

CARLOS D. BUSTAMANTE, Ph.D.
UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE PATENT TRIAL AND APPEAL BOARD

IPR2025-00026

QIAGEN SCIENCES, LLC, :
Petitioner, :
:
v. :
:
TECAN GENOMICS, INC, :
Patent Owner. :
----- X

DEPOSITION OF:

CARLOS D. BUSTAMANTE, Ph.D.
NEW YORK, NEW YORK
WEDNESDAY, OCTOBER 8, 2025

REPORTED BY:

SILVIA P. WAGE, CCR, CRR, RPR
JOB NO. 7620048

CARLOS D. BUSTAMANTE, Ph.D.

October 8, 2025

9:13 a.m.

Deposition of CARLOS D. BUSTAMANTE, Ph.D.,
held at the offices of GOODWIN PROCTER,
LLP, The New York Times Building,
620 Eighth Avenue, New York, New York,
pursuant to agreement before SILVIA P.
WAGE, a Certified Shorthand Reporter,
Certified Realtime Reporter, Registered
Professional Reporter, and Notary
Public for the States of New Jersey,
New York and Pennsylvania.

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3

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CARLOS D. BUSTAMANTE, Ph.D.

I N D E X

PAGE

WITNESS: CARLOS D. BUSTAMANTE, Ph.D.

EXAMINATION BY MS. TRAUPMAN 6

E X H I B I T S

NO.	DESCRIPTION	PAGE
-----	-------------	------

NONE

PREVIOUSLY MARKED EXHIBITS

NO.	DESCRIPTION	PAGE
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Exhibit QIAGEN 1005	US Patent Application US2007/0020640	98
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Exhibit QIAGEN 1006	US Patent Application US2012/0165202	30
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Exhibit Tecan 2107	Declaration of Carlos D. Bustamante, Ph.D.	8
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CARLOS D. BUSTAMANTE, Ph.D.

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DEPOSITION SUPPORT INDEX

- - -

Direction to Witness Not to Answer
Page Line

Request for Production of Documents
Page Line

Stipulations
Page Line

Question Marked
Page Line

Reservation
Page Line

118 20

Motion to Strike
Page Line

91 17

1 CARLOS D. BUSTAMANTE, Ph.D.
2 CARLOS D. BUSTAMANTE, Ph.D.,
3 CBD Consulting Group, 600 Grapetree
4 Drive, Apartment 11BN, Key Biscayne,
5 Florida 33149, after having been
6 duly sworn, was examined and testified
7 as follows:
8 THE STENOGRAPHER: Thank you. 09:13:42
9 You may proceed. 09:13:43
10 EXAMINATION BY MS. TRAUPMAN: 09:13:45
11 Q. Good morning. We're going on 09:13:45
12 the record at 9:13 a.m. in proceeding IPR 09:13:46
13 2025/00026. 09:13:52
14 Good morning, Dr. Bustamante. 09:13:55
15 A. Good morning. 09:13:57
16 Q. My name is Matt Traupman from 09:13:58
17 Quinn Emanuel. 09:14:00
18 I'm going to be asking you some 09:14:01
19 questions here today, okay? 09:14:03
20 A. I understand. 09:14:04
21 MR. TRAUPMAN: And are we 09:14:05
22 doing appearances on the record 09:14:06
23 or... 09:14:07
24 MS. CIPRIANO: We didn't 09:14:07
25 yesterday. 09:14:08

1 CARLOS D. BUSTAMANTE, Ph.D.

2 MR. TRAUPMAN: We didn't 09:14:09

3 yesterday, okay. 09:14:09

4 Well, I will dispense with 09:14:10

5 that as well. Fine with me. 09:14:12

6 Q. So, Dr. Bustamante, I know 09:14:14

7 you're familiar with the procedure of a 09:14:17

8 deposition considering my colleagues 09:14:19

9 spent the delightful day with you 09:14:22

10 yesterday. So I know you're familiar 09:14:24

11 with the procedure. 09:14:26

12 But just to remind you, please make 09:14:26

13 sure you allow me to finish asking my 09:14:30

14 questions before you begin answering to 09:14:32

15 give the Court Reporter a clean record, 09:14:35

16 and I will, likewise, extend the same 09:14:37

17 courtesy or, at least, do my best to 09:14:39

18 extend the same courtesy to you and let 09:14:41

19 you finish your answers before I ask my 09:14:43

20 next question. 09:14:47

21 And if any of my questions are 09:14:47

22 unclear, please let me know. I'll do my 09:14:51

23 best to clarify them. 09:14:53

24 But if I don't have a request from 09:14:55

25 you, I'll assume that you understand the 09:14:58

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	question, okay?	09:15:00
3	A. I understand.	09:15:01
4	(There is a discussion off	09:15:13
5	the record.)	09:15:28
6	Q. Is there any reason why you	09:15:28
7	can't testify today truthfully and	09:15:29
8	accurately, Dr. Bustamante?	09:15:31
9	A. Not to my knowledge.	09:15:32
10	Q. Great.	09:15:33
11	Alright. Can you just, for the	09:15:35
12	record, state your name and business	09:15:36
13	address, please?	09:15:39
14	A. I'm Carlos Bustamante and the	09:15:40
15	business address is 600 Grapetree Drive,	09:15:44
16	Apartment 11BN, Key Biscayne, Florida	09:15:49
17	33149.	09:15:50
18	Q. Thank you.	09:15:51
19	I understand from your Counsel that	09:15:53
20	you have a copy of your Declaration in	09:15:57
21	front of you; is that correct?	09:16:00
22	A. It is.	09:16:01
23	(Deposition Exhibit Tecan	09:16:01
24	2107, Declaration of Carlos D.	09:16:01
25	Bustamante, Ph.D., was previously	09:16:01

1 CARLOS D. BUSTAMANTE, Ph.D.
2 marked for identification.) 09:16:02
3 Q. Great. 09:16:02
4 Can you confirm that that 09:16:05
5 Declaration is in proceeding ending in 09:16:07
6 00026? 09:16:10
7 A. I see that it says 00026 here. 09:16:12
8 Q. Great. 09:16:15
9 And it's exhibit Tecan Exhibit 2107, 09:16:16
10 correct? 09:16:20
11 A. It is Tecan Exhibit 2107. 09:16:21
12 Q. And you have -- if you flip 09:16:23
13 to the back -- all 116 pages of that 09:16:25
14 Declaration? 09:16:27
15 A. I haven't checked every page, 09:16:30
16 but I presume I have all 116 pages. 09:16:32
17 Q. I'm going to presume as such. 09:16:35
18 MR. TRAUPMAN: Counsel, by the 09:16:37
19 way, I have an extra copy. 09:16:38
20 Do you need a copy? 09:16:39
21 MS. CIPRIANO: No, I'm good. 09:16:40
22 MR. TRAUPMAN: Okay. 09:16:41
23 Q. And is it safe for me to 09:16:46
24 assume, Dr. Bustamante, that you had a 09:16:48
25 chance to review your Declaration in 09:16:50

1 CARLOS D. BUSTAMANTE, Ph.D.
2 preparing for the deposition today? 09:16:52
3 A. I have reviewed my Declaration 09:16:53
4 in preparation for today's deposition. 09:16:57
5 Q. Great. 09:16:59
6 And, as you were reviewing your 09:17:00
7 Declaration, did you notice any errors, 09:17:04
8 any omissions, anything you wanted to 09:17:06
9 correct in your Declaration? 09:17:09
10 A. There may be a few typos, but 09:17:11
11 I don't believe that we're going to 09:17:13
12 submit a correction. 09:17:16
13 Q. Okay, great. 09:17:17
14 If you do happen to see any typos 09:17:19
15 or any errors in your Declaration, as we 09:17:23
16 on go explore it today, please let me 09:17:26
17 know, okay? 09:17:29
18 A. Okay. 09:17:30
19 Q. Okay. So I'd like to just 09:17:33
20 start with some preliminary measures. 09:17:44
21 You had a chance in preparing your 09:17:48
22 Declaration in this proceeding to review 09:17:50
23 QIAGEN's petition for inter parties 09:17:54
24 review on the '357 patent, correct? 09:17:56
25 A. I did. 09:17:58

1 CARLOS D. BUSTAMANTE, Ph.D.

2 Q. And you also had a chance to 09:17:58

3 review the Declaration of Dr. Metzker that 09:18:00

4 was submitted in connection with QIAGEN's 09:18:03

5 IPR on the '357 patent, correct? 09:18:10

6 A. I did review it. 09:18:12

7 I don't have a copy in front of me. 09:18:13

8 Q. Well, I can give you a copy. 09:18:14

9 But, you know, you recall reviewing 09:18:17

10 it? 09:18:18

11 A. I do recall reviewing it. 09:18:19

12 Q. And it's listed in your 09:18:20

13 materials considered, if you need to 09:18:22

14 refresh your memory. 09:18:23

15 And is it fair to say you didn't 09:18:24

16 respond to every point raised in QIAGEN 09:18:28

17 and Dr. Metzker's -- QIAGEN's petition 09:18:33

18 and Dr. Metzker's Declaration, correct? 09:18:35

19 A. That is correct. I was not 09:18:38

20 asked to respond to all of the -- all of 09:18:39

21 the elements of the petition or the 09:18:46

22 Declaration. 09:18:48

23 Q. Okay. So what were you asked 09:18:48

24 to do? 09:18:50

25 A. What I was asked to respond 09:18:50

1 CARLOS D. BUSTAMANTE, Ph.D.
2 to is what is included in the Declaration. 09:18:52
3 Q. Okay. Who made that request, 09:18:53
4 as to what you should respond to or not 09:18:56
5 respond to, in the QIAGEN IPR and the 09:18:58
6 Metzker Declaration? 09:19:03
7 MS. CIPRIANO: So objection to 09:19:04
8 the extent it gets into privileged 09:19:05
9 information. 09:19:06
10 You can answer the question 09:19:07
11 as phrased. 09:19:08
12 A. As you know, I'm not an 09:19:10
13 attorney and I am here as a scientific 09:19:12
14 expert and I was asked to prepare the 09:19:15
15 Declaration alongside the requests from 09:19:22
16 Counsel. 09:19:26
17 Q. Okay. So I just want to 09:19:26
18 understand. 09:19:28
19 Was it Counsel who selected which 09:19:29
20 parts of QIAGEN's IPR and which parts of 09:19:35
21 Dr. Metzker's Declaration you were to 09:19:39
22 respond to? 09:19:40
23 MS. CIPRIANO: Objection, to 09:19:41
24 the extent that it gets into 09:19:42
25 privileged information. 09:19:44

1 CARLOS D. BUSTAMANTE, Ph.D.
2 MR. TRAUPMAN: This is his 09:19:45
3 opinion. I totally disagree with 09:19:46
4 that Counsel. 09:19:47
5 I want to know -- he said he 09:19:48
6 didn't respond to all of the 09:19:50
7 petition and all of its contents 09:19:53
8 in Dr. Metzker's Declaration and 09:19:56
9 I'm trying to understand who made 09:19:58
10 that selection. 09:19:59
11 That is not privileged. That 09:20:00
12 is the subject matter of his 09:20:01
13 Declaration. 09:20:03
14 MS. CIPRIANO: Well, the 09:20:03
15 subject matter of his Declaration 09:20:03
16 is in the Declaration. 09:20:05
17 But how the conversations 09:20:06
18 came to how he -- 09:20:07
19 MR. TRAUPMAN: I'm not asking 09:20:09
20 about the conversations, Counsel. 09:20:10
21 MS. CIPRIANO: I disagree. 09:20:10
22 MR. TRAUPMAN: I'm asking 09:20:12
23 about -- well, we can get on the 09:20:13
24 phone with the Board, if you'd like, 09:20:15
25 because this is clearly not 09:20:16

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	privileged.	09:20:17
3	Q. Let me ask you a different	09:20:18
4	question, Dr. Bustamante.	09:20:19
5	Who selected which points in	09:20:20
6	QIAGEN's IPR and which points in Dr.	09:20:24
7	Metzker's Declaration you would respond	09:20:27
8	to?	09:20:28
9	A. I was asked to respond to	09:20:28
10	certain elements of the petition and in	09:20:30
11	reviewing the materials worked with	09:20:35
12	Counsel to address them, including Dr.	09:20:40
13	Metzker's Declarations [sic], as well as	09:20:44
14	other materials.	09:20:45
15	Q. Right.	09:20:46
16	And so, as you testified before,	09:20:46
17	there are parts of the IPR and parts of	09:20:52
18	Dr. Metzker's Declaration that you don't	09:20:55
19	address, correct?	09:20:57
20	A. That is correct.	09:21:00
21	Q. Who made the decision not to	09:21:00
22	address certain parts of Dr. Metzker's	09:21:02
23	Declaration and QIAGEN's IPR?	09:21:05
24	A. Those were, I think, two	09:21:09
25	separate questions.	09:21:11

1 CARLOS D. BUSTAMANTE, Ph.D.
2 So, on the QIAGEN IPR, I was asked 09:21:12
3 to respond to certain elements, which I 09:21:14
4 did. 09:21:16
5 And then in reviewing Dr. Metzker's 09:21:16
6 Declaration, I made a decision in 09:21:23
7 conjunction with Counsel around what 09:21:26
8 elements to include. 09:21:27
9 Q. Okay. So, when you say, 09:21:30
10 "elements," you're talking about claim 09:21:32
11 limitations? 09:21:33
12 A. No. I'm saying what aspects 09:21:34
13 of the Declaration I felt were relevant 09:21:39
14 to address, the parts of the petition I 09:21:43
15 was asked to opine upon. 09:21:49
16 Q. Okay. And when you say, "the 09:21:51
17 parts of the petition that you were asked 09:21:53
18 to opine upon," there are certain claim 09:21:54
19 limitations set forth in the petition? 09:21:58
20 A. It includes claim limitations 09:22:00
21 and other aspects of the petition, as laid 09:22:03
22 out, including the matters of anticipation 09:22:11
23 and obviousness, as indicated in the 09:22:20
24 petition. 09:22:22
25 Q. Okay. So is it fair to say 09:22:22

1 CARLOS D. BUSTAMANTE, Ph.D.
2 that the only elements of the petition 09:22:24
3 that you were asked to respond to are 09:22:36
4 what's set forth in your Declaration; is 09:22:39
5 that correct? 09:22:41
6 A. What is set forth in the 09:22:41
7 Declaration is what I was asked to opine 09:22:43
8 on. 09:22:44
9 Q. And is it fair to say you 09:22:48
10 haven't formed opinions on any subject 09:22:49
11 matter that's not set forth in your 09:22:51
12 Declaration? 09:22:53
13 A. I'm not prepared to discuss 09:22:53
14 opinions that aren't set forth in the 09:22:57
15 Declaration. 09:23:00
16 Q. Great. 09:23:00
17 Okay. And I'm going to look at 09:23:01
18 just the Table of Contents. But, of 09:23:07
19 course, if you want to look at the parts 09:23:10
20 of the Table of Contents -- the parts of 09:23:13
21 the Declaration that correspond to what's 09:23:16
22 set forth in the Table of Contents, feel 09:23:18
23 free to, Dr. Bustamante. 09:23:20
24 But looking on Page Romanette (ii) 09:23:22
25 of your Declaration, that's Page 3 of 116, 09:23:24

Page 16

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	you see section Roman Numeral VIII,	09:23:28
3	"Porreca fails to disclose the claimed	09:23:33
4	inventions"? Do you see that?	09:23:36
5	A. Sorry. I lost you there for	09:23:39
6	a minute.	09:23:41
7	Q. Yeah. Look at Page 3 of 116.	09:23:42
8	A. Page 3 of 116, yes.	09:23:44
9	Q. Are you there?	09:23:46
10	A. I am; Roman Numeral VIII.	09:23:47
11	Q. Yeah.	09:23:47
12	You can see --	09:23:47
13	A. "Porreca fails to disclose	09:23:49
14	the claimed inventions."	09:23:51
15	Q. Perfect, the third line.	09:23:52
16	And there is a section that spans	09:23:53
17	from Page 56 to Page 62.	09:23:55
18	Do you see that?	09:24:01
19	A. I am there.	09:24:01
20	Q. Okay. And is it fair to say	09:24:02
21	that the only opinion you offer regarding	09:24:05
22	"Porreca failing to disclose the claimed	09:24:12
23	inventions" is with respect to the	09:24:16
24	limitation in Claim 1 that reads,	09:24:18
25	"Ligating an adapter to each of a	09:24:21

1 CARLOS D. BUSTAMANTE, Ph.D.
2 plurality of nucleic acid fragments 09:24:23
3 wherein each adapter... and indexing site 09:24:25
4 unique to a subset of the adapters... 09:24:30
5 amplifying the adapter ligated fragments 09:24:33
6 into amplicons," correct? 09:24:35
7 A. That is accurate. 09:24:38
8 Q. So do you have any opinions 09:24:39
9 with respect to whether or not Porreca 09:24:41
10 does or does not disclose any other 09:24:42
11 limitation in Claim 1, other than what's 09:24:45
12 set forth in your Declaration? 09:24:48
13 A. What I'm prepared to discuss 09:24:50
14 today is that element in Claim 1. 09:24:52
15 Q. Okay. And if you go to -- if 09:24:54
16 you go to Page 61 -- well, it's 64 of 116. 09:24:57
17 Let's just use the numbers at the 09:25:02
18 bottom of the page, so we're all on the 09:25:04
19 same page. 09:25:07
20 If you go there, you see a 09:25:07
21 subsection b, "dependent Claims 2 to 10"? 09:25:09
22 A. I see that section in my 09:25:11
23 Declaration. 09:25:13
24 Q. And there your opinion -- 09:25:13
25 your opinion is that dependent Claims 2 09:25:19

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	to 10 are not rendered invalid, in view	09:25:23
3	of Porreca, is based upon your opinions	09:25:27
4	with respect to Claim 1, correct?	09:25:29
5	A. Correct. As I state, "It is	09:25:32
6	my opinion that a POSA would not	09:25:35
7	understand Porreca to disclose the	09:25:35
8	limitations of Claim 1."	09:25:35
9	THE STENOGRAPHER: Can you	09:25:35
10	just read a little slower?	09:25:35
11	THE WITNESS: I apologize.	09:25:39
12	A. I'm just reading from my	09:25:41
13	Declaration.	09:25:42
14	"It is my opinion that a POSA would	09:25:43
15	not understand Porreca to disclose the	09:25:44
16	limitations of Claim 1."	09:25:46
17	Since that is the independent claim,	09:25:48
18	the dependent claims follow from that.	09:25:51
19	Q. And you don't have any	09:25:54
20	independent opinions with respect to why	09:25:55
21	any of the dependent claim limitations	09:25:57
22	are not satisfied by Porreca, correct?	09:26:01
23	A. I do not discuss any	09:26:02
24	independent claims in the Declaration.	09:26:05
25	Q. And if you go back to Page 3	09:26:11

1 CARLOS D. BUSTAMANTE, Ph.D.
2 of 116, I'm going to move a little farther 09:26:13
3 down in your Table of Contents to 09:26:19
4 Section 9 titled, "Schmitt and McCloskey 09:26:21
5 failed to disclose the claimed 09:26:24
6 inventions." 09:26:26
7 Do you see that? 09:26:26
8 A. I do. 09:26:27
9 Q. And that section goes from 09:26:27
10 Page 62 to 65 of your Declaration. 09:26:29
11 Do you see that? 09:26:32
12 A. I do. 09:26:32
13 Q. Okay. So it seems like you've 09:26:33
14 already jumped ahead. 09:26:35
15 Just for the record, you're looking 09:26:36
16 at Page 65 of 116 of your Declaration, 09:26:37
17 correct, sir? 09:26:40
18 A. I am. 09:26:41
19 Q. Great. 09:26:41
20 And you'd agree with me -- and, 09:26:42
21 again, feel free to flip through the few 09:26:45
22 pages in this section -- the only 09:26:47
23 limitation of Claim 1 that you allege is 09:26:50
24 not disclosed by the combination of 09:26:52
25 Schmitt and McCloskey is the limitation 09:26:56

Page 20

1 CARLOS D. BUSTAMANTE, Ph.D.
2 reading, "identifying sequence reads with 09:26:59
3 identical identifier and target sequences 09:27:02
4 as duplicates," correct? 09:27:05
5 A. That is accurate. 09:27:06
6 Q. And if you go ahead to Page 67 09:27:13
7 of 116, please, there is a subsection b 09:27:16
8 regarding dependent Claims 2 to 10. 09:27:26
9 Do you see that? 09:27:29
10 A. Sorry, Page 67. 09:27:29
11 Yes, I see it. 09:27:30
12 Q. Are you with me, sir? 09:27:32
13 A. I am. It -- I -- 09:27:34
14 Q. Yeah, I'm trying -- 09:27:35
15 A. -- 64 on the 67. 09:27:36
16 Q. I get it. 09:27:37
17 And for that very reason, I'm going 09:27:38
18 to try throughout the day today to use 09:27:40
19 the page number that's like at the very 09:27:42
20 bottom associated with the exhibit. 09:27:44
21 A. Okay. 09:27:46
22 Q. Because that is a uniform 09:27:46
23 methodology of numbering pages for every 09:27:48
24 exhibit. So, hopefully, that will allow 09:27:51
25 us to stay on the same page. 09:27:53

Page 21

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Is that okay with you, sir? 09:27:54
3 A. That sounds fantastic. 09:27:55
4 Q. Okay. 09:27:57
5 A. Thank you. 09:27:57
6 Q. So, if we're on Page 67 of 09:27:58
7 116 of your Declaration -- are you there, 09:28:01
8 sir? 09:28:04
9 A. I am. 09:28:04
10 Q. Great. 09:28:04
11 And there you see at the bottom of 09:28:05
12 the page a subsection labeled, "Dependent 09:28:06
13 Claims 2 to 10"? Do you see that? 09:28:10
14 A. I do. 09:28:11
15 Q. And you'd agree with me that 09:28:11
16 your basis for disputing the -- let me 09:28:15
17 strike that and ask a better question. 09:28:21
18 Your sole basis for alleging that 09:28:23
19 the combination of Schmitt and McCloskey 09:28:25
20 do not invalidate dependent Claims 2 to 09:28:28
21 10 is based on your opinions with respect 09:28:31
22 to Claim 1, correct? 09:28:33
23 A. That is what I have written. 09:28:34
24 Q. Thank you. 09:28:38
25 And if you go to -- I'm sorry to 09:28:43

Page 22

1 CARLOS D. BUSTAMANTE, Ph.D.
2 bounce around a little bit. 09:28:47
3 We're staying in the same section 09:28:48
4 on Schmitt and McCloskey to Page 65 of 09:28:50
5 116. 09:28:53
6 Are you there? 09:28:56
7 And if you go just from Paragraphs 09:28:57
8 -- it's subsection a, which is your 09:29:01
9 opinions with respect to the "identifying 09:29:03
10 sequence reads with identical identifier 09:29:10
11 and target sequences of duplicates." 09:29:11
12 Do you see that? 09:29:12
13 A. Uh-huh, I do. 09:29:13
14 Q. Thank you. 09:29:14
15 And that spans Paragraphs 125 to 09:29:16
16 130 of your Declaration, correct? 09:29:19
17 A. That is correct. 09:29:23
18 Q. Alright. And you'd agree 09:29:23
19 with me that the only two paragraphs of 09:29:25
20 the Schmitt reference that you discuss in 09:29:30
21 Paragraphs 125 to 130 are Paragraphs 85 09:29:34
22 and 98 and I'll call your attention 09:29:40
23 particularly to Paragraph 127 through 129. 09:29:43
24 A. That is what I've written in 09:29:48
25 Paragraphs 127 and through 129. 09:29:51

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Q. Right. 09:29:53
3 So your opinions with respect to, 09:29:54
4 again, the identifying sequence reads 09:29:59
5 limitations of Claim 1 with respect to 09:30:01
6 the combination of Schmitt and McCloskey 09:30:04
7 are based on your analysis of Paragraphs 09:30:07
8 85 and 98 of Schmitt, correct? 09:30:10
9 MS. CIPRIANO: Objection, to 09:30:11
10 the extent that it misstates the 09:30:12
11 document. 09:30:13
12 A. The paragraph reads that the 09:30:14
13 Petitioner relies on Paragraphs 85 and 98 09:30:21
14 of Schmitt for disclosure of this 09:30:23
15 limitation. 09:30:24
16 So that's where I focused in 09:30:25
17 responding. But I, of course, have read 09:30:28
18 the entirety of Schmitt and relied on the 09:30:32
19 entirety of the document in analyzing the 09:30:34
20 Petitioner's petition. 09:30:37
21 Q. Right. 09:30:42
22 And, of course, as cited here, you 09:30:42
23 read the entirety of the petition as 09:30:44
24 well, correct? 09:30:46
25 A. I have read the entirety of 09:30:47

1 CARLOS D. BUSTAMANTE, Ph.D.
2 the petition. 09:30:48
3 Q. Right. 09:30:49
4 Did you read the institution 09:30:50
5 decision? 09:30:52
6 A. I have read the institution 09:30:52
7 decision. 09:30:54
8 (There is a discussion off 09:30:54
9 the record.) 09:31:13
10 Q. Okay. I'd like to go to a 09:31:13
11 different section of your Declaration, if 09:31:16
12 we could, Dr. Bustamante. 09:31:19
13 If you go to Page 53 of 116, please. 09:31:23
14 Are you there? 09:31:40
15 A. I am. 09:31:41
16 Q. And here you're discussing the 09:31:41
17 -- there is a section called, "Relevant 09:31:49
18 Prior Art." 09:31:51
19 Do you see that? 09:31:52
20 A. I do. 09:31:52
21 Q. And there is a subsection a 09:31:56
22 titled, "Porreca Exhibit 1006." 09:32:01
23 Do you see that? 09:32:06
24 A. I do. I don't have a copy of 09:32:07
25 Porreca in front of me. 09:32:09

