10 BY MR. JONES:

11 Q. You'll agree with me that prior to
12 2009, at least some of the patients who were
13 taking guaiac FOBT tests were healthy people where
14 the risk of disease was relatively low?

15 A. Correct.

16 Q. And another type of fecal colorectal
17 cancer screening test that was being used by 2009
18 was a FIT test, right?

19 A. Correct.

20 Q. And those are also called iFOBT tests?

21 A. Correct.

22 Q. So generally speaking, through the
23 documents that we've reviewed, your understanding
24 is that FIT tests and iF- -- FIT tests and iFOBT

1 tests are interchangeable?

2 A. Correct.

3 Q. FIT tests also require fecal
4 manipulation by the patient, right?

5 A. They do.

6 Q. And prior to 2009, these tests were
7 also being used by healthy people where the risk
8 of disease was relatively low?

9 A. Correct.

10 Q. So you'll agree with me that before
11 2009, at least some healthy patients were willing
12 to do some fecal manipulation when undertaking
13 colorectal cancer diagnostic assays, right?

14 A. Yes.

15 Q. If you look at paragraph 42 of your
16 declaration.

17 Are you there?

18 A. I do.

19 Q. Okay. So in this paragraph, you have a
20 quote from a 2006 paper by Hoepffner, I'll go
21 with.

22 A. I see that.

23 Q. That's Exhibit 1023 in this case,
24 right?

1 A. That's correct.

2 Q. And your quote is, An ideal screening
3 test must be noninvasive, acceptable to patients,
4 simple, have high sensitivity and specificity,
5 inexpensive, cost-effective, easy to implement
6 across a large population, and should be effective
7 in reducing morbidity and mortality from CRC in
8 the screened population.

9 Do you see that?

10 A. I do.

11 Q. So this quote from Hoepffner describes
12 the characteristics of an ideal screening test,
13 right?

14 A. Correct.

15 Q. Does an ideal screening test exist?

16 MS. FERNANDS: Objection.

17 THE WITNESS: Well, that's the --
18 that's the kind of definition of what ideal
19 is. You're trying to get to something ideal,
20 as close as possible.

21 BY MR. JONES:

22 Q. But you're not aware of a test, even
23 today, that would be an ideal screening test,
24 correct?

1 MS. FERNANDS: Objection.

2 THE WITNESS: I would say -- I would
3 say by its definition, what an ideal test is,
4 it might not -- it cannot possibly exist
5 because it's the -- it's the goal to which
6 all the tests are trying to -- which other
7 tests are trying to achieve.

8 So by definition, something that
9 is completely unreachable. Some tests just
10 get closer to the ideal test than others. An
11 ideal test would be a hundred percent
12 sensitive; a hundred percent specific; would
13 not require -- would cost zero dollars; would
14 not require any effort on the part of a
15 patient.

16 This test does not exist for any
17 disease. It's an ideal.

18 BY MR. JONES:

19 Q. So the ideal test is aspirational?

20 A. Aspirational. But just some tests
21 are -- they do get quite close to that, and they
22 can be quite good.

23 Q. Uh-huh. So of these characteristics of
24 an ideal test, you'll agree with me that sometimes

1 one of these characteristics might need to be
2 moved slightly away from the ideal in order to
3 move other characteristics closer to the ideal,
4 correct?

5 A. That's correct.

6 Q. Would you agree with me that different
7 of these characteristics listened here -- listed
8 here could be more important to different people
9 or under different circumstances?

10 MS. FERNANDS: Objection.

11 THE WITNESS: Generally, I do agree
12 with that; that depending on -- on the
13 population, what type of disease or
14 characteristics of the screening population,
15 follow-up test -- the follow screening tests,
16 different characteristics can be sacrificed
17 in order to improve some others.

18 In fact, actually,
19 Exact Sciences' test is -- I mean, can be one
20 example of that. We -- we know -- we've
21 looked at -- let's say, just talked about
22 claim 3. We talked about that it requires
23 splitting the sample.

24 Ideally, you would not split the

1 sample. Ideally, you would use just one
2 preservative and one -- one sample. That
3 would make -- make the test a little easier,
4 easier for patients, easier to process. But
5 if you wanted to go this route, you would
6 sacrifice -- if you had to sacrifice its
7 diagnostic performance, that's the -- that's
8 the question; would you -- would you do that?
9 And that would not be desirable.

10 So that is an example where in
11 order to improve the diagnostic performance,
12 you would sacrifice some other attributes,
13 for example, how easy it is to implement or
14 its cost, just to give one example. And
15 there are many examples like that.

16 BY MR. JONES:

17 Q. Do you have an understanding as to why
18 the Cologuard test has a patient split the sample
19 rather than ship the sample in a single
20 preservative?

21 MS. FERNANDS: Objection, outside the
22 scope.

23 THE WITNESS: So the -- and let me just
24 clarify. Are you referring to Cologuard

1 product or the patent?

2 BY MR. JONES:

3 Q. Cologuard product.

4 A. Cologuard product.

5 So in Cologuard product, you split the
6 sample in order to use different buffers,
7 different preservatives to preserve one part of
8 the sample for nucleic acid analysis. In case of
9 Cologuard specifically, its DNA, DNA methylation,
10 and -- and KRAS analysis. The second portion, of
11 course, for blood proteins.

12 The essence of the test is the
13 combination of these two sets of markers, which
14 improves the performance of the test, which is the
15 essential feature of the test that gave its over
16 40 percent sensitivity and I believe close to
17 90 percent specificity for advanced adenomas,
18 which was substantially higher than any other
19 available test other than colonoscopy, obviously.

20 So this was a required step, to use
21 different preservatives and analyze them --
22 analyze the samples separately. I would presume
23 that if it had been possible to use just one
24 sample, one preservative, it would have been a

1 much more easier and obvious preferred solution,
2 especially considering that preservatives that
3 preserve both nucleic acids and -- such as DNA,
4 RNA, and blood proteins, they had been available.

5 So that's a -- that's an example --
6 that's a good example of sacrifice that
7 Exact Sciences had to do in their Cologuard
8 product in order to get to better diagnostic
9 performance.

10 Q. Do you have an understanding of why
11 Cologuard didn't use one of these readily
12 available buffers to preserve both hemoglobin and
13 DNA?

14 MS. FERNANDS: Objection, outside the
15 scope.

16 THE WITNESS: I -- I don't think I can
17 comment on that because I'm not familiar with
18 internal R&D process that happened at
19 Exact Sciences.

20 From -- what I can say is that
21 from the perspective of somebody working in
22 the field, somebody skillful in the art, it
23 would have been the first thing to try and
24 more obvious thing to do, of course, to just

1 use one preservative in one sample.

2 If this were me developing the
3 test, I would try that first. And I would
4 only go to two samples -- two preservatives
5 if the first route did not work. But like I
6 said, I cannot comment on the R&D process
7 that led to Cologuard development.

8 BY MR. JONES:

9 Q. So if there was a single buffer that
10 could be used to preserve fecal DNA and fecal
11 hemoglobin in a way that allowed downstream
12 analysis, according to the Cologuard process, you
13 would have expected Exact Sciences to have used
14 that buffer --

15 MS. FERNANDS: Objection.

16 BY MR. JONES:

17 Q. -- in their Cologuard?

18 MS. FERNANDS: Objection, out --

19 THE WITNESS: That's not --

20 MS. FERNANDS: Go ahead.

21 THE WITNESS: That's not exactly what I
22 said. So maybe let me clarify.

23 The buffers that preserve both
24 nucleic acids and hemoglobin, blood proteins,

1 they had been known, and they had been in
2 existence -- they were in existence well
3 before 2009.

4 So one -- I did not say that one
5 would have to create one or invent one. This
6 kind of buffers were available, and they were
7 known. These buffers would preserve -- the
8 same buffer would preserve nucleic acids and
9 proteins. They could have been used.

10 What I was trying to say is that
11 this would have been much more obvious and
12 easier thing to do. So somebody -- a person
13 skillful in the art would prefer to use or
14 propose to use two different buffers, not
15 because they wouldn't know that this kind of
16 buffers existed, but because there must have
17 been a specific diagnostic/biochemical reason
18 that allowed the use of this two different
19 buffers, preserve the samples in such a way
20 that their diagnostic output would -- would
21 be superior to the one that could have been
22 obtained from just a single buffer.

23 But, again, importantly, I just
24 want to make sure that I, you know, did not

1 misspoke, is that one would not have to
2 invent or develop from scratch a buffer that
3 preserves both.

4 Those buffers had been in
5 existence for, in fact, many decades prior to
6 2009. One example -- I -- I think I
7 mentioned this in my declaration -- is the
8 combination of Tris and EDTA. It preserves
9 both -- this buffer would preserve both DNA
10 and proteins. Sometimes with the addition of
11 physiological concentration of salt, such as
12 sodium chloride, would preserve both DNA and
13 proteins.

14 BY MR. JONES:

15 Q. If you were developing a diagnostic
16 assay for testing fecal DNA, wouldn't you optimize
17 your stabilization buffer to preserve DNA?

18 MS. FERNANDS: Objection, outside the
19 scope.

20 THE WITNESS: Would you mind repeating
21 the question?

22 BY MR. JONES:

23 Q. If you were developing -- if one of
24 skill in the art was developing a fecal diagnostic

1 assay for detecting DNA, wouldn't they optimize
2 their stabilization buffer to preserve DNA as well
3 as they can?

4 MS. FERNANDS: Objection.

5 THE WITNESS: Presume they would.

6 BY MR. JONES:

7 Q. And if someone was developing a fecal
8 diagnostic assay that was testing for hemoglobin
9 in the stool, wouldn't one skilled in the art
10 optimize that -- the stabilization buffer to
11 preserve hemoglobin in the stool as well as it
12 possibly could?

13 MS. FERNANDS: Objection.

14 THE WITNESS: They would. However, I
15 think there's an important caveat. I think
16 you specifically mentioned that they would go
17 into, let's say, R&D steps or research steps,
18 development steps to optimize the buffer.

19 I think what you're referring to,
20 specific steps, new steps that would lead to
21 the development of a better buffer. That I
22 would not agree with, at least not generally.

23 In a lot of circumstances, in a
24 lot of labs, they would use existing buffers,

1 commercially available in particular, or
2 previously reported, the combinations,
3 recipes, quote, unquote, that were known in
4 the field without necessarily going into a
5 specific step of altering them, changing
6 them, developing something new.

7 And I think that's what you might
8 have meant -- meant when you said optimizing.
9 If I'm developing an assay, for example,
10 for -- you know, for example, a diagnostic
11 assay for nucleic acids -- for example,
12 nucleic acids in the stool, I don't
13 necessarily have to develop my own buffer. I
14 may not have expertise in doing that. I'm --
15 for whatever reasons.

16 There are companies and people
17 and articles that have spent time developing
18 that. What -- all I have to do is to use
19 the either commercially available product or
20 the one that has been proven to work well in
21 my -- in my as- -- in the same way as when --
22 if I want to -- to program on a computer or
23 use Word, I don't necessarily going to go and
24 build my computer to optimize it, but I would

1 probably buy the one that is known to have
2 Word product -- Microsoft product on it,
3 right? So the same thing here.

4 So I think it -- I think the
5 answer to your question really depends on
6 what you mean by -- by developing or
7 optimizing.

8 If it's new development,
9 innovative steps, new -- new recipes,
10 generally, the answer is no. But you clearly
11 would select the buffer that is known -- has
12 been proven to work for your sample.

13 I would -- if you're developing a
14 DNA assay, you would not use a buffer that
15 digests DNA, obviously.

16 BY MR. JONES:

17 Q. So a person of skill in the art would
18 preferably use a buffer that had been proven to
19 work in the -- for the preservation of their
20 analyte of choice?

21 A. Correct.

22 Q. So a person of skill in the art who was
23 testing for DNA would use a buffer that had been
24 proven to stabilize fecal DNA, right?

1 MS. FERNANDS: Objection.

2 THE WITNESS: That would be proven to
3 stabilize DNA. They would certainly use the
4 buffer that is known to stabilize DNA.

5 BY MR. JONES:

6 Q. And you'll agree with me that by 2009,
7 there were buffers that had already been designed
8 and optimized for preservation of fecal DNA,
9 right?

10 MS. FERNANDS: Objection, outside the
11 scope.

12 THE WITNESS: I would say so. And one
13 of the -- one of the better known ones --
14 known ones had a combination of, as I have
15 mentioned, Tris and EDTA.

16 (Reporter clarification.)

17 THE WITNESS: EDTA. Sorry. So Tris is
18 T R I S. T is capitalized. EDTA is E --
19 Edward, data, Thomas, apple. All capital --
20 capitalized.

21 BY MR. JONES:

22 Q. And if one of skill in the art were
23 testing hemoglobin in a stool sample in their
24 assay, that person would preferably use a buffer

1 that had been proven to stabilize blood proteins?

2 A. Correct.

3 MS. FERNANDS: Objection.

4 BY MR. JONES:

5 Q. Are you aware of whether the
6 commercially available FIT kits that are available
7 in the art as of 2009 use the buffer containing
8 Tris-EDTA?

