

IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF NORTH CAROLINA

NATERA, INC.,

Plaintiff,

vs.

NEOGENOMICS LABORATORIES, INC.,

Defendant.

Civil Action
No. 1:23CV629

Greensboro, North Carolina
March 11, 2025

TRANSCRIPT OF CLAIM CONSTRUCTION PROCEEDINGS

BEFORE THE HONORABLE CATHERINE C. EAGLES
CHIEF SENIOR UNITED STATES DISTRICT JUDGE

APPEARANCES:

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ANDREW SHORES, ESQ.
WILLIAMS MULLEN

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Proceedings reported by stenotype reporter
Transcript produced by computer-aided transcription.

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I N D E X

PLAINTIFF'S WITNESS:

DIRECT

CROSS

Dr. Metzker

By Ms. Haberny

78

By Ms. Durie

83

P R O C E E D I N G S

(Court in session 9:33 a.m.)

THE COURT: First, if everybody would identify themselves to assist the court reporter and me.

Here for the plaintiff?

MR. VAN ARNAM: Rob Van Arnam from Williams Mullen. You've met them before, but Sandra Haberny and Tara Srinivasan. Dr. Metzker is our expert. Drew Shore. In-house counsel, Sean Boyle and Nashita Doshim.

THE COURT: I think I may have seen everybody before. Have I seen Mr. Shores?

MR. SHORES: You have, Your Honor.

THE COURT: Here for the defendant, or NeoGenomics.

MS. REECE: John Morrow from Womble, Bond. With me is Matthew Kreeger and Duralyn Durie. We have Dr. Nile Leonard, who is our technical expert. J.D. Wooten is in the courtroom, he is with our firm. In-house counsel, we have Meghan Van Horn and Frank Daucherty.

THE COURT: Good to see everybody.

So I read everything, and I have just under three hours. I need to stop at 12:29 or so, and that means I'm going to give each of you not quite an hour and a half, because we will have to take a morning break. So you get, what, an hour and 21 minutes, or something like to that.

I'm pretty much open to hearing what you have to

1 say, starting -- I will tell you where I am. I did think that
2 the motion -- let's see, the motion to supplement the record
3 included a bunch of argument to the merit. I mean, I'm not
4 really opposed to considering whatever evidence you all want
5 to present, because you can present it to me today.

6 What I'm inclined to do is, to let NeoGenomics
7 present that. You know, you've already presented it, but I'm
8 going to strike it, because that's not a vehicle for
9 additional argument. I did skim it, and it looks like this is
10 about the merits, and so I never really studied it. I sort of
11 did the same to Natura's response on the merits.

12 I'm going to allow the supplement of the record with
13 the depositions. I think it was Dr. Metzker's deposition.
14 I'm not going to -- we don't have to strike them, but I'm not
15 going read them, the parts that go on the merits, which is a
16 lot.

17 I have these word limits for a reason, and I would
18 appreciate you all not trying to get around them with other
19 motions.

20 Now when we turn to the claim construction, I see
21 there is basically four disputed, the one about the isolated
22 cell-free DNA. I don't really have any questions about that.

23 The one about performing high-throughput sequencing
24 of the amplified DNA, I don't really have any questions about.
25 I'm not preventing you from addressing those.

1 The ones I would like you to address are the other
2 two, performing sequencing, wherein an SNV mutation is
3 detected from the sequence reads, and wherein an SNV mutation
4 is detected from the sequence reads.

5 That's where I'm having the limits of my high school
6 chemistry are very challenged. I learned a lot in this case
7 and I would say I know more than a high school chemistry
8 student even before this case but, you know, it is definitely
9 a layman's understanding, and of course the jury is not going
10 to be people with Ph.Ds in chemistry or whatever your experts
11 have Ph.Ds in. I say chemistry as sort of a big over-arching
12 completely inaccurate categorization, I'm sure.

13 You all are going to have to explain this one to me
14 with a little more detail. And you can put on evidence. You
15 can argue. I don't care how you use your hour and 20 minutes.
16 What I would -- you can use it all in one chunk, or if you
17 want to reserve some time to respond to what the other side
18 does, that's fine, too.

19 I'm going to do my best -- you all are going to
20 laugh when I say this, I'm going to do my best to be quiet.
21 Nobody laughed. I thought you all would get a kick out of
22 that, because I'm always asking you all questions, but I'm
23 going to try to just listen. That's my goal for myself today,
24 to really give you all a chance to explain it to me.

25 So I'm going to let the plaintiff go first. It is

1 9:37. Proceed.

2 **MS. HABERNY:** Good morning, Your Honor. This is
3 Sandra Haberny for Natera.

4 I would first just like to tell Your Honor that we
5 don't intend to affirmatively call Dr. Metzker to testify,
6 however, he is here and present if Your Honor has any
7 questions for him or would like to clarify any of his
8 testimony.

9 So based on Your Honor's opening comments, I would
10 like to start with the second term in our list of terms, which
11 is, performing high-throughput sequencing of the amplified DNA
12 comprising the plurality of target loci to obtain sequence
13 reads, wherein an SNV mutation that is present in less than or
14 equal to 0.015% of the cell-free DNA having the SNV locus is
15 detected from the sequence reads.

16 So Natera contends that the entire step should be
17 construed, starting from performing, all the way through from
18 the sequence reads. Natera contends it needs to be construed
19 with all of its language.

20 NeoGenomics, wants to keep the language about
21 obtaining sequence reads out of the term and they want to do
22 that for reasons I'll explain in detail in a moment.

23 First, I would like to frame what the dispute is.
24 Can we have Slide 16, please.

25 **THE COURT:** I'm going to apologize if I'm turning

1 away from you, but the screen is to my left, so in order to
2 see your screen, I have to not look at you.

3 **MS. HABERNY:** Of course, Your Honor.

4 **THE COURT:** Go ahead.

5 **MS. HABERNY:** Okay. So Natera's proposal is to
6 construe the entire step in context, because what is important
7 here is, that the, is detected, which is really the dispute
8 between the parties, happens during a single sequencing step
9 to obtain sequence reads. I would like to emphasize, that the
10 part two, obtain sequence reads, is what NeoGenomics would
11 like to keep out of this construction.

12 So NeoGenomics's proposal reads that portion of the
13 step out and also ignores the fact that there is a wherein
14 clause that the, is determined, occurred in.

15 Slide 17, please. So NeoGenomics is trying to frame
16 this as a dispute over whether the terms detect and determine,
17 Can be used interchangeably, but that's not what this dispute
18 is about at all.

19 Natera's contention is, that the real dispute is
20 over where, when, and how, SNVs are detected, not over whether
21 detected and determined mean the same thing.

22 So Natera's position is that detecting happens in
23 the sequencer during sequencing with the fluorescent signal.

24 **THE COURT:** Something funny is happening with my
25 screen. I'm blacking in and out. Does anybody know why that

1 is happening? It's not deliberate, right? You're not trying
2 to make me think I'm in the twilight zone?

3 **MS. HABERNY:** No, Your Honor.

4 **THE COURT:** We'll hope for the best. Go ahead.

5 **MS. HABERNY:** We have handed up a hard copy of the
6 slide, if that's easier for Your Honor to follow.

7 **THE COURT:** If you tell me the page, it will be.

8 **MS. HABERNY:** I'm on Slide 17.

9 **THE COURT:** Great. Thank you. At least until it
10 stops blinking.

11 **MS. HABERNY:** I apologize, but I don't know what is
12 going on.

13 **THE COURT:** That's all right.

14 **MS. HABERNY:** So again, NeoGenomics wants to frame
15 this dispute as one over whether the terms detect and
16 determine can be used interchangeably, but that is not what
17 this dispute is about. The real dispute is over where, when,
18 and how the SNV is detected.

19 So Natera's position is consistent with the claim
20 language, and a person of skill in the arts understanding of
21 the science is, that detecting happens in the sequencer during
22 sequencing with the capture of fluorescent signals.

23 NeoGenomics, on the other hand, is contending, and
24 this is based on essentially a mischaracterization of the
25 specification, and the expert testimony, and it's contrary to

1 its own expert's testimony, NeoGenomics is contending that
2 detecting happens in a computer using algorithms to analyze
3 and correct for errors, and this is in furtherance of its
4 non-infringement theory that it is performing detecting in its
5 overseas server. So that's how the dispute really should be
6 viewed.

7 Tellingly, NeoGenomics's construction has been a
8 moving target. If Your Honor turns to Slide 18, please.
9 NeoGenomics's construction has changed over time. In its
10 opening brief, NeoGenomics claims that the term should have
11 its plain and ordinary meaning, wherein an SNV mutation is
12 determined to be present from sequence reads. So it is
13 essentially writing out the actual claim language, is
14 detected, and replacing it with, determined to be present.
15 But then in its responsive brief, that changed quite a bit.
16 Now NeoGenomics's position becomes more clear. It's trying to
17 read in not just determined to be present, but an analysis, a
18 computational mathematical analysis to determine whether the
19 SNV is present, and that's not what the claim says at all.

20 So if Your Honor would turn to Slide 19. In fact,
21 Your Honor has recognized the same problem with NeoGenomics's
22 construction when the Court interpreted the analogous term in
23 the '454 Patent. So the '454 Patent, Claim One and, again,
24 the '454 Patent Your Honor previously construed is a sister
25 patent of the '596, and it shares the same specification and

1 the same priority.

2 So that patent included a final term, sequencing the
3 amplicons to obtain sequence reads, and detecting the SNVs
4 from the frequency reads. Your Honor construed that to mean
5 that the sequencing and detecting are all part of the same
6 sequencing step, and that was Natera's construction.

7 The '596 Patent claim that we're discussing right
8 now is analogous. It's slightly different, though, performing
9 high-throughput sequencing of the amplified DNA to obtain
10 sequence reads, wherein an SNV is detected from the sequence
11 reads. So it's the same notion, just written slightly
12 differently using a variant clause, but it should be construed
13 similarly, that the '596 Patent term means detecting SNVs from
14 the sequence reads occurs during sequencing to obtain those
15 sequence reads.

16 So we can take this one step at a time, first
17 focusing on grammar. If Your Honor turns to Slide 21, please.
18 So similar to the term in the '454 Patent, here it is clear
19 from the use of punctuation, indentation and grammar --

20 **THE COURT:** You would be glad to know that I know a
21 lot more about grammar than I do about sequencing amplicons.

22 **MS. HABERNY:** That's true of almost every one. So
23 here, the grammar, indentation, just the general framing
24 linguistically of the claim, indicates that the sequencing and
25 detecting happen together, and that's especially true here,

1 because the claim says, you sequence to obtain sequence reads.
2 NeoGenomics doesn't dispute that sequence reads are generated
3 during sequencing in the sequencer.

4 So you have here a semicolons punctuation separating
5 the different steps, so I don't think there is any dispute
6 that the last performing step indented on its own after a
7 semicolon is separated in the same way the other steps in the
8 claim are separated. And there is a wherein clause with a
9 comma before it, not a semicolon, and that indicates that the
10 wherein clause is part of that last performing step,
11 performing a high-throughput sequencing step, and it's
12 describing what happens, wherein that sequencing step is
13 occurring.

14 **THE COURT:** If you were doing an outline, the first
15 performing would be like a little i or something, and the
16 second one, the one we're talking about, would be the two
17 ii's.

18 **MS. HABERNY:** Little ii's.

19 **THE COURT:** That's not there, but that's how you are
20 seeing it?

21 **MS. HABERNY:** Yes, Your Honor. That's how it is
22 indicated based on the indentation here.

23 **THE COURT:** Okay. Go ahead.

24 **MS. HABERNY:** So NeoGenomics is contending that
25 sequencing -- or, I'm sorry, detection happens after

1 sequencing, but the English language alone doesn't support
2 that here. This determining step is in the wherein clause, so
3 it is wherein an SNV mutation that is present in less than or
4 equal to 0.015% of the cell-free DNA having the SNV locus is
5 detected from the sequence reads. That wherein clause, based
6 on where it's placed, the comma before it and the overall
7 setup of the claim is modifying high-throughput sequencing to
8 obtain sequence reads. That wherein clause happens during
9 sequencing the sequence reads.

10 Now just to be clear from the linguistics,
11 NeoGenomics's expert, does not offer any opinion that a person
12 of skill in the art which understands English language
13 differently, so there is really no rebuttal based on the
14 expert testimony that a person of skill in the art would
15 understand the plain English of this language as it is
16 written.

17 So if we could turn to Slide 23. I would like to
18 now look at how NeoGenomics is attempting to deviate from the
19 plain and ordinary meaning, and Natera's construction is
20 consistent with the claim language and a person of skill in
21 the art's understanding of the science.

22 For this portion, I would like to focus on that
23 wherein clause that contains the is detected term in the
24 context of the rest of the claim.

25 If we could turn to Slide 24, please. Here are the

1 competing proposals. So Natera's proposal reflects the claim
2 language and science, and Natera proposes the plain and
3 ordinary meaning such as the wherein clause informs the
4 mechanics of how the high through-input sequencing is
5 performed. The wherein clause indicates that the detection
6 occurs during sequencing in the sequencer to obtain sequence
7 reads. Even NeoGenomics's technical expert and multiple
8 corporate witnesses agreed. NeoGenomics's proposal says it
9 detect means, determined to be present, but their construction
10 really is a lot more than that. The construction is not just
11 determined to be present, and we saw this as it came out in
12 their responsive brief. It is determined to be present
13 through an algorithm after sequencing is complete, and that's
14 not following the claim language. It is reading in data
15 processing limitations after sequencing that are not there and
16 that are not supported by the intrinsic record, and it
17 misunderstands the science.

18 So if we can turn to Slide 25, please.

19 If you can first take a look at the science to put
20 this into context. So the specification of the '596 Patent
21 discloses that the preferred embodiment for sequencing, use
22 sequencers from a company called Illumina. Specifically,
23 there are multiple disclosures of preferred embodiment using
24 what is called Illumina HiSeq sequencer. And the
25 specification incorporates the product specifications from

1 that high speed sequencer into the disclosure.

2 If we turn to Slide 26 and take a look at the
3 Illumina specifications that are incorporated in the
4 specification Illumina itself describes its sequencing
5 technology as a method that detects single bases as they are
6 incorporated into DNA template strands. So there is a
7 detection of each base in the sequencer, and that's the
8 understanding that a person of skill in the art reading the
9 specification would have.

10 So if we go to Slide 27, please. We have here some
11 slides that we previously showed Your Honor, I believe it was
12 during the tech tutorial a long time ago, November of '23, I
13 believe. So I'll briefly go over this again, just to refresh
14 Your Honor's memory about how sequencing works.

15 **THE COURT:** I remember the ladders. Good idea to go
16 over it again with me.

17 **MS. HABERNY:** The ladders being built during
18 sequencing.