Page 25

1 CARLOS D. BUSTAMANTE, Ph.D.

2 Q. I understand. 09:32:10

3 And I can, certainly, give you one. 09:32:11

4 But I'm really just asking about the 09:32:12

5 organization of your Declaration, sir. 09:32:14

6 And here is it fair to say that you 09:32:16

7 are providing your summary of the 09:32:22

8 teachings of Porreca, correct? 09:32:25

9 A. I am discussing Porreca, as 09:32:28

10 relevant prior art, and my understanding 09:32:30

11 of Porreca, as it relates to the petition, 09:32:32

12 put forth before the Court. 09:32:37

13 Q. Right. 09:32:38

14 And so, for instance, on Page 55 of 09:32:39

15 116, you have copied Figure 4 of Porreca, 09:32:41

16 correct? 09:32:44

17 A. I believe that is an accurate 09:32:45

18 representation of Figure 4 of Porreca. 09:32:46

19 Q. The citation is, actually, at 09:32:49

20 the very top of the page. 09:32:51

21 A. Yes. 09:32:52

22 Q. Page 56, if you flip the page. 09:32:53

23 No one is questioning whether that's 09:32:55

24 accurate. 09:32:58

25 I'm just asking if that's Porreca. 09:32:58

1 CARLOS D. BUSTAMANTE, Ph.D.

2 A. That's Porreca. 09:32:59

3 Q. If you go down to the next 09:33:00

4 page, Page 56 of 116. 09:33:02

5 A. 56 of 116? 09:33:05

6 Q. Yeah. 09:33:06

7 Do you see Paragraph 105? 09:33:07

8 A. I see Paragraph 105. 09:33:09

9 Q. Right. 09:33:11

10 And here I understand this paragraph 09:33:12

11 to be talking about -- this paragraph to 09:33:13

12 be talking about Figure 4, which we just 09:33:18

13 looked at on Page 55, 4A, 4B and 4C, 09:33:20

14 correct? 09:33:25

15 A. That's correct. I discuss 09:33:26

16 4A, 4B and 4C, which are different 09:33:28

17 embodiments of Porreca. 09:33:32

18 Q. Correct. 09:33:33

19 And at the end, though, you cite 09:33:34

20 Schmitt Exhibit 1007 at 105. 09:33:36

21 Do you see that? 09:33:40

22 A. I do see that. That may be in 09:33:43

23 relevance to what comes in Paragraph 106. 09:33:50

24 Q. Right. And that's my -- yeah. 09:33:53

25 So, I guess, I'm wondering why you 09:33:55

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	cited Schmitt when discussing Figures 4A	09:33:59
3	through 4C of Porreca.	09:34:04
4	A. So, in the beginning of	09:34:06
5	Paragraph 105, I cite to Porreca, as	09:34:09
6	Exhibit 1006.	09:34:16
7	And in Paragraph 106, I cite to	09:34:18
8	Schmitt. That may be a carryover and	09:34:21
9	meant to indicate what's coming in the	09:34:26
10	next paragraph.	09:34:27
11	I apologize for the error.	09:34:28
12	Q. Ah, I see.	09:34:31
13	So that Schmitt 1007, EX 1007, you	09:34:32
14	believe is supposed to be a subsection	09:34:37
15	heading, just a typo; is that your	09:34:40
16	testimony?	09:34:42
17	A. That Schmitt 1007 should start	09:34:50
18	-- that should start a section -- 106,	09:34:54
19	107 should refer to Exhibit 1007, which	09:34:57
20	is Schmitt.	09:35:03
21	Q. I see.	09:35:05
22	Okay. So that's -- I'm trying to	09:35:06
23	understand.	09:35:08
24	You believe that's just a typo in	09:35:08
25	your Declaration?	09:35:11

1 CARLOS D. BUSTAMANTE, Ph.D.

2 A. It is a formatting error. It 09:35:12

3 should have a letter that carries through 09:35:14

4 and should be its own section. 09:35:22

5 I apologize for the oversight. 09:35:23

6 Q. No worries. 09:35:25

7 A. It's referring to Schmitt, as 09:35:26

8 the -- Paragraphs 106 and 107 refer to 09:35:28

9 Schmitt. 09:35:31

10 Q. In other words, just so the 09:35:31

11 record is clear -- and totally. I make 09:35:33

12 plenty of typos myself. So I'm just 09:35:35

13 trying to understand the organization of 09:35:37

14 your Declaration. 09:35:39

15 Your opinions in the overall 09:35:39

16 section, "Relevant Prior Art," your 09:35:46

17 opinions with respect to Porreca end with 09:35:48

18 the words, "connected via a ligase.", and 09:35:50

19 your opinions for Schmitt pick up with 09:35:53

20 the word, "Schmitt Exhibit 1007"; is that 09:35:55

21 your testimony? 09:35:58

22 A. Give me a minute to -- 09:35:59

23 Q. Yeah, please. 09:36:01

24 A. -- confirm. 09:36:02

25 I believe sitting here today right 09:36:30

1 CARLOS D. BUSTAMANTE, Ph.D.
2 now today that that should be a separate 09:36:33
3 section that outlines the prior art 09:36:36
4 relevant to Schmitt. 09:36:41
5 Q. Got it. Thanks for clarifying 09:36:41
6 that. 09:36:43
7 So, if we stay here on Figure 105 09:36:44
8 -- or excuse me, Paragraph 105 of your 09:37:07
9 Declaration where you're discussing 09:37:11
10 Figures 4A to 4C of Porreca, you say, 09:37:12
11 "Figure 4A shows a padlock probe also 09:37:16
12 known as a molecular inversion probe or 09:37:21
13 MIP." 09:37:25
14 Do you see that? 09:37:25
15 A. I do. 09:37:25
16 Q. Alright. And you'd agree with 09:37:26
17 me that a MIP is one way to -- that 09:37:30
18 Porreca discloses as one way of amplifying 09:37:37
19 DNA, correct? 09:37:41
20 A. Could I please get a copy of 09:37:42
21 Porreca? 09:37:44
22 Q. Sure. 09:37:45
23 A. Thank you. 09:37:45
24 (Deposition Exhibit QIAGEN 09:37:45
25 1006, US Patent Application 09:37:45

1 CARLOS D. BUSTAMANTE, Ph.D.
2 US2012/0165202, was previously 09:37:45
3 marked for identification.) 09:38:09
4 (There is a discussion off 09:38:09
5 the record.) 09:38:10
6 MR. TRAUPMAN: For the record, 09:38:10
7 I have presented the witness with 09:38:13
8 a copy of QIAGEN Exhibit 1006, which 09:38:15
9 is US Patent Application Publication 09:38:19
10 US 2012/0165202 and -- 09:38:22
11 Q. Is there a problem, sir? 09:38:32
12 A. I need my glasses. 09:38:33
13 I apologize. 09:38:34
14 MR. TRAUPMAN: Well, should we 09:38:35
15 take a break? 09:38:36
16 MS. CIPRIANO: Yeah, let's 09:38:37
17 take two seconds to run down the 09:38:39
18 hall. 09:38:41
19 A. Two-minute break to get my 09:38:41
20 glasses. 09:38:43
21 Q. No problem. 09:38:44
22 A. I apologize. 09:38:45
23 (Recess taken 9:38 to 9:41 09:38:50
24 a.m.) 09:40:56
25 Q. Okay. 09:41:57

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Alright. We ready? 09:41:59
3 MS. CIPRIANO: Yeah. 09:42:00
4 A. I have my glasses. Thank you. 09:42:01
5 Q. No worries. 09:42:03
6 Alright. We're back on the record 09:42:04
7 after a short break for attending to Zoom 09:42:07
8 and glasses. 09:42:10
9 So I had marked a copy of QIAGEN 09:42:11
10 Exhibit 1006 or given you a copy, Dr. 09:42:16
11 Bustamante. 09:42:19
12 And you'd agree with me this is what 09:42:19
13 we've referred to today and in your 09:42:21
14 Declaration as "the Porreca application," 09:42:24
15 correct? 09:42:26
16 A. That is correct. 09:42:27
17 Q. Okay. And, of course, you had 09:42:27
18 a chance to review this document both in 09:42:29
19 drafting your Declaration and preparing 09:42:32
20 for your deposition here today, correct? 09:42:34
21 A. That is correct. 09:42:37
22 Q. Okay. So let's just orient 09:42:37
23 ourselves with Porreca. 09:42:40
24 We see just on the front cover the 09:42:45
25 abstract of Porreca. It reads that -- 09:42:48

1 CARLOS D. BUSTAMANTE, Ph.D.
2 the first sentence of the Abstract says, 09:42:56
3 "Aspects of the invention relates to 09:42:58
4 methods and compositions that are useful 09:43:00
5 to reduce bias and increase the 09:43:02
6 reproducibility of multiplex analysis of" 09:43:05
7 gene loci -- or excuse me, "genetic 09:43:09
8 loci," correct? 09:43:12
9 A. That's what I read. 09:43:14
10 Q. Right. 09:43:16
11 And it uses the words "multiplex 09:43:17
12 analysis" there in the first sentence of 09:43:19
13 the Abstract. 09:43:20
14 Can you tell us what you understand 09:43:21
15 "multiplex analysis" to be referring to? 09:43:23
16 A. "Multiplex analysis" refers to 09:43:25
17 the simultaneous analysis of, in this 09:43:27
18 case, multiple genetic loci. 09:43:36
19 Q. Okay. And "multiple genetic 09:43:41
20 loci," as used throughout the Porreca 09:43:44
21 application, can refer to multiple loci 09:43:47
22 from one individual, correct? 09:43:49
23 A. There are -- that is one use 09:43:54
24 of the word "multiplexing." 09:44:00
25 Q. Right. 09:44:01

1 CARLOS D. BUSTAMANTE, Ph.D.
2 And another use of "multiple genetic 09:44:01
3 loci" in Porreca is samples from different 09:44:05
4 individuals, correct? 09:44:08
5 A. I think, that's the same 09:44:11
6 target. 09:44:13
7 Q. I said "multiple genetic 09:44:13
8 loci" from one individual. 09:44:15
9 A. That's -- that is one 09:44:16
10 definition of "multiplexing." 09:44:18
11 Q. And another is multiple 09:44:19
12 samples from different individuals, 09:44:21
13 correct? 09:44:23
14 A. It's a second definition of 09:44:23
15 "multiplexing." 09:44:25
16 Q. And you would understand the 09:44:25
17 reference to "multiplex analysis of 09:44:27
18 genetic loci" in the first sentence of 09:44:29
19 the Abstract of Porreca to be referring 09:44:32
20 to both, correct? 09:44:34
21 A. We would need to carefully 09:44:41
22 look at where in the document "multiplex" 09:44:43
23 is being used given that at times the 09:44:48
24 general term "multiplexing" means 09:44:58
25 different samples -- samples from 09:45:03

1 CARLOS D. BUSTAMANTE, Ph.D.
2 different individuals being simultaneously 09:45:08
3 sequenced, and at other times when we say 09:45:12
4 "multiplexing," we mean simultaneously 09:45:15
5 analyzing genetic loci across a single 09:45:19
6 individual. 09:45:22
7 Q. Right. 09:45:24
8 And having read Porreca or Porreca, 09:45:25
9 excuse me, which one or maybe both is 09:45:27
10 Porreca referring to in the applications? 09:45:33
11 A. I'd like to make sure we check 09:45:35
12 any use of "multiplexing," because I do 09:45:40
13 believe at times they may be used 09:45:42
14 interchangeably. 09:45:45
15 Q. Right. 09:45:46
16 Here in the Abstract, what do you 09:45:47
17 understand? 09:45:48
18 When you just read the Abstract, 09:45:48
19 what do you understand it to be referring 09:45:50
20 to? 09:45:51
21 A. (The witness reviews the 09:45:57
22 exhibit.) 09:45:58
23 I'm not a hundred percent sure you 09:45:58
24 can deduce it from the Abstract itself, 09:46:04
25 because it also says, "a plurality of 09:46:06

1 CARLOS D. BUSTAMANTE, Ph.D.
2 genetic loci" and "a plurality of 09:46:09
3 samples." 09:46:10
4 So I think reading the Abstract in 09:46:11
5 a vacuum, "multiplex analysis for 09:46:17
6 plurality of genetic loci in a plurality 09:46:19
7 of samples" is using that term 09:46:21
8 interchangeably. 09:46:24
9 We do need to make sure, 09:46:28
10 specifically, when we're talking about 09:46:29
11 different embodiments what is being done 09:46:31
12 in that embodiment. 09:46:36
13 Q. Right. 09:46:42
14 And, I mean, I did a word search, 09:46:42
15 as I was preparing for this deposition 09:46:46
16 today -- 09:46:48
17 A. Okay. 09:46:48
18 Q. -- of the word "multiplex" or 09:46:48
19 some variant of "multiplex" like 09:46:50
20 "multiplexed" or "multiplexing" -- 09:46:53
21 A. Okay. 09:46:54
22 Q. -- in Porreca. 09:46:54
23 It shows up over 40 times. 09:46:56
24 Does that surprise you that number? 09:47:00
25 A. It doesn't surprise me. 09:47:02

1 CARLOS D. BUSTAMANTE, Ph.D.
2 That's why I said, in different context, 09:47:03
3 "multiplex" refers to one of those 09:47:05
4 definitions; in other context, it refers 09:47:07
5 to another. So it's -- it's used in 09:47:09
6 multiple ways. 09:47:14
7 Q. Within Porreca you're saying? 09:47:15
8 A. Within Porreca, it wouldn't 09:47:19
9 surprise me if "multiplexing" is used to 09:47:22
10 refer to either of those because in the 09:47:26
11 literature, both of those meanings are 09:47:30
12 attributable to the word "multiplex." 09:47:35
13 I would caveat by saying, in 09:47:38
14 general, when we use the word 09:47:45
15 "de-multiplexing," we refer to different 09:47:48
16 samples that have been analyzed at the 09:47:54
17 same time, different samples from 09:47:57
18 different individuals. 09:47:59
19 But "multiplexing across loci" is 09:48:00
20 also a very standard use of the word 09:48:05
21 "multiplexing." So it could appear in 09:48:08
22 both. 09:48:12
23 And happy to discuss any particular 09:48:12
24 use of "multiplex" in context of how it's 09:48:15
25 used. 09:48:18

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Q. Right. 09:48:18
3 But you would agree with me a 09:48:18
4 person who's skilled in the art would 09:48:20
5 understand "multiplex" could, again, 09:48:21
6 refer to either samples -- multiple 09:48:24
7 samples from one individual or multiple 09:48:27
8 samples from different individuals, right? 09:48:29
9 MS. CIPRIANO: Objection, 09:48:31
10 asked and answered. 09:48:31
11 Q. Go ahead. 09:48:36
12 A. With the caveat that it 09:48:36
13 depends on context. So that's my caveat. 09:48:38
14 Q. Great. 09:48:41
15 Okay. And so I'd like to go and 09:48:43
16 look at some various aspects of the 09:48:50
17 Porreca disclosure and go over with you. 09:48:54
18 And, just to orient you, if you go 09:48:58
19 to page -- it's 18 of Exhibit 1006. 09:49:00
20 You see at the bottom left column 09:49:13
21 that begins the section of the "Summary 09:49:16
22 of the Invention"? Do you see that? 09:49:18
23 A. I do see that. 09:49:19
24 Q. What's your understanding of 09:49:20
25 what the "Summary of Invention" section 09:49:22

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	of a patent's specification is?	09:49:24
3	MS. CIPRIANO: Objection,	09:49:26
4	foundation.	09:49:27
5	A. As you're aware, I'm not a	09:49:33
6	lawyer. But my understanding is that the	09:49:36
7	"Summary of the Invention" discusses how	09:49:42
8	the embodiments are -- describes the	09:49:47
9	embodiments -- the potential embodiments	09:49:55
10	of the claims in the invention.	09:49:58
11	Q. Okay. I just want you to know	09:50:05
12	that we've start -- you know, just keep	09:50:07
13	looking, that we're in the "Summary of	09:50:08
14	the Invention" section, and as you go	09:50:09
15	forward to Page 20 of Exhibit 1006 and go	09:50:11
16	to Paragraph 27.	09:50:16
17	Are you there?	09:50:19
18	A. Give me one minute.	09:50:21
19	Okay. Give me a second just to	09:50:24
20	re-read.	09:50:26
21	Q. Yeah, feel free to re-read	09:50:27
22	that paragraph.	09:50:29
23	A. Thank you.	09:50:30
24	Okay, I've read Paragraph 27.	09:50:47
25	Q. Great.	09:50:49

Page 39

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	And I just want you to confirm,	09:50:49
3	just as a preliminary matter,	09:50:54
4	Paragraph 27 is part of the "Summary of	09:50:57
5	the Invention," correct?	09:50:58
6	A. It appears after the "Summary	09:51:03
7	of the Invention" section.	09:51:05
8	Q. Right.	09:51:05
9	And, just to make sure we draw that	09:51:06
10	to a full conclusion, if we pop forward	09:51:10
11	to Page 27, you see that the summary of	09:51:12
12	the invention continues all the way	09:51:17
13	through to the end of Paragraph 81 and	09:51:19
14	then a new subsection begins with, "brief	09:51:21
15	description of the drawings."	09:51:24
16	Do you see that?	09:51:25
17	A. I do.	09:51:25
18	Q. So, if we go back to 27.	09:51:26
19	A. (The witness complies.)	09:51:29
20	Q. Okay. So the first sentence	09:51:34
21	in Paragraph 27 states, "In some	09:51:40
22	embodiments, the isolated nucleic acid	09:51:43
23	fragments are products of a	09:51:45
24	circularization selection based	09:51:47
25	preparative method, e.g., molecular	09:51:50

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	inversion probe capture products."	09:51:55
3	Do you see that?	09:51:57
4	A. I do.	09:51:57
5	Q. Okay. And so, here in	09:51:58
6	Paragraph 27, they're talking about how	09:52:03
7	nucleic acid can be prepared for genetic	09:52:08
8	analysis, correct?	09:52:13
9	A. Well, I think, it is saying	09:52:25
10	that the nucleic acid products are the	09:52:26
11	result of a circularization preparative	09:52:32
12	method, namely, molecular inversion probe.	09:52:38
13	Q. Right.	09:52:39
14	And when they refer to "preparative	09:52:40
15	method," someone who's skilled in the art	09:52:42
16	would understand that you're preparing	09:52:44
17	certain nucleic acids for genetic	09:52:47
18	analysis; for instance, genotyping is	09:52:49
19	referenced in the paragraph previously in	09:52:52
20	Paragraph 26, correct?	09:52:55
21	A. Let me take a look at	09:52:57
22	Paragraph 26.	09:52:59
23	Okay, I see -- I re-read Paragraph	09:52:59
24	26.	09:53:26
25	Q. Let me just ask you.	09:53:26

1 CARLOS D. BUSTAMANTE, Ph.D.
2 What would a person skilled in the 09:53:28
3 art understand the words "preparative 09:53:30
4 method" to be referring to in Paragraph 09:53:33
5 27? 09:53:35
6 A. It would refer to method of 09:53:35
7 preparing a library. 09:53:41
8 Q. Okay. And what would the 09:53:43
9 library -- a library of nucleic acids, of 09:53:47
10 course, correct? 09:53:49
11 A. Presumably, yes. 09:53:51
12 Q. And what would that library 09:53:51
13 of nucleic acids be used for in the 09:53:53
14 context of Paragraph 27? 09:53:56
15 A. It could be used for 09:53:59
16 genotyping it. Could be used for 09:54:01
17 sequencing. 09:54:03
18 Here it's simply saying, isolated 09:54:06
19 nucleic acids are the product of, you 09:54:09
20 know, molecular inversion probe capture 09:54:10
21 products. 09:54:15
22 Q. Right. 09:54:15
23 And you'd agree with me that part 09:54:15
24 of the library preparation process would 09:54:17
25 be -- is amplifying the nucleic acid, 09:54:20

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	correct?	09:54:24
3	A. "Amplifying a nucleic acid"	09:54:27
4	is often a part of a library prep method.	09:54:27
5	Q. Great.	09:54:30
6	And so, again, one library prep	09:54:32
7	method, according to Paragraph 27, are	09:54:35
8	MIPs, a circularization-based protocol,	09:54:38
9	correct?	09:54:41
10	A. In one embodiment, you're	09:54:41
11	using MIPs.	09:54:44
12	Q. And then if you read the next	09:54:45
13	paragraph of Paragraph 27 it said, "In	09:54:46
14	other embodiments, the isolated nucleic	09:54:49
15	acids are products of an	09:54:52
16	amplification-based preparative method."	09:54:54
17	Do you see that?	09:54:56
18	A. I do. Because that would be	09:54:56
19	a separate embodiment from the first	09:54:58
20	embodiment.	09:54:59
21	Q. So you would agree with me	09:54:59
22	that's not MIPs, correct?	09:55:02
23	A. In my reading, MIPs is one	09:55:06
24	embodiment and this would be a second	09:55:08
25	embodiment.	09:55:11

1 CARLOS D. BUSTAMANTE, Ph.D.

2 Q. Okay, great. 09:55:11

3 And so "this," meaning, 09:55:16

4 amplification-based preparative methods, 09:55:19

5 correct? 09:55:22

6 A. Correct. 09:55:23

7 Q. Alright. And if we go to the 09:55:25

8 last sentence of Paragraph 27, "In other 09:55:28

9 embodiments, the isolated nucleic acids 09:55:30

10 are products of hybridization-based 09:55:32

11 preparative methods." 09:55:35

12 Do you see that? 09:55:36

13 A. I do. 09:55:37

14 Q. So you agree with me Paragraph 09:55:38

15 27 is now disclosing a third preparative 09:55:40

16 method for preparing a DNA or nucleic 09:55:43

17 acid library, correct? 09:55:46

18 A. The third sentence is a 09:55:47

19 separate embodiment, which in this case 09:55:48

20 is making use of hybridization-based. 09:55:50

21 Q. Right. 09:55:52

22 So three embodiments for library 09:55:53

23 preparation are described in Paragraph 27; 09:55:55

24 MIPS, amplification-based and 09:55:59

25 hybridization-based, correct? 09:56:01

1 CARLOS D. BUSTAMANTE, Ph.D.
2 A. Those are three different 09:56:04
3 embodiments. 09:56:05
4 Q. Right. 09:56:05
5 And they're all discussed in 09:56:06
6 Paragraph 27, right? 09:56:08
7 A. I would agree with that. 09:56:08
8 Q. Okay. And if we then just 09:56:17
9 orient ourselves, if you look at then 09:56:23
10 Paragraph 28, that's talking about the 09:56:27
11 circularization or MIP-based preparative 09:56:31
12 method, correct? 09:56:34
13 A. Let me read Paragraph 28, 09:56:35
14 please. 09:56:36
15 Q. Sure. 09:56:37
16 A. I've read Paragraph 28. 09:57:09
17 Q. My question simply was, that 09:57:12
18 is just a description -- that paragraph 09:57:14
19 is discussing the circularization-based 09:57:16
20 or MIP-based preparative method, correct? 09:57:19
21 A. It is discussing the 09:57:24
22 preparative method -- the MIPs preparative 09:57:25
23 method and it also states at the end that 09:57:30
24 in some embodiments, the MIP capture is 09:57:32
25 indicative of the presence of a 09:57:37

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	polymorphism as well.	09:57:40
3	Q. So it's going beyond	09:57:41
4	preparative method?	09:57:43
5	A. It's going slightly beyond	09:57:43
6	preparative method.	09:57:46
7	Q. Got it.	09:57:46
8	But you would agree with me	09:57:47
9	Paragraph 28 does not discuss the other	09:57:49
10	two preparative methods disclosed in	09:57:51
11	Paragraph 27, correct?	09:57:53
12	A. My reading of 28 is it is --	09:57:56
13	it is speaking about MIPS.	09:57:59
14	Q. Great.	09:58:00
15	And then if we go to the next	09:58:01
16	paragraph, 29, that's talking about the	09:58:03
17	second preparative method discussed in	09:58:05
18	Paragraph 27, the amplification-based	09:58:08
19	method, correct?	09:58:10
20	By the way, feel free to read	09:58:11
21	Paragraph 29.	09:58:13
22	A. Thank you.	09:58:14
23	I finished reading 29.	09:58:15
24	Q. And you'd agree with me	09:58:37
25	Paragraph 29 is discussing the	09:58:38

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	amplification-based preparative method,	09:58:41
3	correct?	09:58:44
4	A. I would agree that that's	09:58:44
5	accurate.	09:58:45
6	Q. Okay. And then if we go to	09:58:46
7	Paragraph 30 of Porreca -- again, feel	09:58:49
8	free to read it, before you answer my	09:58:54
9	question.	09:58:55
10	You'd agree with me that Paragraph	09:58:56
11	30 is talking about the	09:58:59
12	hybridization-based preparative method,	09:59:02
13	correct?	09:59:04
14	A. (The witness reviews the	09:59:08
15	exhibit.)	09:59:09
16	Thank you.	09:59:09
17	I would agree that Paragraph 30 is	09:59:18
18	discussing hybridization-based	09:59:21
19	preparative methods.	09:59:23
20	Q. Right.	09:59:23
21	And so, just to summarize, we've now	09:59:24
22	talked about 27 introduces three	09:59:26
23	preparative methods and then the	09:59:28
24	following three paragraphs -- 28, 29 and	09:59:29
25	30 -- discuss each one of those three	09:59:32

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	preparative methods in more detail,	09:59:35
3	correct?	09:59:37
4	A. That's accurate.	09:59:40
5	Q. And then 31 says, "It should	09:59:41
6	be appreciated that any of the	09:59:46
7	circularization, amplification and/or	09:59:48
8	hybridization-based methods described	09:59:50
9	herein may be used in connection with one	09:59:53
10	or more of the tiling/staggering, tagging,	09:59:55
11	size detection and/or sensitivity	09:59:59
12	enhancing algorithms disclosed herein,"	10:00:02
13	correct?	10:00:06
14	A. That's what it says in	10:00:06
15	Paragraph 31.	10:00:09
16	Q. Right.	10:00:09
17	So this is a teaching from Porreca	10:00:10
18	that any of the three preparative methods	10:00:11
19	can be used in connection with the	10:00:13
20	various -- again, "tiling/staggering,	10:00:16
21	tagging, size detection and/or sensitivity	10:00:20
22	enhancing algorithms" described in the	10:00:24
23	application, correct?	10:00:25
24	A. It is discussing the	10:00:26
25	applicability of the algorithms.	10:00:28