9 A. I did not review that.

10 Q. Okay. We got a little sidetracked from
11 that line of questions.

12 Okay. So turning your attention back
13 to paragraph 42 of your declaration --

14 A. Uh-huh.

15 Q. -- and the characteristics of an ideal
16 screening test set forth by the Hoepffner
17 reference.

18 Do you see that?

19 A. Right.

20 Q. And I believe I asked you that you
21 agree with me that different of these
22 characteristics could be more important than
23 others under different circumstances, right?

24 A. Generally, I -- I agree with that.

1 Q. So, for example, a particularly
2 impoverished remote community might sacrifice test
3 performance for a cheaper test that they could
4 actually afford, right?

5 A. That's a reasonable example, yes.

6 Q. On the other hand, there are still
7 individuals who prefer a colonoscopy to, for
8 example, Cologuard despite colonoscopy's higher
9 cost and inconvenience?

10 A. Correct, because it has higher -- for
11 two reasons. We talked -- we have talked about
12 it. One of them is higher accuracy for advanced
13 adenomas. And second, that it's also therapeutic
14 procedure at the same time as a diagnostic.
15 That's the gold standard.

16 Q. And you'd agree with me that by
17 definition, Cologuard is not an ideal screening
18 test, right?

19 A. Well, like -- as I mentioned, the word
20 "Ideal screening test" is really aspirational.
21 Thank you for using the right word. Aspirational
22 is a good -- good term here.

23 It's -- it's not perfect. No test is
24 perfect. But at the time and still is -- when it

1 was introduced and still is, it does offer a
2 combination -- combination of characteristics and
3 attributes that are considerably -- you know,
4 collectively, they're considerably superior to any
5 other product available in clinical medicine as a
6 first-tier screening test.

7 Q. But I mean, for example, Cologuard is
8 more expensive than a FIT test, right?

9 A. Exactly. That would be an additive.

10 Q. And Cologuard has a specificity that's
11 lower than a FIT test --

12 MS. FERNANDS: Objection.

13 BY MR. JONES:

14 Q. -- right?

15 A. I think it depends on exactly lesion --
16 the type of lesion we're talking about. For some
17 of them, it -- it is a little lower.

18 Q. And Cologuard's ability to detect
19 colorectal cancer is not as high as colonoscopy --

20 MS. FERNANDS: Objection.

21 BY MR. JONES:

22 Q. -- for example?

23 A. Could you define ability to detect
24 colorectal cancer? What do you specifically mean

1 by that?

2 Q. Cologuard's sensitivity for colorectal
3 cancer is not as high as colonoscopy, right?

4 A. Assuming that colonoscopy is the gold
5 standard, and that's how most of this
6 sensitivity/specificity are calculated. By
7 definition, no other test would be as sensitive as
8 colonoscopy.

9 Now, we're meaning, of course, such --
10 aspects such as miss rate -- that colonoscopy does
11 have miss rate, but it's treating it as a gold
12 standard, which is frequently done in -- in
13 scientific reporting. It -- Cologuard would miss
14 some cancers.

15 Q. And colonoscopy is still considered the
16 gold standard?

17 A. It does.

18 Q. And the Cologuard test requires a
19 patient to undergo more fecal manipulation than a
20 DNA-only test would, right?

21 A. That's correct.

22 MS. FERNANDS: Objection.

23 BY MR. JONES:

24 Q. In paragraph 45 of your declaration --

1 it's on page 19. I'm talking about your second
2 declaration.

3 You say in paragraph 45, The situation
4 remained until the introduction of the Cologuard
5 test by Exact Sciences, which, through the
6 combination of fecal DNA analysis and
7 identification of blood proteins in the stool,
8 offered excellent sensitivity and specificity for
9 early-stage colorectal cancers and robust
10 sensitivity and excellent specificity for advanced
11 adenomas.

12 Do you see that?

13 A. I see that.

14 Q. Cologuard was released in 2014, right?

15 A. I believe so.

16 Q. So it was released five years after the
17 priority date of the '746 patent?

18 A. Correct.

19 Q. How come in this sentence you use the
20 word "excellent" to describe sensitivity and
21 specificity for colorectal cancers and "excellent"
22 to -- for the specificity for advanced adenomas
23 but only "robust" for the Cologuard sensitivity
24 for advanced adenomas?

1 A. I would have to say that when we were
2 writing this, the sentence would not read as well
3 if you were to repeat the same word twice. I
4 wouldn't read too much into "excellent" versus
5 "robust." I think both of them convey that these
6 are good values.

7 I don't think there is a conventional
8 definition or agreement of what sensitive or
9 specificity would be classified as excellent
10 versus robust. I think both words convey my
11 excitement over what this performance
12 characteristics are. We have to put them in
13 perspective.

14 The -- the question is how they compare
15 with the state of the art in 2014, when the test
16 came out, or even today, how they compare with the
17 other available tests. And to me, as somebody who
18 has been working in the field of colorectal cancer
19 screening, probably the most important endpoint is
20 advanced adenomas because as I mentioned, I think,
21 repeatedly in -- in this declaration, these are
22 the lesions that we really need to screen for if a
23 test is to be used as a prescreen for colonoscopy
24 or the first-tier screening.

1 Cologuard until today remains the test
2 that has the best combination of sensitivity and
3 specificity for advanced adenomas; considerably
4 higher than any other test. Again, all of these
5 numbers are relative to colonoscopy, of course.

6 So words "excellent, robust" just
7 convey my excitement. It does not necessarily
8 mean that "robust" is more or less excellent than
9 "excellent." Clearly, for Cologuard, just like
10 any other test on the market, the diagnostic
11 performance for CRC would be greater than for
12 advanced adenomas.

13 A test that is more sensitive to
14 adenomas and less sensitive -- more specific to
15 CRC has not been developed. It doesn't exist.

16 Q. And Cologuard's sensitivity for
17 colorectal cancers is above 90 percent; is that
18 right?

19 A. Cologuard sensitivity for CRCs --

20 Q. Yes.

21 A. -- is -- I can't remember the exact
22 number. It's close to 90 percent. It's -- yeah,
23 it's up there.

24 Q. And Cologuard sensitivity for advanced

1 adenomas, is it consistent that its sensitivity is
2 around 42 percent?

3 A. That's correct.

4 Q. Oh, I should point out that at the very
5 bottom of the page -- at least as reported in
6 2014, you write that Cologuard tests achieved
7 92.3 percent sensitivity and 86.6 percent
8 specificity for colorectal cancer.

9 Do you see that?

10 A. I'm just finding exact numbers. The
11 numbers sound --

12 Q. It's on the very -- bottom line of
13 page 19.

14 A. 19. Oh, yeah. Right at -- my page.
15 Yes, that's correct.

16 Cologuard test achieved 92.3 percent
17 sensitivity and 86.6 percent specificity for CRC.
18 Of course, it says that.

19 Q. Okay. So --

20 A. Good. I'm glad we established that.

21 Q. It refreshes your recollection --

22 A. Yes.

23 Q. -- that Cologuard sensitivity for
24 colorectal cancer is somewhere above 90 percent?

1 A. Above 90 percent. Correct.

2 Q. Okay. You attribute Cologuard's
3 sensitivity and specificity for colorectal cancers
4 and advanced adenomas to its combination of fecal
5 DNA analysis and identification of blood proteins
6 in the stool.

7 Do you see that on the first sentence
8 of paragraph 45?

9 A. I do. Yeah, I see -- yes, I see that.

10 Q. Do you know how many DNA markers
11 Cologuard tests for in its fecal DNA analysis
12 step?

13 A. I may have to look it up to be -- to
14 give the exact number. I believe it's nine.

15 Q. So I'll give you Exhibit 1080, which is
16 Cologuard's Physicians Brochure.

17 And do you recognize Exhibit 180 [sic]?

18 A. I do.

19 Q. This is an exhibit that you considered
20 while preparing your declaration?

21 A. Correct. Yes.

22 Q. If we look at page 3, in the Cologuard
23 Overview, the second paragraph.

24 Do you see that?

1 A. Right.

2 Q. Does that refresh your recollection
3 with respect to how many DNA markers --

4 A. So it sounds like ten. I think I said
5 nine. I think the correct number should be ten
6 then.

7 Q. Do you know what Cologuard's
8 sensitivity for colorectal cancer would have been
9 if it only analyzed one of these ten DNA markers?

10 A. I don't think that has been disclosed.
11 So I -- I -- obviously, no, I don't know.

12 Q. Would you expect it to be lower?

13 A. I would --

14 MS. FERNANDS: Objection.

15 THE WITNESS: I would expect it to
16 be -- I would expect it to be lower --

17 BY MR. JONES:

18 Q. And --

19 A. -- if only one marker is used --

20 Q. If only --

21 A. -- for the entire test.

22 Q. If one DNA marker and hemoglobin was
23 used?

24 A. I would expect it to be lower in part

1 based on the -- or primarily based on the fact
2 that the test does use ten DNA markers. It would
3 be very hard for me to imagine that anybody would
4 use -- would add more markers -- use more markers
5 and have a more complicated prediction rule for no
6 increase in diagnostic performance.

7 So I -- I presume it should be a fair
8 statement, that a single DNA marker and the -- and
9 the, let's say, blood proteins -- one marker for
10 blood proteins would give lower diagnostic
11 performance.

12 Q. So one -- if you only used one of the
13 ten DNA markers and the blood protein marker,
14 you'd expect worse diagnostic performance?

15 A. I would, but I cannot -- obviously, I
16 cannot say how low. Is it lower by 1 percent? Is
17 it lower by 5 percent? I wouldn't know that.

18 Q. It's not something you investigated?

19 MS. FERNANDS: Objection.

20 THE WITNESS: Something -- I don't
21 think this could be -- could be learned from
22 the -- from the materials that I have at
23 hand.

24 BY MR. JONES:

1 Q. Have you seen any data with respect to
2 what Cologuard's sensitivity and specificity for
3 colorectal cancer would be if they only tested
4 those ten DNA biomarkers and did not test
5 hemoglobin?

6 A. I cannot say these numbers were
7 explicitly reported. They might have been. I do
8 not remember seeing that. This performance could
9 easily be inferred, at least from the Imperiale
10 reference, because they provide -- they provide
11 fairly complete information on the performance of
12 combination, including sensitivity, specificity,
13 the area under the curve.

14 They also provide the same statistics
15 for -- for their blood protein marker, which they
16 compare with essentially immuno-FOBT and has very
17 similar performance, as they mentioned in the
18 article as well, and they quantify the -- the
19 added value of the combination versus FOBT alone.

20 So from this data report in the -- in
21 the article, it's fairly easy to infer what the
22 performance be for the combined DNA rule. So a
23 combination of those ten markers.

24 So this is different from dividing this

1 DNA test that has ten markers into individual
2 markers; that part I cannot tell you what it would
3 be because I just don't have the data. It can --
4 maybe it's available. I just haven't seen it.

5 But like I said, if you look at the ten
6 DNA markers together as one rule, that is very
7 easy to see and calculate from the Imperiale data
8 because they have sufficient information on that
9 as a single component.

10 Q. Did you provide that calculation in
11 your declaration anyplace?

12 A. I don't think so. Yeah, I don't think
13 so.

14 MR. JONES: Why don't we take a break.
15 (Whereupon, a break was taken,
16 after which the following
17 proceedings were had:)

18 BY MR. JONES:

19 Q. So if you can turn to paragraph 141 of
20 your declaration. Okay.

21 I was in the wrong declaration. Okay.
22 Paragraph 141 of your declaration.

23 A. Right. I see it.

24 Q. Okay. So in this paragraph, you

1 discuss the use of what you call an AND rule or an
2 OR rule when assessing -- when using biomarker
3 combinations; is that right?

4 A. Correct.

5 Q. And these are rules that can be used,
6 for example, when two biomarkers are used to
7 assess a sample, right?

8 A. Examples of two rules. Examples of
9 some rules.

10 Q. These are -- yeah, the AND rule and the
11 OR rule are rules, potentially among other rules,
12 that can be used --

13 A. Correct.

14 Q. -- when two biomarkers are --

15 A. Correct.

16 Q. -- used?

17 So with the AND rule -- actually,
18 stepping back.

19 So for these clarifying questions,
20 let's assume that there's -- it's a two-biomarker
21 assay.

22 A. Okay.

23 Q. Okay. And we'll call them biomarker A
24 and biomarker B.

1 A. Okay.

2 Q. Okay. So when the AND rule is used,
3 the sample would only be considered diagnostically
4 positive if both biomarker A and biomarker B are
5 detected in the sample?

6 A. With the AND rule, right. Correct.

7 Q. So in that case, the sample was
8 positive for biomarker A but negative for
9 biomarker B; it would be considered diagnostically
10 negative?

11 A. Correct.

12 Q. And would you agree with me that when
13 biomarkers are combined using the AND rule, the
14 combined test can only be equal to -- be equal to
15 or less than the individual tests and
16 sensitivity -- sorry. Let me take that back.

17 Would you agree with me that when the
18 AND rule is used, the sensitivity of the combined
19 test can only be equal to or less than the
20 sensitivity of each individual test?

21 A. Yes.

22 Q. And when the AND rule is used, the
23 specificity of the combined test can only be equal
24 to or greater than that of each individual test,

1 right?