19 **THE COURT:** Yes.

20 **MS. HABERNY:** So detection occurs using fluorescent
21 signals, when the sequencer reads the sequence. So what
22 happens is, you have a single-stranded piece of DNA, which is
23 the piece of the letter you have to complete, and the
24 sequencer adds on each complementary base as it goes along,
25 and each time it adds a base, that base is tagged with a

1 certain color, and there are four possible bases that can be
2 added; A, T, G, and C. Each one is labeled with a different
3 color.

4 If we go to Slide 28, we can see that there are
5 these labeled nucleotides floating around. They get added on
6 and this happens again and again in cycles.

7 If go to Slide 29, you have it the second time, and
8 the fluorescence lights up, and that happens all the way to
9 the end of the strand. And so each base that's added on has a
10 fluorescent signal that lights up.

11 If we go to Slide 30, please, there is a camera in
12 the sequencer that captures the fluorescence at each cycle
13 that actually takes a picture of the color. Each time a new
14 base is added on, the color lights up and the camera takes a
15 picture, and that color corresponds to the base that's added.
16 When the camera captures that color corresponding to each
17 piece, the base is detected.

18 If we turn to Slide 31, please. This is a cartoon
19 of what it looks like. So you'll have, for example, strand
20 one, you'll have four strands that they're sequencing at the
21 same time. In cycle one, the camera captured a picture of a
22 base A being added. In cycle two in strand one, the camera
23 takes a picture of another A being added. Cycle three, that's
24 the third one down being added along the ladder, the camera
25 captures a G being added. Cycle four, a T, and so on.

1 This is how the fluorescent signals corresponding to
2 the bases are detected inside the sequencer when pictures of
3 them are captured.

4 If we could go to Slide 32, this is how the
5 sequencer can detect the SNVs during sequencing. So the way
6 the claim is set up is through targeted amplification. So
7 we're not putting everything, every bit of DNA we got out of
8 the sample into the sequencer, but we have amplified it in a
9 targeted manner, and the amplicons that are sequencing have
10 defined start and end positions, and the SNV will either be
11 present or not at a certain position on that amplicon. Their
12 design path of the SNV are in certain positions, and if the
13 SNV is present at the position where it is supposed to be, it
14 would be detected through its corresponding color in the
15 sequencer.

16 If we go to Slide 33, NeoGenomics, before it
17 developed its noninfringement driven construction here, agreed
18 with Natera, so this is NeoGenomics's picture of amplification
19 and sequencing from its tech tutorial to the Court, and
20 NeoGenomics itself here is showing that the sequencer is
21 capturing the bases that are present in the DNA being
22 sequenced.

23 If we turn to Slide 34, NeoGenomics's expert,
24 Dr. Lennon, agreed with this when he testified at trial in
25 another case. So this is testimony from Dr. Lennon's opinion

1 at this trial in a case called *Archer DX versus Qiagen*, and
2 he's being asked here about what happens in sequencing. You
3 have the sequencing primer, it's spitting out of the sequencer
4 A, G, T, C, and he's being asked the question. The actual
5 thing -- about the actual thing where a sequence is getting
6 spit out of the machine, and Dr. Lennon, NeoGenomics's expert,
7 called that the detection step. And then it's clarified.

8 So the sequencing step, right?

9 Answer, Yes, sir. It is where we're doing the
10 interrogation of the colors to understand what bases are
11 there. They are being detected, as Dr. Lennon acknowledged.
12 And this is the same sequencing and detecting that happens in
13 the '596 Patent. This is what happens in every Illumina
14 machine.

15 **THE COURT:** And that case, *Archer DX* versus --

16 **MS. HABERNY:** *Qiagen*.

17 **THE COURT:** A little hard to pronounce. It also
18 involved a patents involving the same sequencer, is that what
19 you are saying?

20 **MS. HABERNY:** It involved sequencing. Other
21 portions are different, but what is key here is, that it is
22 just describing what happens in the sequencer, and what
23 happens in the sequencer involved in that case is the same
24 thing that happens in this case and essentially any sequencing
25 that uses the Illumina sequencers.

1 If we go to Slide 35, Dr. Lennon testified to the
2 same thing here in this case. So he was asked in his
3 deposition, open-ended question:

4 Can you explain to me what occurs in the process of
5 sequencing in the high-throughput sequencer?

6 He said -- he gives an explanation and he says at
7 the end, The camera, essentially, takes a photograph or
8 detects any emission spectra signal that comes off of those
9 incorporated bases.

10 So there is no dispute, that this is how sequencing
11 works. All the experts agree that the product literature says
12 that there are bases that are called in the sequencer,
13 fluorescent signal is emitted, it is captured, photographed in
14 the sequencer, and that is detection.

15 Let's take a look at Slide 36. This is Dr. Forshew.
16 Dr. Forshew was a NeoGenomics's corporate representative on
17 Rule 36 topics regarding technology, and he also said, The
18 sequencer does measure, to my understanding, a most probable
19 color. He's talking about detecting the colors corresponding
20 to the SNVs in the sequencer.

21 The next, Slide 37, the same thing from another
22 NeoGenomics's corporate representative. He says, The SNVs are
23 detected through the sequencer where the sample is run.

24 So prior to claim construction, every one was
25 agreeing with this. Now NeoGenomics is changing course and

1 contradicting its experts and its witnesses testimony.

2 All of this is consistent with the patent's own
3 definition of sequencing to produce sequence reads.

4 If we go to Slide 38, please. This is the expressed
5 definition in the patent. It's not an embodiment. It's not
6 an example. It's a definition in the definition section, and
7 it is a definition of sequence reads, and that's why it is
8 important for Your Honor to consider the whole claim term,
9 including, to obtain sequence reads, because sequence reads
10 are defined as data representing a sequence of nucleotide
11 bases that were measured. It is plain logic that bases have
12 to be detected in order to be represented in that data of the
13 sequence of nucleotide bases. That's why it's important for
14 Your Honor to consider the whole claim term, including, to
15 obtain sequence reads, because sequence reads are defined as
16 data representing a sequence of nucleotide bases that were
17 mentioned.

18 It's plain logic that bases have to be detected in
19 order to be represented in that data in the sequence of
20 nucleotide bases. The patent specification defined these
21 sequence reads as raw data generated in the sequencer.

22 Now I'll bring up the part of this definition the
23 quality score, because what NeoGenomics real construction
24 seems to be getting at is, a notion of algorithmic error
25 correction after sequencing.

1 I'd just like to point out that in this definition
2 the patent expressly acknowledges that a sequence reading may
3 have an associated quality score at each base position
4 indicating the probability that the nucleotide has been called
5 correctly. So the sequencer is already dealing with the
6 possibility of false positives or true positives or the bases
7 called correctly. There may be false positives as in any
8 detection, there's always going to be a false positive.

9 If Your Honor thinks about a Covid test, for
10 example, 99 percent of the time when the little line turns
11 pink on the Covid test, the person has Covid. Every once in
12 awhile, there's a false positive. There is a line there, but
13 the person doesn't have Covid. That doesn't negate all the
14 true positives and, in fact, the sequencer itself has a
15 mechanism for indicating what might be a false positive or an
16 error or noise or whatever NeoGenomics wants to call it.

17 If we can turn to Slide 39, please. Here's what the
18 Illumina's product specification says about that. So this is
19 Illumina's product literature that's referenced in the patent
20 specification. Here it shows that base calls are made one at
21 a time, right? So these are the scores, the probability of
22 incorrect base calls that's a function of the Q score in the
23 sequencer. And so it's here showing in the product
24 literature, that there are mechanisms for the machine itself
25 to indicate a probability of true versus false positives.

1 If we turn to Slide 40, Dr. Metzger explained this,
2 even if you get errors, you're still detecting SNVs as
3 claimed, right? So you may, much of the time be detecting an
4 SNV, that practices the claim If you detect an error, maybe
5 that error doesn't practice the claim, but it doesn't negate
6 all of the detection of the SNVs that did happen practicing
7 the claim.

8 So, I mean, if I may analogize this to an engine
9 light coming on in an old car. So it may light up nine times
10 out of ten. It may light up at nine times out of ten and
11 there's an actual problem with the engine. The engine light
12 detected a problem with the engine. Maybe every once in a
13 while it lights up. And when you go to the mechanic and he
14 says, oh, you must reset, that doesn't negate all the other
15 times that an error was -- or an engine problem was actually
16 detected.

17 So if we go to Slide 41, please. NeoGenomics's
18 expert, Dr. Lennon, actually put in a declaration with the IPR
19 of the '596 Patent. So if Your Honor recalls, there was a
20 proceeding in the Patent Trademark Office challenging the '596
21 Patent. Dr. Lennon submitted a declaration and he said, NGS,
22 which are the sequencing, the Illumina and other platforms,
23 typically also generate quality scores. And he says,
24 sequencing platforms that carry up NGS use a variety of
25 sequencing and detection biochemistry. So he, himself, is

1 describing detection biochemistry in the sequencer. So what
2 is NeoGenomics's explanation for this, or how do they deal
3 with it?

4 If we go to Slide 42, please. First, NeoGenomics
5 tries to change the meaning of detected to something that all
6 of that other overwhelming evidence does not support, and they
7 replace it with, determined to be present.

8 By the way, that's not the plain and ordinary
9 meaning as NeoGenomics contends, because detecting and
10 determine to be present, are not the same thing.
11 Determination requires some further level of thought or
12 analysis, and it's not synonymous in the way NeoGenomics is
13 using it.

14 So if we turn to Slide 43, that's actually made
15 clear in the NeoGenomics's responsive brief. So after reading
16 the opening briefs, NeoGenomics digs in a little more and
17 makes clear the extent to which it is trying to rewrite the
18 claim. And this time, rewrites out pretty much the entire
19 wherein clause and replaces it with, the sequence reads are
20 analyzed after sequencing to determine whether the SNV is
21 present. And, again, none of that downstream analysis is part
22 of the claim, and there is no support in the claim or the
23 specification for this rewrite.

24 So NeoGenomics points to one passage that it
25 contends to define this term. If we turn to Slide 44 -- and

1 there's no support in the claim or the specification for this
2 rewrite. This is actually a mischaracterization of this
3 passage, and it is certainly not a clear and an unambiguous
4 definition of detecting single nucleotide variants from the
5 sequence reads.

6 This is a section of the specification, if we go to
7 Slide 45, it is very hard to read on the slide, so we tried to
8 unpack it a little bit paragraph by paragraph.

9 So the first sentence here refers to detecting
10 SNV's, but it is critical to note that the claim requires
11 detecting SNVs from sequence reads.

12 Let's walk through this section. So the first
13 paragraph describes detecting SNVs generally. It says this
14 can be done on a system, various teachings regarding
15 functional and structural features. It is a general
16 description.

17 If we go to Slide 46, this is what NeoGenomics is
18 latching onto. So there is an embodiment, and it is an
19 embodiment for determining whether a single nucleotide variant
20 is present. And this is actually an embodiment of downstream
21 analysis after detection. It's a post hoc analysis, and it's
22 here describing generating estimates of error reads,
23 determining probabilities, you know, a lot of mathematical
24 calculations.

25 I would like to note on Slide 47, this same section

1 with the same title, has an embodiment for determining whether
2 an SNV is present where the sample is plasma, where it is
3 circulating tumor DNA, and clearly, not even NeoGenomics would
4 stretch to argue that this paragraph describes how detection
5 occurs.

6 So what is happening in this section, and this is
7 really the only section NeoGenomics relies on in the intrinsic
8 record. What is happening here is, the patentee is describing
9 other aspects of detection things you can do downstream after
10 detection, and where you can get the SNVs from to detect them.

11 This, again, certainly is not a definition. By no
12 means is this a clear and unambiguous definition of sequencing
13 SNVs to obtain sequence reads and detecting SNVs. That's not
14 a definition.

15 What is a definition is on Slide 48, and this,
16 again, is a term that NeoGenomics tried to omit for what it
17 wants to be construed. And this definition defines sequence
18 reads as the data, the raw data reflected in the nucleotide
19 bases that are present in what is being sequenced.

20 So you detect SNVs from the sequence reads because
21 as the sequence reads are being generated, they reflect the
22 bases that are being called on Slide 48. And this, again, is
23 the term that NeoGenomics tried to omit from what it wants to
24 be construed. And this definition defines sequence reads as
25 the data, the raw data reflected, and the nucleotide bases

1 that are present in what's being sequenced.

2 So you detect SVS from the sequence reads because as
3 the sequence reads are being generated, they reflect the bases
4 that are being called in the sequencer, and the technique is
5 just capturing that signal.

6 So NeoGenomics would like to make this term all
7 about errors and error corrections, but all the error
8 correction stuff is something that occurs after sequencing in
9 the common products, in the commercial products. So
10 NeoGenomics is looking at its own product and saying, we do
11 downstream analysis after sequencing, and then trying to read
12 that into the claim.

13 And I would posit the following analogy. So imagine
14 you have a method for preparing a batter.

15 **THE COURT:** Like cake batter?

16 **MS. HABERNY:** Yes. Preparing a batter that is
17 useful for baking a cake. Okay. Preparing a batter that's
18 useful for baking a cake batter. You have to butter the pan,
19 preheat the oven, actually put it in there and bake it, and
20 there is a lot of things that happen after.

21 What NeoGenomics wants to do is, take a fully baked
22 cake and read it into a method for making a batter. So it is
23 really focusing on downstream processes after detection
24 occurs. It is trying to substitute claim terms, detecting for
25 determining to be present, and then further with analysis, and

1 none of that is in the claims, so the Court should adopt
2 Natura's construction. It reflects the science. It reflects
3 a person of skills understanding of the science and the
4 English language, plain language and NeoGenomics's
5 construction is not plain and ordinary meaning. It rewrites
6 the claim.

7 **THE COURT:** So I just ask you sort of a technical
8 question. So your construction says plain and ordinary
9 meaning. That's what NeoGenomics says. And then you say,
10 which means that the terms are part of, and then it goes on.
11 So when you say the terms right there, what are you
12 talking about?

13 **MS. HABERNY:** Yes, Your Honor. So this -- to
14 clarify, Natera's position is, that the plain and ordinary
15 meaning includes the wherein clause. The wherein clause that
16 recites is detected, informs sequencing to obtain sequence
17 reads, and that necessarily means that the SNV mutations are
18 detected during sequencing to obtain sequence reads.

19 **THE COURT:** I just didn't really get -- I mean, I
20 understand your argument. The way that it is worded is a
21 little confusing to me, because I'm not sure what the
22 term -- it is like, okay, I'm going to define these terms by
23 using the words, the term. I didn't really even explain that
24 very clearly. I'm not quite following.

25 **MS. HABERNY:** If Your Honor would go back to

1 Slide 2, please. This is where the confusion may come in,
2 because the parties proposed to construe this last step in two
3 different ways.