1 CARLOS D. BUSTAMANTE, Ph.D.

2 Q. Well let's just understand. 10:00:30

3 Is everything -- "tiling/staggering, 10:00:34

4 tagging, size detection and/or 10:00:38

5 sensitivity enhancing," those are all 10:00:40

6 algorithms? 10:00:43

7 A. No. Tiling and staggering, 10:00:44

8 tagging, size selection are not 10:00:46

9 algorithms. 10:00:48

10 Q. Right. 10:00:49

11 So there is a sensitivity enhancing 10:00:49

12 algorithm that can be used with all three 10:00:51

13 preparative processes, right? 10:00:54

14 A. That would be my read. 10:00:56

15 Q. Right. 10:00:57

16 But you could also use tiling -- 10:00:58

17 what is "tiling/staggering," sir? 10:00:59

18 A. As discussed both in Porreca 10:01:09

19 and in the literature, "tiling/staggering" 10:01:11

20 is the design of probes that overlap a 10:01:15

21 given region of interest. 10:01:20

22 Q. Alright. And Porreca is 10:01:20

23 teaching that technique can be used with 10:01:22

24 any of the three preparative methods 10:01:28

25 discussed in Paragraphs 27 through 30, 10:01:30

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	correct?	10:01:33
3	A. Uh-huh.	10:01:33
4	Q. You have to answer audibly,	10:01:34
5	sir.	10:01:35
6	A. Yes, correct.	10:01:36
7	Q. And then next up is "tagging."	10:01:39
8	Do you see that?	10:01:41
9	A. I do.	10:01:41
10	Q. Okay. And, again, Porreca is	10:01:42
11	saying that can be used with any of the	10:01:46
12	three preparative methods disclosed in	10:01:49
13	Paragraphs 27 to 30, correct?	10:01:52
14	A. That would be my read.	10:01:54
15	Q. And what is "tagging," sir?	10:01:56
16	A. "Tagging" can have multiple	10:02:00
17	meanings depending on the context;	10:02:02
18	usually, adding a molecular tag.	10:02:10
19	Q. Okay. And next up is "size	10:02:12
20	detection," right?	10:02:17
21	A. I see "size detection."	10:02:20
22	Q. Okay. And, again, Porreca in	10:02:22
23	Paragraph 31 is saying "size detection"	10:02:27
24	can be used with any of the three	10:02:29
25	preparative methods disclosed in	10:02:31

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	Paragraphs 27 through 30, correct?	10:02:35
3	A. That would be my read.	10:02:39
4	Q. Alright. And then last are	10:02:42
5	"sensitivity enhancing algorithms."	10:02:43
6	Do you see that?	10:02:46
7	A. I do.	10:02:46
8	Q. What's a "sensitivity	10:02:47
9	enhancing algorithm"?	10:02:49
10	A. "Sensitivity enhancing	10:02:51
11	algorithm" would be downstream analysis	10:02:53
12	of the resulting data generated by the	10:02:56
13	experiment.	10:03:03
14	Q. Again, you would agree with	10:03:05
15	me Paragraph 31 of Porreca is telling a	10:03:07
16	person who's skilled in the art that	10:03:10
17	sensitivity enhancing algorithms can be	10:03:11
18	used with any of the three preparative	10:03:14
19	methods disclosed in Paragraphs 27	10:03:17
20	through 30, correct?	10:03:19
21	A. That's what it states in	10:03:21
22	Paragraph 31.	10:03:23
23	Q. Okay.	10:03:31
24	Alright. Let's go ahead to	10:03:40
25	Paragraph 66, please. And I know you're	10:03:48

1 CARLOS D. BUSTAMANTE, Ph.D.
2 going to ask, not unreasonably. 10:03:55
3 Why don't you go ahead and take the 10:03:57
4 opportunity to read Paragraph 66 and let 10:03:59
5 me know when you're done. 10:04:01
6 A. Thank you. 10:04:02
7 (The witness reviews the exhibit.) 10:04:03
8 I read Paragraph 66. 10:04:42
9 Q. Okay. And, as an initial 10:04:44
10 matter, you'd agree with me that Paragraph 10:04:47
11 66 is still part of the "Summary of the 10:04:49
12 Invention," right, sir? 10:04:51
13 A. (The witness reviews the 10:04:58
14 exhibit.) 10:04:58
15 I would agree that Paragraph 66 is 10:04:58
16 within the section of the patent that is 10:05:06
17 the "Summary of the Invention." 10:05:09
18 Q. And you'd also agree with me 10:05:10
19 that Paragraph 66 is talking about the 10:05:12
20 amplification-based preparative method, 10:05:15
21 correct? 10:05:17
22 A. That is how Paragraph 66 10:05:20
23 starts, yes. 10:05:21
24 Q. Well, right. 10:05:21
25 Well, the whole -- the contents of 10:05:22

1 CARLOS D. BUSTAMANTE, Ph.D.
2 what you just read is talking about the 10:05:24
3 amplification-based preparative method, 10:05:27
4 correct? 10:05:30
5 A. I believe that is correct. 10:05:30
6 Q. It does not talk about the 10:05:31
7 hybridization-based preparative method in 10:05:32
8 Paragraph 66, does it? 10:05:34
9 A. It does not. 10:05:35
10 Q. And it does not talk about 10:05:36
11 the circularization-based preparative 10:05:37
12 method in Paragraph 66, does it? 10:05:40
13 A. It doesn't. 10:05:41
14 Q. And I'll just call your 10:05:42
15 attention to the first words of Paragraphs 10:05:44
16 67 and 68. 10:05:47
17 Those other two methods are 10:05:47
18 disclosed in the next two paragraphs, 10:05:49
19 right? 10:05:51
20 A. Given me a moment to read. 10:05:52
21 Q. Sure. 10:05:54
22 A. (The witness reviews the 10:05:55
23 exhibit.) 10:06:34
24 Thank you. 10:06:34
25 I would agree that Paragraph 67 is 10:06:35

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	discussing hybridization-based	10:06:39
3	preparative methods and Paragraph 68 is	10:06:40
4	discussing circularization	10:06:43
5	selection-based preparative methods.	10:06:45
6	Q. Right.	10:06:46
7	Again, three different preparative	10:06:48
8	methods discussed in Porreca, correct?	10:06:50
9	A. Three different embodiments	10:06:53
10	as --	10:06:53
11	Q. Correct.	10:06:53
12	A. -- discussed earlier on.	10:06:55
13	Q. Right.	10:06:55
14	And if I call your attention to the	10:06:56
15	end of Paragraph 66, about two-thirds of	10:06:59
16	the way down, roughly -- there's no lines	10:07:08
17	numbers, unfortunately -- it says,	10:07:12
18	"Primers may also include additional	10:07:14
19	nucleic acids that are not complementary	10:07:17
20	to target sequences but that facilitate	10:07:19
21	downstream applications including, for	10:07:21
22	example, restriction sites and identifier	10:07:24
23	sequences e.g., source sequences."	10:07:26
24	Do you see that?	10:07:28
25	A. I do.	10:07:29

1 CARLOS D. BUSTAMANTE, Ph.D.

2 Q. And you'd agree with me the 10:07:29

3 reference to "identifier sequences," 10:07:32

4 that's a form of "tagging" that we read 10:07:33

5 about in Paragraph 31, correct? 10:07:36

6 A. Presumably, it would be a 10:07:41

7 "form of tagging." 10:07:43

8 Q. Right. 10:07:44

9 And that's, again, in relation to 10:07:45

10 embodiment, other than a MIP embodiment, 10:07:48

11 correct? 10:07:50

12 A. This would be for the 10:07:52

13 application [sic] based embodiment. 10:07:53

14 Q. "Amplification." 10:07:55

15 A. Sorry. 10:07:56

16 What did I say? 10:07:56

17 Q. You said, "application." 10:07:58

18 A. I apologize. 10:07:59

19 The amplification-based embodiment, 10:08:00

20 thank you. 10:08:02

21 Q. Okay. So, if we go to 10:08:53

22 Paragraph 100. 10:09:00

23 And, again, why don't you take your 10:09:07

24 time and read that paragraph, sir, and 10:09:09

25 then I'll ask you questions about it. 10:09:13

1 CARLOS D. BUSTAMANTE, Ph.D.

2 A. Thank you. 10:09:14

3 (The witness reviews the exhibit.) 10:09:25

4 Thank you. I read Paragraph 100. 10:09:46

5 Q. And I'm focusing on the first 10:09:49

6 sentence that states, "In some 10:09:50

7 embodiments, two or more independent 10:09:53

8 samples may be obtained from a subject 10:09:54

9 and independently analyzed." 10:09:56

10 Do you see that? 10:09:58

11 A. I do. 10:09:58

12 Q. And that is one of the two 10:09:58

13 possibilities of multiplexing that we 10:10:00

14 talked about earlier, two samples from 10:10:02

15 one subject, correct? 10:10:04

16 A. Usually, when we refer to 10:10:16

17 "multiplexing." We mean different samples 10:10:19

18 from different individuals being analyzed 10:10:21

19 in a given experiment or multiple loci 10:10:26

20 from the same individual. 10:10:32

21 Q. Right. 10:10:38

22 If you go to the next sentence, "In 10:10:38

23 some embodiments, two or more independent 10:10:40

24 samples are obtained at approximately the 10:10:42

25 same time point." 10:10:44

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Do you see that? 10:10:45
3 A. I do. 10:10:45
4 Q. Right. 10:10:46
5 And that's two or more samples from 10:10:46
6 the same individual, in the context of 10:10:52
7 Paragraph 100, correct? 10:10:55
8 A. These are two independent 10:10:58
9 samples from the same individual. 10:10:59
10 Q. Right. 10:11:00
11 And, again, that would be, as you 10:11:01
12 just, I think, testified, an example of 10:11:02
13 "multiplexing," correct? 10:11:05
14 A. Again, normally, we think of 10:11:06
15 "multiplexing" as the analysis of multiple 10:11:08
16 samples simultaneously from different 10:11:12
17 individuals. But two independent samples 10:11:15
18 from the same individual could fit within 10:11:17
19 the definition of "multiplexing." 10:11:21
20 Q. Okay. And then why don't you 10:11:22
21 go forward to Paragraph 102. Go ahead 10:11:28
22 and read that to yourself and I'll ask 10:11:33
23 you questions. 10:11:35
24 A. (The witness reviews the 10:11:36
25 exhibit.) 10:11:36

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Thank you. I've finished reading 10:13:20
3 Paragraph 102. 10:13:24
4 Q. Okay. The first sentence of 10:13:24
5 Paragraph 102 states, "It should be 10:13:28
6 appreciated that aspects of the invention 10:13:30
7 may be useful for high throughput cost 10:13:32
8 effective yet reliable genotyping of 10:13:35
9 multiple patient samples, e.g., in 10:13:39
10 parallel, for example, in multiplex 10:13:43
11 reactions." 10:13:45
12 Do you see that? 10:13:46
13 A. I do. 10:13:46
14 Q. Okay. And this sentence is 10:13:46
15 talking about the other form of 10:13:50
16 "multiplexing" that you talk about where 10:13:52
17 you have two different samples from two 10:13:54
18 different patients, correct? 10:13:58
19 A. It could be multiple samples 10:14:02
20 from different patients. 10:14:04
21 Q. Let me be more precise. 10:14:05
22 That's a fair point. 10:14:06
23 More than one sample from more than 10:14:08
24 one patient, correct? 10:14:10
25 A. Could be, yes. 10:14:11

1 CARLOS D. BUSTAMANTE, Ph.D.

2 Q. Could be -- 10:14:12

3 A. I mean, it says, "multiple 10:14:14

4 patient samples." So you're genotyping 10:14:16

5 multiple patient samples. 10:14:16

6 Q. Right. 10:14:18

7 So samples from more than one 10:14:18

8 patient, that is what that sentence is 10:14:20

9 talking about, correct? 10:14:22

10 A. Agreed. 10:14:23

11 Q. Okay. And, again, you would 10:14:26

12 agree, as it states in that sentence, that 10:14:28

13 that is a form of multiplex, correct? 10:14:30

14 A. It is -- yes, it says, "for 10:14:32

15 example, in parallel, for example, in 10:14:36

16 multiplex reactions." 10:14:39

17 Q. Okay. And this sentence 10:14:39

18 doesn't refer to any particular 10:14:44

19 preparative method, correct? 10:14:46

20 A. (The witness reviews the 10:14:51

21 exhibit.) 10:14:51

22 That sentence does not refer to a 10:14:51

23 preparative method. However, there are 10:14:57

24 different preparative methods that are 10:15:01

25 discussed throughout the rest of the 10:15:04

1 CARLOS D. BUSTAMANTE, Ph.D.
2 paragraph. 10:15:05
3 Q. Right. 10:15:05
4 Okay. And then farther down about, 10:15:06
5 I don't know, ten or so -- eight lines 10:15:20
6 from the bottom of the left-hand column 10:15:22
7 of Page 28 of Exhibit 1006, there is a 10:15:25
8 statement or a sentence that reads, "In 10:15:30
9 some embodiments, samples from different 10:15:32
10 subjects are tagged with subject 10:15:36
11 specific, e.g., patient specific tags" -- 10:15:39
12 excuse me, let me start over. 10:15:43
13 "In some embodiments, samples from 10:15:45
14 different subjects are tagged with 10:15:47
15 subject specific, e.g., patient specific 10:15:51
16 tags, e.g., unique sequence tags, so that 10:15:54
17 the information from each product can be 10:15:56
18 assigned to an identified subject." 10:16:00
19 Do you see that? 10:16:02
20 A. I do. 10:16:02
21 Q. And that sentence describes a 10:16:02
22 form of "tagging" that we talked about in 10:16:07
23 Paragraph 31, correct? 10:16:10
24 A. Well, let's look back at 10:16:17
25 Paragraph 31 and ensure that we're using 10:16:19

Page 60

1 CARLOS D. BUSTAMANTE, Ph.D.
2 "tagging" in the same way. 10:16:21
3 So similar to how "multiplexing" 10:16:41
4 can have multiple meanings, "tagging" can 10:16:43
5 have multiple meanings. 10:16:46
6 And I think it's important to be 10:16:50
7 careful in differentiating tags that are 10:16:52
8 random molecular tags versus patient 10:17:00
9 sample tags that are part of the 10:17:08
10 experimental design. 10:17:14
11 So I would read Paragraph 31 to be 10:17:17
12 referring to "tagging" in the sense of 10:17:27
13 molecular tags. 10:17:33
14 Whereas here we're referring to 10:17:36
15 "tagging" using subject specific tags. 10:17:38
16 Q. What is your understanding of 10:17:43
17 what a "subject specific tag" is? 10:17:44
18 A. A "subject specific tag" would 10:17:47
19 -- I think, sometimes this is used in the 10:17:54
20 form of de-multiplexing. So these are 10:17:56
21 alternate forms of -- usually, it's an -- 10:17:59
22 Illumina P5, P7 universal primers that 10:18:04
23 are set up in the reaction in such a way 10:18:08
24 that as the individual libraries are 10:18:10
25 prepped from different patients, each of 10:18:15

1 CARLOS D. BUSTAMANTE, Ph.D.
2 those patients is receiving a predefined 10:18:18
3 nucleotide sequence that is known as part 10:18:30
4 of the design of the universal primer. 10:18:32
5 So they're alternative forms of the 10:18:38
6 universal primer. 10:18:40
7 Q. Okay. So this predefined 10:18:41
8 nucleic acid sequence, is it a molecular 10:18:43
9 tag? 10:18:47
10 A. Again, it depends on the -- 10:18:52
11 the word "tag" is, unfortunately, like 10:18:58
12 the word "barcode," used with multiple 10:19:02
13 meanings. So, in this particular context, 10:19:05
14 when they're saying patient specific 10:19:11
15 tags, in the way this is usually 10:19:19
16 implemented, it means the use of molecular 10:19:21
17 signatures that are predefined and used 10:19:32
18 to follow the library prep through in 10:19:37
19 such a way that all of the molecules that 10:19:44
20 are derived through sequencing will carry 10:19:47
21 that patient specific information. 10:19:51
22 Q. Okay. So, again, you talked 10:19:54
23 about predefined nucleic acid sequence, 10:19:56
24 along with the Illumina P5 and P7 10:20:00
25 parameters. 10:20:00

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Are they molecular tags, sir? 10:20:03
3 A. In one definition of 10:20:05
4 "molecular tags," but in a different 10:20:08
5 definition of "molecular tags" they 10:20:10
6 wouldn't be tagging individual molecules, 10:20:12
7 in the sense that we're normally talking 10:20:22
8 about when we talk about random molecular 10:20:27
9 barcoding. 10:20:31
10 Q. Alright. And so understanding 10:20:31
11 -- you understand the same inventors have 10:20:34
12 written the entirety of Porreca, right? 10:20:37
13 A. Yes. 10:20:40
14 Q. Right. 10:20:41
15 And so you'd expect words to be used 10:20:41
16 consistently throughout this disclosure, 10:20:44
17 correct? 10:20:46
18 A. But they could have multiple 10:20:48
19 meanings like multiplex. 10:20:49
20 Q. Do you think the inventors of 10:20:51
21 Porreca intended to use "multiplex" in 10:20:54
22 different ways in different parts of the 10:20:57
23 patent application, sir? 10:20:59
24 A. By our own discussion, they're 10:21:01
25 using the word "multiplex" in different 10:21:03

1 CARLOS D. BUSTAMANTE, Ph.D.
2 ways. We've been "multiplexing" samples 10:21:05
3 and "multiplexing" loci. 10:21:09
4 Q. Right. 10:21:10
5 And so isn't the logical conclusion 10:21:11
6 to mean that they use "multiplex" to 10:21:14
7 include both? 10:21:15
8 A. They're unclear -- it might 10:21:20
9 be unclear in a given setting, which one 10:21:24
10 of the two meanings. 10:21:27
11 Q. Well, would you agree with me 10:21:27
12 with the general proposition that the 10:21:29
13 same word found repeatedly throughout a 10:21:31
14 patent application should have the same 10:21:33
15 meaning? 10:21:34
16 MS. CIPRIANO: Objection to 10:21:34
17 form. 10:21:37
18 A. Could you clarify that 10:21:37
19 question? 10:21:40
20 Q. No, I really can't. It's a 10:21:40
21 simple proposition. 10:21:43
22 When you read patents or patent 10:21:44
23 applications, sir, and see the same word 10:21:46
24 multiple times, do you assume that it has 10:21:48
25 the same meaning, or do you think the 10:21:51

1 CARLOS D. BUSTAMANTE, Ph.D.
2 authors have context-dependent meanings 10:21:53
3 where the same word is used differently 10:21:55
4 throughout a patent application? 10:21:58
5 MS. CIPRIANO: Same objection. 10:21:59
6 A. As we've discussed earlier, 10:22:03
7 the word "multiplex" can have multiple 10:22:04
8 meanings. 10:22:06
9 Q. Right. I'm not asking you 10:22:06
10 about the word "multiplex." 10:22:08
11 I'm asking, in general, as a 10:22:09
12 proposition, when you read a patent 10:22:12
13 application, do you understand when the 10:22:13
14 same word is used throughout that 10:22:15
15 application that it has a consistent 10:22:16
16 meaning throughout that application? 10:22:18
17 MS. CIPRIANO: Same 10:22:20
18 objections. 10:22:20
19 A. It could multiple meanings. 10:22:21
20 The same way "multiplex" can have multiple 10:22:22
21 meanings, "tag" can have multiple 10:22:24
22 meanings. 10:22:26
23 So, when they're referencing "tags," 10:22:26
24 we need to be specific -- 10:22:28
25 Q. Okay? 10:22:28

1 CARLOS D. BUSTAMANTE, Ph.D.

2 A. -- about which of the meanings 10:22:30
3 of "tags" it could have. 10:22:31

4 Q. Okay. So, in Paragraph 31, 10:22:33
5 it uses the word "tagging." We looked a 10:22:34
6 the that before. 10:22:37

7 A. We did. We may need to go 10:22:38
8 back to Paragraph 31. 10:22:39

9 Q. You can read it. It just 10:22:40
10 simply says the word, "tagging." But you 10:22:41
11 can feel free to look at it. 10:22:44

12 Do you see that? 10:22:46

13 A. I do. 10:22:46

14 Q. Okay. So, when Paragraph 102 10:22:46
15 uses the words "tagged" or "tags," is 10:22:50
16 that a form of "tagging," as that word is 10:22:55
17 used in 31; yes or no, sir? 10:22:59

18 A. Yes, but because the word 10:23:02
19 "tag" has multiple meanings, it could be 10:23:07
20 ambiguous, as to whether they're 10:23:09
21 referencing molecular tags or sample 10:23:11
22 barcodes. 10:23:13

23 Q. It could be "ambiguous" where? 10:23:15

24 A. It is unclear whether in 10:23:20
25 Paragraph 31 "tagging" here is referencing 10:23:22

1 CARLOS D. BUSTAMANTE, Ph.D.
2 sample barcodes, which are predetermined, 10:23:28
3 or random barcodes, which are part of the 10:23:31
4 different preparative methods. 10:23:40
5 In my opinion -- again, we could 10:23:42
6 dig more into this. Given that this is 10:23:47
7 in the library prep method, it's more 10:23:48
8 likely to be discussing the preparative 10:23:55
9 methods and how they use "tagging," which 10:23:59
10 do differ and meaning molecular random 10:24:02
11 barcodes versus sample barcodes. 10:24:11
12 Q. Okay. So, just so I 10:24:12
13 understand your testimony, you read the 10:24:14
14 word "tagging" in Paragraph 31 to not 10:24:17
15 include the sentence in Paragraph 102 10:24:23
16 that states, "In some embodiments, samples 10:24:29
17 from different subjects are tagged with 10:24:31
18 subject specific, e.g., patient specific 10:24:33
19 tags, e.g., unique sequence tags so that 10:24:36
20 the information from each product can be 10:24:39
21 assigned to an identified subject," 10:24:41
22 correct? 10:24:43
23 MS. CIPRIANO: Objection, 10:24:43
24 to the extent it misstates the 10:24:44
25 testimony. 10:24:46

1 CARLOS D. BUSTAMANTE, Ph.D.
2 A. What I said is it is 10:24:46
3 "ambiguous." 10:24:48
4 And so we have to be careful, 10:24:48
5 because some embodiments, as outlined in 10:24:51
6 Porreca, include the possibility for 10:24:53
7 sample barcodes, as part of the prep 10:24:57
8 method, and some do not. 10:25:00
9 Q. Right. 10:25:01
10 So you're saying to Paragraph 31 is 10:25:02
11 "ambiguous" as to "tagging." 10:25:05
12 So it could be what you've been 10:25:07
13 saying molecular identifiers or it could 10:25:10
14 be barcodes or, I guess, it could be both, 10:25:13
15 correct? 10:25:19
16 A. I think we have to read 10:25:21
17 "tagging" here in reference to each of the 10:25:23
18 preparative methods. 10:25:30
19 In the embodiments, as discussed in 10:25:32
20 Porreca, some preparative methods can 10:25:34
21 include sample barcodes. Some do not 10:25:38
22 include sample barcodes. And given that 10:25:41
23 -- particularly, in reference to Figure 4, 10:25:47
24 that is really around molecular random 10:25:51
25 barcodes. 10:25:54

1 CARLOS D. BUSTAMANTE, Ph.D.

2 And so my read of this would be, if 10:25:56
3 we're talking about preparative methods, 10:25:59
4 "tagging" is largely referring to 10:26:01
5 molecular barcodes that are randomers 10:26:04
6 versus when we're talking about "tags," 10:26:10
7 in the context of patient tags. We're 10:26:12
8 talking about different versions of the 10:26:16
9 P5, P7 adapters that have predefined 10:26:21
10 identifiers. 10:26:32

11 But, again, we can -- we need to 10:26:32
12 look carefully at each of the embodiments 10:26:35
13 to make sure which one is using which 10:26:37
14 definition of "tags," because it was 10:26:39
15 multiply used throughout the patent. 10:26:41

16 10:26:44
17 Q. Alright. And the sentence 10:26:44
18 that we've been looking at in 102 that 10:26:48
19 begins, "In some embodiments, samples 10:26:52
20 from different subjects are tagged with 10:26:53
21 subject specific e.g., patient specific 10:26:55
22 tags" -- I'm not going to read the rest 10:26:58
23 of that sentence. 10:26:59

24 You would agree with me, though, 10:27:00
25 that that sentence does not mention any 10:27:01

1 CARLOS D. BUSTAMANTE, Ph.D.
2 particular preparative method? 10:27:03
3 A. It simply says, "in some 10:27:12
4 embodiments." 10:27:14
5 Q. Right. 10:27:14
6 Okay. Let's go onto Paragraph 140, 10:27:16
7 please. And you can read that to 10:27:34
8 yourself. 10:27:37
9 A. (The witness reviews the 10:28:27
10 exhibit.) 10:28:27
11 Thank you. I finished reading 10:28:48
12 Paragraph 140. 10:28:50
13 Q. Okay. And Paragraph 140 10:28:51
14 starts with, "In some embodiments, the 10:28:59
15 invention relates to compositions 10:29:02
16 comprising pools" -- parent libraries -- 10:29:04
17 "of preparative nucleic acids that each 10:29:07
18 compromise 'differentiator tag sequences' 10:29:10
19 for detecting and reducing the effects of 10:29:13
20 bias and for genotyping target nucleic 10:29:16
21 acid sequences." 10:29:23
22 Do you see that? 10:29:23
23 A. I do. 10:29:23
24 Q. And when they're talking 10:29:23
25 about "preparative nucleic acid sequences" 10:29:25

1 CARLOS D. BUSTAMANTE, Ph.D.
2 in those sentences, they're talking about 10:29:27
3 nucleic acids that have undergone one or 10:29:29
4 perhaps more one of the various 10:29:32
5 preparative methods that we've discussed, 10:29:34
6 correct? 10:29:36
7 A. Presumably, yes. It's 10:29:37
8 referring to the preparative methods, 10:29:40
9 including those that have been discussed. 10:29:41
10 Q. Right. 10:29:43
11 By the way, having read Porreca, can 10:29:44
12 you point me to any place in Porreca 10:29:47
13 where they disclose a preparative method, 10:29:49
14 other than the three we've already 10:29:51
15 discussed today? 10:29:53
16 A. I believe those are the three 10:29:55
17 preparative methods largely used -- 10:29:57
18 Q. Okay. 10:29:59
19 A. -- and discussed. 10:30:00
20 Q. Okay. So, again, sitting 10:30:01
21 here today, you can't point me to a fourth 10:30:03
22 preparative method disclosed in Porreca? 10:30:05
23 A. I would need to re-read this 10:30:07
24 in detail to make sure that there isn't a 10:30:09
25 fourth. 10:30:11