2 A. Correct.

3 Q. Okay. Now, switching to the OR rule,
4 in the OR rule, a sample is only considered --
5 sorry. Scratch that.

6 With the OR rule, a sample is
7 considered positive if either biomarker is
8 detected in the sample, right?

9 A. Yes.

10 Q. So the sample would only be considered
11 negative if neither of the two biomarkers are
12 detected in the sample?

13 A. Yes.

14 Q. So if the sample is positive for
15 biomarker A but negative for biomarker B, the
16 sample would be considered diagnostically
17 positive?

18 A. Correct.

19 Q. And if the sample were positive for
20 biomarker B but negative for biomarker A, then the
21 sample would also be considered diagnostically
22 positive, right?

23 A. Yes.

24 Q. Would you agree with me that when the

1 OR rule is applied, the sensitivity of the
2 combined test can only be equal to or better than
3 the sensitivity for each individual test?

4 A. Yes.

5 Q. And you'll agree with me that when the
6 combined -- when the OR rule is applied, the
7 specificity of the combined test can only be equal
8 to or less than the specificity of each individual
9 test?

10 A. Correct.

11 Q. And you mentioned in paragraph 141 that
12 the OR rule was used when reporting the combined
13 results in Lenhard, right?

14 A. Yes.

15 Q. I'm handing you Exhibit 1004.
16 And do you recognize this as the
17 reference you referred to as Lenhard in your
18 declaration?

19 A. I do.

20 Q. So in Lenhard, the authors tested stool
21 samples using both of DNA methylation marker HIC1
22 and a gFOBT test, right?

23 A. Yes.

24 Q. If you look at Table 1, you'll agree

1 with me that this table provides the results of
2 the HIC1 assays and the FOBT test on individual
3 samples?

4 A. Yes, these are individual samples of
5 patients with CRC.

6 Q. Right. So these are -- all these
7 patients in Table 1 have CRC?

8 A. Correct.

9 Q. Okay. And if you look at example
10 patient No. 4 --

11 A. Right.

12 Q. -- this is a sample that came from a
13 patient where they did not report any symptoms,
14 right?

15 A. That's my understanding.

16 Q. And with this patient, the HIC1 assay
17 was tested -- came up positive in this patient,
18 right?

19 A. Yes.

20 Q. In this patient, the FOBT test came up
21 negative, right?

22 A. Yes.

23 Q. So this is a case where the HIC1 assay
24 detected cancer in the patient that was not

1 detected by the FOBT assay, right?

2 A. Correct.

3 Q. And if you look at sample No. 17.

4 A. Uh-huh. Right.

5 Q. This is also a sample where the patient
6 did not report any symptoms?

7 A. Yes.

8 Q. And this is a patient -- this is a
9 sample where the HIC1 test came up negative,
10 right?

11 A. Yes.

12 Q. And in this sample, the FOBT test came
13 up positive, right?

14 A. Correct.

15 Q. So this is an example of a sample where
16 the FOBT test caught a cancer that was not
17 detected by the HIC1 test, right?

18 A. Correct.

19 Q. If you go to Table 4.

20 A. Table 4.

21 Q. Yeah. You'll agree with me that this
22 table provides positivity rates for fecal DNA
23 assay alone, FOBT alone, and the combination of
24 the tests?

1 A. Correct.

2 Q. And for the combination of the tests,
3 Lenhard here uses the OR rule that we discussed,
4 right?

5 A. Yes.

6 Q. And you'll agree with me that when the
7 OR rule is applied here in Lenhard, the
8 sensitivity of the combined test could only be the
9 same or higher than the sensitivity of each
10 individual test, right?

11 A. Yes.

12 Q. And you'll also agree with me that each
13 individual test that -- if each individual test
14 detects cancer incidence missed by the other test,
15 then the combined test will necessarily have some
16 level of higher sensitivity than each individual
17 test, right?

18 A. Yes, higher or -- in principle, it can
19 be higher or the same.

20 Q. But if the -- if each test detects
21 patients that are positive, that the other test
22 misses, then wouldn't it necessarily be higher?

23 A. I would say higher or the same. It can
24 still be the same -- have the same sensitivity as

1 one of the tests.

2 Q. Sorry. If both tests detect cancer --
3 so if the HIC1 test detects cancers that are
4 missed by the FOBt and the FOBt test also detects
5 cancers that are missed by the HIC1, when using
6 the OR rule, wouldn't the sensitivity need to be
7 at least some level higher for the combined test?

8 A. Right. In -- right. In this specific
9 example that you gave, when one test misses one
10 cancer and another test misses another, the
11 sensitivity would be and can only be higher.

12 Q. Okay.

13 A. What I was referring to is that in --
14 in general, sensitivity might be higher or the
15 same. You can also construct the case when -- it
16 can be the same as that of the more sensitive
17 test.

18 If -- for example, if test A detects,
19 you know, five, let's say, out of ten cancers and
20 test B detects three of those, but they are --
21 three out of five does not detect any other ones,
22 the sensitivity of the combination would be the
23 same as the sensitivity of the first test.

24 Q. Right.

1 A. That's what I was referring to.

2 Q. So, for example, for the adenoma
3 detection in Lenhard, the combined test has a
4 higher sensitivity than the FOBT test alone, but
5 as it's reported, has the same sensitivity as the
6 DNA -- as the HIC1 test alone?

7 A. Correct. That's a good example, yes.

8 Q. In this case, where -- in the case of
9 the cancers, where both -- where both the HIC1
10 test detects cancers that are missed by the FOBT
11 and the FOBT test detects cancers with -- that are
12 missed by the HIC1, in that case, the sensitivity
13 has to be higher to some extent?

14 A. In this case, it's higher.

15 Q. So if you go to paragraph 66 of your
16 declaration, and if you go to -- so in this
17 paragraph -- it's part of a section where you're
18 providing some data analysis concerning the
19 Lenhard results, right?

20 A. Correct.

21 Q. In the very last sentence of this
22 paragraph, on the bottom of page 30, you say, This
23 data shows that it's possible that the real
24 sensitivity of HIC1 with the gFOBT could be lower

1 than that of HIC1 alone. Right?

2 A. It does say that.

3 Q. Given that Lenhard is using the OR rule
4 in their data analysis of the combined test, you'd
5 agree with me that this is not an accurate
6 statement?

7 A. So that's a good question. So let me
8 clarify.

9 In the constrained case of the OR rule,
10 that is indeed used in Lenhard. If this -- if the
11 use of the OR rule is the prerequisite for -- for
12 the analysis, then what you said is correct.

13 The real sensitivity of HIC1 combined
14 with gFOBT would not be lower than HIC1 alone. It
15 could be the same. It would not -- we would not
16 be able to say whether it's higher. It could be
17 the same. It would not be lower.

18 What this sentence refers to is --
19 are -- it makes a more general statement where no
20 specific rule or the rule of combining the markers
21 is assumed as a required step. And in -- in --
22 and that is a correct statement.

23 Q. So in this paragraph, paragraph 66,
24 you're analyzing the data presented in Table 4 of

1 Lenhard, right?

2 A. Correct. So the -- right. If we
3 read -- let's read this sentence again.

4 This data shows that it's possible that
5 the real sensitivity of HIC1 with gFOBT could be
6 lower than that of HIC1.

7 The sentence does not say that this
8 data shows that in the specific example of
9 Lenhard, the way -- the way the markers were
10 combined with the OR rule, the real sensitivity of
11 HIC1 with gFOBT could be lower.

12 So it does not has this clause that in
13 case if OR rule is used. It refers to HIC1 in
14 combination with gFOBT. So that is still a
15 correct statement, but I agree with you. If -- if
16 the statement had explicit reference to the use of
17 Lenhard's OR rule, the way Lenhard used that,
18 we -- we would have to say the real sensitivity of
19 HIC1 with gFOBT could be the same as HIC1 alone.

20 But that's not what this -- that's not
21 how the sentence is written.

22 Q. If you look at the figure right above
23 that sentence where you graph the probability
24 density and positivity rates of HIC1 versus

1 combined.

2 Do you see that?

3 A. Right.

4 Q. So the combined positivity rate that
5 you're plotting here is based on the OR rule,
6 right?

7 A. This probabilities are based on the --
8 on the distribution of data from table -- Table 4.
9 So yes, it assumes the OR -- OR rule. So let me
10 make one thing very, you know, clear here. And I
11 understand, it might be kind of fine point, is
12 that what Table 4 reports is the sensitivity and
13 specificity. We're talking about sensitivity in
14 this case.

15 The Table 4 reports the means of the
16 distribution. It reports one particular
17 realization given the dataset of -- of that
18 particular paper. If we're looking at
19 sensitivity, we have to look at Table 1. There
20 are 26 patients.

21 For this 26 patients, exactly the way
22 they are, exactly the way the HIC1 methylation
23 came out, the -- exactly the way FOBT came out, if
24 you look at exactly this dataset, these are the

1 values of sensitivity you're going to get for HIC1
2 and FOBT and the combined test.

3 It does not mean that if we were to
4 extend this dataset and look at the real
5 performance, which is what -- the real sensitivity
6 of HIC1 or gFOBT or the combination, it could only
7 be assessed when you look at a much larger
8 dataset.

9 The -- the values of sensitivity that
10 we would get in this case could be different and
11 probably would be different than the ones reported
12 for -- in Table 4 for this particular study.

13 And -- too many papers here.

14 And what this graph on page 30 shows is
15 the probability where this values would lie. So
16 we conclude, therefore, that if -- that the real,
17 let's say, sensitivity of HIC1 combined with
18 gFOBT, for example, could be lower than -- or
19 higher than the one -- the value reported here in
20 this paper for -- for HIC1.

21 It is a matter of probability. All we
22 can talk about, distributions.

23 Q. Yeah. Wouldn't you agree with me that
24 no matter how many cancer samples are tested and

1 how many times you repeat the test, if you're
2 applying the OR rule, the combined test will never
3 have a sensitivity that's lower than the HIC1 test
4 alone?

5 A. For a -- for a given dataset, yes.

6 Q. Okay. So --

7 A. Only when applied to a given dataset --
8 to the same dataset.

9 Q. But as long as you're -- but you'd
10 compare these tests using the same dataset, right?
11 You wouldn't be -- like a -- one of skill in the
12 art wouldn't be taking one dataset and running the
13 HIC1 and one dataset -- one set of samples to test
14 the HIC1 and one set of samples to test the
15 combined test?

16 A. Correct. Correct.

17 Q. That wouldn't be a scientifically sound
18 comparison, right?

19 A. For sure. For sure.

20 Q. Okay. And then isn't the issue with
21 this analysis that's presented in -- in this
22 figure that's on page 30 that it assumes that the
23 HIC1 sensitivity is going to be unrelated to the
24 combined sensitivity?

1 MS. FERNANDS: Objection.

2 THE WITNESS: No, it does not. It
3 doesn't assume that. What it shows is the
4 probability density functions of the true --
5 real sensitivity for either -- either test in
6 different realizations.

7 For -- for any fixed dataset, of
8 course, if the OR rule is used, then the
9 sensitivity of combination cannot be lower
10 than the sensitivity of HIC1 in this case,
11 but if you repeat this experiment multiple,
12 multiple times, according to the statistics,
13 you would get two distributions, and they
14 would overlap.

15 BY MR. JONES:

16 Q. But you'll agree with me, when the
17 combined test is compared to the individual HIC1
18 test, on any single dataset, you're never going to
19 see a sensitivity of the combined test that's
20 lower than the individual test?

21 A. Yes, I agree with that. And I believe
22 that's what paragraph -- what -- 146, I think,
23 right? When the AND and OR rules are -- 141 --
24 paragraph 141, when the AND and OR rules are

1 discussed, these aspects are inferred in this --
2 in this paragraph.

3 Q. If you look at paragraph 67 of your
4 declaration.

5 A. I see.

6 Q. So here you -- in this paragraph, you
7 use a data in Table 4 to calculate the probability
8 that the sensitivity of the combined -- sorry.
9 Let me start that over.

10 In this paragraph, you describe a
11 calculation where you calculated the probability
12 that the combined marker test has a sensitivity
13 that's the same as the HIC1 test alone; is that
14 right?

15 A. Could you point the sentence?

16 Q. Sorry. It's the -- it's the last --

17 A. Just want to make sure I'm on the right
18 part of the paragraph.

19 Q. It's the last sentence of the
20 paragraph.

21 Because a normal distribution, the
22 standard deviation -- and it says, We can use
23 Table 4 data to calculate the probability of the
24 sensitivity of the combined marker being the same

1 as that for HIC1 alone and the p-value.

2 A. Correct. Yes, I see that.

3 Q. And so the p-value is the chances of --
4 the statistical chances of the -- in this case, of
5 the combined assay being the same as -- sorry.
6 Let me start that off because there's too many
7 clauses here.

8 A. Okay.

9 Q. Okay. In this case, the p-value
10 represents the statistical probability that the
11 sensitivity of the combined assay is the same as
12 the sensitivity of the HIC1 assay alone?

13 A. Almost correct. Conceptually you're
14 correct. Just to be correct mathematically, let
15 me just add one slight thing, but conceptually
16 does not change what you said.

17 So the p-value is the probability of
18 obtaining the outcome, let's say, as extreme as
19 what was inferred; in this case, that the
20 combination has higher sensitivity than HIC1 under
21 the assumption or if the new hypothesis is
22 correct, the new hypothesis being that they are
23 the same.