4 So Natera proposed to construe what is highlighted
5 here, the whole highlighted portion, which we are calling the
6 second term. NeoGenomics wants to break that apart and ignore
7 the portion that recites, to obtain sequence reads.
8 NeoGenomics doesn't want that in there, but it is highly
9 critical to understanding the claim. They want to only
10 construe what comes before and after it, performing the
11 sequencing of amplified DNA. And then the second term they
12 want -- they want to skip over the obtaining sequence reads
13 and a separate term to construe the wherein clause, wherein
14 the SNVs is detected.

15 **THE COURT:** So your -- would it be accurate to say,
16 which means that the terms, being that whole entire phrase, is
17 read as a whole?

18 **MS. HABERNY:** Yes, Your Honor.

19 **THE COURT:** That's what you are actually saying?

20 **MS. HABERNY:** And that means, necessarily, that the
21 SNV is detected during sequencing to obtain sequence reads.

22 **THE COURT:** Okay.

23 **MS. HABERNY:** So, Your Honor, if Your Honor has no
24 more questions on that term, I would like to just quickly
25 slide through the isolated self-read DNA term, which is the

1 first one.

2 **THE COURT:** Okay.

3 **MS. HABERNY:** There are competing proposals here for
4 this. If we go to Slide 4, please. And, really, there are
5 two real disputes. One is, what is the antecedent basis for
6 the isolated cell-free DNA. So both parties agree there is an
7 antecedent basis. The dispute is, what it is.

8 Natera's position is, that the antecedent basis is
9 isolated cell-free DNA from biological samples at different
10 time points.

11 NeoGenomics's position would just read that
12 different time point portion out of the antecedent basis term,
13 and I'll walk through that.

14 The second dispute is whether --

15 **THE COURT:** This is like -- feels like deja vu.

16 **MS. HABERNY:** It should, Your Honor, because it is
17 very similar to what Your Honor decided in Natera's favor
18 previously.

19 **THE COURT:** You use as much more of your time as you
20 think appropriate.

21 **MS. HABERNY:** I would like to conserve as much time
22 for everyone as possible, so I'll try to be efficient.

23 The second dispute is whether the claim requires
24 pooling the samples for assaying. So if we go to Slide 5,
25 this is the dispute regarding the antecedent basis of the

1 isolated cell-free DNA, and here Natera contends that you must
2 look at the term as a whole again. So it's highlighted here
3 in the claim, the cell-free DNA isolated from a plurality of
4 biological samples obtained from the subject at different time
5 points.

6 NeoGenomics wants to write the different time points
7 out of the claim and use only part of what's describing the
8 isolated -- or this cell-free DNA isolated, what's described
9 as only partially ignoring the full description of it.

10 What NeoGenomics is arguing just doesn't make sense
11 in the context of the claim, which if Your Honor looks at the
12 preamble, it's a method for monitoring the progress.

13 So if we go to Slide 6, please. This is a cartoon
14 depicting monitoring cancer progression. That means you
15 monitor it over time. You do it all at once with pooled
16 samples. You're not going to monitor progression. You're
17 going to look after the fact and say, it's too late now to do
18 anything about it.

19 So this cartoon shows time point one, you take a
20 sample, you assay it. Time point two, a month later or
21 however long later, take another sample. And nothing in the
22 claim says you can't do this.

23 The claim -- if we look back at Slide 5, the claim
24 just says isolating cell-free DNA from a plurality of
25 biological samples obtained from the subject at different time

1 points. It doesn't say assay them all at the same time. It
2 doesn't say assaying a plurality of different biological
3 samples all at the same time.

4 This claim permits you to assay it at one time
5 point, assay again later at a different time point, as long
6 you have done that with more than one, you've assayed a
7 plurality, even if you did them separately at different time
8 points.

9 So if we look -- sorry to move around, Your Honor,
10 but at Slide 7, there's only basically two ways that
11 NeoGenomics's construction could work. One of them is, if you
12 pooled different time points, that is being shown here, and
13 waited and assayed them altogether, which, again, would be too
14 late and you wouldn't be monitoring cancer progression.

15 If Your Honor looks at Slide 8, the other way that
16 NeoGenomics's construction would work is, you pooled multiple
17 samples at each time point and then assay them, but nothing in
18 the claim remotely comes close to saying that. There's
19 no support in the specification, either, or in the scientific
20 understanding of a person skilled in the art.

21 So if Your Honor goes to Slide 9, please,
22 NeoGenomics purports to rely on the intrinsic record in the
23 specification, but it completely ignores the disclosure, which
24 is here on the left-hand side of Slide 9. Completely ignores
25 the disclosure of repeat testing, so that means you do one,

1 then you do another one later over multiple time points.
2 Instead, it focuses on this completely irrelevant disclosure
3 on the right-hand side of Slide 9 about different samples that
4 could be from blood or tissue or could be from saliva or some
5 other source. NeoGenomics is saying you have to compile
6 together in pools different samples or two blood draws at the
7 same time, and that's not monitoring cancer progression,
8 ignoring the disclosure that talks about monitoring cancer
9 progress, and it is not reflected in the claim language.

10 If Your Honor looks at Slide 10, this is, again,
11 just more unclaimed embodiments that NeoGenomics is relying
12 on. It's relying on disclosure. It doesn't mention cell-free
13 DNA at all, which is in the claim. Doesn't mention monitoring
14 cancer progression. And there's really no reconciling view in
15 NeoGenomics's position that you should pool different samples
16 from different sources of different blood draws with the
17 language it wants to a read out of the claim, which is
18 different time points.

19 So on Slide 11, it should be rejected. Plain and
20 ordinary meaning should control, and NeoGenomics's pooling
21 requirement should be rejected, and the different time point
22 language should be honored.

23 If Your Honor has no questions about this, I'll turn
24 it over to my colleague, Tara Srinivasan to address the last
25 term.

1 **THE COURT:** All right.

2 **MS. SRINIVASAN:** Good morning, Your Honor.

3 **THE COURT:** You might need to get closer to the mic.
4 Pull the base towards you and get close to it.

5 **MS. SRINIVASAN:** The last term in dispute
6 is performing high-throughput sequencing of amplified DNA.

7 **THE COURT:** Hold on. The court reporter is
8 straining. Move that base closer to you, really, really,
9 close. You're an opera singer -- no, those opera singers
10 don't need microphones. Bad. You're a country music star.
11 Go ahead.

12 **MS. SRINIVASAN:** No one wants to hear that.

13 So the last term in dispute is performing
14 high-throughput sequencing of the amplified DNA. This is a
15 term in the '596 Patent that is very similar to what the Court
16 previously construed for the '454 Patent. We are prepared to
17 address any discussion that they bring up in rebuttal, but to
18 the extent that Your Honor doesn't have any further questions,
19 I can walk through our argument, or I can stop there.

20 **THE COURT:** It is your time. I don't have any
21 questions about -- wait a minute. Which one are talking
22 about?

23 **MS. SRINIVASAN:** If you look at Slide 61, the term
24 at issue is performing. And this is a term NeoGenomics
25 contends should be construed to prevent intermediate steps

1 between the targeted multiplex amplification and the
2 high-throughput sequencing.

3 Go to Slide 62. On 62, you can see the parties'
4 competing proposals. Natera's proposal is the plain and
5 ordinary meaning, which would permit intermediate steps
6 between the targeted multiplex amplification, but before the
7 high-throughput sequencing.

8 NeoGenomics's proposal, on the other hand, requires
9 that the claim be limited to exclude intermediate steps
10 between the target and multiplex amplification and the
11 high-throughput sequencing.

12 If we go to Slide 63, this is a term that is very
13 similar to what the Court previously has examined and ruled on
14 in the '454 Patent at the preliminary injunction proceeding
15 during the last claim construction hearing, and most recently
16 on the motion for reconsideration that NeoGenomics filed.

17 **THE COURT:** But you are not asking me to construe
18 that phrase separately from the rest of the claim, correct?

19 **MS. SRINIVASAN:** That's correct.

20 **THE COURT:** If I go your way, I don't even need to
21 say plain and ordinary meaning, which permits intermediate
22 steps after multiplex amplification or before sequencing, or
23 do you think I do need to say that?

24 **MS. SRINIVASAN:** I think the best way for Your Honor
25 to look at the claim is on Slide 2, and because NeoGenomics

1 has a noninfringement position for that portion of the term,
2 it would be helpful if the Court is able to both address the
3 term as a whole as Natera has briefed, but also that
4 performing high-throughput sequencing of the amplified DNA
5 would permit intermediate steps between the targeted multiplex
6 amplification at sequencing.

7 **THE COURT:** Okay.

8 **MS. SRINIVASAN:** I think with that, Your Honor,
9 we'll rest and reserve our time for rebuttal.

10 **THE COURT:** Thank you.

11 For the defendant.

12 **MS. DURIE:** Thank you, Your Honor, and good morning.
13 Daralyn Durie, for NeoGenomics. I would like to start -- if
14 Your Honor has our set of slides.

15 **THE COURT:** I do.

16 **MS. DURIE:** I think given the technical issues, I'll
17 just use the paper copies. I would like to start at Slide 11,
18 which sets out what the dispute is. That is, I think,
19 ostensibly going to occupy our time today.

20 So the entire term is this performing
21 high-throughput sequencing of the amplified DNA, wherein an
22 SNV mutation that is present in less than or equal to 0.015
23 percent of the cell-free DNA having the SNV locus is detected
24 from the sequence reads.

25 So from NeoGenomics's point of view, the only word

1 there that is in dispute is the meaning of the word detected,
2 and I'll say the extent to which it is in dispute is a little
3 bit of an open question, I think, and we'll talk about that.
4 But the rest of it, we believe from a language point of view,
5 the parties don't disagree about what it means.

6 So by way of example, the sequence reads, I think
7 both sides agree the sequence reads are the output of the
8 sequencer that takes an image and correlates it with a base.

9 If Your Honor would flip forward for a moment to
10 Slide 22, I just want to use the visual here to show what I'm
11 talking about. I'll come back to the argument piece of it.

12 Your Honor should see an image that has a bunch of
13 little colored dots on Slide 22, and that is what you see when
14 you are looking -- if you were to actually look at the
15 sequencer. What you have is all of these reactions happening,
16 and each of those colors represents a base. So yellow might
17 be C. Red might be T, et cetera. The sequencer is saying, in
18 essence, I see that color, and that color yellow means that it
19 is a C, or that color blue means that it is a T. So that is
20 sort of just a visual to help anchor us as to what is going on
21 in the sequencer.

22 If we go back to Slide 11 and we look at the claim
23 language, we're talking about the sequence reads. I think
24 every one agrees, the sequence reads are saying, I see a blue,
25 that means it's T, or I see a red, that means it is a C.

1 That's the sequence reads.

2 The thing we're disagreeing about is, what it means
3 to say that an SNV mutation that's present in the DNA is
4 detected from those sequence reads. Our proposition is that
5 in this context, the word detected means that it is determined
6 to be present.

7 Natera hasn't offered a different construction of
8 detected. They are saying it carries -- well, they are saying
9 the Court doesn't need to construe it. We think that it means
10 the same thing as determined to be present.

11 Now if you turn to Slide 12, Natera supported
12 some -- or cited some dictionaries in their brief. I would
13 note that we think those dictionary definitions of what
14 detects means, actually very much support our position, to
15 discover or identify the presence or existence of. That is
16 what we think it means to determine whether the SNV mutation
17 is present, to determine, discover or identify whether that
18 SNV mutation is actually present.

19 Now this issue about whether in the context of the
20 claim saying that you are detecting the SNV mutation from the
21 sequence read is the same thing, as to whether you are
22 determining the SNV mutation is present.

23 **THE COURT:** If you think it means the same thing,
24 then why are we even here? I mean, I'm not following. And,
25 why does it matter?

1 **MS. DURIE:** A very good question. Claim
2 construction is often, maybe some what frustratingly, an
3 exercise in taking a word and providing a definition of it,
4 and the goal of that is if there is a dispute between the
5 parties as to what that word means, I will say here, as we
6 look through what Natera has put forward, sometimes it appears
7 there is a dispute, sometimes it appears that there is not
8 with respect to what the word detect means, but we think just
9 as a matter of English and in the context of the claim, the
10 definition of detect, if you are detecting something, you are
11 determining that it is present. We think it would be helpful
12 for the jury to have that.

13 We don't think it is essential, but I think it is
14 helpful for the jury, because Natera has been, frankly, a
15 little all over the map as to whether they think that's right
16 or not right, that that is in fact what detect means.

17 If you go to Slide 13, Your Honor, I tried to get at
18 this in Dr. Metzker's deposition, because Natera's position is
19 that detect doesn't mean it is determined to be present. They
20 said our construction is wrong, but they haven't said what
21 about it is wrong, why that is not a correct understanding of
22 what that word means.

23 I asked Dr. Metzker: Okay. So what needs to happen
24 in your view to go from detecting the SNV to determining the
25 SNV is present?

1 I was trying to understand what is the difference
2 here in our two respective positions. And his answer was:

3 I have no idea. I haven't considered what needs to
4 be done to go from one term to the other. I just think that
5 construction is wrong.

6 So part of why we're asking for the construction is,
7 we think the clarity will be helpful because they are clearly
8 going to argue that's not what detect means, although they
9 haven't proffered any alternative construction.

10 Now if Your Honor turns to Slide 14, I tried to push
11 in the deposition a little bit on this question of, what does
12 detect mean. I asked Dr. Metzker. Now, the way that you
13 understand the use of the term detect in the context of the
14 patent, is that the same as how you understand persons of
15 skill in the art use the term detect in the context of
16 sequencing generally? And his answer was, No. So he is
17 apparently arguing for some nonstandard definition but, again,
18 it is not entirely clear to us what that is.

19 Now when we look at the patent, and if Your Honor
20 turns to Slide 15, the patent uses detect and determining
21 whether a variant is present, we think interchangeably. It
22 means the same thing.

23 In certain aspects, provided herein are methods for
24 detecting single nucleotide variants in a sample.
25 Accordingly, provided herein is a method for determining

1 whether a single nucleotide variant is present. We think
2 those mean the same thing.

3 If you go to Slide 16, we provided a number of
4 examples where we think that specification is using these
5 terms interchangeably. Interestingly in Dr. Metzker's
6 deposition, he frequently used terms interchangeably as well.

7 If Your Honor turns to Slide 17, I was asking him
8 about the wherein clause, that disputed clause.

9 I said: So what, if any, are the mechanics of the
10 claim that are required as a function of the wherein clause?

11 He said, Well, the mechanics are performing some
12 kind of sequencing process where base calls are being made.
13 The mechanics are going through that process of being able to
14 identify the base at that location, and the ability to either
15 determine or to detect the presence or absence of the SNV
16 mutation.