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	But my recollection is that it	10:30:12
3	focuses largely on those three	10:30:14
4	preparative methods.	10:30:15
5	Q. And when they talk about in	10:30:15
6	the first sentence of Paragraph 130	10:30:17
7	[sic], "a preparative nucleic acid," a	10:30:18
8	person of skill in the art would	10:30:21
9	understand that the preparative nucleic	10:30:23
10	acid is a nucleic acid that has gone	10:30:25
11	through one of the preparative methods,	10:30:27
12	correct?	10:30:28
13	And I misspoke. I said, "130." I	10:30:30
14	meant to say 140.	10:30:32
15	A. Yes, we're in Paragraph 140.	10:30:35
16	I agree.	10:30:37
17	Q. Yeah.	10:30:39
18	So I don't know if I misspoke or	10:30:40
19	the Court Reporter got the thing wrong,	10:30:43
20	but I want to have a clear record.	10:30:45
21	A. Okay.	10:30:45
22	Q. So we're in Paragraph 140.	10:30:46
23	And I know you know that, but I want the	10:30:48
24	record to be clear.	10:30:50
25	A. Yeah.	10:30:51

1 CARLOS D. BUSTAMANTE, Ph.D.

2 Q. In Paragraph 140, in the 10:30:52

3 second -- going onto the third line of 10:30:54

4 that paragraph, when it says, "preparative 10:30:56

5 nucleic acids," a person who is skilled 10:30:59

6 in the art would understand that those 10:31:01

7 words are referring to nucleic acids that 10:31:03

8 have undergone one of the preparative 10:31:05

9 methods disclosed in Porreca, correct? 10:31:08

10 A. That is correct. As one 10:31:12

11 would read this patent, you would be 10:31:15

12 directed to one of those preparative 10:31:18

13 methods. 10:31:20

14 Q. And if you go about halfway 10:31:27

15 down that paragraph it states, "For 10:31:39

16 example, in the context of a multiplex 10:31:47

17 nucleic acid capture reaction, 10:31:51

18 differentiator tag sequences provide a 10:31:54

19 basis for differentiating between 10:31:56

20 multiple independent target nucleic acid 10:31:59

21 capture events." 10:32:01

22 Do you see that? 10:32:03

23 A. I do. 10:32:04

24 Q. Okay. What do you understand 10:32:05

25 a "multiplex nucleic acid capture 10:32:09

1 CARLOS D. BUSTAMANTE, Ph.D.
2 reaction" to be referring to? 10:32:12
3 A. Well, I would read this 10:32:17
4 paragraph as indicating that you are using 10:32:19
5 one of the capture methods discussed, 10:32:36
6 which could include the MIPs preparative 10:32:42
7 method, for example, and in that method, 10:32:50
8 you have a differentiator tag sequence. 10:32:54
9 Q. Would you agree that the 10:32:57
10 hybridization-based preparative method is 10:33:03
11 also a capture reaction? 10:33:07
12 A. I would agree that it is a 10:33:15
13 capture reaction. Whether in 10:33:18
14 hybridization you'd have a differentiator 10:33:21
15 tag sequence, as part of the capture 10:33:24
16 reaction, is unclear, as used here. 10:33:26
17 Q. Alright. And then in the 10:33:36
18 next sentence it says, "Also, in the 10:33:39
19 context of multiplex nucleic acid 10:33:41
20 amplification reaction, differentiator 10:33:45
21 tag sequences provide a basis for 10:33:47
22 differentiating between multiple 10:33:49
23 independent, primary amplicons of a 10:33:51
24 target nucleic acid, for example." 10:33:54
25 Do you see that? 10:33:56

1 CARLOS D. BUSTAMANTE, Ph.D.

2 A. I do. 10:33:57

3 Q. Alright. And you'd agree 10:33:57

4 with me that the "a multiplex nucleic 10:34:00

5 acid amplification reaction" is referring 10:34:05

6 to the amplification-based preparative 10:34:06

7 method, correct? 10:34:09

8 A. It's referring to an 10:34:13

9 "amplification-based preparative method." 10:34:14

10 Q. Alright. 10:34:22

11 Alright. And then the last 10:34:28

12 sentence states, "Figure 4A through 4C 10:34:31

13 depict various non-illuminating examples 10:34:36

14 of methods for combining differentiator 10:34:39

15 tag sequence and target sequences," 10:34:43

16 correct? 10:34:45

17 A. That is correct. 10:34:46

18 Q. So if you look at -- go 10:34:57

19 forward to 4A. 10:35:01

20 Figure 4A, actually, called 10:35:05

21 Figure 4A through C. It's on Page 5 of 10:35:09

22 Exhibit 6. 10:35:12

23 A. So it's back. 10:35:13

24 Q. Yes, forward in the document. 10:35:15

25 A. It's Page 5 in the document. 10:35:21

1 CARLOS D. BUSTAMANTE, Ph.D.

2 Q. Are you there? 10:35:23

3 A. Yeah. 10:35:24

4 Q. You see Figures 4A through C 10:35:24

5 in front of you, sir? 10:35:26

6 A. Yes. 10:35:28

7 Q. Okay, perfect. 10:35:28

8 A. It's not forward in the 10:35:28

9 document. It's backwards in the document. 10:35:29

10 Q. It's backwards in my brain. 10:35:32

11 So anyways apologies. We've arrived -- 10:35:34

12 A. We've arrived at Figure 4. 10:35:37

13 Q. We've arrived at Figure 4? 10:35:38

14 Alright. So Figure 4A is labeled a 10:35:40

15 "padlock probe." 10:35:47

16 Do you see that? 10:35:48

17 A. I do. 10:35:48

18 Q. And you would agree with me 10:35:49

19 that this is showing a molecular inversion 10:35:50

20 probe, correct? 10:35:53

21 A. Yes, it -- I -- my read of 10:35:56

22 this, this is a molecular inversion probe, 10:35:59

23 which is a type of padlock probe. 10:36:01

24 Q. So this would be used in the 10:36:03

25 circularization-based preparative method 10:36:08

1 CARLOS D. BUSTAMANTE, Ph.D.
2 that we discussed, correct? 10:36:10
3 A. I would agree with that. 10:36:13
4 Q. Okay. And then Figure 4B has 10:36:14
5 two adapters labeled "adapter 1" and 10:36:20
6 "adapter 2" shown, correct? 10:36:24
7 A. I see that. 10:36:25
8 Q. Right. 10:36:26
9 And does Figure 4B apply to any 10:36:26
10 particular preparative method in your 10:36:32
11 opinion? 10:36:35
12 A. We should look at the figure 10:36:43
13 legend, to be clear. 10:36:47
14 Q. Yeah. That's fine. It's 10:36:49
15 Paragraph 89 [sic], I believe. 10:36:53
16 A. I believe that is correct. 10:36:54
17 Q. Sorry, 85. I misspoke. 10:36:55
18 A. It is 85, which says, 10:37:00
19 "Figures 4A, B and C depict various 10:37:02
20 non-limiting methods for combining 10:37:02
21 differentiator tags and target sequences." 10:37:06
22 And "NNN depicts" -- 10:37:10
23 (Stenographer clarification.) 10:37:12
24 A. "NNN depicts a differentiator 10:37:13
25 tag sequence." 10:37:15

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Okay. So going back -- would you 10:37:19
3 mind repeating your question for me? 10:37:37
4 Q. Yeah, I just want to know 10:37:38
5 what your opinion is as to whether or not 10:37:39
6 Figure 4B depicts any particular -- any 10:37:41
7 one of three or more of the three 10:37:47
8 preparative methods that we discussed in 10:37:50
9 Paragraph 27 to 30 of Porreca. 10:37:53
10 A. Yeah, I would -- I would 10:37:55
11 surmise sitting here today that that is, 10:38:03
12 presumably, a depiction of the 10:38:10
13 amplification-based preparative method. 10:38:12
14 Q. Okay. And then going down to 10:38:14
15 Figure 4C, it has "ligation" listed in 10:38:17
16 the middle of that figure. 10:38:24
17 Do you see that? 10:38:25
18 A. I do. 10:38:26
19 Q. Okay. And similar question. 10:38:26
20 Does Figure 4C depict any of the 10:38:30
21 preparative methods disclosed in 10:38:35
22 Figures 27 to 30 of Porreca? 10:38:38
23 A. It's that -- that one's a bit 10:38:43
24 more unclear, because it says, "molecule 10:38:46
25 of interest," and you're just ligating on 10:38:49

1 CARLOS D. BUSTAMANTE, Ph.D.
2 the -- make sure I use the patent's 10:38:54
3 terminology. 10:39:04
4 I believe what they refer to it as 10:39:14
5 the "differentiator tag sequences." And 10:39:16
6 you're appending them to a "molecule of 10:39:19
7 interest." 10:39:22
8 From this figure alone, it is 10:39:24
9 unclear how that "molecule of interest" 10:39:25
10 was derived. 10:39:28
11 Q. Okay. So could that "molecule 10:39:38
12 of interest" in Figure 4C have been 10:39:44
13 obtained through a hybridization-based 10:39:46
14 preparative method? 10:39:49
15 A. A hybridization-based approach 10:39:49
16 would be one way that a molecule of 10:39:52
17 interest may have been obtained. 10:39:54
18 Q. Okay. Could a molecule of 10:39:55
19 interest have been obtained in Figure 4C 10:39:57
20 through an amplification-based preparative 10:39:59
21 method? 10:40:11
22 A. It could have. 10:40:11
23 Although in the context of an 10:40:13
24 amplification-based method, I'm not sure 10:40:15
25 how you would interpret the experiment 10:40:20

1 CARLOS D. BUSTAMANTE, Ph.D.
2 afterwards. But it is unclear from the 10:40:23
3 figure alone, but in theory it could be. 10:40:28
4 Although I would venture to say that you 10:40:40
5 probably wouldn't do the experiment in 10:40:46
6 that way. 10:40:47
7 Q. Okay. Why don't we take a 10:40:50
8 break. We've been going over an hour. 10:40:52
9 A. Okay. Thank you. 10:40:55
10 (Recess taken 10:40 to 10:54 10:40:56
11 a.m.) 10:54:32
12 MR. TRAUPMAN: Back on the 10:54:32
13 record. 10:54:33
14 Q. Welcome back, Dr. Bustamante. 10:54:33
15 A. Thank you. 10:54:35
16 Q. Before we took a break, we 10:54:37
17 were looking at the Porreca patent 10:54:39
18 application, Exhibit 1006. 10:54:42
19 Do you have that still in front of 10:54:45
20 you? 10:54:46
21 A. I do. 10:54:46
22 Q. Okay, great. 10:54:47
23 Can you please turn to Paragraph 149 10:54:48
24 of that document. It's on Page 33. 10:54:55
25 A. Yes. 10:55:01

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Q. Alright. And, again, why 10:55:02
3 don't you read that to yourself and then 10:55:03
4 we can talk about it. 10:55:06
5 A. (The witness reviews the 10:55:23
6 exhibit.) 10:55:23
7 I've read the section. 10:55:23
8 Q. Okay. And this, of course, 10:55:24
9 is a paragraph that you're familiar with, 10:55:26
10 correct? 10:55:27
11 A. I am familiar with this 10:55:28
12 paragraph. 10:55:29
13 Q. Yeah. 10:55:29
14 You've offered some opinions in your 10:55:30
15 Declaration on this paragraph, correct? 10:55:33
16 A. That is correct. 10:55:35
17 Q. Okay. And you know you can 10:55:36
18 feel free to refer to -- I'm not trying 10:55:39
19 to trick you. You can feel free to refer 10:55:41
20 to your Declaration, if you want. 10:55:44
21 I believe the relevant paragraph is 10:55:46
22 117 of Exhibit 2107. 10:55:50
23 But, as the case with all of my 10:55:56
24 questions, feel free to look at whatever 10:55:58
25 you'd like, Dr. Bustamante. 10:56:00

1 CARLOS D. BUSTAMANTE, Ph.D.

2 A. Thank you for the opportunity 10:56:01

3 to re-read this paragraph. 10:56:04

4 (The witness reviews the exhibit.) 10:56:17

5 Q. Alright. So 149, please, sir, 10:56:51

6 of Exhibit 1006. And the first sentence 10:56:53

7 reads, "The skilled artisan will 10:57:00

8 appreciate that as part of a MIP library 10:57:03

9 preparation process, adapters may be 10:57:06

10 ligated onto the ends of the molecules of 10:57:09

11 interest," correct? 10:57:12

12 A. That's what it states. 10:57:14

13 Q. Right. 10:57:15

14 And so the MIP library preparation 10:57:16

15 process is -- 10:57:18

16 (Stenographer clarification.) 10:57:18

17 Q. The MIP library preparation 10:57:22

18 process is one of the three preparative 10:57:24

19 processes that we looked at in Paragraphs 10:57:28

20 27 to 30 of Porreca, correct? 10:57:32

21 A. MIPs is one of the library 10:57:35

22 preparation processes that we've 10:57:37

23 discussed. 10:57:38

24 Q. Right. 10:57:38

25 And, specifically, in Paragraphs 27 10:57:39

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	to 30, correct?	10:57:41
3	A. I can go back and	10:57:44
4	double-check, but I believe it is 27	10:57:45
5	through 30, as we discussed earlier.	10:57:47
6	I agree.	10:57:56
7	Q. And it's your opinion, correct	10:58:00
8	me if I'm wrong, that the entirety of this	10:58:05
9	paragraph is discussing only the MIP	10:58:09
10	preparative process, correct?	10:58:15
11	A. (The witness reviews the	10:58:20
12	exhibit.)	10:58:20
13	This paragraph is discussing the MIP	10:58:36
14	preparative process and adapters for PCR	10:58:42
15	primer sites and/or sequencing primer	10:58:54
16	sites.	10:58:57
17	Q. Okay. Would a person that's	10:58:58
18	skilled in the art who reads Paragraph 149	10:59:01
19	understand that it applies to any of the	10:59:03
20	other two preparative processes disclosed	10:59:06
21	in Paragraphs 27 to 30 of Porreca, other	10:59:09
22	than the MIP preparative process?	10:59:12
23	A. It is referring to the MIP	10:59:15
24	preparative process.	10:59:18
25	Q. And only the MIP preparative	10:59:18

1 CARLOS D. BUSTAMANTE, Ph.D.
2 process, in your opinion, correct? 10:59:20
3 A. That's what is stated here. 10:59:22
4 Q. Well that's your opinion, 10:59:25
5 right, sir? 10:59:27
6 A. My opinion is that this 10:59:29
7 paragraph is referencing the MIP library 10:59:30
8 process -- preparative process, as it 10:59:36
9 states. 10:59:38
10 Q. Right. And I want to get 10:59:38
11 your -- understand your testimony. 10:59:41
12 Your opinion is that a person 10:59:43
13 skilled in the art who reads Paragraph 149 10:59:45
14 would understand that the contents of 10:59:48
15 Paragraph 149 are not applicable to the 10:59:51
16 other preparative processes, correct? 10:59:54
17 A. My testimony is that Paragraph 11:00:00
18 149 clearly states that it is referencing 11:00:02
19 the MIP library preparative process. 11:00:05
20 Q. Would a person who is skilled 11:00:06
21 in the art, sir, who reads Paragraph 149 11:00:10
22 in the larger context of Porreca 11:00:11
23 understand that Paragraph 149 can apply 11:00:13
24 to preparative processes, other than the 11:00:16
25 MIP preparative process? 11:00:19

1 CARLOS D. BUSTAMANTE, Ph.D.
2 MS. CIPRIANO: Objection, 11:00:21
3 asked and answered. 11:00:22
4 A. I believe I've answered the 11:00:26
5 question. 11:00:28
6 Q. Well, I want to hear your 11:00:28
7 answer, please. You don't just get to 11:00:30
8 refer back to an earlier answer. 11:00:32
9 I know your Counsel likes coaching 11:00:34
10 you. We'll deal with that as necessary. 11:00:36
11 My question, sir, though -- and I 11:00:37
12 can re-read it for you. 11:00:40
13 Would a person of skill in the art 11:00:42
14 who reads Paragraph 149, in the larger 11:00:43
15 context of Porreca, understand that 11:00:46
16 Paragraph 149 can apply to preparative 11:00:48
17 processes, other than the MIP preparative 11:00:51
18 process? 11:00:53
19 MS. CIPRIANO: Same objection. 11:00:53
20 A. Your -- if I understand your 11:00:57
21 question correctly, you're asking me 11:01:02
22 whether Paragraph 149 refers to the MIP 11:01:08
23 library preparation process, which I've 11:01:14
24 stated it does. 11:01:19
25 And I also believe you've asked me 11:01:20

1 CARLOS D. BUSTAMANTE, Ph.D.
2 would somebody reading this skilled in 11:01:22
3 the art understand that what is written 11:01:26
4 here could also apply to other methods. 11:01:28
5 And I would have to say that 11:01:33
6 somebody could read this and understand 11:01:35
7 it would apply to other methods. 11:01:37
8 But, as stated in 149, as written 11:01:38
9 in the patent, it is referencing the MIP 11:01:43
10 library process. 11:01:46
11 Q. Okay. So let's talk a little 11:01:52
12 bit more about that. 11:01:57
13 So you provide in your Declaration 11:01:59
14 an overview of the MIP library process, 11:02:08
15 correct? 11:02:14
16 And I refer you, specifically, to 11:02:16
17 the section or paragraphs beginning 11:02:18
18 around Paragraphs 70 on Page 35 of 11:02:21
19 Exhibit 2107. 11:02:26
20 You in Paragraph 30 refer to 11:02:28
21 "capture-by-circularization methods." 11:02:31
22 And I think we've agreed already 11:02:34
23 today that that is just another word for 11:02:36
24 the MIP preparative process, correct? 11:02:39
25 A. MIPs are one example of 11:02:42

1 CARLOS D. BUSTAMANTE, Ph.D.
2 capture-by-circularization. 11:02:47
3 Q. So, in Paragraphs 70 through 11:02:48
4 76, you depict the 11:02:54
5 capture-by-circularization methodology, 11:02:56
6 correct? 11:02:58
7 A. That is correct. 11:02:58
8 Q. And you'd agree that would 11:02:59
9 apply to MIPs, a MIP preparative process, 11:03:01
10 correct? 11:03:04
11 A. Yes, a MIP preparative 11:03:07
12 process is an example of the 11:03:10
13 capture-by-circularization, as discussed 11:03:14
14 here. 11:03:15
15 Q. Right. 11:03:15
16 And I don't want to belabor in the 11:03:16
17 interest of time this process too much, 11:03:20
18 but you have a capture in the 11:03:24
19 capture-by-circularization process. 11:03:28
20 You have a capture probe, correct? 11:03:29
21 A. Yes, we have a capture probe 11:03:33
22 in -- 11:03:35
23 Q. Correct. 11:03:36
24 And that anneals to the DNA or 11:03:37
25 nucleic acid of interest, correct? 11:03:43

1 CARLOS D. BUSTAMANTE, Ph.D.

2 A. Correct. 11:03:45

3 Q. And then you form the -- after 11:03:45

4 you polymerase that to form a fully 11:03:53

5 circular nucleic acid, correct? 11:03:56

6 A. Yes, after gap filling. 11:03:59

7 (Stenographer clarification.) 11:04:05

8 A. Gap filling. 11:04:05

9 Q. Right. 11:04:05

10 And then you, ultimately, as shown 11:04:05

11 in Paragraph 74, end up with the nucleic 11:04:07

12 acid of interest in a linear form with 11:04:14

13 additional nucleic acids attached to 11:04:19

14 either end of the nucleic acid of 11:04:21

15 interest, correct? 11:04:22

16 A. Paragraph 74 does not yet 11:04:25

17 have the linear material that's depicted 11:04:27

18 at the end of 75. 11:04:37

19 Q. Well, actually, I just want 11:04:38

20 to correct you. 11:04:40

21 I think it's the end of 74, because 11:04:41

22 75 doesn't begin until below those linear 11:04:44

23 strands. 11:04:50

24 A. Sorry. The graphical figure 11:04:51

25 -- you are correct, sorry. 11:04:54

1	CARLOS D. BUSTAMANTE, Ph.D.	
2	Below 74 is the figure and the	11:04:55
3	entire figure is put together in 75.	11:04:58
4	Q. Correct.	11:05:01
5	Okay. In the interest of	11:05:02
6	efficiency, the figure at the end of 75	11:05:05
7	represents the entire process, correct?	11:05:09
8	A. It's a representation of the	11:05:12
9	process.	11:05:13
10	Q. Right, right.	11:05:13
11	And your understanding of Porreca	11:05:14
12	Paragraph 130 -- excuse me, 149 -- let me	11:05:19
13	start over, for a clean record.	11:05:22
14	Your understanding of Porreca	11:05:24
15	Paragraph 149 is that the adapters would	11:05:25
16	be added after Step F of the work flow in	11:05:29
17	Paragraph 75 of your Declaration, correct?	11:05:39
18	A. They would be added after	11:05:43
19	Step F, yeah.	11:05:45
20	Q. Correct, okay.	11:05:46
21	So, again, after the probe has been	11:05:47
22	captured and amplified, correct?	11:05:54
23	A. They would be -- they would	11:06:01
24	be added after F, after it's been	11:06:10
25	amplified.	11:06:14

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Q. Okay. And that's -- okay, 11:06:14
3 great. 11:06:18
4 So, if you go back to Porreca, 11:06:19
5 Exhibit 1006, Paragraph 149, I want to 11:06:21
6 look at the second sentence. 11:06:27
7 A. Uh-huh. 11:06:29
8 Q. The second sentence talks 11:06:29
9 about -- let me start over. The second 11:06:33
10 sentence states, "Adapters often contain 11:06:36
11 PCR priming [sic] sites (for amplification 11:06:41
12 or emulsion PCR) and/or sequencing 11:06:44
13 priming [sic] sites." 11:06:49
14 Do you see that? 11:06:50
15 A. I do. 11:06:51
16 Q. Okay. And your understanding 11:06:52
17 is that sentence is talking about adapters 11:06:55
18 used in a MIP preparative process, 11:06:59
19 correct? 11:07:02
20 A. So the adapters would -- for 11:07:05
21 the adapters to be ligated on, they would 11:07:12
22 need to be ligated on to the end product 11:07:15
23 of the MIP preparative process. 11:07:20
24 Q. Right. 11:07:21
25 But you told me before that 11:07:22

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Paragraph 149 of Porreca was talking 11:07:25
3 about a MIP preparative process, correct? 11:07:27
4 A. It is. 11:07:29
5 Q. Right. 11:07:29
6 And so this second sentence in 149 11:07:29
7 is talking about adapters used in a MIP 11:07:32
8 preparative process, correct, in your 11:07:34
9 opinion? 11:07:39
10 A. So, in the MIP preparative 11:07:40
11 process, you're using the molecular 11:07:44
12 inversion probes to generate the amplified 11:07:47
13 target of interest. 11:07:50
14 For adapters to be ligated on, they 11:07:52
15 must be ligated onto the double-stranded 11:07:54
16 material. 11:07:57
17 Q. Okay. [MOTION] I move to 11:07:57
18 strike as nonresponsive. 11:07:58
19 My question, sir, is the second 11:07:59
20 sentence of Paragraph 149 that states, 11:08:01
21 "Adapters often contain PCR priming [sic] 11:08:04
22 sites (for amplification or emulsion PCR) 11:08:06
23 and/or sequencing priming [sic] sites," 11:08:11
24 that sentence refers to adapters used in 11:08:12
25 a MIP preparative process, in your 11:08:14

1 CARLOS D. BUSTAMANTE, Ph.D.
2 opinion, correct? 11:08:16
3 A. They would be used on the end 11:08:21
4 result of the MIP preparative process. 11:08:22
5 Q. Right. 11:08:24
6 Alright. And you see that the 11:08:25
7 sentence talks about a primer that has a 11:08:30
8 "PCR priming [sic] site and/or" a PCR -- 11:08:33
9 "and/or sequencing priming [sic] site." 11:08:37
10 Do you see that? 11:08:39
11 A. I do. 11:08:40
12 Q. Okay. So I want to take the 11:08:40
13 "and" example, okay? 11:08:42
14 You see it's "and/or." Let's focus 11:08:45
15 on "and." 11:08:47
16 So I want to understand an adapter 11:08:48
17 that has a "PCR priming [sic] site" and a 11:08:52
18 "sequencing priming [sic] site." 11:08:57
19 Are you with me, sir? 11:08:58
20 A. Okay. I'm just trying to 11:09:03
21 follow. 11:09:06
22 Q. The sentence uses the words 11:09:07
23 "and/or." 11:09:09
24 Do you see that? 11:09:10
25 A. Yes. 11:09:10

1 CARLOS D. BUSTAMANTE, Ph.D.

2 Q. It says, an adapter can have 11:09:10

3 -- there's three possibilities with an 11:09:13

4 "and/or" logic operator, correct? 11:09:14

5 As you read -- a person who is 11:09:18

6 skilled in the art that reads this 11:09:20

7 sentence -- I want to make sure you agree 11:09:22

8 with me here, sir. 11:09:24

9 According to the sentence, an 11:09:25

10 adapter can have "PCR priming [sic] site," 11:09:27

11 possibility No. 1, or a "sequencing 11:09:28

12 priming [sic] site" by itself, that's 11:09:31

13 possibility No. 2, and then the "and" 11:09:33

14 part of this sentence, just as a matter 11:09:36

15 of logic, sir, it can have a "sequencing 11:09:39

16 priming [sic] site" and a "PCR priming 11:09:41

17 [sic] site." 11:09:43

18 Would you agree with that? 11:09:44

19 MS. CIPRIANO: Objection to 11:09:46

20 form. 11:09:51

21 A. Could you break that question 11:09:51

22 up for me? 11:09:53

23 Q. No, I really can't. 11:09:54

24 A. Okay. 11:09:56

25 Q. This is really simple logic, 11:09:56

1 CARLOS D. BUSTAMANTE, Ph.D.
2 sir. It talks about an adapter that 11:09:58
3 contains a "PCR priming [sic] site and/or 11:10:01
4 a sequencing priming [sic] site." 11:10:04
5 Do you see those words in the 11:10:07
6 second sentence of Paragraph 149? 11:10:08
7 A. I do see those words. 11:10:10
8 Q. Okay. "And/or," do you 11:10:11
9 understand what those words mean? 11:10:13
10 A. I do understand. 11:10:15
11 Q. What does "and/or" mean to 11:10:15
12 you, sir? 11:10:17
13 A. "And/or" would mean "PCR 11:10:20
14 primer site" or a "sequencing primer 11:10:21
15 site" or "PCR primer site" and 11:10:25
16 "sequencing primer sites." 11:10:28
17 Q. Thank you. 11:10:30
18 So three possibilities, right? 11:10:30
19 A. Those would be three 11:10:31
20 possibilities. 11:10:33
21 Q. Okay. So I want to take the 11:10:33
22 third possibility that you mentioned, 11:10:34
23 sir, of an adapter with both a PCR 11:10:36
24 priming site and a sequencing priming 11:10:41
25 site. 11:10:44