24 Q. Okay. So --

1 A. It's just a small mathematical
2 difference, just to be mathematically correct.
3 But conceptually you got it right.

4 Q. I want you to be mathematically
5 correct.

6 So here the no hypothesis would be that
7 the combined test would be -- has the same
8 sensitivity as the HIC1 test alone --

9 A. Correct.

10 Q. -- right?

11 And obviously, in their results, the
12 sensitivity of the combined test was higher to
13 some extent than the test alone, and so the
14 p-value is the chances that you'd get those
15 results if -- if, in fact, the sensitivities were
16 the same?

17 A. That is correct. And this is because
18 any number reported in a study like this, in
19 particular Table 4, it's just the mean of
20 observe- -- of the observation for a particular
21 finite size -- in this case, smallish dataset --
22 and there's always a distribution that we would
23 obtain if we were to repeat the study multiple
24 times.

1 So we technically don't know what
2 exactly the sensitivity of HIC1 is or the
3 sensitivity of the combination. So
4 hypothetically, if data like this shows that the
5 combination has 65 percent sensitivity for all
6 cancers, is the first row in Table 4, versus
7 42 percent in HIC1, the p-value would -- would
8 assess the probability of getting the same result
9 at random.

10 Q. Yeah. So the probability of -- the
11 chance -- the probability of getting the results
12 are reported in Lenhard for the combined tests
13 versus the HIC1 test alone, if there was no
14 difference between the tests, would be 13 percent?

15 A. That's correct.

16 Q. Okay.

17 A. So yeah, let -- let me maybe clarify
18 this with an analogy. Let's say if you have a
19 coin; I have a coin. You toss it several times.
20 It may fall on the same side, right?

21 Q. Yes.

22 A. Let's say heads. You get all heads; I
23 get all tails. We might make an observation that
24 your coin only has -- is different from mine.

1 Only has heads, and my coin only has tails.

2 So if the question is, what is the
3 probability of obtaining the same result if we
4 actually both had a fair coin? What is the
5 probability of making a judgment that is -- that
6 the coins are unfair?

7 And in -- in scientific community,
8 across pretty much all fields, especially
9 medicine, there is a consensus that a couple of
10 values that are typically used as threshold of
11 statistical significance of results, the more
12 rigorous threshold is .01 p-value, which means
13 1 percent probability. A little less rigorous is
14 .05, so 5 percent probability.

15 In our experiment with coins, what this
16 values would be analogous of is the following.

17 If your coin falls on the same side
18 four times in a row and my coin falls on a
19 different side four times in a row, that could
20 respond to p-value close to .01. P-value of .05
21 corresponds to close -- gets close to the -- your
22 coin getting tossed on the same side three times
23 in a row. And the same thing for me. Three
24 times.

1 The p-value of .13 that is here,
2 actually, is fairly close to the p-value we would
3 obtain if your coin -- you toss your coin, you get
4 two heads in a row, and I get two tails in a row.
5 So you throw it twice. Head and head. I get tail
6 and tail.

7 The probability of -- so the p-value of
8 this experiment would be very close to .13. So if
9 you were to make a conclusion that your coin has
10 only heads and my coin only has tails, p-value of
11 making that conclusion is .13 -- well, it's close
12 to -- close to .13.

13 I don't know if I made it more clearer
14 or less clearer.

15 Q. No. This p-value calculation doesn't
16 take into account that the results of these -- the
17 combined tests and the result of the HIC1 test
18 alone are actually linked to each other, right?

19 A. They -- they consider them as
20 independent observations.

21 Q. Okay. But they aren't actually
22 independent observations in this case, right?

23 A. In a sense that they rely on the same
24 dataset -- patient dataset, no, they're not.

1 Q. And, in fact, every single incident
2 where it tested positive for the HIC1 test, it
3 necessarily also tested positive for the combined
4 test, right?

5 A. Could you repeat that? I'm sorry.

6 Q. Every sample that tested positive for
7 the HIC1 test alone also would have been a
8 positive score for the combined test here?

9 A. Correct.

10 Q. So given the fact that some tests
11 tested positive for the HIC1 -- some cancers
12 tested positive for the HIC1 but not for the FOBT
13 and other cancers tested positive for the FOBT but
14 not for the HIC1, mean that regardless of degree,
15 there must be some increase in specificity for the
16 combined test than either test alone?

17 MS. FERNANDS: Objection.

18 THE WITNESS: So you see, you said must
19 be an increase, and I'm not sure I can,
20 again, mathematically, say that. I don't
21 think we can say that because you may not
22 have -- you might not have an increase for
23 any dataset.

24 I agree with you that the

1 sensitivity for a -- if we fix a dataset, the
2 sensitivity of a combination cannot go lower.

3 BY MR. JONES:

4 Q. And will you agree with me that if you
5 fix a dataset and one test catches positives that
6 are missed by the other and the other test catches
7 positives that are missed by the first test, the
8 sensitivity must be, to some extent, higher?

9 A. Yes. And -- but -- yes, I agree with
10 that.

11 Q. And you'll agree with me that under
12 this situation, that kind of discrepancy wouldn't
13 be picked up by a p-value, right?

14 A. No, p-value analysis is still valid,
15 and it's used all the time for -- in this kind of
16 studies, including Lenhard themselves, when they
17 look at -- like on page -- what is it? Page 6,
18 the last paragraph, right before the discussion,
19 where they compare -- so the point of this
20 paragraph is to compare HIC1 versus FOBT, and they
21 say things such as HIC1 assay was only slightly
22 more sensitive for all cancers compared to FOBT,
23 42 versus 35 percent p-value equals .19, and they
24 have analysis -- more subgroup analysis in this

1 paragraph.

2 So they -- and there -- so there are --
3 p-value -- p-value analysis used in -- in this
4 kind of circumstances all the time. I think
5 what -- the part that we -- we need to
6 understand -- and I understand that somewhat --
7 somewhat confusing topic is the question of
8 probability versus reported mean.

9 When we look at the dataset like what
10 we have in Table 1, we are already looking at
11 the -- at the output of both tests -- let's say,
12 test A versus test B. They are fixed, right.

13 So in this case, obviously, sensitivity
14 cannot be -- if you use the OR rule, the
15 sensitivity cannot go below the -- the sensitivity
16 of the -- one of the tests.

17 However, we have to remember that in
18 this case, we're looking at the -- at one
19 observation of a random dataset. If we were to
20 take the very, very same patients and run the same
21 tests again, we could, in principle and in
22 practice, get somewhat different readouts for FOBT
23 or HIC1.

24 And I'm not talking about getting

1 patients in different circumstances. Just take
2 the very same samples. Because each time you do
3 measurement, there is an uncertainty. There is a
4 noise involved and an uncertainty of measurements.
5 There's always some sort of error.

6 So some of this HIC1 readouts or FOBT
7 readouts could potentially be different. Some of
8 the pluses may turn into minuses and vice versa.
9 So we always have to remember that we are dealing
10 with the probability distribution, and -- and
11 that's where things like p-values come in handy,
12 to see if the -- if the -- how -- how likely it is
13 this kind of output could be obtained as a random
14 chance.

15 Q. When Lenhard applies the p-values here,
16 in the part on -- did you say page 6; is that
17 right?

18 What -- I'm sorry. I can look it up.
19 Page 6, right?

20 A. Uh-huh.

21 Q. You mention the p-values that Lenhard
22 is applying.

23 In this case, they're comparing the
24 HIC1 test to the FOBT test, right?

1 A. Uh-huh.

2 Q. And in that case, the results of the
3 HIC1 test and FOBT test, they aren't linked to
4 each other, right?

5 A. They're not linked. They're on the
6 same set of patients. They're not linked, yes.

7 Q. Right. They don't apply a p-value when
8 comparing the combined test to either test
9 individually, do they?

10 A. They do not. They provide
11 confidence -- I believe they provide confidence
12 intervals for each. They don't -- they don't have
13 a p-value.

14 For the combined test -- they say, so
15 the mean, what they observed, was 65 percent. The
16 confidence interval, on that number, is 44 to
17 83 percent. And for HIC1 is the average -- the
18 mean is 42 for their dataset, and the
19 confidence -- 95 percent confidence interval is 23
20 to 63 percent.

21 (Reporter clarification.)

22 THE WITNESS: Right. So for the
23 combined dataset, the observed mean is
24 65 percent for all cancers. The 95 percent

1 confidence interval is 44 percent to
2 83 percent. And for HIC1 alone, the mean is
3 42 percent sensitivity. The confidence
4 interval is 23 to 63 percent.

5 BY MR. JONES:

6 Q. Okay. So if you look at paragraph 68
7 of your declaration, you say, By widely accepted
8 convention, result is said to be statistically
9 significant if the p-value is less than .05, which
10 is considered a loose criterion, or a p-value of
11 less than .01, which is a strict criterion.

12 Do you see that? Paragraph 68, right?

13 A. Yeah, I see that.

14 Q. And then you say, p-values below .1 and
15 higher than .05 are considered to be marginally
16 significant, and most observers would not accept a
17 result of p-value of greater than .05.

18 A. Correct. Yeah.

19 Q. Then you go on to say that the p-value
20 of .13 is not statistically significant according
21 to this conventional definition, right?

22 A. Correct.

23 Q. Then you say, Based on this p-value, a
24 person of skill in the art would not consider a

1 claim of increased sensitivity for all colorectal
2 cancers for the combination of HIC1 and gFOBT as
3 compared to HIC1 sufficiently substantiated. Is
4 that right?

5 A. Correct.

6 Q. And if you look at paragraph 76 -- it's
7 on page 37.

8 A. Yes.

9 Q. In this paragraph, you discuss the
10 sensitivities -- sorry. Scratch that. Start
11 over.

12 In this paragraph, you discuss the
13 specificities of the test performed in Lenhard,
14 right?

15 A. Yes.

16 Q. Lenhard does not explicitly provide the
17 specificity of the combined test, does it?

18 A. I -- I don't think so. But to be sure,
19 I would have to look at it again.

20 Q. Do you recall calculating the
21 specificity based on Table 3?

22 A. I certainly did. But I always
23 calculate my statistics myself.

24 Q. Okay.

1 A. So yes, I did calculate it.

2 Q. But you're not aware of anyplace in
3 Lenhard where it provides a specificity for the
4 combined test?

5 A. I don't remember them providing
6 specificity for the combined test. It -- it can
7 be easily calculated based on their data. But
8 yes, I don't remember them providing a number.

9 Q. There's no place in Lenhard where the
10 authors explicitly say that the combined test has
11 a lower specificity than the individual tests,
12 does it?

13 A. I don't remember them saying that. I
14 don't remember them analyzing specificity of the
15 combined test.

16 Q. So certainly Lenhard --

17 A. Yeah.

18 Q. -- Lenhard doesn't say anywhere that
19 the specificity of the combined test is
20 unacceptable, right?

21 A. They -- since they don't analyze
22 specificity, over the combined test, I -- I don't
23 think they qualify how good or bad it is.

24 Q. And in your declaration, you calculate

1 that the specificity of the combined test is
2 89 percent, right?

3 A. It sounds about right.

4 Q. I think you say it in paragraph 73, if
5 you want to check it.

6 So about halfway down, in paragraph 73,
7 you say, Based on the data in Lenhard, in this
8 particular combination -- if this particular
9 combination is optimized for sensitivity, the
10 result is that the sensitivity and specificity for
11 cancers are 65 percent and 89 respectively.
12 Right?

13 A. Correct.

14 Q. And when you say optimized for
15 sensitivity there, you're referring to using the
16 OR test?

17 A. Yes.

18 Q. In your declaration, do I -- do I
19 identify anyplace in the art where it states that
20 a specificity of 89 percent for a fecal colorectal
21 cancer test would be unacceptable?

22 A. No.

23 Q. Cologuard's specificity that we just
24 looked at reported in the 2014 --

1 A. 86 percent --

2 Q. -- was 86 percent, right?

3 A. 86, yeah.

4 Q. About --

5 A. 86.6, yeah.

6 Q. Okay. If you look at the sentence
7 bridging pages 37 and 38 of your declaration, back
8 in paragraph 76, you state that using the data in
9 Table 3 to calculate the probability of the
10 specificity of the combined HIC1 and gFOBT markers
11 being the same as HIC1 alone results in a p-value
12 of .12. This is also not statistically
13 significant.

14 Do you see that?

15 A. Yes, I do.

16 Q. So combining the HIC1 and FOBT tests in
17 Lenhard did not result in a statistically
18 significant drop in specificity compared to the
19 HIC1 test alone, did it?

20 A. I'm sorry. Can you repeat that?

21 Q. The combination of the HIC1 test and
22 FOBT tests in Lenhard did not have a statistically
23 significant -- okay. Sorry. Let me do that.

24 The specificity of the combined HIC1

1 and FOBT test was not statistically significantly
2 lower than the specificity of the HIC1 test alone,
3 right?

4 A. Correct. Yes.

5 Q. So a person with skill in the art would
6 not consider a claim of decreased specificity in
7 the combined test as compared to HIC1 alone to be
8 sufficiently substantiated, would they?

9 A. That is correct. And that is why we
10 provided -- you know, that's why I calculated this
11 and provided my declaration, to -- to make sure
12 that, you know, we are consistent.