17 I included further down on that slide a further
18 place in his deposition where he said, determining or
19 detecting. I think that reflects the fact that persons of
20 skill in the art do use these terms interchangeably, because
21 they really do mean the same thing; that when we talk about
22 detecting something, we really are talking about determining
23 whether that thing is present.

24 If Your Honor turns to Slide 18, we see this here.
25 I asked him, So you go through all of these steps. You know

1 the position of the interest. You get the readout of the
2 sequencer. You know it should be a T. The readout of the
3 sequencer tells you it's a T. So let me pause there.

4 You've got a construct where you know your variant
5 of interest is in a particular position in the DNA. So let's
6 say its position (indiscernible) and you know the variant
7 would be at T. And the sequencer tells you there's a T there.
8 So have you detected that variant? And it says, I think I've
9 explained this many times, Based on the fluorescence intensity
10 at that cycle, so based on that color, based on the way the
11 multiplex PCR assay has been designed, you will measure the
12 fluorescence intensity and determine whether it's present or
13 absent.

14 That's exactly our point. That's exactly our claim
15 construction. That is what is required to determine whether
16 it is present or absent.

17 So I want to suggest what we have here is not
18 actually a claim construction. I think both sides agree that
19 because that's what it means and Dr. Metzker frequently used
20 that way in his deposition, that's the way it is used in the
21 patent.

22 What we really have here is a factual question,
23 which is in a given system where is it and what information is
24 being used to make that determination about whether there is a
25 variant present? And I want to distinguish between detecting

1 the color and detecting whether there is in fact a variant
2 that is present in the DNA sample, which is the thing that the
3 claim requires.

4 So if we continue and if Your Honor turns to Slide
5 19, this distinction came out in Dr. Metzker's deposition. So
6 I asked him: So if I see the fluorescent signal, the machine
7 sees the fluorescent signal and it makes the base call, has it
8 determined whether an SNV is present? At that place in his
9 deposition, the answer was, No. And, I think that's correct,
10 and that's because additional information is needed in order
11 to be able to make that determination. The reason for that,
12 and I'll talk more about this is, things like errors that can
13 happen during the amplification process.

14 So persons of skill in the art recognize, as he
15 admitted here, seeing the fluorescent signal and making the
16 base call, you are not determining whether an SNV is present.

17 I want to know -- he also in his deposition, said
18 the opposite. If you turn to the next slide, Slide 20: And
19 so is it your position that that base call then is sufficient
20 to determine whether an SNV mutation is present? Answer: It
21 is, based on the way the claim is constructed, yes.

22 I think the first answer was sort of a general
23 answer, seeing a fluorescent signal is not sufficient to
24 determine whether an SNV is present. He then later flipped
25 that and tried to say, well, in the context of the claim, it

1 means something different. And there really is no support for
2 that, that what the claim is talking about when it says if you
3 making this evaluation, that it is talking that you are
4 detecting. That it is talking about anything other than the
5 ordinary meaning of what it means to detect whether that SNV
6 mutation is present.

7 Now I said there is a difference between detecting
8 the color and detecting the presence of the mutation, as
9 Dr. Metzker acknowledged in that first colloquy.

10 If we go to Slide 21, what Your Honor will see is,
11 that frequently what Natera talks about is detecting these --
12 detecting fluorescents, detecting color or detecting base.
13 They do that in the brief. We highlighted here. That's also
14 the point that they were making with Dr. Lennon's testimony.

15 In their slides at Slide 34, they have called out a
16 portion of Dr. Lennon's testimony, and Your Honor asked a
17 question about that. And if we look at Slide 34 of Natera's
18 presentation, the question was about the sequencing read. It
19 is saying the next one is an A, the next one is a G, the next
20 one is a T, the next one is a C. So it is actually -- It is
21 actually a participant in the actual thing where a sequence is
22 getting spit out of the machine; right? And he says, Right.
23 We call that the detection step. So the sequencing step,
24 right? It is where we're doing the interrogation of the
25 colors to understand what bases are there.

1 That's absolutely correct. You are detecting the
2 things -- you are detecting -- at that point, you are
3 determining what that base is, but that is different from
4 detecting whether that base is or is not a single nucleotide
5 variant, which requires understanding what the expectation is.

6 It also requires looking at the data to figure out,
7 for example, whether there is an error that came in during the
8 process of amplification, such that you may see a C and the
9 color may be a C, and it may be a C, but that's not a
10 single-nucleotide variant, because in the original sample it
11 was a G. And that is part of the error correction that
12 happens to then make a variant call as opposed to a base call.
13 You make a base call, then it is true, you do analysis and you
14 make a variant call. What the claim is about is making a
15 variant call.

16 Now if we take a look at the next slide, Slide 22,
17 this, I think, really encapsulates the factual dispute between
18 the parties, not the claim construction dispute, but the
19 factual dispute which is something I think we should take up
20 at the right time in the context of summary judgment or trial.

21 I asked Dr. Metzker, Sure. You said color is enough
22 to identify a base. And we agree with that, color will
23 identify the base. Is color enough to identify a single
24 nucleotide variant? And his answer was, Yes. In this view of
25 the world, yes. And because a base at a given location is

1 either going to be represented by the normal base or the SNV
2 mutated base.

3 So that really is the crux of the question, is color
4 enough to identify a single nucleotide variant. And Dr.
5 Metzger and Natera's position is, that you have identified a
6 single nucleotide variant in the DNA, even if there's no
7 variant there.

8 I actually asked him in his deposition, Page 67,
9 beginning at line 23. And I said, So you have detected a SNV
10 mutation, even though no SNV mutation is present in the
11 patient sample? Answer: Based on sequence and detection of
12 fluorescent signals in the sequencer, that is correct.
13 Nothing is perfect.

14 Just to be clear, Natera's position is, color is
15 enough to detect or to identify a single nucleotide variant,
16 even if there is no single nucleotide variant. In other
17 words, you can detect something that doesn't exist. That's
18 the ultimate crux of the dispute between the parties.

19 We think detecting something means actually looking
20 to see whether it is present. They think detecting from
21 sequence reads means looking at the color and saying there is
22 a single nucleotide variant, even if it is not actually there
23 in the sample.

24 Now if we go to Slide 23, this point about the
25 grammar of the claim, I think, is important. You are

1 performing high-throughput sequencing. You are getting
2 sequencing reads, and then you are detecting -- you are
3 performing this detecting step from the sequencing reads.

4 Natera has said that we are reading language out of
5 the claim. I don't think we are. The only thing that we are
6 asking the Court to do is, to say detecting means determining
7 that it is present. But that detection happens from the
8 sequence reads.

9 What Natera wants to say is, the sequence reads are
10 themselves the detection. And that is not just as a matter of
11 English. What it means to say is that you are detecting from
12 the sequence reads. That means you are using the sequence
13 reads to detect, which is exactly what we are saying.

14 So if we take a look at the next slide, Slide 24,
15 this is a slide that we took from Natera's tutorial back in
16 the context of the preliminary injunction motion. The title
17 at the very top is added, but the rest of it is their slide.
18 And so they were showing here what happens with sequencing.
19 You generate sequence reads. You see the colors and then you
20 get the T, G, T, G, T, and that's data and those are sequence
21 reads.

22 If you take a look at the next slide, I was asking
23 in Dr. Metzker's deposition about the sequencing data, that A,
24 T, C, G. My question was: I was asking how the variants that
25 are in the sequencing data from the cell-free DNA are

1 identified.

2 I'm sorry, this was from his deposition in the
3 preliminary injunction in this context. Do you know how that
4 is done?

5 **THE COURT:** You are asking him, or somebody is
6 asking him about how NeoGenomics does it, right?

7 **MS. DURIE:** That's exactly right.

8 **THE COURT:** Okay.

9 **MS. DURIE:** So you get -- NeoGenomics obviously does
10 sequencing, right. You get an output that is that A, C, T,
11 whatever -- and it was not me. I apologize. But the question
12 he was asked is, how the variants that are in the sequencing
13 data are identified. And he said, and this was obviously
14 before this claim construction dispute had arisen. He said,
15 Well, my understanding, based on the public documents, is they
16 used high-throughput sequencing to generate sequence reads.
17 That's what we saw in the prior slide. And then there's a
18 bioinformatic pipeline to identify whether the variants that
19 are in the assays are detected or not.

20 **THE COURT:** What patent was he talking about here,
21 and what language in what patent was he talking about because
22 it couldn't have been this one?

23 **MS. DURIE:** It was the '454. I don't think, and
24 I'll be interested to see what Natera says about this, but I
25 don't think the parties are arguing that the terms mean

1 different things across the two patents.

2 **THE COURT:** I don't understand that. Didn't I rule
3 against you in the '454 Patent?

4 **MS. DURIE:** No. The Court didn't address this, not
5 this issue. This was not an issue in terms of what it means
6 to detect a variant. There are some things, obviously, that
7 we lost on, and there is a reason I'm starting -- the reason
8 I'm starting here is this is new territory.

9 **THE COURT:** Okay.

10 **MS. DURIE:** And, in fact, in the context of the
11 '454, I think Natera and Dr. Metzker adopted exactly what we
12 are saying here now, which is, what it means to identify
13 whether the variants are detected, variant detection. That,
14 as a factual matter, it happens from the sequencing data, but
15 you get the sequence reads, and then there is a bioinformatic
16 pipeline to identify whether the variants are detected. That
17 is exactly what we are saying, and in that context in
18 preliminary injunction proceedings, Dr. Metzker clearly very
19 readily testified, because it is consistent with the ordinary
20 usage, that that's what it means to detect a variant, as
21 opposed to simply detecting the base, the A, the C, the T.

22 If you turn to Slide 26, when we're thinking about
23 sort of what's a good way to exemplify this, the difference
24 between a base call and a variant detecting mutation. So you
25 can think of it, I think, as like you have a crime scene and

1 there's a bunch of forensic evidence. There might be a bunch
2 of fingerprints. There might be a bunch of hair. You collect
3 all of that evidence. I think in Dr. Metzger's current view
4 of the world, not his view of the world at this PI stage for
5 today, Natera's position is, as soon as you've collected that
6 evidence, you have identified the suspect. What we're saying
7 is, no, you've identified the fingerprints. You collected the
8 fingerprints, but in order to know whether you've identified
9 the suspect, you need to actually analyze the data.

10 I want to be clear, sometimes that analysis is done
11 on the sequencer -- I'll get to this in a bit -- sometimes it
12 is not. There is more than one way to do it, but that's
13 really the thrust of what we're saying is a factual matter is
14 the question, what analysis is required in order to know
15 whether that variant is present.

16 Now I said I think Dr. Metzker agreed with us in the
17 context of preliminary injunction. He also agreed with us in
18 his testimony in another case.

19 This is now Slide 27, which was a recent trial
20 between Guardant and Natera. Dr. Metzker was Natera's expert
21 there. He was asked about sequencing that was being detected.
22 And he said, The sequencing step then actually decodes the
23 genetic material into information, which is shown as the
24 bioinformatics pipeline. And now we just have the letters,
25 our As, Cs, Gs and Ts, but this is where we can then analyze

1 whether mutations are present that we are looking for to
2 either make a determination whether a circulating-tumor DNA is
3 present or not. Again, that's exactly what we are saying.

4 **THE COURT:** So you are equating circulating-tumor
5 DNA to an SNV?

6 **MS. DURIE:** Yes, because if we take a look at the
7 claim, and I'll go to Natera's deck for this, because they
8 have the whole claim laid out on Slide 21, but what we are
9 looking to see in this last requirement is, we are detecting
10 an SNV, and it is an SNV mutation that is present at this low
11 frequency of the cell-free DNA. So it is -- we are looking to
12 see whether that SNV mutation is present in the cell-free DNA.
13 That's the sample that has been taken from the patient. It
14 might be blood, it might be something else. But we are
15 looking for the presence of the SNV in the sample.

16 So I think in substance, yes, that circulating tumor
17 DNA, that C, T DNA is being identified by looking at the
18 presence of these single nucleotide variants.

19 I think the point really here, and it is consistent
20 with the testimony from the preliminary injunction, the
21 letters, the A, C, G, T, is different from that determination.

22 If we go to Slide 28, Natera's CEO, Dr. Rabinowitz,
23 testified in the *Guardant* trial, and his testimony was the
24 same. How does Signatera tell you whether a patient's cancer
25 is recurring? We target the 16 variants in the blood. We

1 take a blood draw from the patient, and we perform this test
2 where we amplify up the DNA. We then sequence the DNA, and we
3 then apply a bunch of signal processing or informatics
4 algorithms to look for the presence of those variants that are
5 unique to that patient's cancer. And that's exactly right.
6 That's completely correct. That wasn't a one-off.

7 If we look at the next slide -- I take that back,
8 actually. I got a copy of it twice.

9 Dr. Metzker, I will say in his deposition, as I said
10 he went back and forth a fair bit, but if you take a look at
11 Slide 30, what he is saying is, in some sense, detecting is
12 the same thing as determining whether a mutation is present.

13 So the question I asked was, I said, In your view of
14 the world, the NSV is detected at the point in time that the
15 case is called, is that fair? And he gave sort of a preamble,
16 and then I said, The way that the SNV is detected at the point
17 in time that the base is called, is that fair?

18 **THE COURT:** Slow down. Where did you start?

19 **MS. DURIE:** I apologize, I started three lines down
20 in the answer.

21 **THE COURT:** Go ahead.

22 **MS. DURIE:** The way that the assaying in cell-free
23 DNA is performed using target specific primers looking for
24 known SNV mutations, you will know which cycle the SNV
25 mutation appears, and the fluorescent color based on which

1 nucleotide is incorporated will tell you whether the SNV
2 mutation is present or absent. That's what he says detecting
3 means, determining whether it is present or absent.

4 **THE COURT:** But he is saying the color tells you
5 that, which is not your detection.

6 **MS. DURIE:** That's right. So he is not fighting
7 about the claim construction question at this stage. It is
8 what is detecting. We think detect means whether it is
9 present or absent. That's the claim construction question.

10 Then there is a question as a factual matter, where
11 does that determination about whether the mutation is present
12 or absent happen? Does it happen on the sequencer, or does it
13 happen in the bioinformatics pipeline.

14 Now as you saw in his testimony in *Guardant*, the
15 testimony at the preliminary injunction here, Dr. Metzger
16 agreed that happens at the bioinformatics platform, but that's
17 not the question for today. That's a fact question about how
18 NeoGenomics's product works.

19 As Your Honor knows, for claim construction we're
20 not supposed to be looking at how the products work. We're
21 just supposed to be looking at how do we understand what the
22 words in the claim mean, and the thing that's significant here
23 is, he's not disagreeing with our view about what the words
24 mean. He is disagreeing about where that happens here, but
25 not what the words mean. It will tell you whether it is

1 present or absent.