1 CARLOS D. BUSTAMANTE, Ph.D.
2 You with me? 11:10:44
3 A. I'm with you. 11:10:45
4 Q. Okay. Can you explain to me 11:10:45
5 how in a MIP preparative process where an 11:10:49
6 adapter is added after amplification, the 11:10:51
7 added adapter has a PCR priming site and 11:10:57
8 a sequencing priming site? 11:11:00
9 A. Well, it would be designed to 11:11:05
10 be ligated onto the ends of the molecules 11:11:08
11 of interest, which would be the end result 11:11:12
12 of the preparative process. 11:11:13
13 Q. Right. 11:11:15
14 And you testified that the end 11:11:15
15 result of the MIP preparative process has 11:11:18
16 already been amplified. 11:11:20
17 So what would be the purpose of a 11:11:21
18 PCR priming site on that adapter, sir, in 11:11:24
19 a MIP preparative process? 11:11:26
20 A. It depends on the design of 11:11:45
21 the PCR primer sites. 11:11:48
22 Q. Okay. What would be the 11:11:48
23 purpose of the PCR priming site in an 11:11:49
24 adapter that's added on after Step F of a 11:11:52
25 MIP preparative process, as used in the 11:11:58

1 CARLOS D. BUSTAMANTE, Ph.D.
2 flow chart in Paragraph 75 of your expert 11:12:01
3 report? 11:12:05
4 A. As it states here, the 11:12:05
5 adapters may "contain PCR primer sites 11:12:07
6 (for amplification or emulsion PCR) 11:12:08
7 and/or sequencing primer sites." 11:12:11
8 So following the logic, it be PCR 11:12:14
9 primer sites for amplification and 11:12:19
10 sequencing primer sites or, if so chosen, 11:12:21
11 for emulsion PCR and sequencing primer 11:12:26
12 sites. 11:12:31
13 Q. Okay. What would be the 11:12:31
14 purpose of a second amplification step? 11:12:32
15 You testified that the MIP process 11:12:35
16 already has an amplification step before 11:12:37
17 the adapters are added? 11:12:40
18 A. My statement is based on the 11:12:45
19 fact that for adapters to be ligated onto 11:12:47
20 the ends of the molecules of interest, 11:12:49
21 because through the MIPs process you've 11:12:55
22 hybridized the probes, it would -- you 11:12:59
23 know, you needed double-stranded DNA to 11:13:09
24 do the ligation. 11:13:12
25 So it would require an experimental 11:13:13

1 CARLOS D. BUSTAMANTE, Ph.D.
2 setup where you want to use those PCR 11:13:16
3 primer sites for additional amplification, 11:13:19
4 emulsion PCR and sequencing. 11:13:21
5 Q. Okay. 11:13:24
6 A. And/or sequencing. 11:13:24
7 Q. Alright. 11:13:25
8 Okay. And then the next sentence 11:13:44
9 states "In addition, barcodes may be 11:13:48
10 included, for example, to uniquely 11:13:52
11 identify individual samples (e.g., 11:13:54
12 patient samples) that have been mixed 11:13:57
13 together." 11:13:59
14 Do you see that? 11:13:59
15 A. I do. 11:14:00
16 Q. And that's, again, referring 11:14:00
17 to multiplexing, correct? 11:14:02
18 A. That's referring to one of 11:14:06
19 the definitions of "multiplexing." 11:14:07
20 Q. Right. 11:14:10
21 And in that definition of 11:14:10
22 "multiplexing," it was known prior to 11:14:12
23 Porreca that you would need to add a 11:14:14
24 unique identifier, such as for a patient 11:14:17
25 sample, correct? 11:14:20

1 CARLOS D. BUSTAMANTE, Ph.D.
2 A. I would agree with that 11:14:21
3 statement. 11:14:22
4 Q. Alright. And then there's a 11:14:28
5 citation at the end of Paragraph 149 to 11:14:30
6 "USPTO Publication Number US 11:14:33
7 2007/0020640A1" to "McCloskey et al." 11:14:39
8 Do you see that? 11:14:45
9 A. I do. 11:14:46
10 Q. And you're familiar with that 11:14:46
11 document as well, right? 11:14:48
12 A. I am. 11:14:50
13 Q. Okay. 11:14:52
14 (Deposition Exhibit QIAGEN 11:14:52
15 1005, US Patent Application 11:14:52
16 US2007/0020640, was previously 11:14:52
17 marked for identification.) 11:14:57
18 Q. I'm going to hand you what's 11:14:57
19 been previously marked as Exhibit 1005. 11:14:59
20 MR. TRAUPMAN: Here's a copy. 11:15:04
21 (There is a discussion off 11:15:06
22 the record.) 11:15:09
23 Q. And Exhibit 1005 is the 11:15:09
24 McCloskey '640 patent application that's 11:15:13
25 referred to at the end of Paragraph 149, 11:15:17

1 CARLOS D. BUSTAMANTE, Ph.D.
2 correct? 11:15:22
3 A. I see that -- the patent 11:15:26
4 application here shares the same 11:15:29
5 publication number and reference to 11:15:30
6 McCloskey. So this is McCloskey. 11:15:33
7 Q. Great. 11:15:34
8 Can you point to me -- feel free to 11:15:35
9 take as much time as you need to review 11:15:41
10 this document, sir. 11:15:43
11 Can you point me to where the 11:15:45
12 McCloskey '640 application discloses an 11:15:47
13 adapter for use in a MIP preparative 11:15:49
14 process? 11:15:52
15 A. (The witness reviews the 11:15:59
16 exhibit.) 11:15:59
17 Sitting right here right now, to my 11:16:27
18 recollection, I do not believe that there 11:16:29
19 is a MIPs preparative process discussed 11:16:30
20 in McCloskey, but happy to continue 11:16:38
21 reading to see if I am mistaken. 11:16:44
22 Q. You would agree with me, for 11:16:47
23 instance, looking at Figure 3 of 11:16:49
24 McCloskey that there is a preparative 11:16:50
25 process where an adapter is added as part 11:16:54

1 CARLOS D. BUSTAMANTE, Ph.D.
2 of either an amplification or 11:16:58
3 hybridization process, correct? 11:17:01
4 A. I -- sorry, figure? 11:17:06
5 Q. Well, to be precise, Figure 3 11:17:11
6 talks about an adapter that's added via 11:17:15
7 ligation, right? 11:17:17
8 A. Yeah. 11:17:18
9 Q. That's what's disclosed there. 11:17:19
10 And Figure 2 -- if you go to 11:17:20
11 Figure 2D, it talks about -- all of 11:17:23
12 Figure 2, talks about an adapter that's 11:17:26
13 added for amplification, correct? 11:17:28
14 A. I believe those were accurate 11:17:33
15 representations of Figures 2A and C -- 2A 11:17:35
16 -- sorry, Figure 2 and Figure 3. 11:17:39
17 Q. Thank you. 11:17:41
18 Okay. So let's go on to Paragraph 11:17:41
19 150. Why don't you read that to 11:18:18
20 yourself. 11:18:21
21 A. (The witness complies.) 11:18:21
22 Thank you. I read Paragraph 150. 11:19:24
23 Q. Okay, great. So let's look 11:19:28
24 at 150. 11:19:31
25 Okay. 150, first sentence states 11:19:32

1 CARLOS D. BUSTAMANTE, Ph.D.
2 that, "The actual incorporation of random 11:19:34
3 differentiator tags sequences can be 11:19:37
4 performed through various methods known 11:19:40
5 in the art. For example, differentiator 11:19:43
6 tag sequences" -- excuse me. Let me 11:19:46
7 start over. 11:19:49
8 "For example, nucleic acids 11:19:49
9 compromising differentiator tag sequences 11:19:50
10 may be incorporated by ligation." 11:19:53
11 Do you see that? 11:19:55
12 A. I do. 11:19:56
13 Q. Okay. Now, you would agree 11:19:56
14 with me that when a differentiator tag 11:20:00
15 sequence is added via ligation, that the 11:20:02
16 differentiator tag is an adapter, correct? 11:20:07
17 A. Let's look at the definition 11:20:18
18 of "adapter" that's used in these 11:20:20
19 proceedings, just to ensure that I give 11:20:22
20 you an accurate answer. 11:20:24
21 Q. Yeah, let's do that. 11:20:25
22 So I believe, if I can call your 11:20:27
23 attention to Paragraphs 90 and 91 of your 11:20:31
24 Declaration. It's Page 47 of 11:20:39
25 Exhibit 2107. 11:20:42

1 CARLOS D. BUSTAMANTE, Ph.D.
2 You state, "I understand that the 11:20:43
3 Board construed 'adaptor' to have the 11:20:45
4 meaning of any oligonucleotide that is 11:20:47
5 attached to the target sequence." 11:20:50
6 Do you see that? 11:20:52
7 A. I do. 11:20:53
8 Q. Okay. You would agree with 11:20:53
9 me that the "differentiator tag" described 11:20:55
10 in the second sentence of Paragraph 150 11:21:00
11 is an oligonucleotide, correct? 11:21:03
12 A. It's an oligonucleotide. 11:21:06
13 Q. Okay. And it's attached to 11:21:07
14 the target sequence, correct? 11:21:08
15 A. It is attached to the target 11:21:10
16 sequence. 11:21:12
17 Q. So, therefore, you would agree 11:21:12
18 with me that "the nucleic acids 11:21:13
19 compromising differentiator tag sequences 11:21:19
20 may be incorporated by ligation," that 11:21:21
21 that sentence is discussing adding an 11:21:23
22 adapter onto the nucleic acid of interest, 11:21:26
23 correct? 11:21:28
24 A. As construed by the Board. 11:21:29
25 Q. And would a person who is 11:21:38

1 CARLOS D. BUSTAMANTE, Ph.D.
2 skilled in the art, based on the entirety 11:21:40
3 of the disclosure of Porreca, understand 11:21:42
4 that the adapter containing the 11:21:44
5 differentiator tag sequence discussed in 11:21:47
6 the second sentence of Paragraph 150, 11:21:49
7 could that include other nucleic acid 11:21:51
8 sequences? 11:21:57
9 A. As written here, the only 11:21:59
10 nucleic acid sequence being discussed is 11:22:05
11 the differentiator tag. 11:22:07
12 Q. Well, let's keep reading 150. 11:22:08
13 Paragraph 150 goes onto say, "This 11:22:11
14 is a flexible method, because molecules 11:22:14
15 having differentiator tag sequence can be 11:22:17
16 ligated to any blunt-ended nucleic acids. 11:22:19
17 The sequencing primers must be 11:22:23
18 incorporated [subsequently] such that 11:22:26
19 they sequence both the differentiator tag 11:22:26
20 sequence and the target sequence. 11:22:28
21 Alternatively, the sequencing adaptors 11:22:31
22 can be synthesized with the differentiator 11:22:34
23 tag sequences at their three prime end 11:22:36
24 (as degenerate basis), so that only one 11:22:40
25 ligation must be performed." 11:22:42

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Do you see that? 11:22:44
3 A. I do. 11:22:44
4 Q. Right. So Paragraph 150 is 11:22:45
5 stressing that the method of adding the 11:22:47
6 differentiator tag is "a flexible method," 11:22:52
7 correct? 11:22:56
8 A. That is what it states. 11:22:56
9 Q. Right. 11:22:57
10 And among the flexibility that it 11:22:58
11 states can be done is that the 11:23:05
12 differentiator tag can be three prime 11:23:12
13 from the sequencing primer and that that 11:23:17
14 nucleic acid can be ligated in a single 11:23:21
15 ligation, correct? 11:23:23
16 A. That's how I would read that 11:23:25
17 sentence. 11:23:26
18 Q. Alright. And then if you go 11:23:27
19 on to read the next sentence in 11:23:30
20 Paragraph 150, it states, "Another method 11:23:34
21 is to incorporate the differentiator tag 11:23:36
22 sequence into a PCR primer, such that the 11:23:38
23 primer structure is ranged with the 11:23:41
24 common adaptor sequence followed by the 11:23:44
25 random differentiator tag sequence 11:23:47

1 CARLOS D. BUSTAMANTE, Ph.D.
2 followed by the PCR priming sequence (in 11:23:48
3 five prime to three prime order)." 11:23:52
4 Do you see that? 11:23:55
5 A. I do see that. 11:23:56
6 Q. Right. 11:23:57
7 So that sentence is disclosing an 11:23:57
8 adaptor with a PCR priming sequence -- 11:24:01
9 let me strike that. 11:24:13
10 That sentence is describing an 11:24:14
11 adaptor with a PCR priming sequence, a 11:24:18
12 sequencing priming sequence and the 11:24:23
13 differentiator tag, correct? 11:24:27
14 A. Give me one moment. 11:24:31
15 Q. Uh-huh. 11:24:33
16 A. Can you simply restate your 11:24:51
17 question, so that I can follow? 11:24:56
18 Q. Yeah. 11:24:58
19 So the sentence reads, "Another 11:24:59
20 method is to incorporate the 11:25:01
21 differentiator tag sequence into a PCR 11:25:03
22 primer, such that the primer structure is 11:25:05
23 arranged with the common adaptor sequence 11:25:07
24 followed by the random differentiator tag 11:25:11
25 followed by the PCR priming sequence (in 11:25:15

1 CARLOS D. BUSTAMANTE, Ph.D.
2 five prime to three prime order)." 11:25:20
3 Do you see that? 11:25:22
4 A. That's what that sentence 11:25:23
5 states. 11:25:24
6 Q. Okay. What do you understand 11:25:24
7 the "common adaptor sequence" to mean? 11:25:26
8 A. It would mean some form of a 11:25:51
9 universal adaptor sequence. 11:25:57
10 Q. Right. 11:25:58
11 And if you read the next sentence, 11:25:59
12 it clarifies that universal adaptor 11:26:01
13 sequence can include a sequencing primer 11:26:03
14 site, because that sentence says, "A 11:26:07
15 differentiator tag sequence and adaptor 11:26:09
16 sequence (which may contain sequencing 11:26:11
17 primer site) are incorporated as tags." 11:26:13
18 Do you see that? 11:26:16
19 A. I do. 11:26:16
20 Q. Okay. You would agree with 11:26:17
21 me that in Paragraph 150, when it talks 11:26:18
22 about a "common adaptor sequence," a 11:26:22
23 person who's skilled in the art would 11:26:24
24 understand that the common adaptor 11:26:25
25 sequence could include a sequencing 11:26:27

1 CARLOS D. BUSTAMANTE, Ph.D.
2 primer -- a sequencing primer site, 11:26:29
3 right? 11:26:32
4 A. That's what it states. 11:26:32
5 Q. Alright. And so you would 11:26:33
6 agree with me then that the sentence that 11:26:37
7 states, "Another method is to incorporate 11:26:44
8 the differentiator tag sequence into a 11:26:47
9 PCR primer, such that the primer structure 11:26:49
10 is arranged with the common adaptor 11:26:52
11 sequence followed by the random 11:26:54
12 differentiator tag followed by the PCR 11:26:57
13 priming sequence (in 5 prime to 3 prime," 11:27:00
14 that sentence describes an adaptor, right? 11:27:02
15 A. It describes an adaptor. 11:27:04
16 Q. And that adaptor has three 11:27:06
17 sequences -- at least, three sequences; 11:27:08
18 sequencing primer site, a differentiator 11:27:13
19 tag and a PCR priming site, correct? 11:27:16
20 A. Sorry, the -- I believe the 11:27:26
21 adaptor in the next sentence may contain 11:27:29
22 the sequencing primer site. 11:27:31
23 Q. Right. 11:27:33
24 As you just testified, the common 11:27:34
25 adaptor sequence in that sentence that 11:27:36

1 CARLOS D. BUSTAMANTE, Ph.D.
2 begins with "Another method" can include 11:27:38
3 a sequencing primer site, right? 11:27:40
4 A. That's, certainly, a 11:27:43
5 possibility. 11:27:45
6 Q. Right. 11:27:45
7 And so the sentence that, again, 11:27:45
8 begins in Paragraph 150 that begins 11:27:47
9 "Another method" is to -- describes an 11:27:50
10 adaptor that can have a sequencing priming 11:27:53
11 site, a PCR priming site and the random 11:27:55
12 differentiator sequence. 11:27:58
13 That's how a person skilled in the 11:27:59
14 art would understand that sentence, in the 11:28:02
15 context of Paragraph 150, right? 11:28:03
16 A. In the context of Paragraph 11:28:05
17 150. 11:28:07
18 Q. Okay. And you would agree 11:28:07
19 with me that the sentence in Paragraph 149 11:28:08
20 that states, "Adaptors often contain PCR 11:28:16
21 priming [sic] sites and/or" -- but 11:28:19
22 focusing on the "and" part -- and 11:28:21
23 "sequencing priming [sic] sites," that 11:28:23
24 the adaptor that we just talked about in 11:28:26
25 Paragraph 150 is consistent with that 11:28:28

1 CARLOS D. BUSTAMANTE, Ph.D.
2 sentence in Paragraph 149, correct? 11:28:30
3 MS. CIPRIANO: Objection to 11:28:32
4 form. 11:28:34
5 A. Could you break that up for 11:28:38
6 me? 11:28:39
7 Q. Yes. So Paragraph 149 says, 11:28:40
8 "Adapters often contain PCR priming [sic] 11:28:42
9 sites and/or" -- but focusing on the 11:28:45
10 "and" site -- and "sequencing priming 11:28:47
11 [sic] sites," right? 11:28:49
12 A. That's correct. 11:28:50
13 Q. Right. 11:28:50
14 And the sentence, as we just went 11:28:51
15 over, in Paragraph 150 that states, 11:28:53
16 "Another method is to incorporate the 11:28:56
17 differentiator" tags -- "the 11:28:58
18 differentiator tag sequence in the PCR 11:29:00
19 primer, such that the primer structure is 11:29:02
20 arranged with the common adaptor sequence 11:29:07
21 followed by the random differentiator tag 11:29:09
22 sequence followed by the PCR priming 11:29:10
23 sequence (in 5 prime to 3 prime order)," 11:29:12
24 that sentence describes an adaptor that 11:29:12
25 can contain a PCR primer site and a 11:29:21

1 CARLOS D. BUSTAMANTE, Ph.D.
2 sequencing primer site, correct? 11:29:22
3 MS. CIPRIANO: Objection to 11:29:24
4 form. 11:29:25
5 A. It can. 11:29:25
6 But if we look at the next line in 11:29:27
7 150 where padlock probes are discussed, 11:29:30
8 there is also a discussion there about 11:29:35
9 the use of differentiator tags. 11:29:37
10 Q. Right. 11:29:39
11 And that's consistent with Figure 4, 11:29:40
12 which shows lots of different ways in 11:29:41
13 Porreca to add the differentiator tag, 11:29:44
14 right? 11:29:46
15 A. It shows three ways of adding 11:29:47
16 the differentiator tag. 11:29:49
17 Q. Right. 11:29:49
18 A. For each of the preparative 11:29:50
19 methods. 11:29:53
20 So, for the MIPs method, you would 11:29:53
21 put them in the MIPs. 11:29:55
22 For the amplification method, 11:29:56
23 presumably, you put them in the design of 11:29:58
24 the capture. 11:30:00
25 And then, presumably, for 11:30:02

1 CARLOS D. BUSTAMANTE, Ph.D.
2 hybridization, you ligate them on through 11:30:05
3 some other method. 11:30:07
4 Q. So switching gears, Dr. 11:30:53
5 Bustamante. 11:30:53
6 You were retained as an expert not 11:30:59
7 just in these IPRs, but in connection with 11:31:04
8 the District Court litigation involving 11:31:08
9 the same patents as the IPRs, correct? 11:31:10
10 MS. CIPRIANO: Objection to 11:31:12
11 scope. 11:31:13
12 A. I'm not sure I can answer 11:31:16
13 that question. 11:31:16
14 Q. Okay. Well, let me ask you a 11:31:17
15 different question. 11:31:19
16 Are you familiar with the fact that 11:31:19
17 Tecan asserted a second patent from the 11:31:26
18 same patent family as the '357 patent 11:31:30
19 against QIAGEN? 11:31:33
20 A. I may or may not be familiar 11:31:37
21 with that. 11:31:39
22 Q. Okay. Are you familiar with 11:31:39
23 the fact that QIAGEN filed an IPR 11:31:41
24 challenging the validity of -- and do you 11:31:44
25 understand that that's the '241 patent? 11:31:47

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Does that ring any bells? 11:31:50
3 A. I am familiar with the patent 11:31:51
4 that is referenced as the '241 patent. 11:31:53
5 Q. Correct. 11:31:55
6 And are you familiar with the fact 11:31:56
7 that QIAGEN filed an IPR challenging the 11:32:00
8 validity of the '241 patent? 11:32:04
9 A. I am familiar with that. 11:32:06
10 Q. Okay. And are you familiar 11:32:08
11 with the fact that in that IPR, QIAGEN 11:32:09
12 asserted that Claim 1 of the '241 patent 11:32:18
13 was anticipated by Porreca? 11:32:23
14 A. I have not reviewed the -- 11:32:28
15 recently the '241 proceedings in 11:32:31
16 preparation for today. 11:32:34
17 Q. Did you review the '241 11:32:37
18 proceedings at some point in your work 11:32:39
19 with Tecan in the opinions you've given 11:32:40
20 on these patents? 11:32:45
21 A. I do recall having reviewed 11:32:48
22 the '241 proceedings in the past. 11:32:50
23 Q. Okay. And so do you 11:32:52
24 understand that -- do you understand that 11:32:54
25 QIAGEN in its '241 IPR also alleged that 11:33:01

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Schmitt anticipated Claim 1 of the '241 11:33:04
3 patent? 11:33:07
4 MS. CIPRIANO: Objection, 11:33:07
5 scope. 11:33:08
6 A. As I stated, I have not 11:33:08
7 recently reviewed the '241 proceedings or 11:33:09
8 petition in preparation for today. 11:33:19
9 Q. Okay. Do you know what 11:33:20
10 happened with the '241 IPR? 11:33:23
11 MS. CIPRIANO: Objection, 11:33:27
12 scope. 11:33:28
13 A. Again, I prepared today to 11:33:28
14 discuss the '357 patent. 11:33:31
15 I may or may not be familiar with 11:33:34
16 what happened to the '241 patent. 11:33:36
17 Q. Well, "may or may not" is a 11:33:38
18 completely nonresponsive answer, sir. 11:33:39
19 So are you familiar with what 11:33:41
20 happened in the '241 proceedings? 11:33:42
21 A. I am broadly familiar, but I'm 11:33:44
22 not prepared to provide an opinion today. 11:33:46
23 Q. I understand. 11:33:49
24 I'm not asking for your "opinion." 11:33:50
25 I'm asking for your knowledge, sir, 11:33:52

1 CARLOS D. BUSTAMANTE, Ph.D.
2 because you are offering opinions here on 11:33:54
3 the '357 patent. And, as, I think, I can 11:33:56
4 show, your knowledge of what the other 11:33:59
5 proceedings is directly relevant to the 11:34:02
6 opinions here today. 11:34:04
7 So I want to try to understand. 11:34:04
8 Do you know what happened to the 11:34:06
9 '241 IPR, sir? 11:34:08
10 A. I am broadly familiar. 11:34:11
11 I don't have a copy of the decision 11:34:13
12 in front of me and so I am -- again, I'm 11:34:15
13 not really prepared to discuss that today. 11:34:20
14 Q. Do you understand that after 11:34:22
15 the Patent Trial and Appeal Board 11:34:24
16 instituted an IPR on the '241 patent, 11:34:28
17 that Tecan chose to disclaim all of the 11:34:29
18 claims of that patent? 11:34:31
19 A. That may be accurate. I'm 11:34:38
20 not sure. Again, as I said -- 11:34:40
21 Q. Are you hearing that for the 11:34:43
22 first time, that the '241 patent was 11:34:45
23 disclaimed; yes or no, sir? 11:34:48
24 MS. CIPRIANO: Objection to 11:34:49
25 form. 11:34:51

1 CARLOS D. BUSTAMANTE, Ph.D.
2 A. Could you restate that 11:34:51
3 question for me? 11:34:52
4 Q. Yes. 11:34:52
5 Did you know prior to coming into 11:34:53
6 the deposition room today that Tecan 11:34:55
7 disclaimed the '241 patent after it had 11:34:57
8 been -- after QIAGEN's IPR had been 11:35:00
9 instituted on that patent? 11:35:03
10 A. I was aware that there was a 11:35:06
11 decision on Tecan's part regarding the 11:35:10
12 '241 patent. As I said, I haven't 11:35:12
13 recently read exactly what that entailed. 11:35:15
14 But it wouldn't -- again, I'm not really 11:35:18
15 prepared to discuss that today, because 11:35:24
16 that's not what I prepared for. 11:35:26
17 Q. Okay. Well, I'll represent to 11:35:27
18 you that Claim 1 of the '241, which I know 11:35:30
19 you've read before, but I'll represent to 11:35:35
20 you that Claim 1 of the '241 patent has a 11:35:40
21 verbatim limitation as what's in the '357 11:35:44
22 patent, specifically, the one that says, 11:35:48
23 "identifying sequence reads with 11:35:51
24 identical identifier and target sequences 11:35:52
25 as duplicates." 11:35:55

1 CARLOS D. BUSTAMANTE, Ph.D.
2 And you recall, if you want to look 11:35:56
3 at your Declaration, that's the one 11:35:58
4 limitation that you allege is not 11:35:59
5 disclosed by Schmitt with respect to the 11:36:04
6 '357 patent, correct? 11:36:09
7 MS. CIPRIANO: Objection to 11:36:12
8 form. 11:36:14
9 A. (The witness reviews the 11:36:24
10 exhibit.) 11:36:25
11 Would you mind repeating the 11:36:25
12 question for me? 11:36:32
13 Q. Yeah. 11:36:32
14 I'll read you the last limitation 11:36:33
15 of the Claim 1 of the '241 patent. It 11:36:35
16 says, "Identifying sequence reads with 11:36:39
17 identical identifier and target sequences 11:36:41
18 as duplicates." 11:36:43
19 That's verbatim the same limitation 11:36:46
20 as what's quoted in your Declaration for 11:36:48
21 the '357 patent, correct? 11:36:51
22 A. I quote in my Declaration, 11:36:53
23 "identifying sequences reads with 11:36:55
24 identical identifier and target sequencing 11:36:56
25 as duplicates." 11:36:59

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Q. Great. 11:36:59
3 And that's the one limitation you 11:37:00
4 discuss in your Declaration with respect 11:37:03
5 to the Schmitt and McCloskey combination 11:37:04
6 Ground 2, correct? 11:37:09
7 A. That's what I discuss in my 11:37:11
8 Declaration. 11:37:12
9 Q. Alright. And the question 11:37:12
10 for you, sir, is, do you know why you and 11:37:17
11 Tecan are disputing the fact that Schmitt 11:37:22
12 discloses that limitation in this 11:37:28
13 proceeding, but that Tecan chose to 11:37:29
14 disclaim the '241 patent with an identical 11:37:33
15 limitation based on identical prior art 11:37:34
16 in the other proceeding? 11:37:36
17 MS. CIPRIANO: Objection, 11:37:37
18 calls for privileged information. 11:37:38
19 MR. TRAUPMAN: If he knows, 11:37:40
20 he can tell me. 11:37:41
21 MS. CIPRIANO: You can answer 11:37:42
22 yes or no. 11:37:44
23 A. I'm not a lawyer and I don't 11:37:45
24 know why Tecan made the decision with 11:37:49
25 Counsel that it made. I can't know that. 11:37:52

1 CARLOS D. BUSTAMANTE, Ph.D.
2 Q. Why don't we take a short 11:37:55
3 break. I might be done. 11:37:57
4 A. Okay. 11:37:59
5 (Recess taken 11:37 to 11:47 11:37:59
6 a.m.) 11:47:58
7 MR. TRAUPMAN: So back on the 11:47:58
8 record. 11:48:00
9 Q. And, Dr. Bustamante, thank you 11:48:01
10 for your time today. 11:48:02
11 I have no further questions for you. 11:48:03
12 A. Thank you. 11:48:05
13 MS. CIPRIANO: And I don't 11:48:06
14 have any questions for you. 11:48:07
15 Thank you. 11:48:08
16 MR. TRAUPMAN: Thank you very 11:48:08
17 much. 11:48:09
18 We can go off the record. 11:48:09
19 (Time noted: 11:48 a.m.) 11:48:13
20 ([RESERVATION] Ms. Cipriano 11:48:33
21 reserves signature.) 11:48:37
22 (Ms. Cipriano's order is 11:48:37
23 recorded on the Stenographer's
24 software.)
25

1 CARLOS D. BUSTAMANTE, Ph.D.

2 CERTIFICATE OF REPORTER

3 I, SILVIA P. WAGE, CSR, CRR, RPR,
4 herby certify that the witness in the
5 foregoing deposition was by me duly sworn
6 to tell the whole truth, nothing but the
7 truth; said deposition was taken down in
8 shorthand by me, a disinterested person,
9 at the time and place therein stated. The
10 testimony of said witness was thereafter
11 reduced to typewriting by computer under
12 my direction and supervision. Before
13 completion of the deposition, review of
14 the transcript [X] was [] was not
15 requested. If requested, any changes
16 made by the deponent (and provided to
17 the reporter) during the period allowed
18 are appended hereto.