13 Neither increase in sensitivity or drop
14 in specificity would be considered
15 statistically -- statistically significant. I
16 wanted to make sure that we are honest and
17 complete, and that's why this p-value is provided.
18 And we do say it's not statistically significant.

19 It's a -- you know, it's a small
20 dataset. The numbers for the sensitivity,
21 specificity are not drastically different for the
22 combined versus HIC1 test. And that's why it's
23 just difficult to make conclusions, just like in
24 the example I gave with tossing the same coin

1 twice.

2 I think, you know, it would be fairly
3 easy to imagine a scenario when your coin gets
4 head twice in a row and so is mine. That's the
5 problem with the smallish studies that don't show
6 huge improvements in diagnostic performance.

7 Q. So if you go to paragraph 73 of your
8 declaration. We just looked at this. It's --
9 halfway through the paragraph it says, Based on
10 the data in Lenhard, if this particular
11 combination is optimized for sensitivity, the
12 result is that the sensitivity and specificity for
13 cancers are 65 percent and 89 percent,
14 respectively. Right?

15 A. Right.

16 Q. In the first sentence, you say that
17 Lenhard also shows that the sensitivity and
18 specificity for HIC1 alone in cancers is
19 44 percent and 98 percent, respectively, right?

20 A. Correct.

21 Q. So combining the test in this dataset
22 resulted in an increase of 21 percentage points to
23 the sensitivity, right?

24 A. You're referring to the increase in

1 sensitivity from 42 to 65 percent?

2 Q. From 44 to 65 percent.

3 A. Right. Correct. Yes. Yes. Yes.

4 Q. And combining the results of the HIC1
5 tests and the FOBT test using the OR rule resulted
6 in a decrease in the specificity of 9 percentage
7 points, right?

8 A. Correct.

9 Q. And then in the next sentence, after
10 you report the 65 percent and 89 percent, you say,
11 Here, although the sensitivity of the combined
12 test is numerically higher, the specificity is
13 considerably lower.

14 Do you see that?

15 A. Yes, I see that.

16 Q. So you consider the reduction in
17 specificity in the combined test as not
18 statistically significant, to be considerably
19 lower?

20 MS. FERNANDS: Objection.

21 THE WITNESS: It is lower. But, again,
22 I -- I have to point out that we discussed --
23 in the other paragraph that you pointed out,
24 we discussed that the drop in specificity is

1 also not statistically significant. So none
2 of them is significant.

3 The increase in sensitivity and
4 the drop in specificity, they're not
5 significant.

6 BY MR. JONES:

7 Q. Do you feel comfortable calling the
8 specificity considerably lower despite the fact
9 that the result -- difference was not
10 statistically significant?

11 MS. FERNANDS: Objection.

12 THE WITNESS: So there's a different
13 terminology. Word "significantly lower"
14 would mean that result is statistically
15 significant based on a predetermined criteria
16 for statistical significance.

17 We don't use word "significantly
18 lower." The sentence says "considerably
19 lower." So it has a very different meaning.

20 BY MR. JONES:

21 Q. So in your mind, the value could be
22 considerably lower than another value even though
23 the difference was not statistically significant?

24 MS. FERNANDS: Objection.

1 THE WITNESS: I think these are two
2 different things. The means may be lower or
3 higher. They might or might not be
4 significantly different. And I think that's
5 what almost essentially -- this is the crux
6 of the matter.

7 If we use Lenhard's reference to
8 argue that sensitivity of the combination is
9 higher than HIC1 and say, Well, that's what
10 this reference shows. It's -- it's a fact.
11 It's a fact that could have been fairly
12 easily observed by a random chance as the
13 statistical analysis of the data shows.

14 So if we look at the -- if we
15 look at the differences in sensitivity and
16 differences in specificity, they are -- they
17 are different.

18 If we argue that 65 percent is
19 higher than 44, there's a difference. 65 is
20 higher. We should also acknowledge that
21 89 percent is different from 98 percent. So
22 the specificity of the combination is lower
23 than the specificity of the -- of HIC1 alone,
24 but either of these results could be obtained

1 as a random chance -- as a result of random
2 chance if the tests performed very similarly
3 to one another.

4 BY MR. JONES:

5 Q. So in this sentence, in paragraph 73,
6 how come you say the sensitivity of the combined
7 test is numerically higher and the specificity is
8 considerably lower?

9 Why do you use the word "numerically"
10 versus "considerably"?

11 A. Those are qualitative terms. If you're
12 asking whether the -- the difference between 65
13 and 44 percent numerically higher than the
14 difference between 98 and 99, the answer is yes,
15 it is numerically higher. None of this
16 differences is significant.

17 Q. Is the difference between 44 percent
18 and 65 percent considerably higher?

19 A. You can say that. The word
20 "considerable" does not imply a particular
21 mathematical criterion or test.

22 Q. Okay. Okay. If you look at
23 paragraph 78.

24 So on the top of page 39, you say,

1 They -- I think that mean -- in this context, I
2 believe it's the authors of Lenhard -- did not
3 conclude that HIC1 should be combined with FOBT.

4 And then you say, Lenhard's conclusion
5 is consistent with the direction of the art at the
6 time.

7 Do you see that?

8 A. Just to make sure we're on the same
9 page, it's 78, right?

10 Q. Paragraph 78.

11 A. 78.

12 Q. Page 39. So it's --

13 A. Oh, okay. That's right. Right.

14 Yes, I see that.

15 Q. And you don't cite any references in
16 support of your opinion that the conclusion is
17 consistent with the direction of the art at the
18 time, do you?

19 A. I did not provide a citation here.

20 Q. Then you say, A POSA at the time would
21 have expected that, by using different methylation
22 markers, some markers would identify indicia of
23 CRC but other markers would not, thus improving
24 test sensitivity without negatively affecting

1 specificity.

2 Do you see that?

3 A. Yes.

4 Q. Lenhard doesn't provide any data
5 showing that combining methylation markers would
6 increase sensitivity, does it?

7 A. No, he did not -- or they did not.

8 Q. Lenhard also doesn't provide any data
9 showing that combining methylation markers would
10 increase sensitivity without negatively affecting
11 specificity, does it?

12 A. They did not. They do reference
13 several other methylation markers that on their
14 own were able to provide very high sensitivity.
15 And the -- as we have just discussed, following
16 the logic of using the OR rule, if you look at a
17 specific dataset and you have two methylation --
18 methylation markers, the sensitivity would not be
19 lower. It would be the same or higher.

20 The higher the sensitivity of each of
21 the markers, the higher the combined sensitivity
22 would be. So following the logic of achieving
23 higher sensitivity when two markers are combined
24 using the OR rule as an FOBT and -- and HIC1, if

1 FOBT is replaced by some of the markers that
2 Lenhard suggested with very high sensitivity, the
3 sensitivity would go up more likely higher than
4 65 --

5 Q. Okay.

6 A. -- percent.

7 Q. So are you referring to the SFRP2
8 methylation marker?

9 A. For example, yes.

10 Q. Is there any other methylation marker
11 for which Lenhard -- other than HIC1 and SFRP2, is
12 there any other methylation markers that Lenhard
13 provides sensitivity values for?

14 A. I don't think so.

15 Q. So let's look at SFRP2 then.

16 So if you look at -- here -- we -- it
17 is probably easier to just look at your
18 declaration.

19 In paragraph 77 of your declaration,
20 you say, Lenhard discusses other methylation
21 markers found in stool, including SFRP2, which
22 detected 77 percent to 90 percent of CRCs, more
23 than the 65 percent detected by HIC1 methylation
24 analysis combined with gFOBT.

1 And it says, Lenhard noted, however,
2 that the specificity of SFRP2 methylation was
3 quite poor, at 77 percent.

4 Do you see that?

5 A. Yes.

6 Q. So if HIC1 were combined with SFRP2
7 methylation marker using the OR rule, you'll agree
8 with me that you would have decreased the
9 specificity of -- compared to HIC1 alone, right?

10 A. We would have to look at actual data.

11 Q. Well, you said the SFRP2 methylation,
12 the specificity is 77 percent, right?

13 A. Uh-huh.

14 Q. When you combine using the OR rule,
15 your specificity is going to be the same as or
16 lower than the lower specificity of the individual
17 marker, right?

18 A. It will be the same or lower, yes.

19 Q. So the specificity of the combined test
20 would be -- combining SFRP2 methylation and HIC1
21 would be no higher than 77 percent?

22 A. It would not be higher than 77, but --

23 Q. And that would be a significant
24 reduction -- well, I don't want to say significant

1 because --

2 A. That implies statistical significance.

3 Q. Yeah. That would be lower than the
4 specificity of 98 percent for the HIC1 alone,
5 right?

6 A. Yes.

7 Q. So if you combine those two markers,
8 using the OR rule -- I mean, using the OR rule, it
9 would result in a lower specificity than the HIC1
10 test alone, right?

11 A. Right. You would get -- what we can
12 say is that the combination would have sensitivity
13 above 77 or 90 percent, depending on where SFRP2
14 actually is. Let's say, 90 -- it doesn't matter.

15 So the sensitivity would be above 77 or
16 90 percent. Where exactly it would fall, we don't
17 know. And the specificity of the combination
18 would fall below 77 --

19 Q. Okay.

20 A. -- or could be 77 or below 77.

21 Q. Okay. And if you combined the HIC1
22 test with the SFRP2 test using the AND rule, the
23 sensitivity of the combined test could be no
24 greater than the sensitivity for HIC1 alone,

1 right?

2 A. Correct.

3 Q. So the sensitivity for the combined
4 test could be no greater than 44 percent?

5 A. Correct.

6 Q. So in that case, using the -- combining
7 HIC1 and SFRP2, you would say that by using these
8 two different methylation markers, you would not
9 be -- you would not -- it would not result in
10 identification of indicia of CRC that -- sorry.
11 Scratch that.

12 When you combine -- you would agree
13 with me that combining the SFRP2 and the HIC1 test
14 does not result in improved test sensitivity
15 without negativity -- negatively affecting
16 specificity regardless of whether you use an AND
17 test or the OR test?

18 A. Yes, I agree with that.

19 Q. Are you aware of any example -- sorry.
20 Scratch that.

21 Do you provide in your declaration any
22 example of where combining different methylation
23 markers results in improved test sensitivity
24 without affecting specificity?

1 A. I did not consider this -- this
2 publications for the purposes of this declaration.
3 In -- so I don't want to -- I cannot speak in
4 hypothetical. If -- the question if it's
5 possible, it is possible.

6 Q. But you're not -- you haven't -- let me
7 scratch that.

8 Are you aware of any specific example
9 where methylation -- prior to 2009, where
10 methylation markers were combined, and it resulted
11 in an increase in test sensitivity without
12 negatively affecting specificity?

13 A. That was not reported in the literature
14 that I reviewed.

15 Q. So despite that -- despite it not being
16 reported in the literature review and despite it
17 not being reported in Lenhard, it's your opinion
18 that a person of skill in the art would have
19 expected that by using different methylation
20 markers, they would have been able to improve test
21 sensitivity without negatively affecting
22 specificity?

23 MS. FERNANDS: Objection.

24 THE WITNESS: So Lenhard does not

1 suggest using SFRP2. In fact, I think
2 they're pretty clear by saying that it's not
3 the marker that they should be using.

4 They giving it as an example of a
5 marker that may have pretty high sensitivity
6 or sensitivity higher than that of HIC1.
7 They do acknowledge very clearly that that's
8 not the methylation marker they would want to
9 combine with HIC1 precisely because its
10 specificity is low.

11 What they're saying is that
12 HIC1 -- we can look at the summary.

13 The study shows HIC1 is a
14 sensitive and specific marker well suited for
15 stool-based CRC screening. Combination of
16 HIC1 --

17 (Reporter clarification.)

18 THE WITNESS: Sorry.

19 HIC1 is a sensitive and specific
20 marker well suited for stool-based CRC
21 screening. Combination of HIC1 with a few
22 additional sensitive and specific methylation
23 markers -- so their criticism of SFRP2 is
24 that it may have the sensitivity; it doesn't

1 have the good specificity.

2 A combination of HIC1 with a few
3 additional sensitive and specific methylation
4 markers -- I emphasize methylation -- may
5 allow for the highly sensitive and specific
6 stool-based detection of CRCs and adenomas.

7 They suggest a few genes based on
8 their understanding of cancer biology,
9 mechanistic biology, such hMLH1 or HPP1.
10 That's what they mentioned. There are
11 clearly others that are known outside of --
12 outside of Lenhard at the time that could
13 have been candidates as well that might fit
14 this role.

15 So I agree with you on SFRP2.
16 But this also agrees with -- with Lenhard's
17 conclusions.

18 BY MR. JONES:

19 Q. Do you know whether if you combined
20 HIC1 with hMLH1, you'd result in an increase in
21 sensitivity without negatively affecting
22 specificity?

23 A. Not based on the -- based on Lenhard or
24 other papers that were brought to me. Most of

1 those papers that I reviewed, they came from
2 Dr. Whitney's deposition; were his literature,
3 prior art analysis.

4 So this is the -- these are the papers
5 I reviewed. I don't believe hMLH1 was discussed
6 in the context of -- in those papers, in the
7 context of combining -- being combined with HIC1.
8 So no, I don't know.