2 Again, if you take a look at Page 31. Dr. Metzker
3 is saying that happens when you see the fluorescent signal,
4 but he admits, you see the fluorescent signal, but the base
5 may not be there.

6 **THE COURT:** Let me ask you this. If I were to
7 interpret this Natera's way, are you saying you would be
8 precluded from offering this -- disputing this factual
9 question?

10 **MS. DURIE:** No. So there is sort of three things
11 that are going on, I think, in the respective constructions.
12 We think that it would be useful to construe the word detect
13 to mean determine to be present. We don't think there is
14 actually a real dispute that that's what that word means.
15 Dr. Metzker frequently uses it that way. But we think that is
16 the plain meaning of it.

17 So does the Court need to construe it? No. We
18 think it is helpful, but because Natera hasn't actually said
19 what is wrong, I think it is fair to say that on the present
20 record, the Court could construe the sides seem to agree that
21 that is what the word detected means.

22 Then the other aspects of Natera's proposal, they
23 don't offer an alternative construction of detect. They say
24 the terms are part of the sequencing step. In and of itself,
25 I think that's fine. I think it leaves open a little bit of

1 question of what that means, but I don't disagree you can
2 think of that as being a single step. And then the wherein
3 clause informs the mechanics of how the --

4 **THE COURT:** Of how the what?

5 **MS. DURIE:** High-throughput sequencing is performed.
6 So that's the last piece of their proposed construction.

7 **THE COURT:** Just for the court reporter, she said,
8 high-throughput.

9 **MS. DURIE:** Sequencing.

10 **THE COURT:** Go ahead.

11 **MS. DURIE:** I have no idea what that means. I asked
12 Dr. Metzker, I didn't get, I think, an answer. I don't know
13 what they think that means, but it informs the mechanics of
14 how the high-throughput frequency is performed.

15 We think the only word that there seems to be any
16 potential disagreement about is detected, and that SNV
17 mutation has to be detected from the sequence reads. That's
18 what the claim says.

19 We don't think there is anymore clarification of
20 that that is required from -- it is definitely an English word
21 that the jury is going to be familiar with, so we don't think
22 that needs further construction.

23 Again, I want to be clear, sort of the ultimate
24 dispute between the parties is, that Dr. Metzker and Natera's
25 position is, you can detect them.

1 So if we take a look at Slide 31, go to Slide 31 in
2 our deck. I asked him about this very directly, and I said,
3 It is your position that even if such errors take place, and I
4 was asking about errors, for example, in the amplification
5 process. So the sequence that is being sequenced is different
6 from the sequence in the sample. You are still detecting an
7 SNV if you see the signal that corresponds to an SNV at the
8 correct location, even if that signal turns out to be an
9 error, right? And he said, In the sequencing process when
10 fluorescence is being detected, the base call is making the
11 base call based on the nucleotide that's being incorporated.
12 I asked him about this very directly. And I said, it's your
13 position that even if such errors take place, and I was asking
14 about errors, for example, in the amplification process. So
15 the sequence that is being sequenced is different from the
16 sequence in the sample, in the cell free damage. You're still
17 detecting an SNV if you see the signal that corresponds to an
18 SNV at the correct location, even if that signal turns out to
19 be an error, right? And he said, In the sequencing process
20 when fluorescence is being detected, the base call is making
21 the base call based on the nucleotide that's been
22 incorporated, which was to say, yes, that in his view of the
23 world, detection means you look at the color signal, you see
24 that it's red, you see that's a C, and even -- and you've
25 detected an SNV, even if there is no SNV.

1 We think that just doesn't make sense as a factual
2 matter. So to just really put a point on this, if we go to
3 Slide 32, again, the claim requires that you are detecting an
4 SNV mutation that is present in the cell-free DNA in the
5 original sample, not present in what is being run through the
6 sequencer after the errors have been introduced through
7 amplification, but in the sample.

8 I asked him, At the point in time when you call the
9 base, and the base is the same as the expected mutation, at
10 that point in time is it your testimony that you have detected
11 an SNV mutation in the patient?

12 Now, that's critical, because that's what the claim
13 requires, you are detecting an SNV mutation in the cell-free
14 DNA in the patient's sample. And he says, I have not provided
15 that opinion. That's not my testimony. It would be detecting
16 an SNV mutation in the sequence read. That's not what the
17 claim requires.

18 **THE COURT:** So you think it says detected from the
19 sequence read, so you say "from" is different from in?

20 **MS. DURIE:** It is, and this is important. It is.
21 So when you are detecting the presence of an SNV mutation from
22 the sequence read, you take the sequence read, that's what you
23 start with.

24 **THE COURT:** I mean, you've told me several times
25 that this is abstract, it is not -- you know, we're not into

1 the factual questions, we're not applying the construction to
2 the product to figure out why it matters.

3 **MS. DURIE:** That is correct.

4 **THE COURT:** But it sounds like that's what you are
5 doing here.

6 **MS. DURIE:** No. I'm trying to explain the way I
7 think the claim works, and I'm trying to do that in the
8 context of science, not how either parties' product works, but
9 the science of the claim says we detect a SNV mutation from
10 the sequence read. What does that mean? You start with the
11 sequence read. That's the A, T, C, G. You are using that to
12 then determine whether there is a SNV mutation in the patient.

13 **THE COURT:** So where is the word, "in the patient,"
14 in that claim?

15 **MS. DURIE:** So it is -- if you take a look, it is
16 the SNV mutation, so you are -- you are performing
17 high-throughput sequencing of the amplified DNA, and then it
18 says, wherein in the amplified DNA starts with a patient's
19 sample, right, you start by getting a tumor biopsy sample or
20 another sample, right, and then that's the thing that you are
21 sequencing.

22 **THE COURT:** But it doesn't say SNV is detected in
23 the sample.

24 **MS. DURIE:** It says that --

25 **THE COURT:** I understand what you are saying.

1 Obviously ultimately this is what we are talking about, has
2 the patient's cancer recurred, right?

3 **MS. DURIE:** It says, wherein an SNV mutation, that's
4 the thing you're detecting, is present in less than or equal
5 to 0.015 percent of the cell-free DNA having the SNV locus.
6 And then it says, wherein the amplified DNA starts with a
7 patient sample, right? You start by getting a tumor biopsy
8 sample or another sample, right? And then that's the thing
9 you're --

10 **THE COURT:** But it doesn't say SNV is detected in
11 the sample. I understand what you're saying. I mean,
12 ultimately this is what we're talking about, has the patient's
13 cancer recurred, right? I mean, don't I infer that correctly?

14 **MS. DURIE:** It says, wherein an SNV mutation, that's
15 the thing you're detecting, is present in less than or equal
16 to 0.015 percent of the cell-free DNA having SNV locus, and
17 you are sequencing the amplified DNA to obtain sequence reads.
18 And then an SNV mutation that is present in a small percentage
19 of the cell free DNA is detected from the sequence reads.

20 So to be clear, if all the claim was about was
21 getting sequence reads, right, you wouldn't need that part
22 about detecting an SNV mutation. You're just basically
23 stopping after sequencing, because that's all the claim is
24 about. But the claim is saying something more. It's saying,
25 you do the sequencing, and then from the sequence reads you

1 detect an SNV mutation that is present in the cell-free DNA,
2 and that's the difference between base calling and variant
3 calling. Base calling is calling the base C, G, T. Variant
4 calling is deciding when the single nucleotide variant is
5 present.

6 When this claim says you are detecting an SNV,
7 single nucleotide variant mutation, that's variant calling.
8 Now again, there is a fact question here that I think the
9 Court will get to, but the claim construction question is,
10 what does it mean to say you are detecting it. Our only point
11 is, you are determining whether it is present.

12 Now if we go back to Slide 32, and I said, Have you
13 detected an SNV mutation in the patient? He says, No. And I
14 said -- and then I said, I'm asking you, as people like you of
15 skill in the art in the field use the word detect, because I
16 kept trying to pressure, like what do we mean here by detect,
17 Would you say that you have detected an SNV mutation in the
18 patient? And he says, I would think you would do a lot more
19 downstream analysis to actually make that determination.

20 So that is exactly our point. What does it mean to
21 detect an SNV mutation? It means to make a determination. It
22 means to make a determination whether it is present, that's
23 it. That's the claim construction question. That's exactly
24 what he was saying. What does it mean? What is required in
25 order to detect? Whatever is required, the thing that you are

1 doing is actually making a determination about whether it is
2 present.

3 Again, if we go to Slide 33, that, we think, is just
4 what the claim says. It is about --

5 **THE COURT:** I'm going to ask you to find a stopping
6 point in the next couple of minutes. You don't have to
7 finish, I just need to stop briefly.

8 **MS. DURIE:** I'm happy to stop now. I mean, I'm
9 perfectly happy to stop now.

10 **THE COURT:** I don't want to interrupt you in the
11 middle of a thought.

12 **MS. DURIE:** Not at all.

13 **THE COURT:** We'll stop here and take a ten minute
14 recess.

15 (Recess taken from 11:05 to 11:19 a.m.)

16 **THE COURT:** All right. I'm ready to continue. You
17 may proceed.

18 **MS. DURIE:** Thank you, Your Honor. I wanted to
19 respond to a couple of things in Natera's presentation, and if
20 Your Honor has it in front of you, I wanted to start with
21 Slide 18.

22 **THE COURT:** I do.

23 **MS. DURIE:** So here, Natera is trying to suggest
24 that our construction is a moving target. I want to be very
25 clear, the construction that we are asking for is that

1 detected means determine to be present, and that's it.

2 In our responsive brief, we tried to simply
3 summarize that by saying the sequence reads are analyzed to
4 determine whether the SNV is present, but we didn't mean
5 anything more than simply the language of the construction.
6 We're asking for the -- we're not asking the Court to make any
7 change to the claim language, but simply to say detected means
8 determined to be present.

9 **THE COURT:** In the patient?

10 **MS. DURIE:** No.

11 **THE COURT:** Everything you have told me right before
12 the break sounded like that.

13 **MS. DURIE:** So that is required by other parts of
14 the claim. It is not required by the meaning of detected.
15 The meaning of detected is determined to be present. The
16 claim requires that the thing that you are detecting, or in
17 our view, determining to be present is an SNV mutation in the
18 cell-free DNA, because that's what the claim says. Neither
19 side is asking Your Honor to construe that. I think we all
20 agree with an SNV mutation is. I think we all agree what the
21 cell-free DNA is.

22 The fact that the thing that is being detected from
23 the sequence reads is an SNV mutation in the cell-free DNA, is
24 simply a feature of those other words in the claim.

25 **THE COURT:** Okay.

1 **MS. DURIE:** Now if we turn to Slide 26, and this is
2 really representative of a lot of what Natera has said.

3 **THE COURT:** In your slides or their's?

4 **MS. DURIE:** Their slide, I apologize.

5 They talk about using SBS technology, using the
6 Illumina sequencer to detect single bases. I want to be
7 clear, we agree with all of that. You can detect a base. You
8 are determining whether or not the base is present. You can
9 detect a variant. You can determine whether or not the
10 variant is present. The word detection in our view means the
11 same thing in both cases. The thing that you are detecting is
12 different.

13 If we turn in their slide deck to Slide 49, I want
14 to clear up one thing here, because it says NeoGenomics
15 mischaracterizes what is required. It says, there's no
16 recited limitations about a --

17 **THE COURT:** I'm sorry, I had a moment. Tell me
18 where you are again.

19 **MS. DURIE:** Slide 49 in their deck.

20 **THE COURT:** Not your fault. Sometimes I just have a
21 little trouble keeping up.

22 **MS. DURIE:** I wanted to respond to the things in
23 their deck, and then I'll come back and make a final point.

24 **THE COURT:** 49 in their's.

25 **MS. DURIE:** They say, No recited limitations about a

1 threshold for accuracy or errors. And I agree with that as
2 far as it goes, but what it does say is, that the thing that
3 you are detecting from the sequence reads is the SNV mutation.

4 It is true in the cell-free DNA that SNV mutation
5 has to be rare. It has to be present at that very low
6 frequency.

7 **THE COURT:** Because that's the whole point of the
8 test, to detect the cancer at the very beginning of the
9 recurrence.

10 **MS. DURIE:** A hundred percent correct. I absolutely
11 agree with that. That is the whole point. But I agree with
12 them that the claim doesn't have a recited limitation about a
13 threshold for accuracy or errors. I agree with that. That's
14 true.

15 Then they go on to say, it only requires detecting
16 at least one SNV from a sequence read in about 7,000 reads.
17 That's nowhere in the claim. That's nowhere in the claim.
18 What the claim says is, you are detecting from the sequence
19 reads an SNV mutation that is present in a very, very tiny
20 fraction of the cell-free DNA. That's the patient sample, the
21 cell-free DNA. That's all it says.

22 So in our view of the world, what that means is, you
23 are looking to see whether --

24 **THE COURT:** Does .015 percent equal one out of
25 7,000?

1 **MS. DURIE:** I think it would. I think that's their
2 point.

3 **THE COURT:** I'm not a math person, but I was just
4 guessing. So what's inaccurate about that?

5 **MS. DURIE:** So nothing says you need to do 7,000
6 reads. What it says is, you have a sample of cell-free DNA.
7 A mutation is present in the sample at a very low frequency.
8 You are then doing this to detect from the sequence reads
9 whether that SNV mutation is present.

10 Now in our view of the world, that means you are
11 determining whether it is present, and that might require
12 looking at however many sequence reads to make that
13 determination. In Natera's view of the world in the matter of
14 claim construction, they said it doesn't matter if it's an
15 error, you detect the SNV as soon as you see that blue light,
16 or that yellow light, but nothing in the claim says you need
17 to look at 7,000 reads. You see a blue light once, maybe
18 that --

19 **THE COURT:** If you only look at five reads, how
20 could you possibly detect it at the point of .015 percent
21 level? I mean, I appreciate -- I hear what you are saying,
22 but you have to look at a whole bunch in order to figure out
23 if you --

24 **MS. DURIE:** Not necessarily. So in Natera's view of
25 the world, and I think this is the odd thing about what they

1 are proposing. In their view of the world, detecting just
2 means you see the base, and the base corresponds with a
3 mutation. You could do one read, let's say that the mutation
4 would be a C in position four. Okay. You take one sequence,
5 you see a C in position four. According to Natera, you have
6 detected an SNV mutation. If that mutation is actually
7 present in the sample at that very low frequency, then you've
8 satisfied the claim.

9 **THE COURT:** That's not how it actually works when
10 you are reading the whole thing. I mean, I don't understand.
11 I'm not --

12 **MS. DURIE:** I guess I'm not seeing what else in the
13 whole thing --

14 **THE COURT:** Well, you were telling me that one in
15 7,000 reads is inaccurate, and I was just asking what that
16 really meant, because, I mean, there is a lot of reads.