19 I further certify that I am not of
20 counsel or attorney for either or any
21 of the parties to the said deposition,
22 nor in any way interested in the event
23 of this cause, and that I am not
24 related to any of the parties thereto.
25 October 17, 2025

1 Linnea Cipriano
2 Lcipriano@goodwinlaw.com

3 October 17, 2025

4 RE: Qiagen Sciences, LLC v. Tecan Genomics, Inc.

5 10/8/2025, Carlos D. Bustamante, Ph.D. (#7620048)

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 calendar-ca@veritext.com.

16 Return completed errata within 30 days from
17 receipt of testimony.

18 If the witness fails to do so within the time
19 allotted, the transcript may be used as if signed.

20

21

22 Yours,

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1 Qiagen Sciences, LLC v. Tecan Genomics, Inc.

2 Carlos D. Bustamante, Ph.D. (#7620048)

3 E R R A T A S H E E T

4 PAGE_____ LINE_____ CHANGE_____

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24 Carlos D. Bustamante, Ph.D.

Date

25

1 Qiagen Sciences, LLC v. Tecan Genomics, Inc.

2 Carlos D. Bustamante, Ph.D. (#7620048)

3 ACKNOWLEDGEMENT OF DEPONENT

4 I, Carlos D. Bustamante, Ph.D., 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 _____
Carlos D. Bustamante, Ph.D. Date

13

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&	102 57:21 58:3	90:5 91:2,6,20	241 111:25
& 3:3,18	58:5 66:14	94:6 98:5,25	112:4,8,12,15
0	67:15 69:18	108:19 109:2,7	112:17,22,25
00026 9:6,7	105 27:7,8,20	150 100:19,22	113:2,7,10,16
1	28:5 30:7,8	100:24,25	113:20 114:9
1 17:24 18:11	106 27:23 28:7	102:10 103:6	114:16,22
18:14 19:4,8	28:18 29:8	103:12,13	115:7,12,18,20
19:16 20:23	107 28:19 29:8	104:4,20	116:15 117:14
22:22 24:5	10:40 80:10	106:21 108:8	26 41:20,22,24
77:5 93:11	10:54 80:10	108:15,17,25	27 39:16,24
112:12 113:2	116 9:13,16	109:15 110:7	40:4,11,18,21
115:18,20	16:25 17:7,8	17 5:22 119:25	41:6 42:5,14
116:15	18:16 20:2,16	120:3	43:7,13 44:8
10 18:21 19:2	21:7 22:7 23:5	18 38:19	44:15,23 45:6
21:8 22:13,21	25:13 26:15	2	46:11,18 47:22
10/8/2025	27:4,5	2 18:21,25 21:8	49:25 50:13
120:5	117 81:22	22:13,20 77:6	51:2,19 78:9
100 55:22 56:4	118 5:19	93:13 100:10	78:22 82:20,25
57:7	11:37 118:5	100:12,16	83:4,21
10016 3:5	11:47 118:5	117:6	28 45:10,13,16
1005 4:11	11:48 118:19	20 5:19 39:15	46:9,12 47:24
98:15,19,23	11bn 6:4 8:16	122:15	60:7
1006 4:13	125 23:15,21	2007/002064...	29 46:16,21,23
25:22 28:6	127 23:23,25	98:7	46:25 47:24
30:25 31:8	129 23:23,25	2012/0165202	295 3:4
32:10 38:19	130 23:16,21	31:10	2a 100:15,15
39:15 60:7	72:6,13 89:12	2025 1:12 2:3	2d 100:11
80:18 82:6	140 70:6,12,13	119:25 120:3	3
90:5	72:14,15,22	2025/00026	3 16:25 17:7,8
1007 27:20	73:2	6:13	19:25 99:23
28:13,13,17,19	149 80:23 82:5	2107 4:14 8:24	100:5,16
29:20	83:18 84:13,15	9:9,11 81:22	107:13 109:23
10118 3:12	84:18,21,23	86:19 101:25	30 4:13 47:7,11
	85:14,16,22	212 3:5,12	47:17,25 49:25
	86:8 89:12,15		50:13 51:2,20

[30 - adapter]

78:9,22 82:20 83:2,5,21 86:20 120:16 31 48:5,15 50:23 51:15,22 55:5 60:23,25 61:11 66:4,8 66:17,25 67:14 68:10 33 80:24 33149 6:5 8:17 35 86:18 357 10:24 11:5 111:18 113:14 114:3 115:21 116:6,21	5 5 75:21,25 107:13 109:23 53 25:13 55 26:14 27:13 56 17:17 26:22 27:4,5	8 8 1:12 2:3 4:14 81 40:13 813-8800 3:12 849-7000 3:5 85 23:21 24:8 24:13 77:17,18 89 77:15	accurately 8:8 acid 18:2 40:22 41:7,10 42:25 43:3 44:17 62:8,23 70:21 70:25 72:7,10 72:10 73:17,20 73:25 74:19,24 75:5 87:25 88:5,12,14 102:22 103:7 103:10 104:14 acids 41:17 42:9,13,19 43:15 44:9 54:19 70:17 71:3 73:5,7 88:13 101:8 102:18 103:16 acknowledge... 122:3 acknowledg... 120:12 actual 101:2 actually 26:19 75:20 88:19 adapter 17:25 18:3,5 77:5,6 92:16 93:2,10 94:2,23 95:6,7 95:18,24 99:13 99:25 100:6,12 101:16,18 102:22 103:4
4	6 6 4:5 75:22 600 6:3 8:15 61 18:16 62 17:17 20:10 620 2:8 3:11 64 18:16 21:15 640 98:24 99:12 65 20:10,16 23:4 66 51:25 52:4,8 52:11,15,19,22 53:8,12 54:15 67 21:6,10,15 22:6 53:16,25 68 53:16 54:3	9 9 20:4 90 101:23 91 5:22 101:23 98 4:11 23:22 24:8,13 9:13 2:4 6:12 9:38 31:23 9:41 31:23	
4 26:15,18 27:12 68:23 76:12,13 110:11 40 36:23 47 101:24 4a 27:13,16 28:2 30:10,11 75:12,19,20,21 76:4,14 77:19 4b 27:13,16 77:4,9 78:6 4c 27:13,16 28:3 30:10 75:12 78:15,20 79:12,19	7 70 86:18 87:3 74 88:11,16,21 89:2 75 88:18,22 89:3,6,17 96:2 76 87:4 7620048 1:25 120:5 121:2 122:2	a a.m. 2:4 6:12 31:24 80:11 118:6,19 above 120:6 122:7 abstract 32:25 33:2,13 34:19 35:16,18,24 36:4 accuracy 120:9 accurate 18:7 21:5 26:17,24 47:5 48:4 100:14 101:20 114:19	

[adapters - anticipated]

adapters 18:4 69:9 77:5 82:9 83:14 89:15 90:10,17,20,21 91:7,14,21,24 96:5,17,19 109:8 adaptor 102:3 104:24 105:8 105:11,23 106:7,9,12,15 106:22,24 107:10,14,15 107:16,21,25 108:10,24 109:20,24 adaptors 103:21 108:20 add 97:23 110:13 added 89:16,18 89:24 95:6,7 95:24 96:17 99:25 100:6,13 101:15 adding 50:18 102:21 104:5 110:15 addition 97:9 additional 54:18 88:13 97:3 additions 122:6 address 8:13,15 14:12,19,22	15:14 agree 20:20 22:15 23:18 30:16 32:12 38:3 42:23 43:21 44:14 45:7 46:8,24 47:4,10,17 51:14 52:10,15 52:18 53:25 55:2 59:12 64:11 69:24 72:16 74:9,12 75:3 76:18 77:3 83:6 87:8 93:7,18 98:2 99:22 101:13 102:8,17 106:20 107:6 108:18 agreed 59:10 86:22 agreement 2:9 ah 28:12 ahead 20:14 21:6 38:11 51:24 52:3 57:21 al 98:7 algorithm 49:12 51:9,11 algorithms 48:12,22,25 49:6,9 51:5,17	allege 20:23 116:4 alleged 112:25 alleging 22:18 allotted 120:19 allow 7:13 21:24 allowed 119:17 alongside 12:15 alright 8:11 23:18 30:16 32:2,6 44:7 49:22 51:4,24 63:10 69:17 74:17 75:3,10 75:11 76:14 81:2 82:5 92:6 97:7 98:4 104:18 107:5 117:9 alternate 61:21 alternative 62:5 alternatively 103:21 ambiguous 66:20,23 68:3 68:11 amplicons 18:6 74:23 amplification 43:16 44:4,24 46:18 47:2 48:7 52:20 53:3 55:14,19	74:20 75:5,6,9 78:13 79:20,24 90:11 91:22 95:6 96:6,9,14 96:16 97:3 100:2,13 110:22 amplified 89:22,25 91:12 95:16 amplifying 18:5 30:18 42:25 43:3 analysis 24:7 33:6,12,15,16 33:17 34:17 36:5 41:8,18 51:11 57:15 analyzed 37:16 56:9,18 analyzing 24:19 35:5 anneals 87:24 answer 5:6 12:10 47:8 50:4 85:7,8 101:20 111:12 113:18 117:21 answered 38:10 85:3,4 answering 7:14 answers 7:19 anticipated 112:13 113:2
--	--	--	---

[anticipation - based]

anticipation 15:22 anyways 76:11 apartment 6:4 8:16 apologies 76:11 apologize 19:11 28:11 29:5 31:13,22 55:18 appeal 1:2 114:15 appear 37:21 appearances 6:22 appears 40:6 appended 119:18 122:7 appending 79:6 applicability 48:25 applicable 84:15 120:8 application 4:12,13 30:25 31:9 32:14 33:21 48:23 55:13,17 63:23 64:14 65:4,13 65:15,16 80:18 98:15,24 99:4 99:12 applications 35:10 54:21 64:23	applies 83:19 apply 77:9 84:23 85:16 86:4,7 87:9 appreciate 82:8 appreciated 48:6 58:6 approach 79:15 approximately 56:24 arranged 105:23 107:10 109:20 arrived 76:11 76:12,13 art 25:18 26:10 29:16 30:3 38:4 41:15 42:3 51:16 72:8 73:6 83:18 84:13,21 85:13 86:3 93:6 101:5 103:2 106:23 108:14 117:15 artisan 82:7 asked 11:20,23 11:25 12:14 14:9 15:2,15 15:17 16:3,7 38:10 85:3,25 asking 6:18 7:13 13:19,22 26:4,25 65:9	65:11 85:21 113:24,25 aspects 15:12 15:21 33:3 38:16 58:6 asserted 111:17 112:12 assigned 60:18 67:21 associated 21:20 assume 7:25 9:24 64:24 attached 88:13 102:5,13,15 120:11 attending 32:7 attention 23:22 53:15 54:14 101:23 attorney 12:13 119:20 120:13 attorneys 3:4 3:10 attributable 37:12 audibly 50:4 authors 65:2 available 120:6 avenue 2:8 3:4 3:11 aware 39:5 115:10	b b 4:6 18:21 21:7 77:19 back 9:13 19:25 32:6 40:18 60:24 66:8 75:23 78:2 80:12,14 83:3 85:8 90:4 118:7 backwards 76:9,10 barcode 62:12 barcodes 66:22 67:2,3,11,11 68:7,14,21,22 68:25 69:5 97:9 barcoding 63:9 based 19:3 22:21 24:7 40:24 43:8,16 44:4,10,20,24 44:25 45:11,19 45:20 46:18 47:2,12,18 48:8 52:20 53:3,7,11 54:2 54:5 55:13,19 74:10 75:6,9 76:25 78:13 79:13,15,20,24 96:18 103:2 117:15
--	--	---	---

basis 22:16,18 73:19 74:21 103:24 beginning 28:4 86:17 begins 38:21 40:14 69:19 108:2,8,8 belabor 87:16 believe 10:11 26:17 28:14,24 29:25 35:13 53:5 71:16 77:15,16 79:4 81:21 83:4 85:4,25 99:18 100:14 101:22 107:20 bells 112:2 best 7:17,23 better 22:17 beyond 46:3,5 bias 33:5 70:20 biscayne 6:4 8:16 bit 23:2 78:23 86:12 blunt 103:16 board 1:2 13:24 102:3,24 114:15 bottom 18:18 21:20 22:11 38:20 60:6	bounce 23:2 brain 76:10 break 31:15,19 32:7 80:8,16 93:21 109:5 118:3 brief 40:14 broadly 113:21 114:10 building 2:7 3:11 business 8:12 8:15 bustamante 1:1 1:10 2:1,5 3:1 4:1,4,15 5:1 6:1,2,14 7:1,6 8:1,8,14,25 9:1 9:24 10:1 11:1 12:1 13:1 14:1 14:4 15:1 16:1 16:23 17:1 18:1 19:1 20:1 21:1 22:1 23:1 24:1 25:1,12 26:1 27:1 28:1 29:1 30:1 31:1 32:1,11 33:1 34:1 35:1 36:1 37:1 38:1 39:1 40:1 41:1 42:1 43:1 44:1 45:1 46:1 47:1 48:1 49:1 50:1 51:1 52:1 53:1 54:1	55:1 56:1 57:1 58:1 59:1 60:1 61:1 62:1 63:1 64:1 65:1 66:1 67:1 68:1 69:1 70:1 71:1 72:1 73:1 74:1 75:1 76:1 77:1 78:1 79:1 80:1,14 81:1,25 82:1 83:1 84:1 85:1 86:1 87:1 88:1 89:1 90:1 91:1 92:1 93:1 94:1 95:1 96:1 97:1 98:1 99:1 100:1 101:1 102:1 103:1 104:1 105:1 106:1 107:1 108:1 109:1 110:1 111:1,5 112:1 113:1 114:1 115:1 116:1 117:1 118:1,9 119:1 120:5 121:2,24 122:2,4,12	call 23:22 53:14 54:14 101:22 called 25:17 75:20 calls 117:18 capture 41:2 42:20 45:24 73:17,21,25 74:5,11,13,15 86:21 87:2,5 87:13,18,19,20 87:21 110:24 captured 89:22 careful 61:7 68:4 carefully 34:21 69:12 carlos 1:1,10 2:1,5 3:1 4:1,4 4:15 5:1 6:1,2 7:1 8:1,14,24 9:1 10:1 11:1 12:1 13:1 14:1 15:1 16:1 17:1 18:1 19:1 20:1 21:1 22:1 23:1 24:1 25:1 26:1 27:1 28:1 29:1 30:1 31:1 32:1 33:1 34:1 35:1 36:1 37:1 38:1 39:1 40:1 41:1 42:1 43:1 44:1 45:1 46:1 47:1
		c	
		c 3:2 75:21 76:4 77:19 100:15 ca 120:15 calendar 120:15	

[carlos - common]

48:1 49:1 50:1 51:1 52:1 53:1 54:1 55:1 56:1 57:1 58:1 59:1 60:1 61:1 62:1 63:1 64:1 65:1 66:1 67:1 68:1 69:1 70:1 71:1 72:1 73:1 74:1 75:1 76:1 77:1 78:1 79:1 80:1 81:1 82:1 83:1 84:1 85:1 86:1 87:1 88:1 89:1 90:1 91:1 92:1 93:1 94:1 95:1 96:1 97:1 98:1 99:1 100:1 101:1 102:1 103:1 104:1 105:1 106:1 107:1 108:1 109:1 110:1 111:1 112:1 113:1 114:1 115:1 116:1 117:1 118:1 119:1 120:5 121:2,24 122:2 122:4,12 carries 29:3 carry 62:20 carryover 28:8 case 33:18 44:19 81:23	cause 119:23 caveat 37:13 38:12,13 cbd 6:3 ccr 1:24 certain 14:10 14:22 15:3,18 41:17 certainly 26:3 108:4 certificate 119:2 certified 2:10 2:11 certify 119:4,19 challenging 111:24 112:7 chance 9:25 10:21 11:2 32:18 change 121:4,7 121:10,13,16 121:19 changes 119:15 120:10 122:6 chart 96:2 check 35:11 83:4 checked 9:15 chose 114:17 117:13 chosen 96:10 cipriano 3:13 6:24 9:21 12:7 12:23 13:14,21	24:9 31:16 32:3 38:9 39:3 64:16 65:5,17 67:23 85:2,19 93:19 109:3 110:3 111:10 113:4,11 114:24 116:7 117:17,21 118:13,20 120:1 cipriano's 118:22 circular 88:5 circularization 40:24 41:11 43:8 45:11,19 48:7 53:11 54:4 76:25 86:21 87:2,5 87:13,19 citation 26:19 98:5 cite 27:19 28:5 28:7 cited 24:22 28:2 claim 15:10,18 15:20 17:24 18:11,14 19:4 19:8,16,17,21 20:23 22:22 24:5 112:12 113:2 115:18 115:20 116:15	claimed 17:3 17:14,22 20:5 claims 18:21,25 19:18,24 21:8 22:13,20 39:10 114:18 clarification 77:23 82:16 88:7 clarifies 106:12 clarify 7:23 64:18 clarifying 30:5 clean 7:15 89:13 clear 29:11 72:20,24 77:13 clearly 13:25 84:18 coaching 85:9 colleagues 7:8 column 38:20 60:6 combination 20:24 22:19 24:6 117:5 combining 75:14 77:20 comes 27:23 coming 28:9 115:5 common 104:24 105:23 106:7,22,24 107:10,24
--	---	---	---

[common - counsel]

109:20 complementary 54:19 complete 122:8 completed 120:16 completely 113:18 completion 119:13 complies 40:19 100:21 compositions 33:4 70:15 comprising 70:16 compromise 70:18 compromising 101:9 102:19 computer 119:11 conclusion 40:10 64:5 confirm 9:4 29:24 40:2 conjunction 15:7 connected 29:18 connection 11:4 48:9,19 111:7 considered 11:13	considering 7:8 consistent 65:15 108:25 110:11 consistently 63:16 construed 102:3,24 consulting 6:3 contain 90:10 91:21 96:5 106:16 107:21 108:20 109:8 109:25 containing 103:4 contains 94:3 contents 13:7 16:18,20,22 20:3 52:25 84:14 context 37:2,4 37:24 38:13 42:14 50:17 57:6 62:13 65:2 69:7 73:16 74:19 79:23 84:22 85:15 108:15 108:16 continue 99:20 continues 40:12 conversations 13:17,20	copied 26:15 copies 120:14 copy 8:20 9:19 9:20 11:7,8 25:24 30:20 31:8 32:9,10 98:20 114:11 correct 8:21 9:10 10:9,24 11:5,18,19 14:19,20 16:5 18:6 19:4,5,22 20:17 21:4 22:22 23:16,17 24:8,24 26:8 26:16 27:14,15 27:18 30:19 32:15,16,20,21 33:8,22 34:4 34:13,20 40:5 41:8,20 42:10 43:2,9,22 44:5 44:6,17,25 45:12,20 46:11 46:19 47:3,13 48:3,13,23 50:2,6,13 51:2 51:20 52:21 53:4,5 54:8,11 55:5,11 56:15 57:7,13 58:18 58:24 59:9,13 59:19 60:23 63:17 67:22 68:15 71:6	72:12 73:9,10 75:7,16,17 76:20 77:2,6 77:16 81:10,15 81:16 82:11,20 83:2,7,10 84:2 84:16 86:15,24 87:6,7,10,20,23 87:25 88:2,5 88:15,20,25 89:4,7,17,20,22 90:19 91:3,8 92:2 93:4 97:17,25 99:2 100:3,13 101:16 102:11 102:14,23 104:7,15 105:13 107:19 109:2,12 110:2 111:9 112:5 116:6,21 117:6 122:8 correction 10:12 corrections 122:6 correctly 85:21 correspond 16:21 cost 58:7 counsel 8:19 9:18 12:16,19 13:4,20 14:12 15:7 85:9
--	---	--	--

[counsel - describes]

117:25 119:20 120:14 course 16:19 24:17,22 32:17 42:10 81:8 court 7:15 26:12 72:19 111:8 courtesy 7:17 7:18 cover 32:24 crr 1:24 119:3 csr 119:3	62:1 63:1 64:1 65:1 66:1 67:1 68:1 69:1 70:1 71:1 72:1 73:1 74:1 75:1 76:1 77:1 78:1 79:1 80:1 81:1 82:1 83:1 84:1 85:1 86:1 87:1 88:1 89:1 90:1 91:1 92:1 93:1 94:1 95:1 96:1 97:1 98:1 99:1 100:1 101:1 102:1 103:1 104:1 105:1 106:1 107:1 108:1 109:1 110:1 111:1 112:1 113:1 114:1 115:1 116:1 117:1 118:1 119:1 120:5 121:2,24 122:2,4,12 data 51:12 date 121:24 122:12 day 7:9 21:18 122:15 days 120:16 de 37:15 61:20 deal 85:10 decision 14:21 15:6 25:5,7	114:11 115:11 117:24 declaration 4:14 8:20,24 9:5,14,25 10:3 10:7,9,15,22 11:3,18,22 12:2,6,15,21 13:8,13,15,16 14:7,18,23 15:6,13 16:4,7 16:12,15,21,25 18:12,23 19:13 19:24 20:10,16 22:7 23:16 25:11 26:5 28:25 29:14 30:9 32:14,19 81:15,20 86:13 89:17 101:24 116:3,20,22 117:4,8 declarations 14:13 declare 122:4 deduce 35:24 deemed 122:6 definition 34:10,14 57:19 63:3,5 69:14 97:21 101:17 definitions 37:4 97:19 degenerate 103:24	delightful 7:9 dependent 18:21,25 19:18 19:21 21:8 22:12,20 65:2 depending 50:17 depends 38:13 62:10 95:20 depict 75:13 77:19 78:20 87:4 depicted 88:17 depiction 78:12 depicts 77:22 77:24 78:6 deponent 119:16 120:13 122:3 deposing 120:13 deposition 1:9 2:5 5:3 7:8 8:23 10:2,4 30:24 32:20 36:15 98:14 115:6 119:5,7 119:13,21 derived 62:20 79:10 described 44:23 48:8,22 102:9 describes 39:8 60:21 107:14
d			
d 1:1,10 2:1,5 3:1 4:1,2,4,15 5:1 6:1,2 7:1 8:1,24 9:1 10:1 11:1 12:1 13:1 14:1 15:1 16:1 17:1 18:1 19:1 20:1 21:1 22:1 23:1 24:1 25:1 26:1 27:1 28:1 29:1 30:1 31:1 32:1 33:1 34:1 35:1 36:1 37:1 38:1 39:1 40:1 41:1 42:1 43:1 44:1 45:1 46:1 47:1 48:1 49:1 50:1 51:1 52:1 53:1 54:1 55:1 56:1 57:1 58:1 59:1 60:1 61:1			