9 Q. So in your sentence, in paragraph 78,
10 where you say, A POSA at the time would have
11 expected that by using different methylation
12 markers, some markers would identify indicia of
13 CRC that other markers would not, thus improving
14 test sensitivity without negatively affecting
15 specificity.

16 Now, you don't provide a citation for
17 that, right?

18 A. I do not. This conclusion is
19 consistent with what is said in Lenhard. So
20 effectively, Lenhard's reasoning is -- I agree
21 with what Lenhard says.

22 I would read that if somebody who is
23 skillful in the art were to read Lenhard's paper
24 and look at their data, they would see what the

1 data and conclusions actually say; that there
2 was -- so HIC1 is, as a methylation marker,
3 potentially promising. There is no justification
4 based on this data to combine HIC1 with FOBT for
5 significantly improved diagnosis.

6 But we do know from -- from other
7 studies that there are other methylation markers
8 that are highly sensitive. There are several
9 markers that are known to be mechanistically
10 linked to -- to carcinogenesis, and that's why it
11 might be promising to combine several methylation
12 markers together.

13 Very importantly, in the discussion
14 today, we have focused on statistics and p-values
15 and the increase in sensitivity for CRCs, but I
16 would like to emphasize this. Something I know I
17 mentioned in the -- earlier as well. That person
18 skillful in the art would look particularly
19 closely at this numbers, sensitivity and
20 specificity, possibility of combination, for
21 advanced adenomas because that's the lesion that
22 needs to be targeted by screening.

23 Not only that, the -- as we know,
24 most -- all cancers in the study, they were --

1 these patients were known to have cancer before
2 they were recruited, and many of them were
3 symptomatic.

4 You pointed out a couple of patients
5 that were asymptomatic, but majority were
6 symptomatic. So this is a highly preselected
7 dataset with fairly large cancers that are
8 extremely rarely seen in the screening population.

9 The data that a person skillful in the
10 art would pay more attention to is how these
11 markers behave when applied to advanced adenomas,
12 and -- and the story for advanced adenomas, as we
13 know, is quite different. There was no increase
14 in sensitivity, and there was a drop in
15 specificity when FOBT was combined with HIC1.
16 That's a story of failed combination.

17 So somebody skillful in the art would
18 say, this data is telling me that we shouldn't --
19 shouldn't go there. And that's the conclusion
20 that Lenhard arrives at as well.

21 So in paragraph 78, I don't cite any
22 additional references because this conclusion
23 follows from Lenhard and agrees with Lenhard.

24 Q. So you're saying that a person skilled

1 in the art would have expected that you could
2 improve -- you could combine different methylation
3 markers to improve test sensitivity without
4 negatively affecting specificity here, right?

5 A. Yes.

6 Q. As you sit here today, are you able to
7 provide any example of a methylation marker that
8 has been combined with HIC1 that increased test
9 sensitivity without negatively affecting
10 specificity?

11 A. I would not like to comment on that
12 because I did not research HIC1 in --

13 Q. Can you --

14 A. -- beyond -- beyond Lenhard.

15 Q. As you sit here today, are you able to
16 provide any example of any methylation markers
17 that, when combined with each other, increase test
18 sensitivity without decreasing specificity?

19 MS. FERNANDS: Objection.

20 THE WITNESS: If the -- if your
21 question refers to any case when several
22 markers can be combined in such a way, it's
23 certainly possible.

24 BY MR. JONES:

1 Q. But you're not aware of a specific
2 example of that as you sit here today?

3 MS. FERNANDS: Objection.

4 THE WITNESS: I would not be able to
5 reference a specific paper on that, but
6 there -- there's a lot of literature that
7 shows a lot of examples when this is
8 possible, and when, in fact, in some cases,
9 both sensitivity and specificity are
10 increased. It also depends how you combine
11 the markers.

12 There are quite a few examples of
13 that. I would not be able to cite a specific
14 paper on that right now.

15 BY MR. JONES:

16 Q. Are you able to provide any examples of
17 that that were published before 2009?

18 A. I would have to do additional search.

19 Q. That's not something you did in
20 preparing your declaration?

21 A. No.

22 Q. So you just don't know whether any
23 examples of that were available in the art prior
24 to 2009?

1 MS. FERNANDS: Objection.

2 THE WITNESS: I -- I would have to --
3 I'd have to look obviously.

4 BY MR. JONES:

5 Q. Okay.

6 MR. JONES: Let's take a break.

7 (Whereupon, a break was taken,
8 after which the following
9 proceedings were had:)

10 BY MR. JONES:

11 Q. So I'm going to be asking questions
12 again about Exhibit 2044, your second declaration.
13 So if you go to page 56 of your declaration.

14 Okay. So on page 56, you start a
15 section of your declaration titled Petitioner Has
16 Not Shown a Motivation For At-Home Sample
17 Separation. Right?

18 A. One second. Page 56, right?

19 Q. Your second -- yes. It's section IX.

20 A. Right. Oh, yeah. Okay. Got it. The
21 title of the section.

22 Q. Yeah, the title. It's -- the title is
23 Petitioner Has Not Shown a Motivation For At-Home
24 Sample Separation, right?

1 A. Right.

2 Q. So you'll agree with me that prior to
3 2009, FIT tests were being used as a fecal
4 diagnostic test, right?

5 A. Yes.

6 Q. And you'd agree with a standard FIT
7 test, like the one disclosed in Vilkin, that test
8 would include at-home separation of a fecal
9 sample?

10 MS. FERNANDS: Objection.

11 THE WITNESS: At-home collection.

12 BY MR. JONES:

13 Q. As part of that at-home collection, the
14 patient separates the part of the fecal sample
15 that's going back to the lab to be tested from the
16 part of the fecal sample that is being discarded,
17 right?

18 MS. FERNANDS: Objection.

19 THE WITNESS: Sure. Yeah, I agree with
20 that.

21 BY MR. JONES:

22 Q. So if you -- if a patient were to use a
23 standard commercially available FIT test,
24 according to manufacturer's expression, that

1 patient would separate the fecal sample at home,
2 correct?

3 A. Well, I think you're using the word
4 "separation" in somewhat two different contexts
5 with different meaning.

6 As we know, FIT does not require
7 dividing the sample into two or separating them
8 into two. It requires getting a sample to a lab.
9 The -- a test like Cologuard or -- or the claims
10 of the patents, they require actual separation of
11 the test into two components.

12 Q. So when you run the FIT test, though,
13 you don't send your whole bowel movement to the
14 lab, right?

15 A. Most of the time, you don't.

16 Q. You send just a part of the bowel
17 movement to the lab?

18 A. Part of the bowel movement, yes.

19 Q. So you separate out a part of the bowel
20 movement you're sending to the lab, and you're
21 discarding the rest, right?

22 A. Usually that's the case. There's
23 nothing, obviously, in the procedure that prevents
24 you from sending your whole sample. It just --

1 typically, it's not done.

2 Q. So typically, they don't send the whole
3 sample. They send just part of the sample even
4 though only a single stabilization buffer is
5 required for the FIT test, right?

6 A. Correct.

7 MS. FERNANDS: Objection.

8 BY MR. JONES:

9 Q. So you'll agree with me that there must
10 be reasons why with a FIT test typically a patient
11 would only send a portion of the fecal sample to
12 the lab instead of the entire bowel movement?

13 MS. FERNANDS: Objection.

14 THE WITNESS: So sending a portion of a
15 fecal sample is not a required step for FIT.
16 What is required is to get a -- a necessary
17 amount -- sufficient amount of stool to the
18 lab.

19 If the amount of stool that is
20 produced in a bowel movement substantially
21 exceeds that, the patient does not have to
22 send the whole sample. But it's not a
23 required step, as opposed to being required
24 in a test like Cologuard, where it's

1 essential to separate.

2 So hypothetically, you can
3 imagine that somebody sends a full sample.
4 It depends -- it depends how much stool is
5 produced.

6 BY MR. JONES:

7 Q. But typically, with a commercial FIT
8 test, prior to 2009, the patient would use a probe
9 to take out a little bit of the FIT test, put it
10 in a tube with a hemoglobin stabilizing buffer,
11 and send only that separated portion out back to
12 the lab, right?

13 A. Typically, yes.

14 Q. And then they discard the rest --

15 A. Discard the rest.

16 Q. -- presumably?

17 Now, if they had sent the entire fecal
18 specimen back to the lab, that would require,
19 presumably, less fecal manipulation on the part of
20 the patient?

21 A. I think it's hard to say. It would
22 also deal with, typically, a bigger amount of
23 stool. I think I would -- to answer that, I would
24 need to -- need probably to look how this is

1 actually done in practice.

2 It's hard for me to evaluate which one
3 is -- which one requires more handling.

4 Q. So requiring two buffers is not a
5 prerequisite for separating a fecal sample at home
6 and sending back part of it to the lab as is done
7 in the FIT test, right?

8 MS. FERNANDS: Objection.

9 THE WITNESS: Just to clarify, are you
10 asking about FIT or Cologuard?

11 BY MR. JONES:

12 Q. Specifically talking about FIT tests --

13 A. Okay.

14 Q. -- as they're performed prior to 2009.

15 A. Uh-huh.

16 Q. Patient does a separation step, and
17 sends one part to the lab and discards the rest,
18 right?

19 A. Right.

20 Q. And the patient does that separation
21 step despite the fact that you only need a single
22 stabilizing buffer for a FIT test, right?

23 A. Correct, in the context that you don't
24 need to send the -- what is typically the full

1 amount of stool that is produced. Now, of course,
2 if less stool is produced, you would have to
3 send -- you may have to send the whole thing.

4 Q. That'd be a really small amount of
5 stool for a FIT test, I think, but presumably,
6 yeah?

7 A. Presumably, yeah.

8 Q. But in most cases, you're sending only
9 a portion of the stool sample back to the lab --

10 A. Correct.

11 Q. -- in the hemoglobin buffer?

12 A. Correct.

13 Q. And that's just kind of how the
14 standard FIT test was being done at the time,
15 right?

16 A. Correct.

17 Q. Okay. If you look at paragraph 120 of
18 your declaration.

19 So here you say, Vilkin does not
20 identify the components of the buffer that is
21 identified as hemoglobin stabilizing buffer,
22 right?

23 A. Right.

24 Q. Vilkin doesn't provide any data showing

1 that the hemoglobin stabilizing buffer is able to
2 stabilize DNA, does it?

3 A. No.

4 Q. Okay. Then you say, Itzkowitz cites
5 to -- sorry.

6 Itzkowitz describes use of a buffer
7 that he refers to as DNA stabilizing buffer,
8 right?

9 A. Correct.

10 Q. And then it says, Itzkowitz cites to
11 Olson after the reference to DNA stabilizing
12 buffer, right?

13 A. Yes.

14 Q. And Itzkowitz doesn't provide any data
15 showing that its DNA stabilizing buffer stabilizes
16 hemoglobin, does it?

17 A. No.

18 Q. And Olson doesn't provide any data
19 showing that the DNA stabilizing buffer stabilizes
20 hemoglobin, does it?

21 A. It does not.

22 Q. My pages are --

23 MR. JONES: Can we take like a
24 one-minute break?

1 MS. FERNANDS: Sure.

2 (Whereupon, a break was taken,
3 after which the following
4 proceedings were had:)

5 BY MR. JONES:

6 Q. Okay. So turning to paragraph 121.

7 Here you note that the Shuber reference
8 discloses a DNA stabilizing buffer as well, right?

9 A. Yes.

10 Q. You'll agree with me that Shuber also
11 does not include any data showing that this buffer
12 stabilizes blood proteins?

13 A. Yes.

14 Q. Now, in Section 9 of your declaration
15 here, you don't disclose any specific buffer that
16 had been experimentally shown to stabilize both
17 fecal nucleic acids and fecal blood proteins, do
18 you?

19 A. So there should be a reference to a
20 patent, a Japanese patent.

21 Q. So this is --

22 A. I'm not going to pronounce the --

23 Q. -- paragraph 123?

24 A. 123, yeah. The Tsuji application.

1 Q. Yeah. There's no videographer. So as
2 long as she writes it right, it will sound -- it
3 will seem like we pronounced it right.

4 So you're talking about the Tsuji
5 application.

6 So the Tsuji -- actually...

7 A. T S U -- T S U J I.

8 Q. Actually, why don't I get a copy of the
9 Tsuji patent.

10 So this is Exhibit 2049. So the front
11 of the exhibit says, Declaration of John Andrews,
12 who's the translator, I understand, and then
13 there's -- I believe the exhibit has what I
14 presume is the Tsuji application on Mr. Andrews'
15 say-so because it's in Japanese. And then there's
16 a purported translation of that declaration by
17 Mr. Andrews -- I mean, by -- of that application
18 by Mr. Andrews.

19 Do you see that?

20 A. I see that.

21 Q. And this is the application you were
22 referring to?

23 A. I believe so.

24 Q. So in this application -- does this

1 application contain any data showing that any
2 buffer stabilizes fecal DNA?

3 A. No. This application is specific to
4 blood proteins.

5 Q. Okay. So do you provide any reference
6 in Section 9, containing experimental data,
7 showing that any buffer for -- preserves fecal DNA
8 and fecal hemoglobin?