17 **MS. DURIE:** So --

18 **THE COURT:** That's how it works, there is a lot of
19 reads.

20 **MS. DURIE:** In a sequencer, and if you are actually
21 going to perform this method to detect cancer, you are going
22 to have more than 7,000 reads.

23 **THE COURT:** That's how it works. Why is that wrong?
24 You were trying to say that's wrong, and I don't understand
25 why that is wrong, or why it matters, even.

1 **MS. DURIE:** So it may not matter, but it is wrong in
2 terms of what the claim requires. They are saying the claim
3 requires detecting basically doing 7,000 reads. The claim
4 doesn't say that. You could detect that SNV mutation from a
5 single read and you would have practiced the claim. So the
6 claim doesn't say do 7,000 reads and then figure out how
7 frequently you see the variant. The claim says, the variant
8 is really rare. That's just true or not true. Either it is
9 or isn't in the cell-free DNA at that very low percentage.
10 That's a fact in the world relative to the claim.

11 So we have a mutation that's in there at a review
12 low. 602fricassee22222222222222222222222222222223, and then you
13 detect it from the sequence reads.

14 Natera is saying as soon as you get a C, you've
15 detected it, even if it is wrong and it's not there. We're
16 the ones who are saying, because this is what happens in
17 science and is what makes sense, detecting it means actually
18 figuring out if it's there, and that's the only thing we're
19 saying.

20 Would it require 7,000 reads to do that? Yeah,
21 probably. I don't disagree in the real world that's how you
22 would do the step of detecting the variant as opposed to just
23 base calling, but they are actually -- because of the way that
24 they are reading detected, they are taking that concept out of
25 the claim and then trying to insert it back in by saying,

1 well, you would do 7,000 reads, and that's not what the claim
2 says.

3 The claim says, you got a really great mutation, you
4 are detecting it from the sequence reads. The ultimate
5 question as a factual matter is going to be how do you do
6 that.

7 So I wanted to end with this sort of concept of
8 errors. If we go to Slide 52 and, again, still in Natera's
9 deck, they cited testimony here from Dr. Metzker. This was
10 his deposition in this case, I believe. No, sorry, this was
11 his deposition -- actually, take it back, I'm not actually
12 sure which deposition they are citing. But the questions was,
13 Can errors make it more difficult to detect SNV mutations? I
14 think it's this case. And he said, Not in the context of the
15 claim. So he is saying in the context of the claim, because
16 he's saying you detect the SNV mutation just by seeing the
17 color, in his view errors don't affect your ability to do
18 that. You can see the color.

19 And then the question was, How about in the context
20 of Forshew, Forshew was the main prior art context that was
21 being talked about in the preliminary injunction proceeding.
22 His answer was, In the real world, we know there are errors,
23 and there are ways of weeding out the errors out of the
24 sequencing data. So he's drawing a distinction between the
25 claims, according to him, errors don't matter. You can

1 practice the claim even if you have a higher error rate. Even
2 if it would swap the signal. In the real world you could weed
3 out those errors.

4 I want to come back to our deck, if I may. If we
5 can flip and go to our deck at Slide 35, because what is
6 interesting here is, that in the context of the preliminary
7 injunction proceedings, Dr. Metzker was distinguishing Forshaw
8 based on error rates, error rates that he is now saying don't
9 matter in the context of the claim.

10 So if we take a look at Slide 35.

11 **THE COURT:** At the preliminary injunction, that was
12 in connection with the '454 Patent, and I didn't rule on the
13 '454 Patent in the preliminary injunction, right?

14 **MS. DURIE:** That's right. I'm using it to make a
15 point only about what detect means.

16 **THE COURT:** I'm not disagreeing with you, I'm just
17 remembering.

18 **MS. DURIE:** Absolutely right.

19 **THE COURT:** There is an obviousness problem with
20 that.

21 **MS. DURIE:** That was the question. The question
22 was, does Forshaw make this obvious.

23 **THE COURT:** And I punted.

24 **MS. DURIE:** Right. What he said is, in talking
25 about Forshaw, he was talking about the limitations. He

1 said -- look at the title. It was, ultra-deep sequencing does
2 not enable detection of rare genetic variants that fall below
3 the sequencing workflow error rate. Now that's 180 degrees
4 from what he is saying today. Today he is saying as we just
5 saw it, error rates don't matter in the claim. What he said
6 back then was, you can't detect rare genetic variants, that's
7 SNVs, that fall below the sequencing workflow error rate. He
8 explained in his declaration why this was, and he said, The
9 limitations of Forshew's approach arise because the errors
10 associated with Forshew's sample library preparation and
11 sequencing work, so that is preparing the DNA and amplifying
12 it. So errors will be introduced in that process before you
13 get to actually looking to see what the colors are, exceed the
14 technique's ability to detect rare genetic DNA variants, as
15 explained in greater detail. Under the Forshew approach, the
16 rare variants are lost in the noise associated with the
17 abundant errors found in the sequence read data.

18 So what he was saying back then is, for purposes of
19 the claim, you can't detect those rare variants in Forshew
20 because they are lost in the noise. What he is saying today
21 is, detection just means looking at the color, so error rates
22 are irrelevant to my ability to detect. I look at a blue, it
23 is blue. I detected the SNV, even if all of these errors and
24 sample preparation mean that there is no variant that is
25 actually present. I have detected the thing. That's his

1 position today.

2 To just come back to the sort of crime scene
3 analogy, what they are really saying is, as soon as you have
4 gathered up your forensic evidence, you've detected the
5 presence of the criminal. We're saying, at the end of the
6 day, detecting means determining the presence of. You've
7 detected fingerprints. You detected hair, but you haven't
8 actually detected the criminal until you figure out what those
9 relate to.

10 We're going to have disagreement down the line, I
11 think, either way, about whether this claim requirement is met
12 for infringement purposes. Again, the only question for today
13 is, what does detect mean, we think. And, we think actually
14 the usage of both sides in connection with the prior
15 proceedings, the *Guardant* case and Dr. Metzker's deposition in
16 this case show those terms are used interchangeably, and
17 that's a fair construction of what it means to detect.

18 Unless the Court has questions on that, I want to
19 touch very briefly on the other term that was addressed.

20 **THE COURT:** All right.

21 **MS. DURIE:** If we can go back to Slide 2. This is
22 the isolated cell-free DNA. All that we are asking the Court
23 to do here is, just to say we think the claim means what the
24 claim says.

25 If you take a look at Slide 4, we reproduced here

1 the relevant part. We're saying the isolated cell-free DNA is
2 the cell-free DNA isolated from the plurality of biological
3 samples obtained from the subject. Natera has criticized this
4 and said we didn't include different time points. We think a
5 different time point is modifying assay, that you do the assay
6 at different time points.

7 I don't necessarily have a problem with including
8 different time points, but I think the right read of the claim
9 is that's modifying the assay, but it doesn't really matter
10 for our purposes. Our only point is, the isolated cell-free
11 DNA is the cell-free DNA that is referenced earlier in the
12 claim, that at a minimum, has been isolated from the plurality
13 of biological samples, because that's what the claim says.

14 Now if you turn to Slide 5, this is what Natera is
15 doing. They are saying it includes cell-free DNA isolated
16 from any of the plurality of biological samples. So they are
17 replacing a plurality with any of the plurality. That's
18 rewriting the claim.

19 We cited some law in our slides. Slide 6, the word
20 "the" has to have an antecedent basis.

21 Slide 7, concept that the Court is familiar with.
22 We cited a few different cases here, *Guardant* as well as
23 *Harris*, which is a 2013 Federal Circuit opinion that where you
24 have "the," there needs to be an antecedent basis, and it
25 means "the thing," not a subset of the thing or any of the

1 thing, as Natera would have it.

2 The other point that I wanted to make --

3 **THE COURT:** The A doesn't mean adding.

4 **MS. DURIE:** A does not mean adding, that's exactly
5 right. That's not what it means.

6 If you look at Slide 9, this is a Federal Circuit
7 case called *Chef America*, and the point of the *Chef America*
8 case is, claim construction is just an exercise saying what
9 the words in the claim mean, not rewriting them to make them
10 make sense. The patentee chooses the claim language and they
11 are stuck with it.

12 In the *Chef America* case, the claim said that you
13 were heating, I think this was frozen pizza, but you are
14 heating it to 400 degrees, and the patentee said, obviously
15 that means at 400 degrees because heating to 400 degrees would
16 cause it to be a charred piece of pizza, so that can't be what
17 we meant. And the Court said, no, you said to 400 degrees,
18 that means to 400 degrees, and you don't get to look at the
19 specification and say that doesn't make a ton of sense and we
20 ought to construe it to mean that the air is 400 degrees,
21 rather and the pizza.

22 **THE COURT:** Do these people not have an oven on the
23 Federal Circuit? I mean, obviously that seems nuts. I'm sure
24 they are right. They understand a lot more than me, but it
25 seems kind of crazy.

1 **MS. DURIE:** I totally get it, and I don't disagree.
2 It does seem kind of crazy. I think there is a lot of things
3 in patent law that are kind of crazy.

4 **THE COURT:** Well, I cannot disagree with you.

5 **MS. DURIE:** But this is one of them.

6 **THE COURT:** I don't know, sometimes it doesn't seem
7 like a real world. It is very a specialized world you people
8 live in, and I don't live there.

9 **MS. DURIE:** No argument from me on that score, and
10 just wait until the jury gets ahold of it, is what I would
11 say. So a hundred percent.

12 The reason I wanted to bring this case to the
13 Court's attention is, this is an incredibly formal exercise.

14 **THE COURT:** That is true.

15 **MS. DURIE:** Claim construction is a very formal
16 exercise, so a lot of Natera's arguments on this claim term is
17 that doesn't really make a whole lot of sense. And the
18 federal circuit's answer to that is, that's not the question.
19 The question is, you look at the words and you figure out what
20 the words mean. All we're saying is, read the words as the
21 words. You don't need to do anything.

22 **THE COURT:** Right. But the words do have to be read
23 in the context of everything that is around them. Correct?

24 **MS. DURIE:** Absolutely. I completely agree, but
25 that was true in *Chef America*, too, and in *Chef America*, the

1 Court says, you can have all the context you want, but heating
2 something to 400 degrees, means heating it to 400 degrees.

3 There is lots of context in that claim about why
4 that is clearly not what the patentee intended, but the
5 Federal Circuit didn't care. I think here the same principle
6 holds.

7 The question for the Court is simply, you look at
8 the words, and if the words -- the words mean what they say.
9 If there is a technical word that you need to interpret, you
10 do that, but the goal here is not to cause the claims to make
11 sense. It is to interpret the words as they appear on the
12 page. That's what the Federal Circuit says, and that's the
13 task at this stage for claim construction.

14 Unless the Court has questions on that, I will sit
15 down.

16 **THE COURT:** Thank you.

17 For plaintiff.

18 **MS. HABERNY:** Thank you, Your Honor. I would like
19 to start with the sequencing and detecting term and first note
20 that Ms. Durie, almost every time that she discussed the claim
21 language and the word detect, she substituted the word
22 identify for detect, and so this should be absolutely clear,
23 the claim says detect, not identified, and Ms. Durie's
24 argument seemed to be assuming its own construction, because
25 she freely discussed the claim as if it said identified, and

1 it doesn't.

2 I would also like to point out that much of
3 NeoGenomics's argument was based on testimony about the
4 product at issue. So this -- I think Your Honor picked up on
5 this. The testimony, much of it that Ms. Durie pointed to,
6 was about how Signatera works, Natera's product, or how RaDaR
7 works, NeoGenomics's product.

8 Again, I would like to go back to the cake analogy
9 and the batter. Signatera is a full product, it's a baked
10 cake. The method here only claims part of that. The method
11 is for preparation of -- for preparing a preparation that is
12 useful for monitoring cancer progression. It is not a method
13 for detecting cancer progression. So much of what Ms. Durie
14 relied on was downstream in the product after the detection
15 occurs there was algorithms that look at errors, and that's
16 not what this method at issue today is about.

17 I also would like to address Ms. Durie's assertion
18 that Natera agrees with NeoGenomics's claim construction.
19 Natera, to be clear, does not agree with NeoGenomics's claim
20 construction.

21 I would also like to point out that when Ms. Durie
22 contends that its construction of detecting to mean determined
23 to be present is its full construction, that is inaccurate.
24 NeoGenomics's construction is requiring analysis, further
25 analysis, and the words determined to be present are not

1 analogous to detect. Determined to be present would shoehorn
2 in this downstream analysis. So you are not only detecting
3 something, it could be a false positive, it could be a true
4 positive, it doesn't matter at that stage, right? It is like
5 the COVID test example. You detect COVID most of the time.
6 That's performing the detection. Every once in awhile, there
7 is a false positive. Maybe you go and the CDC determines
8 false positive rates and reports that out. That's not part of
9 the detection.

10 **THE COURT:** So your position would be that if I
11 construe the patent the way you want, that also would do away
12 with the factual question that Ms. Durie talked about, when
13 does the detection occur?

14 **MS. HABERNY:** Your Honor, I don't believe that
15 that's a factual question. So Natera is the patentee here.
16 Natera chose the word detect. Natera stated in the claim
17 language, the SNV is detected from the sequence reads. That's
18 not a question of fact, that's how detection occurs.

19 So again, going back to sequence reads and how they
20 are generated, it's sequencing by synthesis, which is the
21 preferred embodiment. One base is added at a time. Once you
22 have two bases that are added, that's already a sequence read.
23 And as you make it longer, the sequence read just gets longer.
24 You are detecting the SNVs from the sequence reads as they are
25 being built. That is the plain language of the claim, and so

1 it is not a factual question at all. It is a question of what
2 does detected from the sequence reads mean, wherein that is
3 part of sequencing to obtain sequence reads. So I would
4 disagree with that assertion.

5 I would like to address NeoGenomics's discussion of
6 all the purported difference between base calling and variant
7 calling. I would posit to Your Honor, that that's just a
8 smokescreen. The SNV is either present or it's not. There
9 may be false positives, true. That's true of every detection
10 method. But the SNV is either there or it's not. When you
11 identify that base, you've detected it, because it is there.
12 That's just a function of its existence in the DNA. You don't
13 need to go back and do error correction and make sure. That's
14 downstream of detection.

15 So this notion of variant calling being different
16 than detecting the base that as a matter of physics is either
17 there or not, is just a non-sequitur.

18 I would also like to point out that NeoGenomics has
19 very little evidence to support its construction. So if we
20 ask what is NeoGenomics's evidence, the vast majority of
21 NeoGenomics's presentation was a mischaracterization of
22 Dr. Metzker's testimony. In just a moment, I would like to
23 ask him to explain.