[describes - drafting]

107:15 108:9 109:24 describing 105:10 description 4:7 4:10 40:15 45:18 design 49:20 61:10 62:4 95:20 110:23 designed 95:9 detail 48:2 71:24 detecting 70:19 detection 48:11 48:21 49:4 50:20,21,23 differ 67:10 different 14:3 25:11 27:16 34:3,12,25 35:2 36:11 37:2,15,17,18 38:8 45:2 54:7 54:9 56:17,18 57:16 58:17,18 58:20 59:24 60:9,14 61:25 63:4,22,22,25 67:4,17 69:8 69:20 110:12 111:15 differentiating 61:7 73:19 74:22	differentiator 70:18 73:18 74:8,14,20 75:14 77:21,24 79:5 101:3,5,9 101:14,16 102:9,19 103:5 103:11,15,19 103:22 104:6 104:12,21,25 105:13,21,24 106:15 107:8 107:12,18 108:12 109:17 109:18,21 110:9,13,16 differently 65:3 dig 67:6 directed 73:12 direction 5:6 119:12 directly 114:5 disagree 13:3 13:21 disclaim 114:17 117:14 disclaimed 114:23 115:7 disclose 17:3,13 17:22 18:10 19:7,15 20:5 71:13 disclosed 20:24 46:10 48:12 50:12,25 51:19	53:18 71:22 73:9 78:21 83:20 100:9 116:5 discloses 30:18 99:12 117:12 disclosing 44:15 105:7 disclosure 24:14 38:17 63:16 103:3 discuss 16:13 18:13 19:23 23:20 27:15 37:23 46:9 47:25 113:14 114:13 115:15 117:4,7 discussed 45:5 46:17 49:18,25 54:8,12 59:25 65:6 68:19 71:5,9,15,19 74:5 77:2 78:8 82:23 83:5 87:13 99:19 103:5,10 110:7 discusses 39:7 discussing 25:16 26:9 28:2 30:9 45:19,21 46:25 47:18 48:24 54:2,4 67:8 83:9,13 102:21	discussion 8:4 25:8 31:4 63:24 98:21 110:8 disinterested 119:8 dispense 7:4 disputing 22:16 117:11 district 111:8 dna 30:19 44:16 87:24 96:23 document 24:11,19 32:18 34:22 75:24,25 76:9,9 80:24 98:11 99:10 documents 5:9 doing 6:22 double 83:4 91:15 96:23 downstream 51:11 54:21 dr 6:14 7:6 8:8 9:24 11:3,17 11:18 12:21 13:8 14:4,6,12 14:18,22 15:5 16:23 25:12 32:10 80:14 81:25 111:4 118:9 drafting 32:19
--	---	--	--

[draw - fair]

draw 40:9 drawings 40:15 drive 6:4 8:15 du 3:8 duly 6:6 119:5 duplicates 21:4 23:11 115:25 116:18,25	44:19 55:10,10 55:13,19 embodiments 27:17 36:11 39:8,9,9 40:22 43:14 44:9,22 45:3,24 54:9 56:7,23 60:9 60:13 67:16 68:5,19 69:12 69:19 70:4,14 emulsion 90:12 91:22 96:6,11 97:4 ended 103:16 ends 82:10 95:10 96:20 enhancing 48:12,22 49:5 49:11 51:5,9 51:10,17 ensure 60:25 101:19 entailed 115:13 entire 89:3,7 entirety 24:18 24:19,23,25 63:12 83:8 103:2 errata 120:11 120:13,16 error 28:11 29:2 errors 10:7,15	esq 3:7,8,8,13 et 98:7 event 119:22 events 73:21 ex 28:13 exactly 115:13 examination 4:5 6:10 examined 6:6 example 54:22 57:12 58:10 59:15,15 73:16 74:7,24 86:25 87:12 92:13 97:10 101:5,8 examples 75:13 excuse 30:8 33:7 35:9 60:12 89:12 101:6 exhibit 4:11,13 4:14 8:23 9:9,9 9:11 21:20,24 25:22 27:20 28:6,19 29:20 30:24 31:8 32:10 35:22 38:19 39:15 47:15 52:7,14 53:23 56:3 57:25 59:21 60:7 70:10 75:22 80:18 81:6,22 82:4,6 83:12 86:19	90:5 98:14,19 98:23 99:16 101:25 116:10 exhibits 4:9 expect 63:15 experiment 51:13 56:19 79:25 80:5 experimental 61:10 96:25 expert 12:14 96:2 111:6 explain 95:4 explore 10:16 extend 7:16,18 extent 12:8,24 24:10 67:24 extra 9:19
e			f
e 3:2,2,16,16 4:2,6 121:3,3,3 e.g. 40:25 54:23 58:9 60:11,15 60:16 67:18,19 69:21 97:11 earlier 54:12 56:14 65:6 83:5 85:8 effective 58:8 effects 70:19 efficiency 89:6 eight 60:5 eighth 2:8 3:11 either 37:10 38:6 88:14 100:2 119:20 element 18:14 elements 11:21 14:10 15:3,8 15:10 16:2 emanuel 3:3,18 6:17 embodiment 36:12 43:10,19 43:20,24,25			f 89:16,19,24 95:24 facilitate 54:20 fact 96:19 111:16,23 112:6,11 117:11 failed 20:5 failing 17:22 fails 17:3,13 120:18 fair 11:15 15:25 16:9 17:20 26:6 58:22

[familiar - give]

familiar 7:7,10 81:9,11 98:10 111:16,20,22 112:3,6,9,10 113:15,19,21 114:10 family 111:18 fantastic 22:3 farther 20:2 60:4 feel 16:22 20:21 39:21 46:20 47:7 66:11 81:18,19,24 99:8 felt 15:13 fifth 3:4 figure 26:15,18 27:12 30:7,11 68:23 75:12,20 75:21 76:12,13 76:14 77:4,9 77:12 78:6,15 78:16,20 79:8 79:12,19 80:3 88:24 89:2,3,6 99:23 100:4,5 100:10,11,12 100:16,16 110:11 figures 28:2 30:10 76:4 77:19 78:22 100:15	filed 111:23 112:7 filling 88:6,8 fine 7:5 77:14 finish 7:13,19 finished 46:23 58:2 70:11 first 33:2,12 34:18 40:20 43:19 53:15 56:5 58:4 72:6 82:6 100:25 114:22 fit 57:18 five 105:3 106:2 flexibility 104:10 flexible 103:14 104:6 flip 9:12 20:21 26:22 florida 6:5 8:16 flow 89:16 96:2 focus 92:14 focused 24:16 focuses 72:3 focusing 56:5 108:22 109:9 follow 19:18 62:18 92:21 105:17 followed 104:24 105:2 105:24,25	107:11,12 109:21,22 following 47:24 96:8 follows 6:7 foregoing 119:5 122:5 form 55:4,7 58:15 59:13 60:22 61:20 64:17 66:16 88:3,4,12 93:20 106:8 109:4 110:4 114:25 116:8 formatting 29:2 formed 16:10 forms 61:21 62:5 forth 15:19 16:4,6,11,14,22 18:12 26:12 forward 39:15 40:10 57:21 75:19,24 76:8 found 64:13 foundation 39:4 fourth 71:21,25 fragments 18:2 18:5 40:23 free 16:23 20:21 39:21 46:20 47:8	66:11 81:18,19 81:24 99:8 front 8:21 11:7 25:25 32:24 76:5 80:19 114:12 full 40:10 fully 88:4 further 118:11 119:19
g			
gap 88:6,8 gears 111:4 gene 33:7 general 34:24 37:14 64:12 65:11 generate 91:12 generated 51:12 genetic 33:7,18 33:19 34:2,7 34:18 35:5 36:2,6 41:7,17 genomics 1:6 120:4 121:1 122:1 genotyping 41:18 42:16 58:8 59:4 70:20 give 7:15 11:8 26:3 29:22 39:18,19 101:19 105:14			

[given - incorporation]

given 32:10 34:23 49:21 53:20 56:19 64:9 67:6 68:22 112:19 122:9 glasses 31:12 31:20 32:4,8 go 10:16 18:15 18:16,20 19:25 21:6 22:25 23:7 25:10,13 27:3 38:11,15 38:17,18 39:14 39:15 40:18 44:7 46:15 47:6 51:24 52:3 55:21 56:22 57:21,21 66:7 70:6 73:14 75:18 83:3 90:4 100:10,18 104:18 118:18 goes 20:9 103:13 going 6:11,18 9:17 10:11 16:17 20:2 21:17 46:3,5 52:2 69:22 73:3 78:2,14 80:8 98:18 good 6:11,14 6:15 9:21	goodwin 2:6 3:10 goodwinlaw.... 3:13 120:2 grapetree 6:3 8:15 graphical 88:24 great 8:10 9:3,8 10:5,13 16:16 20:19 22:10 38:14 39:25 43:5 44:2 46:14 80:22 90:3 99:7 100:23 117:2 ground 117:6 group 6:3 guess 27:25 68:14	hearing 114:21 held 2:6 herby 119:4 hereto 119:18 122:7 high 58:7 hopefully 21:24 hour 80:8 huh 23:13 50:3 90:7 105:15 hundred 35:23 hybridization 44:10,20,25 47:12,18 48:8 53:7 54:2 74:10,14 79:13 79:15 100:3 111:2 hybridized 96:22	identifiers 68:13 69:10 identify 97:11 identifying 21:2 23:9 24:4 115:23 116:16 116:23 ii 16:24 illumina 61:22 62:24 illuminating 75:13 implemented 62:16 important 61:6 include 15:8 54:18 64:7 67:15 68:6,21 68:22 74:6 103:7 106:13 106:25 108:2 included 12:2 97:10 includes 15:20 including 14:12 15:22 54:21 71:9 incorporate 104:21 105:20 107:7 109:16 incorporated 101:10 102:20 103:18 106:17 incorporation 101:2
	h	i	
	h 4:6 121:3 halfway 73:14 hall 31:18 hand 60:6 98:18 happen 10:14 happened 113:10,16,20 114:8 happy 37:23 99:20 heading 28:15 hear 85:6	identical 21:3 23:10 115:24 116:17,24 117:14,15 identification 9:2 31:3 98:17 identified 60:18 67:21 identifier 21:3 23:10 54:22 55:3 97:24 115:24 116:17 116:24	

[increase - ligase]

increase 33:5 independent 19:17,20,24 56:7,23 57:8 57:17 73:20 74:23 independently 56:9 index 5:3 indexing 18:3 indicate 28:9 indicated 15:23 indicating 74:4 indicative 45:25 individual 33:22 34:8 35:6 38:7 56:20 57:6,9 57:18 61:24 63:6 97:11 individuals 34:4,12 35:2 37:18 38:8 56:18 57:17 information 12:9,25 60:17 62:21 67:20 117:18 initial 52:9 instance 26:14 41:18 99:23 instituted 114:16 115:9	institution 25:4 25:6 intended 63:21 inter 10:23 interchangea... 35:14 36:8 interest 49:21 78:25 79:7,9 79:12,17,19 82:11 87:17,25 88:12,15 89:5 91:13 95:11 96:20 102:22 interested 119:22 interpret 79:25 introduces 47:22 invalid 19:2 invalidate 22:20 invention 33:3 38:22,25 39:7 39:10,14 40:5 40:7,12 52:12 52:17 58:6 70:15 inventions 17:4 17:14,23 20:6 inventors 63:11 63:20 inversion 30:12 41:2,12 42:20 76:19,22 91:12	involving 111:8 ipr 6:12 11:5 12:5,20 14:6 14:17,23 15:2 111:23 112:7 112:11,25 113:10 114:9 114:16 115:8 ipr2025-00026 1:3 iprs 111:7,9 isolated 40:22 42:18 43:14 44:9 j jersey 2:13 job 1:25 john 3:8 johnyang 3:7 jumped 20:14 k keep 39:12 103:12 key 6:4 8:16 know 7:6,10,22 10:17 11:9 12:12 13:5 39:11,12 42:20 51:25 52:5 60:5 72:18,23 72:23 78:4 81:17 85:9 96:23 113:9 114:8 115:5,18	117:10,24,25 knowledge 8:9 113:25 114:4 known 30:12 62:3 97:22 101:4 knows 117:19 l l 3:16 labeled 22:12 76:14 77:5 laid 15:21 largely 69:4 71:17 72:3 larger 84:22 85:14 lawyer 39:6 117:23 lcipriano 3:13 120:2 left 38:20 60:6 legal 120:23 legend 77:13 letter 29:3 libraries 61:24 70:16 library 42:7,9,9 42:12,24 43:4 43:6 44:17,22 62:18 67:7 82:8,14,17,21 84:7,19 85:23 86:10,14 ligase 29:18
---	--	---	--

[ligate - method]

ligate 111:2 ligated 18:5 82:10 90:21,22 91:14,15 95:10 96:19 103:16 104:14 ligating 17:25 78:25 ligation 78:15 96:24 100:7 101:10,15 102:20 103:25 104:15 likely 67:8 likes 85:9 likewise 7:16 limitation 17:24 18:11 20:23,25 24:15 115:21 116:4 116:14,19 117:3,12,15 limitations 15:11,19,20 19:8,16,21 24:5 limiting 77:20 line 5:6,9,12,15 5:18,21 17:15 73:3 110:6 121:4,7,10,13 121:16,19 linear 88:12,17 88:22	lines 54:16 60:5 linnaea 3:13 120:1 listed 11:12 78:15 literature 37:11 49:19 litigation 111:8 little 19:10 20:2 23:2 86:11 llc 1:4 120:4 121:1 122:1 llp 2:7 3:3,10 loci 33:7,8,18 33:20,21 34:3 34:8,18 35:5 36:2,6 37:19 56:19 64:3 logic 93:4,15,25 96:8 logical 64:5 look 16:17,19 17:7 34:22 38:16 41:21 45:9 60:24 66:11 69:12 75:18 77:12 81:24 90:6 100:23 101:17 110:6 116:2 looked 27:13 66:5 82:19 looking 16:24 20:15 39:13 69:18 80:17	99:23 lost 17:5 lots 110:12 m made 12:3 13:9 14:21 15:6 117:24,25 119:16 122:5 make 7:12 29:11 35:11 36:9 40:9 69:13 71:24 79:2 93:7 making 44:20 marked 4:9 5:15 9:2 31:3 32:9 98:17,19 material 88:17 91:16 materials 11:13 14:11,14 matt 6:16 matter 13:12 13:15 16:11 40:3 52:10 93:14 matters 15:22 matthew 3:7 matthewtrau... 3:6 mccloskey 20:4 20:25 22:19 23:4 24:6 98:7 98:24 99:6,6 99:12,20,24	117:5 mean 35:4 36:14 56:17 59:3 64:6 94:9 94:11,13 106:7 106:8 meaning 44:3 64:15,25 65:16 67:10 102:4 meanings 37:11 50:17 61:4,5 62:13 63:19 64:10 65:2,8,19,21,22 66:2,19 means 34:24 62:16 meant 28:9 72:14 measures 10:20 memory 11:14 mention 69:25 mentioned 94:22 method 40:25 41:12,15 42:4 42:6 43:4,7,16 44:16 45:12,20 45:22,23 46:4 46:6,17,19 47:2,12 52:20 53:3,7,12 59:19,23 67:7 68:8 70:2 71:13,22 74:7
--	--	---	--

[method - non]

74:7,10 75:7,9 76:25 77:10 78:13 79:14,21 79:24 103:14 104:5,6,20 105:20 107:7 108:2,9 109:16 110:20,22 111:3 methodology 21:23 87:5 methods 33:4 44:4,11 46:10 47:19,23 48:2 48:8,18 49:24 50:12,25 51:19 53:17 54:3,5,8 59:24 67:4,9 68:18,20 69:3 71:5,8,17 72:4 72:11 73:9,13 74:5 75:14 77:20 78:8,21 86:4,7,21 101:4 110:19 metzker 3:17 11:3 12:6 metzker's 11:17,18 12:21 13:8 14:7,13 14:18,22 15:5 michael 3:17 middle 78:16 mind 78:3 116:11	minute 17:6 29:22 31:19 39:18 mip 30:13,17 45:11,20,24 55:10 82:8,14 82:17 83:9,13 83:22,23,25 84:7,19,25 85:17,22 86:9 86:14,24 87:9 87:11 90:18,23 91:3,7,10,25 92:4 95:5,15 95:19,25 96:15 99:13 mips 43:8,11 43:22,23 44:24 45:22 46:13 74:6 82:21 86:25 87:9 96:21 99:19 110:20,21 misspoke 72:13 72:18 77:17 misstates 24:10 67:24 mistaken 99:21 mixed 97:12 molecular 30:12 40:25 41:12 42:20 50:18 61:8,13 62:8,16 63:2,4 63:5,8 66:21	67:10 68:13,24 69:5 76:19,22 91:11 molecule 78:24 79:6,9,11,16,18 molecules 62:19 63:6 82:10 95:10 96:20 103:14 moment 53:20 105:14 morning 6:11 6:14,15 motion 5:21 91:17 move 20:2 91:17 multiple 33:18 33:19,21 34:2 34:7,11 37:6 38:6,7 50:16 56:19 57:15 58:9,19 59:3,5 61:4,5 62:12 63:18 64:24 65:7,19,20,21 66:19 73:20 74:22 multiplex 33:6 33:11,15,16 34:17,22 36:5 36:18,19 37:3 37:12,24 38:5 58:10 59:13,16 63:19,21,25	64:6 65:7,10 65:20 73:16,25 74:19 75:4 multiplexed 36:20 multiplexing 33:24 34:10,15 34:24 35:4,12 36:20 37:9,15 37:19,21 56:13 56:17 57:13,15 57:19 58:16 61:3,20 64:2,3 97:17,19,22 multiply 69:15 n n 3:2,16 4:2 name 6:16 8:12 necessary 85:10 122:6 need 9:20 11:13 31:12 34:21 36:9 65:24 66:7 69:11 71:23 90:22 97:23 99:9 needed 96:23 new 1:11,11 2:7 2:8,8,13,14 3:5 3:5,11,12,12 40:14 nnn 77:22,24 non 75:13 77:20
--	---	---	---

[nonresponsive - overall]

nonresponsive 91:18 113:18 normally 57:14 63:7 notary 2:12 122:13,19 note 120:10 noted 118:19 122:7 notice 10:7 nucleic 18:2 40:22 41:7,10 41:17 42:9,13 42:19,25 43:3 43:14 44:9,16 54:19 62:8,23 70:17,20,25 71:3 72:7,9,10 73:5,7,17,20,25 74:19,24 75:4 87:25 88:5,11 88:13,14 101:8 102:18,22 103:7,10,16 104:14 nucleotide 62:3 number 21:19 36:24 98:6 99:5 numbering 21:23 numbers 18:17 54:17 numeral 17:2 17:10	o o 3:16 objection 12:7 12:23 24:9 38:9 39:3 64:16 65:5 67:23 85:2,19 93:19 109:3 110:3 111:10 113:4,11 114:24 116:7 117:17 objections 65:18 obtained 56:8 56:24 79:13,17 79:19 obviousness 15:23 october 1:12 2:3 119:25 120:3 offer 17:21 offered 81:14 offering 114:2 office 1:2 offices 2:6 okay 6:19 7:3 8:2 9:22 10:13 10:17,18,19 11:23 12:3,17 15:9,16,25 16:17 17:20 18:15 20:13 21:21 22:2,4	25:10 28:22 31:25 32:17,22 33:19 36:17,21 38:15 39:11,19 39:24 40:20 41:5,23 42:8 44:2 45:8 47:6 50:10,19,22 51:23 52:9 55:21 57:20 58:4,14 59:11 59:17 60:4 62:7,22 65:25 66:4,14 67:12 70:6,13 71:18 71:20 72:21 73:24 76:7 77:4 78:2,14 78:19 79:11,18 80:7,9,22 81:8 81:17 83:17 86:11 89:5,20 90:2,2,16 91:17 92:12,13 92:20 93:24 94:8,21 95:4 95:22 96:13 97:5,8 98:13 100:18,23,25 101:13 102:8 102:13 106:6 106:20 108:18 111:14,22 112:10,23 113:9 115:17	118:4 oligonucleoti... 102:4,11,12 omissions 10:8 one's 78:23 operator 93:4 opine 15:15,18 16:7 opinion 13:3 17:21 18:24,25 19:6,14 67:5 77:11 78:5 83:7 84:2,4,6 84:12 91:9 92:2 113:22,24 opinions 16:10 16:14 18:8 19:3,20 22:21 23:9 24:3 29:15,17,19 81:14 112:19 114:2,6 opportunity 52:4 82:2 order 105:3 106:2 109:23 118:22 organization 26:5 29:13 orient 32:22 38:18 45:9 outlined 68:5 outlines 30:3 overall 29:15
--	--	--	---

[overlap - patient]

overlap 49:20 oversight 29:5 overview 86:14 own 29:4 63:24 owner 1:7 3:10	paragraph 23:23 24:12 27:7,8,10,11,23 28:5,7,10 30:8 39:16,22,24 40:4,13,21 41:6,19,20,22 41:23 42:4,14 43:7,13,13 44:8,14,23 45:6,10,13,16 45:18 46:9,11 46:16,18,21,25 47:7,10,17 48:15 50:23 51:15,22,25 52:4,8,10,15,19 52:22 53:8,12 53:25 54:3,15 55:5,22,24 56:4 57:7,21 58:3,5 60:2,23 60:25 61:11 66:4,8,14,25 67:14,15 68:10 70:6,12,13 72:6,15,22 73:2,4,15 74:4 77:15 78:9 80:23 81:9,12 81:15,21 82:3 83:9,13,18 84:7,13,15,17 84:21,23 85:14 85:16,22 86:20	88:11,16 89:12 89:15,17 90:5 91:2,20 94:6 96:2 98:5,25 100:18,22 102:10 103:6 103:13 104:4 104:20 106:21 108:8,15,16,19 108:25 109:2,7 109:15 paragraphs 23:7,15,19,21 23:21,25 24:7 24:13 29:8 47:24 49:25 50:13 51:2,19 53:15,18 82:19 82:25 83:21 86:17,18 87:3 101:23 parallel 58:10 59:15 parameters 62:25 parent 70:16 part 40:4 42:23 43:4 52:11 61:9 62:3 67:3 68:7 74:15 82:8 93:14 99:25 108:22 115:11 particular 37:23 59:18	62:13 70:2 77:10 78:6 particularly 23:23 68:23 parties 10:23 119:21,24 parts 12:20,20 14:17,17,22 15:14,17 16:19 16:20 63:22 past 112:22 patent 1:2,2,7 3:10 4:11,13 10:24 11:5 30:25 31:9 52:16 63:23 64:14,22 65:4 65:12 69:15 73:11 80:17 86:9 98:15,24 99:3 111:17,18 111:18,25 112:3,4,8,12 113:3,14,16 114:3,15,16,18 114:22 115:7,9 115:12,20,22 116:6,15,21 117:14 patent's 39:2 79:2 patents 64:22 111:9 112:20 patient 58:9,24 59:4,5,8 60:11
--	--	---	---

[patient - porreca]

60:15 61:8 62:14,21 67:18 69:7,21 97:12 97:24 patients 58:18 58:20 61:25 62:2 pcr 83:14 90:11 90:12 91:21,22 92:8,8,17 93:10,16 94:3 94:13,15,23 95:7,18,21,23 96:5,6,8,11 97:2,4 104:22 105:2,8,11,21 105:25 107:9 107:12,19 108:11,20 109:8,18,22,25 pennsylvania 2:14 percent 35:23 perfect 17:15 76:7 performed 101:4 103:25 period 119:17 person 38:4 42:2 51:16 72:8 73:5 83:17 84:12,20 85:13 93:5 102:25 106:23 108:13 119:8	petition 10:23 11:17,21 13:7 14:10 15:14,17 15:19,21,24 16:2 24:20,23 25:2 26:11 113:8 petitioner 1:4 3:4 24:13 petitioner's 24:20 ph.d. 1:1,10 2:1 2:5 3:1,17 4:1 4:4,16 5:1 6:1 6:2 7:1 8:1,25 9:1 10:1 11:1 12:1 13:1 14:1 15:1 16:1 17:1 18:1 19:1 20:1 21:1 22:1 23:1 24:1 25:1 26:1 27:1 28:1 29:1 30:1 31:1 32:1 33:1 34:1 35:1 36:1 37:1 38:1 39:1 40:1 41:1 42:1 43:1 44:1 45:1 46:1 47:1 48:1 49:1 50:1 51:1 52:1 53:1 54:1 55:1 56:1 57:1 58:1 59:1 60:1 61:1 62:1 63:1 64:1 65:1 66:1 67:1 68:1	69:1 70:1 71:1 72:1 73:1 74:1 75:1 76:1 77:1 78:1 79:1 80:1 81:1 82:1 83:1 84:1 85:1 86:1 87:1 88:1 89:1 90:1 91:1 92:1 93:1 94:1 95:1 96:1 97:1 98:1 99:1 100:1 101:1 102:1 103:1 104:1 105:1 106:1 107:1 108:1 109:1 110:1 111:1 112:1 113:1 114:1 115:1 116:1 117:1 118:1 119:1 120:5 121:2,24 122:2 122:4,12 phone 13:24 phrased 12:11 pick 29:19 place 71:12 119:9 please 7:12,22 8:13 10:16 21:7 25:13 29:23 30:20 45:14 51:25 70:7 80:23 82:5 85:7	plenty 29:12 plurality 18:2 35:25 36:2,6,6 point 11:16 56:25 58:22 71:12,21 99:8 99:11 112:18 points 14:5,6 polymerase 88:4 polymorphism 46:2 pools 70:16 pop 40:10 porreca 17:3 17:13,22 18:9 19:3,7,15,22 25:22,25 26:8 26:9,11,15,18 26:25 27:2,17 28:3,5 29:17 30:10,18,21 32:14,23,25 33:20 34:3,19 35:8,8,10 36:22 37:7,8 38:17 47:7 48:17 49:18,22 50:10,22 51:15 54:8 63:12,21 68:6,20 71:11 71:12,22 73:9 78:9,22 80:17 82:20 83:21 84:22 85:15
--	---	--	---

[porreca - proceeding]