9 MS. FERNANDS: Objection.

10 THE WITNESS: The data that we provide,
11 including reference provided by Dr. Whitney,
12 shows that buffers constructed the same way,
13 for example, using Tris-EDTA and certain salt
14 concentrations were independently shown to
15 preserve nucleic acids as per Shuber, Olson,
16 and other references.

17 And what the Tsuji application
18 shows, that a similarly constructed buffer
19 would also preserve hemoglobin.

20 BY MR. JONES:

21 Q. Tsuji referenced the buffer that they
22 disclosed is not identical to the buffers
23 disclosed in Shuber and Olson and Itzkowitz, is
24 it?

1 MS. FERNANDS: Objection.

2 THE WITNESS: So the reference you
3 mentioned, they provide ranges of individual
4 components such as Tris-EDTA, for example.
5 So I don't think I can compare exact numbers
6 because these are ranges.

7 BY MR. JONES:

8 Q. Okay.

9 A. But it's fairly easy to see that there
10 are essentially equivalent --

11 Q. Okay. Let's look --

12 A. -- buffers.

13 Q. -- at page 3 of Tsuji, starting at
14 paragraph 18, labeled Examples of Embodiment.

15 So this starts off with -- are you
16 there?

17 A. Page?

18 Q. 3 of the translation. I guess it's
19 page 153 at the bottom.

20 A. Yeah.

21 Q. I -- I have no idea where that page 153
22 came from.

23 A. So 18, right, Examples of Embodiment?

24 Q. Yeah, paragraph 18.

1 A. Uh-huh.

2 Q. Okay. So it starts off with, An
3 aqueous solution consisting of .2-mol/l glycine,
4 .1 percent bovine serum albumin, and .1 percent
5 sodium azide, and .9 percent sodium chloride was
6 prepared, and the chelating agents shown in
7 Table 1 were dissolved in varying concentrations
8 in this solution, and the pH was adjusted to 8
9 with one normal aqueous sodium hydroxide solution.

10 Do you see that?

11 A. Yes.

12 Q. Does the buffer in Itzkowitz contain
13 glycine?

14 A. So in -- it doesn't or it doesn't have
15 to. The -- this particular paragraph refers to a
16 very specific example of embodiment. That is
17 clearly not -- doesn't cover all possibilities for
18 a buffer like that.

19 What I think --

20 Q. Is -- I'm sorry.

21 A. -- is important is to -- what I refer
22 is the -- one of the previous paragraphs -- I
23 think it's, let's say, 10, where the -- the
24 composition of a buffer is -- is explained.

1 Q. Does paragraph 10 provide any data
2 showing that the buffer that is provided there
3 stabilizes anything?

4 MS. FERNANDS: Objection, vague.

5 THE WITNESS: This particular paragraph
6 does not.

7 BY MR. JONES:

8 Q. In fact, the only data that shows that
9 any buffer in Tsuji stabilizes anything is in the
10 Examples of Embodiment section, right?

11 A. Correct.

12 Q. Okay.

13 A. Yeah.

14 Q. And so the buffer that's actually
15 tested in Tsuji contains glycine, right?

16 A. Yes.

17 Q. And you'll agree with me, the buffer in
18 Itzkowitz does not contain glycine, right?

19 A. I would have to look at Itzkowitz
20 again. I will be happy to do it right now to see
21 if it does or does not.

22 Glycine is not an active compound of a
23 buffer. The active components are EDTA, which is
24 a divalent iron chelator, and Tris, which is a pH

1 buffer, to maintain pH.

2 So I wouldn't necessarily find presence
3 or absence of glycine critical. But if you want
4 me to opine whether Itzkowitz contains it, I would
5 be happy to -- to reexamine it.

6 Q. So where in the examples of the
7 embodiment does it describe the buffer having
8 Tris?

9 A. In -- in the Japanese application?

10 Q. Yes.

11 A. So what I refer -- let's say, para- --
12 maybe paragraph 10, line -- yeah, like line 13 on
13 page 152 -- or after line 13.

14 Q. So this lists possible ingredients in
15 buffers, including a phosphate buffer, a glycine
16 buffer, a Tris-HCl buffer, a borate buffer, or the
17 like, right?

18 A. Correct.

19 Q. So it says, It could be a glycine
20 buffer or a Tris-HCl buffer, right?

21 A. Right. This is where Tris is
22 mentioned. Now, EDTA is mentioned in paragraph --
23 discussed in paragraph 11.

24 Q. So in the examples, though, the ones

1 they actually tested here, they use a glycine
2 buffer, right?

3 A. Right.

4 Q. So they don't use a Tris buffer in any
5 experiments disclosed in Tsuji, do they?

6 A. Yes, I agree with that.

7 Q. So you'll agree with me that the buffer
8 that they actually tested in Tsuji, that they
9 provide data for, is actually different from the
10 buffers disclosed in Itzkowitz, Olson, and Shuber,
11 right?

12 A. The buffer that they tested is -- is a
13 little different, yes.

14 Q. And in addition to glycine, it also
15 contains bovine serum albumin?

16 A. Yes.

17 Q. That's not in the buffers of Olson and
18 Shuber and Itzkowitz, is it?

19 A. I would -- I would need to check. The
20 focus of the disclosure of the buffers
21 in Itzkowitz and Olson was on other active
22 components like Tris and EDTA. So I would need to
23 check if they mention the presence of bovine serum
24 albumin, which is a -- which is frequently used in

1 a lot of buffers.

2 Q. And the buffer in Tsuji that they test
3 also contains sodium azide?

4 A. Correct.

5 Q. Then if you look at paragraph 21 -- or
6 actually -- okay. So --

7 A. Paragraph 21 of the --

8 Q. Of the Tsuji reference.

9 A. Okay.

10 Q. And feel free to read paragraphs 19 and
11 20. I just don't think it's relevant to the
12 question, but you can read it.

13 It says, Next, the human hemoglobin was
14 dissolved in varying concentrations in the
15 chelating reagent solution prepared above, and
16 healthy human feces was further added to a
17 concentration of 4 mg/ml.

18 A. I see that.

19 Q. And then the solution was mixed with
20 the latex antibody reagent, and it was tested for
21 agglutination as observed by the naked eye, right?

22 A. Correct.

23 Q. And then in paragraph 22, they say, The
24 human hemoglobin solution was left to stand at

1 25 degrees Celsius for six days and then mixed
2 with latex reagent to observe the agglutination
3 image. The results are shown in Table 2. Is that
4 right?

5 A. Right.

6 Q. So if you look at Table 2 -- so in
7 Table 2, how well would you say the buffer
8 disclosed in Tsuji preserved the hemoglobin in the
9 sample?

10 Let me take a step back.

11 You'll agree with me that Table 2 does
12 not provide quantitative results of hemoglobin
13 stability, right?

14 A. I think so.

15 Q. It's just a qualitative assessment of
16 whether the antibodies aggregated, right?

17 A. Right.

18 Q. So you can't really tell just how well
19 this buffer stabilized hemoglobin based on this
20 table, can you?

21 MS. FERNANDS: Objection.

22 THE WITNESS: Because they -- since
23 they don't provide explicit relationship
24 between what they describe as double plus or

1 single plus, I would not be able to convert
2 this to quantitative -- to make a
3 quantitative assessment.

4 It's -- it's an assessment based
5 on naked-eye observation and they
6 parameterized it using the double plus, plus,
7 plus-minus, or minus notations.

8 So it is a visual observation.
9 It's not a quantitative measurement.

10 BY MR. JONES:

11 Q. And they certainly didn't test in
12 this whether this buffer that they describe --
13 sorry. Let me make a clear question.

14 They didn't test in Tsuji whether the
15 buffer they describe preserves DNA, did they?

16 A. No.

17 Q. And they didn't -- didn't test whether
18 that buffer preserves RNA either, right?

19 A. No.

20 Q. And you certainly couldn't say whether
21 this buffer preserves hemoglobin at the same level
22 as the buffer that's disclosed in Vilkin?

23 A. I don't think Vilkin discloses specific
24 buffer -- specific formulation of a buffer. So I

1 wouldn't be able to make this comparison.

2 Q. Okay. Do you know -- can -- there's no
3 way to know -- okay. Scratch that.

4 So even if Tris-EDTA buffers did
5 preserve hemoglobin in stool, say the DNA
6 stabilizing buffer in Olson or Shuber, there's no
7 way to know from the data we have available
8 whether it preserved hemoglobin in stool as well
9 as the buffer in Vilkin, for example, right?

10 A. So I think there are two -- two
11 statements -- or two parts of your question. As
12 of the question whether preservative such as
13 disclosed in Olson and other citations,
14 Tris-EDTA-based buffers, whether they would
15 preserve hemoglobin, I think the answer is clearly
16 yes.

17 I don't think it's -- it's not a
18 hypothetical. It's a very well-established
19 combination that has been used to preserve
20 proteins for decades -- for very long time.

21 Whether this buffer would preserve
22 hemoglobin better than Vilkin, I cannot say. I
23 cannot compare them for, you know, two reasons.
24 One of them, this would require actual comparison,

1 experimental validation.

2 And the second, Vilkin doesn't
3 disclose -- at least I'm not aware of Vilkin
4 disclosing a specific formulation of the buffer.
5 So I cannot really opine on how they would
6 compare.

7 Q. Nowhere in your declaration do you
8 actually provide data showing that a Tris -- how
9 well a Tris-EDTA buffer preserves fecal
10 hemoglobin, do you?

11 A. I don't provide data on Tris-EDTA
12 preserving hemoglobin, but as we just discussed,
13 we do provide data on the -- from the Japanese
14 patent on a similarly constructed buffer -- a
15 similarly constructed preservative, that according
16 to this application preserves hemoglobin
17 specifically in feces.

18 What I would like to point out is the
19 construction of the buffers for DNA preservation
20 as in Olson and the one in the Tsuji application,
21 they are based on the same principles, and they
22 are very similar, even though in the specific
23 embodiment, as you mentioned, Tris is -- Tris was
24 not used, but the construction is the same. Use

1 combination of two components with specific
2 function.

3 They use -- you use certain
4 concentration of salt. You use pH buffer to keep
5 the preservative in the physiological range,
6 whether it's glycine or Tris or anything else. So
7 even though specific formulations might be
8 different, they are very similar to constructor.

9 Q. So Tsuji is a patent application from
10 1991, right?

11 A. Correct.

12 Q. And Tsuji is in Japanese, right?

13 A. Yes.

14 Q. How did the Tsuji reference come to
15 your attention?

16 A. Counsel showed it to me.

17 Q. Did you conduct any searches
18 independently to try and identify a reference
19 showing Tris-EDTA-based buffers preserving fecal
20 hemoglobin?

21 A. I did not conduct search to find
22 references that Tris-EDTA would preserve
23 hemoglobin. I was aware of multiple references
24 where Tris-EDTA was used to preserve proteins.

1 Q. Did you try and find any references
2 showing Tris-EDTA preserving hemoglobin that were
3 after 1991?

4 A. I did not.

5 Q. Did you try and find any references
6 that showed Tris-EDTA-based buffers preserving
7 hemoglobin that were in English?

8 A. I did not try.

9 Q. I'm just wondering why you settled for
10 a Japanese language application from 1991 to show
11 this point.

12 You don't use foreign language
13 references anyplace else in your declaration?

14 MS. FERNANDS: Objection.

15 THE WITNESS: So this particular
16 reference was brought to my attention by
17 counsel, and when I reviewed it, what I -- I
18 found it relevant. And I found it relevant
19 because, A, it was a fairly old reference,
20 from 1990.

21 Second, the construction of the
22 buffer was very similar, based on same
23 principles, the same physical chemical
24 principles.

1 And third, they discuss
2 preservation of hemoglobin, but even more
3 importantly, they discuss preservation of
4 hemoglobin in fecal matter.

5 It satisfied all the criteria,
6 both -- of the subject matter. It looked
7 like a very appropriate reference.

8 BY MR. JONES:

9 Q. Did you look for any references that
10 tested Tris-EDTA buffers for preservation of fecal
11 hemoglobin -- sorry. Scratch that.

12 Have you -- did you identify any
13 references that showed quantitatively how well
14 Tris-EDTA buffers preserved fecal hemoglobin?

15 A. I did not conduct a search. I -- I was
16 happy with this reference.

17 Q. So the reference you're happy with
18 tested a buffer that was not Tris-EDTA
19 qualitatively in 1991 and was published in
20 Japanese; is that right?

21 MS. FERNANDS: Objection.

22 THE WITNESS: I did not consider the
23 language as being an important factor.

24 Would -- I paid more attention to, that it

1 was specifically related to blood proteins in
2 the stool and a similar construction --
3 essentially the same construction.