24 Beyond that, NeoGenomics points to a dictionary, a
25 single passage in the specification which I discussed with

1 Your Honor in detail. NeoGenomics spent about ten seconds on
2 it, and that's it. So there really is, other than
3 mischaracterizing Dr. Metzker's testimony, there really is no
4 support for their claim.

5 With that, I would like to ask Dr. Metzker to
6 explain a few of the passages that Ms. Durie pointed to, and I
7 would like to ask Your Honor whether the Court would prefer he
8 go to the witness box or --

9 **THE COURT:** He'll need to be sworn. Before you do
10 that -- hold on. I just kind of want to go back to something
11 I asked you the first time around. So your construction of
12 the entire phrase, to use a nontechnical term, from performing
13 high-throughput sequencing from the sequence reads says, plain
14 and ordinary meaning, which means that the terms are part
15 of -- and I'm just like trying to understand what that means.
16 The terms are part of the terms. I don't get that.

17 Do you see what I mean? Your construction of that
18 whole phrase, I just don't get what -- I mean, "the terms," it
19 seems circular.

20 **MS. HABERNY:** The term -- I apologize, Your Honor, I
21 would like to clarify.

22 **THE COURT:** I just -- if I go with you, I don't want
23 to say it that way, because I find that confusing. But, I
24 mean, I get your point, and I'm not saying I'm going to rule
25 your way, but if I ruled your way, that is confusing to me.

1 **MS. HABERNY:** I would say that the plain and
2 ordinary meaning, which means that the SNVs are detected as
3 part of performing the high-throughput sequencing to obtain
4 sequence reads as part of that sentence.

5 Your Honor, this is analogous to the claim
6 construction order on the '454 Patent that's docket 280 at
7 Page 11, where Your Honor found that sequence and detecting
8 are part of the same sequencing step.

9 Here, because there is this wherein clause, our
10 plain and ordinary meaning is that the SNV mutation is
11 detected as part of the performing high-throughput sequencing
12 to obtain sequence read step.

13 **THE COURT:** Okay. I'm going to think about this a
14 little bit. Now I think Ms. Durie stood up.

15 **MS. DURIE:** I did, and I object, because what I
16 heard from counsel at the beginning of the presentation was,
17 that they were only going to call Dr. Metzker if Your Honor
18 had questions in order to respond to them and he was simply
19 here to answer Your Honor's questions.

20 I made my presentation and allocated my time all on
21 that basis, and I went through. Now we're at the end of the
22 time and they want to call him. I would want to have the
23 opportunity to cross-examine him, but I don't have time.

24 **MS. HABERNY:** Your Honor, that was in my opening
25 presentation.

1 **THE COURT:** How long do you expect him to talk?

2 **MS. HABERNY:** A few minutes.

3 **THE COURT:** If I have to go past 12:30 to give you a
4 few minutes of cross, I'll let you do that, but we're not
5 going to take long because we don't have that. You can come
6 up and be sworn.

7 You don't have to qualify him. I have heard Dr.
8 Metzker a number of times, and I basically remember.

9 (The witness was affirmed.)

10 **DIRECT EXAMINATION**

11 **BY MS. HABERNY:**

12 **Q.** Dr. Metzker, in your deposition that Ms. Durie took in
13 this case, did you ever use the term "detect," interchangeably
14 with "determined to be present," in the context of the claim
15 at issue today?

16 **A.** No, I did not.

17 **Q.** And can you explain Ms. Durie's statement that you did
18 use them interchangeably?

19 **THE COURT:** Well, sustained. He can't explain her
20 statements.

21 **MS. HABERNY:** I'm sorry.

22 **Q.** Can you explain what you meant in the testimony that
23 Ms. Durie pointed to when she stated that you used them
24 interchangeably?

25 **A.** Yes. So early in the deposition, I used the word

1 determined, and then was trying to correct myself to mean
2 detect, but even in the context it was always within the
3 sequencing process itself. It was never to imply that there
4 is some downstream analysis that needs to be taken. It was
5 always in the context of sequencing and detecting the SNV from
6 the sequence read.

7 **Q.** Would you please turn to Slide 19 of NeoGenomics. Do you
8 have the slide deck?

9 **A.** I do not.

10 **THE COURT:** Ms. Winchester is giving him her copy
11 temporarily.

12 **THE WITNESS:** This is Natera's.

13 **THE COURT:** That's the other one. I have a stack of
14 slide decks. I want you to know I keep them. Possibly I look
15 at them after everything is decided and I move on to the next
16 issue, but I don't throw them away.

17 **BY MS. HABERNY:**

18 **Q.** Thank you. Would you please turn to Slides 19 and 20 in
19 NeoGenomics's slide deck.

20 **A.** Yes. I'm there.

21 **Q.** Can you please explain what you mean by the testimony
22 that's there?

23 **A.** Yes. So the question was based on a more general
24 understanding of sequencing and not specific to Claim One of
25 the '596 Patent, and in that context, I answered, "No, I don't

1 think it has," because this was a general question and
2 thoughts related to the claim .

3 **Q.** And what would be the difference between the claim and
4 the general question?

5 **A.** The claim has very specific steps, including targeted
6 multiplex PCR, and in doing so, there is a predetermined
7 position of the SNV, and when the sequencing process hits that
8 particular cycle, it can detect the SNV from the sequence read
9 during the sequencing process.

10 **Q.** Would you please turn to Slide 27 of NeoGenomics's slide
11 deck.

12 **A.** Yes. I'm there.

13 **THE COURT:** I don't understand what you mean when
14 you say, this is a general question. Are you saying it is not
15 about the patent at all? I don't understand that.

16 **THE WITNESS:** She was asking me more about
17 sequencing in general, just --

18 **THE COURT:** Sequencing like out in the world?

19 **THE WITNESS:** Out in the world, and there is lots of
20 ways that can occur.

21 **THE COURT:** Okay. Go ahead.

22 **MS. HABERNY:** Thank you.

23 **THE COURT:** What page did you have him turn to?

24 **MS. HABERNY:** I apologize. Slide 27 of
25 NeoGenomics's deck.

1 **THE COURT:** No need to apologize. I sometimes have
2 to get you all to repeat because there is a lot of numbers and
3 stuff going on. Go ahead.

4 **BY MS. HABERNY:**

5 **Q.** And this is testimony that Ms. Durie referred to from
6 your opinions at the *Guardant* trial. Can you please explain
7 what you meant in your testimony that's on Slide 27?

8 **A.** I'll do my best. The question appears to be incomplete.
9 It appears that I'm being asked about is how the Signatera
10 product works, and I was trying to give a very general
11 description of the Signatera product.

12 **Q.** Were you opining here on the method of the claim in the
13 '596 Patent?

14 **A.** I was not.

15 **Q.** And were you present for every one's testimony at the
16 *Guardant* trial?

17 **A.** Yes, I was.

18 **Q.** Were you present for Dr. Rabinowitz's testimony?

19 **A.** Yes, I was.

20 **Q.** Can you turn to Slide 28 of NeoGenomics deck?

21 **A.** Yes. I'm there.

22 **Q.** Can you explain what you heard Dr. Rabinowitz answering
23 with testimony about?

24 **A.** Yes. So here --

25 **THE COURT:** I'm sorry, ask that again.

1 **BY MS. HABERNY:**

2 **Q.** Can you explain what you heard Dr. Rabinowitz testify?

3 **THE COURT:** Beyond what is written there? I don't
4 understand your question.

5 **MS. HABERNY:** We can move on.

6 **THE COURT:** Okay.

7 **BY MS. HABERNY:**

8 **Q.** Would you go to Slide 30 of NeoGenomics's deck, please.

9 **A.** Yes, I'm there.

10 **Q.** Would you please explain what you were describing here in
11 this testimony?

12 **A.** Right. So again, I don't have a lot of context. This
13 appears to be -- I'm not sure whether it is related to the
14 claim or not, but what I was explaining, if it was specific to
15 the claim and it involves targeting multiplex PCR, where you
16 have predetermined start and stop sites and a predetermined
17 position for the SNV, that once the nucleotide that has its
18 color is incorporated, the fluoresce color, based on which
19 nucleotide is incorporated, will tell you whether the mutation
20 is present or not. But that, again, is during the sequencing
21 process.

22 **Q.** And finally the last slide I'll ask you about is Slide 35
23 of NeoGenomics's deck.

24 **A.** Yes. I'm there.

25 **Q.** Would you please explain what you meant by this paragraph

1 in your declaration that's on Slide 35?

2 **A.** Yes. So this is a paragraph where I'm describing the
3 Forshew reference and I'm describing what Forshew was
4 reporting from their paper, and they had an inability to
5 detect rare genetic DNA variants using their method.

6 **Q.** And does that have anything to do with detecting SNVs in
7 the '596 Patent claim?

8 **A.** It does not.

9 **MS. HABERNY:** Those are all the questions that I
10 have.

11 **THE COURT:** All right.

12 Ms. Durie.

13 **MS. DURIE:** Thank you.

14 **CROSS-EXAMINATION**

15 **BY MS. DURIE:**

16 **Q.** Dr. Metzker, good morning. Let's start where you just
17 left off with your discussion of Forshew. Now you were
18 submitting a reply declaration in connection with the
19 preliminary injunction proceedings, right?

20 **A.** I believe that's correct.

21 **Q.** And you were talking about how Forshew was different from
22 the claims that were at issue in those proceedings. Fair?

23 **A.** I believe that's correct.

24 **Q.** Okay. And you said that Forshew did not have the ability
25 to detect rare genetic DNA variants because of errors in the

1 sample library preparation and sequencing workflow process,
2 right?

3 **A.** In part, yes.

4 **Q.** Now in Forshew, Forshew had the ability to look at the
5 fluorescent signal and see whether there was a blue or a
6 yellow or a red or a green, right?

7 **A.** Yes. They were using the Illumina technology.

8 **Q.** So they could make a base call; blue, yellow, red, green,
9 C, T, G, right?

10 **A.** Right. Well, in their sequencing method, which is
11 different from the claimed method.

12 **Q.** Just to be clear, in Forshew they were using a sequencer
13 as it spit out a color and allowed them to make a base call.
14 Correct?

15 **A.** I agree in the general world of sequencing, yes.

16 **Q.** Let's go back to what you said about Slide 19 in the
17 NeoGenomics's deck. This was the question from your
18 deposition --

19 **A.** Can I have a moment to get to that page?

20 **Q.** Sure. Slide 19. You just testified about it.

21 **THE COURT:** We're slow page flippers. Me, too. Go
22 ahead.

23 **BY MS. DURIE:**

24 **Q.** And the question was: So if I see the fluorescent signal,
25 the machine sees the fluorescent signal and it makes the base

1 call, has it determined whether an SNV is present? And your
2 testimony at the deposition was, No, I don't think it has.
3 And what you just said is, well, I wasn't talking about the
4 claim, I was just talking about how sequencing works in
5 general.

6 **A.** That's correct.

7 **Q.** Let's take a look at the cited testimony. It is on Page
8 44 of your deposition. You'll see the quotation is there at
9 Page 44. We have extra copies.

10 Your Honor, may I approach?

11 **THE COURT:** Is this on the docket somewhere?

12 **MS. DURIE:** It was attached to our motion to
13 supplement the record.

14 **THE COURT:** All right.

15 **MS. DURIE:** We have a copy, I think, for the Court
16 as well. Your Honor, there is a tab five in the binder.

17 **THE COURT:** What is in this notebook generally?

18 **MS. DURIE:** This was our motion for leave to
19 supplement at tab -- I think -- I apologize, I got it wrong.
20 Impeachment material for Dr. Metzker and tab five is
21 deposition.

22 **THE COURT:** I'm asking you, is it in tab five on the
23 docket?

24 **MS. DURIE:** It is on the docket as an exhibit to the
25 motion to supplement.

1 **THE COURT:** Okay. Hold on. Now where did you say
2 to go?

3 **MS. DURIE:** Document 380-1 of -- let's go to Page
4 43, and 44, Your Honor.

5 **BY MS. DURIE:**

6 **Q.** So the cited testimony from the slide, Dr. Metzker,
7 appears at the bottom of Page 44, right? The last four lines
8 on Page 44.

9 **THE COURT:** Why don't you give everybody a minute,
10 including me, just to take a look at the context there so we
11 can all read it before the questions.

12 Okay. So I'm actually slightly confused, because I
13 don't understand how the answer at line 25 at the bottom of
14 Page 44, is consistent with the five -- I'm just approximating
15 the previous answers, where he appears to say something
16 completely different.

17 **BY MS. DURIE:**

18 **Q.** Let's walk through that, Your Honor. Starting at Page 43
19 I said to the witness, I'm trying to understand the difference
20 between detecting SNV, your construction, that is
21 Dr. Metzker's construction, and Dr. Lennon's construction
22 determining whether it is present.

23 **THE COURT:** So just in the previous answer, we're
24 talking about the claim, right?

25 **MS. DURIE:** Right.

1 **THE COURT:** This claim at issue, I presume.

2 **MS. DURIE:** Correct.

3 **THE COURT:** Go ahead.

4 **BY MS. DURIE:**

5 **Q.** And then at the top of 44 I said, So you go through the
6 claim steps. You detect the fluorescence, you make the base
7 call. You have in your view detected the SNV, right? The
8 answer was, Correct. So that's detecting SNV and,
9 Dr. Metzker, that's in the context of the claim, right?

10 **A.** Yes.

11 **Q.** And then I asked, Have you also in your view, determined
12 the SNV to be present? Your answer, sir, was, Well, I've
13 detected it. I think that's the right term to use. That's
14 the claim term, it's been detected. You were talking about the
15 claim, right?

16 **A.** In that section, yes.

17 **Q.** And then I said, Okay. And you said, It has been
18 detected because the florescent is -- I mean, the sequencer is
19 the detector. It is detecting signals corresponding to which
20 nucleotide is added at that position. We could also call that
21 base calling, right, detecting which nucleotide is at that
22 position?

23 **A.** Yes. In the context of the claim, it is still detecting
24 the SNV.

25 **Q.** That's not my question. That thing that you are

1 referencing there, detecting signals corresponding to which
2 nucleotide is added at that position, another word for that
3 would be base call.

4 **A.** In general, that's correct.

5 **Q.** And then I continued, Your Honor, and I said, Right. But
6 the reason I'm asking you about Dr. Lennon's terminology is
7 that you said it is wrong. Okay. And you said it's wrong in
8 substance. So I want to understand what you think the
9 substance is. So if I see the fluorescent signal, the machine
10 sees the fluorescent signal, and it makes the base call, has
11 it determined whether an SNV is present? Your answer was, No.
12 Right?

13 **A.** It was, no, I do not think it has. And then I explain on
14 Page 45, that it is a different application.

15 **Q.** Let's go to Page 45. You said, and I think Dr. Lennon
16 describes it in a very different application of what determine
17 means, but I don't think in the SBS method it's been
18 determined, it's been detected.