89:11,14 90:4 91:2 97:23 103:3 110:13 112:13 posa 19:6,14 possibilities 56:13 93:3 94:18,20 possibility 68:6 93:11,13 94:22 108:5 potential 39:9 precise 58:21 100:5 predefined 62:2,7,17,23 69:9 predetermined 67:2 preliminary 10:20 40:3 prep 43:4,6 62:18 67:7 68:7 preparation 10:4 42:24 44:23 82:9,14 82:17,22 85:23 112:16 113:8 preparative 40:25 41:11,14 42:3 43:16 44:4,11,15 45:11,20,22,22 46:4,6,10,17	47:2,12,19,23 48:2,18 49:13 49:24 50:12,25 51:18 52:20 53:3,7,11 54:3 54:5,7 59:19 59:23,24 67:4 67:8 68:18,20 69:3 70:2,17 70:25 71:5,8 71:13,17,22 72:4,7,9,11 73:4,8,12 74:6 74:10 75:6,9 76:25 77:10 78:8,13,21 79:14,20 82:18 83:10,14,20,22 83:24,25 84:8 84:16,19,24,25 85:16,17 86:24 87:9,11 90:18 90:23 91:3,8 91:10,25 92:4 95:5,12,15,19 95:25 99:13,19 99:24 110:18 prepare 12:14 prepared 16:13 18:13 41:7 113:13,22 114:13 115:15 115:16 preparing 10:2 10:21 32:19	36:15 41:16 42:7 44:16 prepped 61:25 presence 45:25 presented 31:7 presumably 42:11 55:6 71:7 78:12 110:23,25 presume 9:16 9:17 previously 4:9 8:25 31:2 41:19 98:16,19 primary 74:23 prime 103:23 104:12 105:3,3 106:2,2 107:13 107:13 109:23 109:23 primer 62:4,6 83:15,15 92:7 94:14,14,15,16 95:21 96:5,7,9 96:10,11 97:3 104:13,22,23 105:22,22 106:13,17 107:2,2,9,9,18 107:22 108:3 109:19,19,25 110:2 primers 54:18 61:22 103:17	priming 90:11 90:13 91:21,23 92:8,9,17,18 93:10,12,16,16 94:3,4,24,24 95:7,8,18,23 105:2,8,11,12 105:25 107:13 107:19 108:10 108:11,21,23 109:8,10,22 prior 25:18 26:10 29:16 30:3 97:22 115:5 117:15 privileged 12:8 12:25 13:11 14:2 117:18 probably 80:5 probe 30:11,12 41:2,12 42:20 76:15,20,22,23 87:20,21 89:21 probes 49:20 91:12 96:22 110:7 problem 31:11 31:21 procedure 7:7 7:11 proceed 6:9 proceeding 6:12 9:5 10:22 117:13,16
--	---	---	---

[proceedings - reads]

proceedings 101:19 112:15 112:18,22 113:7,20 114:5	protocol 43:8 provide 73:18 74:21 86:13 113:22	91:19 93:21 105:17 111:13 111:15 115:3 116:12 117:9	read 19:10 24:17,23,25 25:4,6 33:9 35:8,18 39:20 39:21,24 41:23 43:12 45:13,16 46:20 47:8 49:14 50:14 51:3 52:4,8 53:2,20 55:4 55:24 56:4 57:22 61:11 64:22 65:12 66:9 67:13 68:16 69:2,22 70:7 71:11,23 73:11 74:3 76:21 81:3,7 82:3 85:12 86:6 93:5 100:19,22 104:16,19 106:11 115:13 115:19 116:14 120:9 122:5
process 42:24 82:9,15,18 83:10,14,22,24 84:2,8,8,19,25 85:18,23 86:10 86:14,24 87:9 87:12,17,19 89:7,9 90:18 90:23 91:3,8 91:11,25 92:4 95:5,12,15,19 95:25 96:15,21 99:14,19,25 100:3	provided 119:16 providing 26:7 public 2:13 122:19 publication 31:9 98:6 99:5 purpose 95:17 95:23 96:14 pursuant 2:9 put 26:12 89:3 110:21,23	questioning 26:23 questions 6:19 7:14,21 14:25 55:25 57:23 81:24 118:11 118:14 quinn 3:3,18 6:17 quinnemanue... 3:6,6,7 quote 116:22 quoted 116:20	reading 19:12 21:2 36:4 43:23 46:12,23 58:2 70:11 86:2 99:21 103:12
processes 49:13 82:19,22 83:20 84:16,24 85:17	q	r	reads 17:24 21:2 23:10 24:4,12 32:25 60:8 82:7
procter 2:6 3:10	qiagen 1:4 4:11 4:13 11:16 12:5 15:2 30:24 31:8 32:9 98:14 111:19,23 112:7,11,25 120:4 121:1 122:1	r 3:2,16 121:3,3 raised 11:16 random 61:8 63:8 67:3,10 68:24 101:2 104:25 105:24 107:11 108:11 109:21	
product 42:19 60:17 67:20 90:22	qiagen's 10:23 11:4,17 12:20 14:6,23 115:8	randomers 69:5 ranged 104:23 reaction 61:23 73:17 74:2,11 74:13,16,20 75:5	
production 5:9	question 5:15 7:20 8:2 12:10 14:4 22:17 45:17 47:9 64:19 78:3,19 85:5,11,21	reactions 58:11 59:16	
products 40:23 41:2,10 42:21 43:15 44:10			
professional 2:12			
proposition 64:12,21 65:12			

[reads - return]

83:18 84:13,21 85:14 93:6 105:19 115:23 116:16,23 ready 32:2 really 26:4 64:20 68:24 93:23,25 114:13 115:14 realtime 2:11 reason 8:6 21:17 120:11 121:6,9,12,15 121:18,21 recall 11:9,11 112:21 116:2 receipt 120:17 receiving 62:2 recently 112:15 113:7 115:13 recess 31:23 80:10 118:5 recollection 72:2 99:18 record 6:12,22 7:15 8:5,12 20:15 25:9 29:11 31:5,6 32:6 72:20,24 80:13 89:13 98:22 118:8,18 recorded 118:23 reduce 33:5	reduced 119:11 reducing 70:19 refer 28:19 29:8 33:21 37:10,15 38:6 41:14 42:6 56:16 59:18,22 79:4 81:18,19 85:8 86:16,20 reference 23:20 34:17 55:3 68:17,23 99:5 referenced 41:19 112:4 120:6 referencing 65:23 66:21,25 84:7,18 86:9 referred 32:13 98:25 referring 29:7 33:15 34:19 35:10,19 42:4 61:12,14 69:4 71:8 73:7 74:2 75:5,8 83:23 97:16,18 refers 33:16 37:3,4 85:22 91:24 refresh 11:14 regarding 17:21 21:8 115:11	region 49:21 registered 2:11 related 119:24 relates 26:11 33:3 70:15 relation 55:9 relevance 27:23 relevant 15:13 25:17 26:10 29:16 30:4 81:21 114:5 reliable 58:8 relied 24:18 relies 24:13 remind 7:12 rendered 19:2 repeatedly 64:13 repeating 78:3 116:11 report 96:3 reported 1:24 reporter 2:10 2:11,12 7:15 72:19 119:2,17 represent 115:17,19 representation 26:18 89:8 representations 100:15 represents 89:7 reproducibility 33:6	request 5:9 7:24 12:3 requested 119:15,15 requests 12:15 require 96:25 required 122:13 reservation 5:18 118:20 reserves 118:21 respect 17:23 18:9 19:4,20 22:21 23:9 24:3,5 29:17 116:5 117:4 respond 11:16 11:20,25 12:4 12:5,22 13:6 14:7,9 15:3 16:3 responding 24:17 rest 59:25 69:22 restate 105:16 115:2 restriction 54:22 result 41:11 92:4 95:11,15 resulting 51:12 retained 111:6 return 120:13 120:16
---	---	---	--

[review - see]

review 9:25 10:22,24 11:3 11:6 32:18 99:9 112:17 119:13 120:7 reviewed 10:3 112:14,21 113:7 reviewing 10:6 11:9,11 14:11 15:5 reviews 35:21 47:14 52:7,13 53:22 56:3 57:24 59:20 70:9 81:5 82:4 83:11 99:15 116:9 right 14:15 24:2,21 25:3 26:13 27:9,24 29:25 33:10,25 35:7,15 36:13 38:2,8 40:8 41:13 42:22 44:21 45:4,6 47:20 48:16 49:10,13,15 50:20 52:12,24 53:19 54:6,13 55:8 56:21 57:4,10 59:6 60:3 63:12,14 64:4 65:9 68:9 70:5 71:10	77:8 82:13,24 84:5,10 87:15 88:9 89:10,10 90:24 91:5 92:5 94:18 95:13 97:20 98:11 99:17,17 100:7 104:4,9 105:6 106:10 107:3,14,23 108:3,6,15 109:11,13 110:10,14,17 ring 112:2 roman 17:2,10 romanette 16:24 room 115:6 roughly 54:16 rpr 1:24 119:3 run 31:17	58:9,17,19 59:4,5,7 60:9 60:13 64:2 67:16 69:19 97:11,12 satisfied 19:22 saying 15:12 37:7,13 41:9 42:18 50:11,23 62:14 68:10,13 says 9:7 33:2 35:25 48:5,14 54:17 59:3,14 66:10 70:3 73:4 74:18 77:18 78:24 93:2 106:14 109:7 115:22 116:16 schmitt 20:4,25 22:19 23:4,20 24:6,8,14,18 27:20 28:2,8 28:13,17,20 29:7,9,19,20 30:4 113:2 116:5 117:5,11 sciences 1:4 120:4 121:1 122:1 scientific 12:13 scope 111:11 113:5,12 search 36:14	second 34:14 39:19 43:24 46:17 73:3 90:6,8,9 91:6 91:19 94:6 96:14 102:10 103:6 111:17 seconds 31:17 section 17:2,16 18:22 20:4,9 20:22 23:3 25:11,17 28:18 29:4,16 30:3 38:21,25 39:14 40:7 52:16 81:7 86:17 see 9:7 10:14 17:2,4,12,18 18:20,22 20:7 20:11 21:9,11 22:11,13 23:12 25:19,23 27:7 27:8,21,22 28:12,21 30:14 32:24 38:20,22 38:23 40:11,16 41:3,23 43:17 44:12 50:8,21 51:6 54:24 56:10 57:2 58:12 60:19 64:23 66:12 70:22 73:22 74:25 76:4,16 77:7 78:17
	s		
	s 3:2,16,16 4:6 121:3 safe 9:23 sample 58:23 61:9 66:21 67:2,11 68:7 68:21,22 97:25 samples 34:3 34:12,25,25 36:3,7 37:16 37:17 38:6,7,8 56:8,14,17,24 57:5,9,16,17		

[see - simultaneously]

90:14 92:6,10 92:14,24 94:5 94:7 97:14 98:8 99:3,21 101:11 102:6 104:2 105:4,5 106:3,18 seems 20:13 selected 12:19 14:5 selection 13:10 40:24 49:8 54:5 sense 61:12 63:7 sensitivity 48:11,21 49:5 49:11 51:5,8 51:10,17 sent 120:14 sentence 33:2 33:12 34:18 40:20 44:8,18 56:6,22 58:4 58:14 59:8,12 59:17,22 60:8 60:21 67:15 69:17,23,25 72:6 74:18 75:12 82:6 90:6,8,10,17 91:6,20,24 92:7,22 93:7,9 93:14 94:6 97:8 100:25	102:10,21 103:6 104:17 104:19 105:7 105:10,19 106:4,11,14 107:6,14,21,25 108:7,14,19 109:2,14,24 sentences 71:2 separate 14:25 30:2 43:19 44:19 sequence 21:2 23:10 24:4 60:16 62:3,8 62:23 67:19 74:8,15 75:15 77:25 101:15 102:5,14,16 103:5,10,15,19 103:20,20 104:22,24,25 105:2,8,11,12 105:21,23,25 106:7,9,13,15 106:16,22,25 107:8,11,13,25 108:12 109:18 109:20,22,23 115:23 116:16 sequenced 35:3 sequences 21:3 23:11 54:20,23 54:23 55:3 70:18,21,25	73:18 74:21 75:15 77:21 79:5 101:3,6,9 102:19 103:8 103:23 107:17 107:17 115:24 116:17,23 sequencing 42:17 62:20 83:15 90:12 91:23 92:9,18 93:11,15 94:4 94:14,16,24 95:8 96:7,10 96:11 97:4,6 103:17,21 104:13 105:12 106:13,16,25 107:2,18,22 108:3,10,23 109:10 110:2 116:24 set 15:19 16:4,6 16:11,14,22 18:12 61:23 setting 64:9 setup 97:2 shares 99:4 sheet 120:11 short 32:7 118:2 shorthand 2:10 119:8 show 114:4	showing 76:19 shown 77:6 88:10 shows 30:11 36:23 110:12 110:15 sic 14:13 55:13 72:7 77:15 90:11,13 91:21 91:23 92:8,9 92:17,18 93:10 93:12,16,17 94:3,4 108:21 108:23 109:8 109:11 sign 120:12 signature 118:21 signatures 62:17 signed 120:19 silvia 1:24 2:9 119:3 similar 61:3 78:19 simple 64:21 93:25 simply 42:18 45:17 66:10 70:3 105:16 simultaneous 33:17 simultaneously 35:2,4 57:16
---	--	---	--

[single - subjects]

single 35:5 104:14 sir 20:17 21:12 22:2,8 26:5 31:11 49:17 50:5,15 52:12 55:24 63:2,23 64:23 66:17 76:5 82:5 84:5 84:21 85:11 91:19 92:19 93:8,15 94:2 94:12,23 95:18 99:10 113:18 113:25 114:9 114:23 117:10 site 18:3 92:8,9 92:17,18 93:10 93:12,16,17 94:3,4,14,15,15 94:24,25 95:7 95:8,18,23 106:14,17 107:2,18,19,22 108:3,11,11 109:10,25 110:2 sites 54:22 83:15,16 90:11 90:13 91:22,23 94:16 95:21 96:5,7,9,10,12 97:3 108:21,23 109:9,11	sitting 29:25 71:20 78:11 99:17 size 48:11,21 49:4,8 50:19 50:21,23 skill 72:8 85:13 skilled 38:4 41:15 42:2 51:16 73:5 82:7 83:18 84:13,20 86:2 93:6 103:2 106:23 108:13 slightly 46:5 slower 19:10 software 118:24 sole 22:18 solutions 120:23 somebody 86:2 86:6 sorry 17:5 21:10 22:25 55:15 77:17 88:24,25 100:4 100:16 107:20 sounds 22:3 source 54:23 spans 17:16 23:15 speaking 46:13 specific 60:11 60:11,15,15	61:15,17,18 62:14,21 65:24 67:18,18 69:21 69:21 specifically 36:10 82:25 86:16 115:22 specification 39:2 spent 7:9 staggering 48:10,20 49:3 49:7,17,19 standard 37:20 start 10:20 28:17,18 39:12 60:12 89:13 90:9 101:7 starts 52:23 70:14 state 8:12 19:5 102:2 stated 84:3 85:24 86:8 113:6 119:9 statement 60:8 96:18 98:3 states 1:2 2:13 40:21 45:23 51:21 56:6 58:5 59:12 67:16 73:15 75:12 82:12 84:9,18 90:10 91:20 96:4	97:9 100:25 104:8,11,20 106:5 107:4,7 108:20 109:15 stay 21:25 30:7 staying 23:3 stenographer 6:8 19:9 77:23 82:16 88:7 stenographer's 118:23 step 89:16,19 95:24 96:14,16 stipulations 5:12 stranded 91:15 96:23 strands 88:23 stressing 104:5 strike 5:21 22:17 91:18 105:9 structure 104:23 105:22 107:9 109:19 subject 13:12 13:15 16:10 56:8,15 60:10 60:15,18 61:15 61:17,18 67:18 67:21 69:21 subjects 60:10 60:14 67:17 69:20
--	--	---	--

[submit - terminology]

submit 10:12	sworn 6:6	66:16,25 67:9	70:24 71:2
submitted 11:4	119:5 122:14	67:14 68:11,17	90:17 91:2,7
subscribed 122:14	synthesized 103:22	69:4	talks 90:8 92:7
subsection 18:21 21:7 22:12 23:8 25:21 28:14 40:14	t	tags 60:11,16 60:16 61:7,8,9 61:13,15 62:15 63:2,4,5 65:23 66:3,15,21 67:19,19 69:6 69:7,14,22 77:21 101:3 106:17 109:17 110:9	94:2 100:6,11 100:12 106:21
subsequently 103:18	t 3:16 4:6 121:3 121:3	66:3,15,21 67:19,19 69:6 69:7,14,22 77:21 101:3 106:17 109:17 110:9	target 21:3 23:11 34:6 54:20 70:20 73:20 74:24 75:15 77:21 91:13 102:5,14 102:15 103:20 115:24 116:17 116:24
subset 18:4	table 16:18,20 16:22 20:3	take 31:15,17 41:21 52:3 55:23 80:7 92:12 94:21 99:9 118:2	teaching 48:17 49:23
sullivan 3:3,18	tag 50:18 61:17 61:18 62:9,11 65:21 66:19 70:18 73:18 74:8,15,21 75:15 77:25 79:5 101:6,9 101:14,16 102:9,19 103:5 103:11,15,19 103:23 104:6 104:12,21,25 105:13,21,24 106:15 107:8 107:12,19 109:18,21 110:13,16	taken 31:23 80:10 118:5 119:7	teachings 26:8
summarize 47:21	tagging 48:10 48:21 49:4,8 50:7,15,16 55:4,7 60:22 61:2,4,12,15 63:6 66:5,10	92:12 94:21 99:9 118:2	tecan 1:6 4:14 8:23 9:9,11 111:17 112:19 114:17 115:6 117:11,13,24 120:4 121:1 122:1
summary 26:7 38:21,25 39:7 39:13 40:4,6 40:11 52:11,17		talk 53:6,10 58:16 63:8 72:5 81:4 86:11	tecans 115:11
supervision 119:12		talked 47:22 56:14 60:22 62:22 108:24	technique 49:23
support 5:3		talking 15:10 27:11,12 36:10 41:6 45:10 46:16 47:11 52:19 53:2 58:15 59:9 63:7 69:3,6,8	tell 33:14 117:20 119:6
supposed 28:14			telling 51:15
sure 7:13 30:22 35:11,23 36:9 40:9 45:15 53:21 69:13 71:24 79:2,24 93:7 111:12 114:20			ten 60:5
surmise 78:11			term 34:24 36:7
surprise 36:24 36:25 37:9			terminology 79:3
switching 111:4			

[testified - understand]

testified 6:6 14:16 57:12 95:14 96:15 107:24 testify 8:7 testimony 28:16 29:21 67:13,25 84:11 84:17 119:10 120:9,17 122:8 thank 6:8 8:18 22:5,24 23:14 30:23 32:4 39:23 46:22 47:16 52:6 53:24 55:20 56:2,4 58:2 70:11 80:9,15 82:2 94:17 100:17,22 118:9,12,15,16 thanks 30:5 theory 80:3 thereto 119:24 thing 72:19 think 14:24 34:5 36:4 41:9 57:12,14 61:6 61:19 63:20 64:25 68:16 86:22 88:21 114:3 third 17:15 44:15,18 73:3 94:22	thirds 54:15 three 44:22 45:2 47:22,24 47:25 48:18 49:12,24 50:12 50:24 51:18 54:7,9 71:14 71:16 72:3 78:7,7 82:18 93:3 94:18,19 103:23 104:12 105:3 106:2 107:16,17 110:15 throughput 58:7 tiling 48:10,20 49:3,7,16,17,19 time 37:17 55:24 56:25 87:17 99:9 114:22 118:10 118:19 119:9 120:18 timeframe 120:8 times 2:7 3:11 34:23 35:3,13 36:23 64:24 titled 20:4 25:22 today 6:19 8:7 10:2,16 18:14 21:18 29:25 30:2 32:13,20	36:16 71:15,21 78:11 86:23 112:16 113:8 113:13,22 114:6,13 115:6 115:15 118:10 today's 10:4 together 89:3 97:13 told 90:25 took 80:16 top 26:20 totally 13:3 29:11 trademark 1:2 transcript 119:14 120:6 120:19 122:5,8 traupman 3:7 4:5 6:10,16,21 7:2 9:18,22 13:2,19,22 31:6,14 80:12 98:20 117:19 118:7,16 trial 1:2 114:15 trick 81:19 true 122:8 truth 119:6,7 truthfully 8:7 try 21:18 114:7 trying 13:9 21:14 28:22 29:13 81:18 92:20	turn 80:23 two 14:24 23:19 31:17,19 46:10 53:17,18 54:15 56:7,12 56:14,23 57:5 57:8,17 58:17 58:17 64:10 77:5 83:20 type 76:23 typewriting 119:11 typo 28:15,24 typos 10:10,14 29:12
			u
			uh 23:13 50:3 90:7 105:15 ultimately 88:10 unclear 7:22 64:8,9 66:24 74:16 78:24 79:9 80:2 under 119:11 undergone 71:3 73:8 understand 6:20 7:25 8:3 8:19 12:18 13:9 19:7,15 26:2 27:10 28:23 29:13 33:14 34:16 35:17,19 38:5

[understand - witness]

41:16 42:3 49:2 63:11 65:13 67:13 72:9 73:6,24 83:19 84:11,14 84:23 85:15,20 86:3,6 92:16 94:9,10 102:2 103:3 106:6,24 108:14 111:25 112:24,24 113:23 114:7 114:14 understanding 26:10 38:24 39:6 61:16 63:10 89:11,14 90:16 unfortunately 54:17 62:11 uniform 21:22 unique 18:4 60:16 67:19 97:24 uniquely 97:10 united 1:2 universal 61:22 62:4,6 106:9 106:12 unreasonably 52:2 urquhart 3:3 3:18 us2007/0020... 4:12 98:16	us2012/0165... 4:14 31:2 use 18:17 21:18 33:23 34:2 35:12 37:14,20 37:24 44:20 49:16 62:16 63:21 64:6 67:9 79:2 97:2 99:13 110:9 used 33:20 34:23 35:13 37:5,9,25 42:13,15,16 48:9,19 49:12 49:23 50:11,24 51:18 61:19 62:12,17 63:15 65:3,14 66:17 69:15 71:17 74:16 76:24 90:18 91:7,24 92:3 95:25 101:18 120:19 useful 33:4 58:7 uses 33:11 66:5 66:15 92:22 using 36:7 43:11 60:25 61:15 63:25 69:13 74:4 91:11 uspto 98:6	usually 50:18 56:16 61:21 62:15 v v 1:5 120:4 121:1 122:1 vacuum 36:5 validity 111:24 112:8 variant 36:19 various 38:16 48:20 71:4 75:13 77:19 101:4 venture 80:4 verbatim 115:21 116:19 verify 120:9 veritext 120:14 120:23 veritext.com. 120:15 versions 69:8 versus 61:8 67:11 69:6 view 19:2 viii 17:2,10 w wage 1:24 2:10 119:3 want 12:17 13:5 16:19 39:11 40:2 72:20,23 78:4	81:20 84:10 85:6 87:16 88:19 90:5 92:12,16 93:7 94:21 97:2 114:7 116:2 wanted 10:8 way 9:19 30:17 30:18 40:12 46:20 54:16 61:2,23 62:15 62:19 65:20 71:11 79:16 80:6 119:22 ways 37:6 63:22 64:2 110:12,15 we've 32:13 39:12 47:21 64:2 65:6 69:18 71:5,14 76:11,12,13 80:8 82:22 86:22 wednesday 1:12 welcome 80:14 went 109:14 witness 4:4 5:6 19:11 31:7 35:21 40:19 47:14 52:7,13 53:22 56:3 57:24 59:20 70:9 81:5 82:4
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[witness - zoom]

83:11 99:15 100:21 116:9 119:4,10 120:8 120:10,12,18 wondering 27:25 word 29:20 33:24 36:14,18 37:12,14,20 62:11,12 63:25 64:13,23 65:3 65:7,10,14 66:5,10,16,18 67:14 86:23 words 29:10,18 33:11 42:3 53:15 63:15 66:15 73:7 92:22 94:5,7,9 work 89:16 112:18 worked 14:11 worries 29:6 32:5 written 22:23 23:24 63:12 86:3,8 103:9 wrong 72:19 83:8	y yang 3:8 yeah 17:7,11 21:14 27:6,24 29:23 31:16 32:3 39:21 72:17,25 76:3 77:14 78:4,10 81:13 89:19 100:8 101:21 105:18 116:13 yesterday 6:25 7:3,10 york 1:11,11 2:7,8,8,14 3:5,5 3:11,12,12
	z
	zoom 3:8 32:7
x	
x 1:7 4:2,6 119:14 xusong 3:8 xusongdu 3:6	

Federal Rules of Civil Procedure

Rule 30

(e) Review By the Witness; Changes.

(1) Review; Statement of Changes. On request by the deponent or a party before the deposition is completed, the deponent must be allowed 30 days after being notified by the officer that the transcript or recording is available in which:

(A) to review the transcript or recording; and

(B) if there are changes in form or substance, to sign a statement listing the changes and the reasons for making them.

(2) Changes Indicated in the Officer's Certificate. The officer must note in the certificate prescribed by Rule 30(f)(1) whether a review was requested and, if so, must attach any changes the deponent makes during the 30-day period.

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Veritext Legal Solutions represents that the foregoing transcript is a true, correct and complete transcript of the colloquies, questions and answers as submitted by the court reporter. Veritext Legal Solutions further represents that the attached exhibits, if any, are true, correct and complete documents as submitted by the court reporter and/or attorneys in relation to this deposition and that the documents were processed in accordance with our litigation support and production standards.

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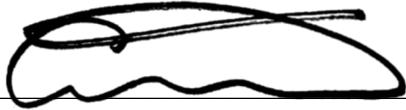
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ERRATA SHEET FOR THE TRANSCRIPT OF:
QIAGEN SCIENCES, LLC., v TECAN GENOMICS, INC.
IPR2025-00026
Deponent: Carlos Bustamante
Deposition Date: October 8, 2025

I wish to make the following changes for the following reasons:

Page:Line	Presently Reads	Should Read	Reason
6:3	"CBD Consulting Group"	"CDB Consulting Group, Inc."	Transcription Error
69:15	"multiply"	"multiple times"	Clarification
88:4	"polymerase"	"polymerize"	Transcription error
107:13	"3 prime,'" "	"3 prime)," "	Transcription error

/s/



Carlos Bustamante

This 11th day of November 2025.