4 BY MR. JONES:

5 Q. Are -- do you know whether -- you'll
6 agree with me that patent applications are not
7 peer reviewed?

8 A. They're not peer reviewed, yeah.

9 Q. Are you aware of whether this patent
10 application ever issued as a patent?

11 A. I did not --

12 Q. Okay.

13 A. -- consider that.

14 Q. Are you familiar with the inventor
15 Takashi Tsuji at all?

16 A. No.

17 Q. So you have no idea what
18 Takashi Tsuji's reputation as a scientist is?

19 A. No, I did not -- I did not investigate
20 that.

21 Q. Are you familiar with the Nitto Denko
22 Corporation?

23 A. No.

24 Q. So you have no --

1 A. Well, I'm familiar with it now. I was
2 not familiar with it.

3 Q. What's your familiarity with it now?

4 A. Just through this -- through this
5 patent.

6 Q. But you are not familiar with what
7 their reputation was like in 1991, were you?

8 A. I don't know.

9 Q. So how do you know that any of the data
10 presented in this application is legitimate?

11 MS. FERNANDS: Objection.

12 THE WITNESS: The data presented in
13 this application agrees very well with the
14 state of the art that has been known for
15 quite some time, for several decades, and
16 clearly well before 2009.

17 In my own work, back in late
18 '90s, and later, and as a graduate student
19 and as a professor, I frequently used this
20 buffers. I use them to preserve nucleic
21 acids. I use them to preserve proteins.

22 What they describe agrees very
23 well with the practice that somebody skillful
24 in the art would know very well and would

1 agree with. It's not a -- this patent does
2 not preserve -- does not report some esoteric
3 knowledge that would need to be independently
4 verified because it contradicts or is not
5 supported by considerable other evidence.

6 And I think in -- I would like to
7 point out that in my declaration in -- let's
8 see where it is.

9 The previous page, page 58,
10 paragraph 122, I -- I think I explain the
11 mechanisms, how this preservatives would work
12 for both DNA proteins. There is no
13 contradiction between the preservation of
14 these two molecules. The principles are the
15 same.

16 For this reason, I did not
17 consider it a good use of my time to
18 investigate Nitto Denko Corporation or the
19 authors of the patents.

20 (Reporter clarification.)

21 THE WITNESS: Or the inventors of the
22 patents.

23 BY MR. JONES:

24 Q. In paragraph 122 of your declaration,

1 where you explain the mechanism, you don't cite to
2 any references, do you?

3 A. No.

4 Q. So the only reference you cite to in
5 support of your contention that Tris-EDTA buffers
6 stabilize human hemoglobin in feces is this patent
7 application, right?

8 A. I think it's -- yes, correct.

9 Q. So in paragraph 124 of your
10 declaration, you cite to a statement -- you say,
11 Prior to 2009, there were also commercially
12 available products such as RNAlater, which were
13 sold as stabilizing both RNA and protein within
14 tissues or cells.

15 Do you see that?

16 A. Yes, I do.

17 Q. Are you aware of any experimental
18 evidence showing that RNAlater preserves
19 hemoglobin in feces?

20 A. I did not check that.

21 Q. Is hemoglobin in feces within tissues
22 or cells?

23 A. It's -- no, it's -- it's extracellular.

24 MR. JONES: Do you recall what time we

1 started? I'm just trying to --

2 MS. FERNANDS: About 12 till the hour.

3 BY MR. JONES:

4 Q. Okay. So I'm going to put before you
5 another reference -- another exhibit.

6 So I'm putting before you Exhibit 1007,
7 which will you agree with me that this is the
8 Kanaoka reference, K A N A O K A, that you discuss
9 in your declaration?

10 A. I agree.

11 Q. You'll agree with me that Kanaoka
12 discloses a discussion of COX2 RNA in fecal
13 samples as a biomarker for cancer, right?

14 A. Correct.

15 Q. And you'll agree with me that COX2 is a
16 human gene?

17 A. It's a -- it's a human gene.

18 Q. You'll agree with me that Kanaoka uses
19 RT-PCR as part of its detection of COX2 RNA?

20 A. I do.

21 Q. If you go to Example 1, which is on
22 page 3, starting at paragraph 55.

23 So in --

24 A. Right.

1 Q. Sorry. So in Example 1 of Kanaoka,
2 you'll agree with me that Kanaoka tested fecal
3 samples for both COX2 mRNA and blood protein using
4 a FIT test, right?

5 A. I'm sorry. Which paragraph are we
6 looking at?

7 Q. In Example 1. It was a general
8 question.

9 But you'll agree with me that in
10 Example 1, they look at -- they examined COX2 mRNA
11 in fecal samples?

12 A. Yes.

13 Q. And you'll agree with me that they also
14 tested those fecal samples using a FIT test?

15 A. They -- they use -- they detected
16 hemoglobin in the stool for comparison and
17 reference.

18 Q. Right.

19 A. Yeah.

20 Q. So they say, Also for comparison and
21 reference, even hemoglobin in the feces of each
22 sample was measured by immunological fecal occult
23 blood test, right?

24 A. Correct.

1 Q. And you understand immunological fecal
2 occult blood test to be referring to a FIT test?

3 A. FIT test, correct.

4 Q. So they tested these samples for both
5 COX2 mRNA and hemoglobin, right?

6 A. Correct.

7 Q. If you look at paragraph 67, you'll
8 agree with me that the FIT test used in Example 1
9 detected cancer in one sample that the COX2 mRNA
10 test missed?

11 A. Correct.

12 Q. If you look at paragraph 68, you'll
13 agree with me that the COX2 RNA test used in the
14 example detected cancer in three samples that the
15 FIT test missed?

16 A. Yes.

17 Q. So if you look at paragraph 187 of your
18 declaration, on page 95.

19 So after bridging the page, you
20 acknowledge here that, Nechvatal also states
21 that -- sorry. Sorry.

22 At the top it says -- you quote
23 Nechvatal's statement.

24 In conclusion, the study suggests that

1 preserving fecal samples at room temperature for a
2 duration of five days in a medium suitable for DNA
3 and RNA analysis is feasible.

4 Do you see that?

5 A. I see the quote, yes.

6 Q. In your declaration, you don't provide
7 any data that shows that Nechvatal's buffer would
8 not preserve fecal samples at room temperature for
9 a duration of five days in a medium suitable for
10 DNA and RNA analysis, do you?

11 A. Sir, can you repeat that?

12 Q. In your declaration, you do not present
13 any data that would show that Nechvatal's buffer
14 would not preserve a fecal sample at room
15 temperature for a duration of five days in a
16 medium suitable for DNA and RNA analysis, do you?

17 A. I'm sorry. And I missed the name.
18 Which -- which buffer? At the beginning of your
19 question, which buffer was it?

20 Q. The buffer used --

21 MS. FERNANDS: I think we've been
22 calling it Nechvatal. I have no idea --

23 MR. JONES: Oh.

24 MS. FERNANDS: I don't know how it's

1 pronounced.

2 BY MR. JONES:

3 Q. Okay. Nechvatal?

4 A. You know what? That's what -- that's
5 what -- that's how I pronounce the name. Maybe
6 I'm wrong.

7 Q. I have no idea how it's pronounced.
8 I've been pronouncing it in my head. I don't know
9 if I have said it out loud before today. It's
10 going to be really confusing on the transcript.

11 A. That's why I didn't recognize the name.

12 Q. So we'll call it Nechvatal. Nechvatal.

13 A. You might be correct. Okay. Well, as
14 long as we know which --

15 MS. FERNANDS: Yeah, I just wanted to
16 clear up the confusion. I think it was a
17 pure pronunciation question.

18 THE WITNESS: Right. I just didn't
19 recognize the name.

20 MR. JONES: Thank you, Anastasia.

21 BY MR. JONES:

22 Q. So my question was -- so Nechvatal --

23 A. And --

24 Q. Nechvatal makes a statement that the

1 study suggests that preserving fecal samples at
2 room temperature for a duration of five days in a
3 medium suitable for DNA and RNA analysis is
4 feasible.

5 My question is, whether or not in your
6 declaration, you provide any data that shows that
7 preserving DNA -- fecal samples at room
8 temperature for a duration of five days in a
9 medium suitable for DNA and RNA analysis is not
10 feasible?

11 A. I -- I don't provide such data.

12 Q. Do you provide any data that would
13 contradict Nechvatal's conclusion?

14 A. No, I don't.

15 MR. JONES: Okay. I have no further
16 questions.

17 MS. FERNANDS: I have no questions for
18 the witness.

19 MR. JONES: Okay. Thank you very much.

20 THE COURT REPORTER: Do you get to read
21 and sign?

22 MS. FERNANDS: We do want it signed,
23 yes.

24 THE COURT REPORTER: Rough drafts?

1 MR. JONES: Rough drafts would be
2 great. And you said three days. That's,
3 honestly, fine given the time frame for me,
4 and I assume you don't even care.

5 MS. FERNANDS: No. No. I don't need
6 to do anything until I see the next thing
7 from you.

8 THE COURT REPORTER: Do you want a
9 rough draft?

10 MS. FERNANDS: I don't need a rough
11 draft, no. There's no reason.

12 THE COURT REPORTER: Do you need
13 regular delivery for your final?

14 MS. FERNANDS: Regular delivery is
15 fine.

16 (Witness excused at 2:43 p.m.)

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1 STATE OF ILLINOIS)
2) SS:
3 COUNTY OF C O O K)
4
5

6 I, Michelle A. Duzan, CSR No.
7 084-004270, a Notary Public within and for the
8 County of Cook, State of Illinois, and a Certified
9 Shorthand Reporter of said state, do hereby
10 certify:

11 That previous to the commencement of
12 the examination of the witness, the witness was
13 duly sworn to testify the whole truth concerning
14 the matters herein;

15 That the foregoing deposition
16 transcript was reported stenographically by me, was
17 thereafter reduced to typewriting under my personal
18 direction and constitutes a true record of the
19 testimony given and the proceedings had;

20 That the said deposition was taken
21 before me at the time and place specified;

22 That I am not a relative or employee or
23 attorney or counsel, nor a relative or employee of
24 such attorney or counsel for any of the parties

1 hereto, nor interested directly or indirectly in
2 the outcome of this action.

3 IN WITNESS WHEREOF, I do hereunto set
4 my hand and affix my seal of office at Orland Park,
5 Illinois, this 11th day of August, 2025.

6
7
8 *Michelle Duzan*
9

10 Notary Public, Cook County, Illinois.

11 My commission expires 11/01/27.

12
13 Michelle A. Duzan, CSR, RMR, CRR

14 CSR No. 084-004270
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1 ANASTASIA FERNANDS

2 anastasiafernands@quinnemanuel.com

3 August 18, 2025

4 RE: Geneoscopy, Inc. v. Exact Sciences Corporation

5 8/7/2025, Vadim Backman (#7492615)

6 The above-referenced transcript is available for
7 review.

8 Within the applicable timeframe, the witness should
9 read the testimony to verify its accuracy. If there are
10 any changes, the witness should note those with the
11 reason, on the attached Errata Sheet.

12 The witness should sign the Acknowledgment of
13 Deponent and Errata and return to the deposing attorney.
14 Copies should be sent to all counsel, and to Veritext at
15 cs-ny@veritext.com

16 Return completed errata within 30 days from
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22 Yours,

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Geneoscopy, Inc. v. Exact Sciences Corporation

Vadim Backman (#7492615)

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Vadim Backman

Date

1 Geneoscopy, Inc. v. Exact Sciences Corporation

2 Vadim Backman (#7492615)

3 ACKNOWLEDGEMENT OF DEPONENT

4 I, Vadim Backman, do hereby declare that I
5 have read the foregoing transcript, I have made any
6 corrections, additions, or changes I deemed necessary as
7 noted above to be appended hereto, and that the same is
8 a true, correct and complete transcript of the testimony
9 given by me.

10
11 _____
12 Vadim Backman

_____ Date

13 *If notary is required

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Federal Rules of Civil Procedure

Rule 30

(e) Review By the Witness; Changes.

(1) Review; Statement of Changes. On request by the deponent or a party before the deposition is completed, the deponent must be allowed 30 days after being notified by the officer that the transcript or recording is available in which:

(A) to review the transcript or recording; and

(B) if there are changes in form or substance, to sign a statement listing the changes and the reasons for making them.

(2) Changes Indicated in the Officer's Certificate. The officer must note in the certificate prescribed by Rule 30(f)(1) whether a review was requested and, if so, must attach any changes the deponent makes during the 30-day period.

DISCLAIMER: THE FOREGOING FEDERAL PROCEDURE RULES ARE PROVIDED FOR INFORMATIONAL PURPOSES ONLY.

THE ABOVE RULES ARE CURRENT AS OF APRIL 1, 2019. PLEASE REFER TO THE APPLICABLE FEDERAL RULES OF CIVIL PROCEDURE FOR UP-TO-DATE INFORMATION.

VERITEXT LEGAL SOLUTIONS

COMPANY CERTIFICATE AND DISCLOSURE STATEMENT

Veritext Legal Solutions represents that the foregoing transcript is a true, correct and complete transcript of the colloquies, questions and answers as submitted by the court reporter. Veritext Legal Solutions further represents that the attached exhibits, if any, are true, correct and complete documents as submitted by the court reporter and/or attorneys in relation to this deposition and that the documents were processed in accordance with our litigation support and production standards.

Veritext Legal Solutions is committed to maintaining the confidentiality of client and witness information, in accordance with the regulations promulgated under the Health Insurance Portability and Accountability Act (HIPAA), as amended with respect to protected health information and the Gramm-Leach-Bliley Act, as amended, with respect to Personally Identifiable Information (PII). Physical transcripts and exhibits are managed under strict facility and personnel access controls. Electronic files of documents are stored in encrypted form and are transmitted in an encrypted

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