19 So you were drawing a distinction between what it
20 means to detect the SNV and to determine whether the SNV is
21 present, right?

22 **A.** Well, no. I was explaining that I disagree -- or I
23 thought Dr. Lennon was using a different application to
24 support his construction of determined to be present.

25 **Q.** I went on and asked you, So what needs to happen, in your

1 view, to go from detecting the SNV to determining the SNV's
2 presence, since you seem to think those meant different
3 things, and your answer was, you have no idea, right?

4 **A.** I did. But I gave more than just, I have no idea.

5 **Q.** Well, let's continue on this question of whether you were
6 talking about the claim.

7 **THE COURT:** Well, I think it is established he is
8 talking about the claim.

9 **MS. DURIE:** May I show one more thing on that point,
10 Your Honor?

11 **BY MS. DURIE:**

12 **Q.** On Page 40, if we go a few pages earlier in the
13 deposition, beginning around line six, Dr. Metzker, we had the
14 following colloquy. Question: Well I'm just trying to
15 understand why you think Dr. Lennon's construction is wrong,
16 and why --

17 **A.** I'm sorry, what line did you start with?

18 **Q.** I'm sorry, Page 40.

19 **THE COURT:** Pause. Let him look at it. And when
20 you are reading, you can read a little slower, because
21 otherwise, the court reporter is, with my permission, going to
22 come over there and strangle you.

23 **MS. DURIE:** Understood. She'll not be the first,
24 and I will endeavor to speak more slowly.

25 **THE COURT:** Go ahead.

1 **BY MS. DURIE:**

2 **Q.** Question: Well, I'm just trying to understand why you
3 think Dr. Lennon's construction is wrong and why you think
4 detected and determined to be present mean different things.
5 So you said, you understand that the SNV mutation is detected
6 at the point that there is a detection of the fluorescent
7 signal, right? You answered, Yes. Okay. Answer: That is
8 correct. Question: And I take it you also think the SNV
9 mutation is not determined to be present at that point, right?
10 Your answer was, That's correct. And that's based on the
11 claim itself and the support in the specification. We can
12 agree, Dr. Metzker, can we not, that when you said the SNV
13 mutation was not determined to be present simply because there
14 was a detection of the fluorescent signal, you were talking
15 about the claim?

16 **A.** Can you repeat that question? That seems a bit
17 convoluted.

18 **Q.** Can we agree that when you said --

19 **THE COURT:** Okay. So -- I'm sorry. The word -- the
20 phrase, determined to be present, are not in the claim, right?

21 **MS. DURIE:** Right.

22 **THE COURT:** And so you're asking him --

23 **BY MS. DURIE:**

24 **Q.** Let me do it this way, Your Honor.

25 Let's go back to Slide 19, in the NeoGenomics's

1 deck. In the NeoGenomics's declaration, we have quoted
2 testimony from you where you said -- you were asked, The
3 machine sees the fluorescent signal and it makes the base
4 call, has it determined whether an SNV is present, right?

5 **A.** No, I do not think it has, but this question was based on
6 my understanding of Dr. Lennon's interpretation.

7 **THE COURT:** Okay. I've caught up.

8 **BY MS. DURIE:**

9 **Q.** So you were saying this wasn't about the claim, it was
10 just about sequencing in general, right, that's what you said
11 on direct?

12 **A.** That's correct. And that is supported by the answer on
13 Page 45.

14 **Q.** And if we go to Page 40, you were asked basically the
15 same question. You also think the SNV mutation is not
16 determined to be present at that point where there is
17 detection of the fluorescent signal, right?

18 **A.** Well, from the context of the claim, I disagree that
19 detect means determined to be present, and I think I was
20 answering it in that context.

21 **Q.** When you said -- when I asked you, I take it you also
22 think that the SNV mutation is not determined to be present at
23 that point where there is a detection of the fluorescent
24 signal. And you said, That's correct.

25 **THE COURT:** That just begs the question about what

1 detected -- whether it means determined to be present. I
2 mean, I've caught up.

3 **MS. DURIE:** My only point here is on direct,
4 Dr. Metzker said he wasn't talking about the claim.

5 **THE COURT:** Yes. You clarified that he was talking
6 about the claim.

7 **MS. DURIE:** He was talking about the claim.

8 **THE COURT:** He was talking about what Dr. Lennon
9 said, and it is actually kind of reasonable to say, I don't
10 know what he meant by determined to be present --

11 **MS. DURIE:** Well --

12 **THE COURT:** -- but on the other hand, I don't know
13 why they are disagreeing -- you know, I don't know --

14 **MS. DURIE:** So --

15 **THE COURT:** Seems like we're kind of going in
16 circles at this point. I appreciate the point you have made.

17 **MS. DURIE:** I guess I would say, Dr. Metzker is not
18 here saying I don't know what Dr. Lennon means by determined
19 to be present. I don't think it is that hard a concept, is
20 the SNV mutation present or not. What he says is, I think you
21 detect it when you see the fluorescent signal.

22 **THE COURT:** He's very consistent about that.

23 **MS. DURIE:** I don't think he determined that it was
24 present. He actually says both things.

25 **THE COURT:** Yeah, because you all think those mean

1 different things. I mean, what is the problem -- that's why
2 we're here, for me to figure that out.

3 **MS. DURIE:** He says variously, it is determined to
4 be present when you see the fluorescent signal and not
5 determined to be present when you see the fluorescent signal.
6 He said both of those things in his deposition.

7 **THE COURT:** Okay. Well --

8 **MS. DURIE:** That's in our slides that we went over a
9 little while ago.

10 **THE COURT:** All right.

11 **MS. DURIE:** But I think the point that I would make
12 here is, Dr. Metzker is acknowledging -- is saying there is a
13 difference between detecting and determining to be present.
14 The difference seems to be, detecting doesn't require any
15 consideration of errors or whether the thing is actually
16 there. That, I think, is the difference between the parties
17 about what detecting means, are you actually looking to see
18 whether there are things there.

19 **THE COURT:** Do you have further questions for the
20 witness?

21 **MS. DURIE:** I have no further questions for the
22 witness.

23 **THE COURT:** I assume you don't have any?

24 **MS. HABERNY:** No questions.

25 **THE COURT:** You can step down. just leave the

1 exhibits, because the clerk or court reporter may need them.

2 **MS. HABERNY:** I believe NeoGenomics has run its
3 time.

4 **THE COURT:** I got to give them a little extra time.
5 I appreciate her argument, but if you have further argument, I
6 don't think you have used all of your time.

7 **MS. HABERNY:** I think we have many minutes left.

8 **THE COURT:** What else do you want to say?

9 **MS. HABERNY:** I just wanted to spend 30 seconds
10 addressing the isolated cell-free DNA term and remind the
11 Court that nothing in the claim precludes assaying a plurality
12 of biological samples separately at different times. So I
13 just want to make that clear, assaying a plurality in the
14 claim language, does not have to be all together at once. You
15 can assay the plurality of samples separately, and I think
16 that NeoGenomics is reading in a requirement that they be
17 assayed all at the same time, and that's just not what the
18 language says.

19 **THE COURT:** Okay. Anything else?

20 **MS. DURIE:** Only --

21 **THE COURT:** Wait. Anything else for the plaintiff?

22 **MS. HABERNY:** I don't believe so, unless Ms. Durie
23 says something that requires a response.

24 **THE COURT:** All right. Now go ahead.

25 **MS. DURIE:** Thank you. The only thing I wanted to

1 say, Your Honor, is that the claim construction dispute that
2 was T-ed up, was the meaning of detect, whether it means
3 determining that it is present, and this notion sort of in
4 general terms that what has happened has happened as part of
5 same stuff. This is not a summary judgment motion. What we
6 heard at the very end of counsel's rebuttal presentation was a
7 request to essentially rule on what would be summary judgment
8 on the factual question of when detect is happening, as
9 opposed to what the word detect means. That would be error.

10 This is not the resolution time to resolve any
11 factual questions about what is happening. The only question
12 is what it means to detect. We think what it means to detect
13 is to determine whether it is present. They think that is
14 wrong. They haven't given you an alternative construction.

15 So it seems so me, the choice for the Court is to
16 say detect just means detect. Every one agrees that it does
17 carry the plain meaning; or, as we would request, to clarify
18 that detecting means determining that it is present. But I
19 think that's the issue and the request that the Court reach
20 and go beyond that to try to rule essentially on summary
21 judgment about whether that detection is happening and how, I
22 think would be error.

23 **THE COURT:** All right.

24 **MS. DURIE:** Thank you.

25 **THE COURT:** I don't think she raised anything new,

1 but I'll give you one minute.

2 **MS. HABERNY:** I would just like to reiterate that
3 the reading in of determined to be present is not based on the
4 intrinsic record. It is not based on evidence. It is based
5 on, again, mischaracterization of testimony, and so there is
6 no support for reading that in.

7 **THE COURT:** All right. So I'm going to take
8 everything under advisement. Hopefully I'll be fairly quick.
9 I'm pretty sure that I already did this, but let me make sure.

10 I realized that the first day of trial is a federal
11 holiday, so I told you all we would pick the jury on Friday.
12 Did I do that?

13 **MS. HABERNY:** Yes.

14 **THE COURT:** Okay, good. I meant to do it, so I'm
15 glad I did it. Based on what I know so far, I do think that
16 we can try the case in four days. We'll pick the jury, get
17 them -- probably won't even take all day, because I don't let
18 you all ask any questions. We'll get the jury picked. We'll
19 get them impaneled. I'll give them their preliminary
20 instructions.

21 We can talk later about whether you want to make
22 opening statements on Friday. They'll almost certainly be
23 timed, depending on how long you think your opening statements
24 might be agreement. I'm asking you to think about this.
25 Obviously we don't have to decide until after summary

1 judgment, if the trial is necessary. But, you know, I'm
2 always thinking about the trial, so just want you all to think
3 about how you want to use that Friday because, you know, the
4 trial is going to be the next four days, at least based on
5 what I understand now, I think we can fairly do that, but I
6 would be willing to let you make your opening statements on
7 Friday, which would give you a little more time. I probably
8 would be willing to, which would give a little more time the
9 following week for your evidence. We don't have to decide. I
10 don't need to hear from you. I'm just telling you, be
11 thinking about this.

12 **MS. DURIE:** May I ask a question? For the trial, am
13 I right in assuming you will just give us a number of hours
14 per side?

15 **THE COURT:** Yes. That is what I'll do, and we'll
16 have to wait until after summary judgment to see what is left
17 and who has the burden of proof on what is left, because, you
18 know, I usually give the person who goes first a little more
19 time because they have to -- there is a little more explaining
20 to be done.

21 You are going to have the burden of proof on
22 obviousness, the defendant is. If that's the only issue,
23 well, you might -- the defendant might get more time. If
24 there are issues on which the plaintiff has the burden of
25 proof, you know, I mean, we're just going to have to figure

1 all of that out later.

2 Yes, I will give you a specific number of minutes,
3 usually. Your time for cross-examination will count for your
4 time, so you can't use up all the other side's time with your
5 cross-examination.

6 If you make an evidentiary objection that takes --
7 you know, that consumes court time beyond, you know, 20
8 seconds or a minute, certainly if I have to have a bench
9 conference or excuse the jury. If you lose, all of that time
10 counts against your time.

11 **MS. DURIE:** I understand.

12 **THE COURT:** That's how I do it in every single case,
13 and I can't think of any reason not to do it here. I hope we
14 will -- if we have to have a trial, that we will get a lot of
15 that worked out on motions in limine.

16 I always allow people, you know, if the jury comes
17 in at 9:30, we'll start at 9:15, and we'll talk about whatever
18 you would like to talk about. I don't like to send the jury
19 in and out. I want to be very efficient with their time when
20 they are here, but that's all down the road, and it also
21 assumes that nobody asks for an extension of time to do
22 anything and that I get the summary judgment motions decided
23 promptly so you all have time to do all the trial prep.

24 I'll just tell you, as you all know, I don't like to
25 mess around. If you are under a little bit of stress in this

1 District, as local counsel probably knows is, a lot of changes
2 with some senior status, which I took senior status, but best
3 I could tell, I'm working like 180 percent, because I'm still
4 the Chief Judge.

5 We have had another judge take senior status. We're
6 kind of swamped, and they haven't nominated anybody for either
7 seat. So I'm just telling you, I'm going to do my absolute
8 best so we can try this case in October, because I would like
9 for it to be over. I suspect you all would like this part of
10 it to be over. I also anticipate whatever happens, somebody
11 is going to appeal.

12 But if I can't do that because of all of this other
13 stuff that is going on and, you know, I keep having to fight
14 with GSA about keeping the Durham courthouse open and blah,
15 blah, you all don't care, but I'm doing the best that I can.

16 If I figure out that I'm not going to be able to get
17 summary judgment done in time for us to try it in October, I
18 will let you know that early, because I respect your time and
19 I know you have other things going on.

20 So I don't expect it to happen, but there is more of
21 a chance than usual that it might happen because of our
22 situation here and the national situation involving budget
23 cuts, primarily to our facilities. That's how we're
24 experiencing it in the moment. So there we are.

25 Anything else you all want to talk about today

1 productively? I saw the CLEA thing was filed. It looks like
2 everything is on track to finish as scheduled, as far as I
3 know.

4 **MS. HABERNY:** On our side, yes.

5 **THE COURT:** Okay. As soon as I am able -- I will
6 get this done pretty quickly. I actually don't anticipate any
7 problems getting this out to you fairly promptly, but summary
8 judgment is a different ball of wax. I would just encourage
9 you to pick your battles, you know, because I usually find it
10 more helpful when you really get into the things that are the
11 most important, because if you make a one paragraph argument,
12 you're liable to get one of those things that says, this is
13 throw-away argument and I'm not even going to address it. So
14 if you really want me to consider it, don't put it in a
15 footnote. I can promise you if you put it in a footnote, it
16 might as well not be there. If it is complete argument in and
17 of itself in a footnote, I'm not doing that. If it's -- in
18 this case a paragraph is equivalent to a footnote.

19 So, please -- you know, what you argue, I really
20 need you all's help, because I'm very fortunate in this case
21 to have very good lawyers on both sides, and I appreciate all
22 of you all's work because you are helping me greatly. It
23 would just help me at summary judgment if you can do it. I
24 mean, you are going to do it however you want to, but I'm
25 trying to tell you what I find helpful, because the purpose of

1 a brief, I'm pretty sure this is true, is to be helpful to me.

2 So to the extent that is helpful to you in figuring
3 out how you are going to brief these issues, we'll do that.

4 Anything else?

5 **MS. DURIE:** No, Your Honor.

6 **MS. HABERNY:** No, Your Honor.

7 **THE COURT:** Okay. Court is adjourned.

8 (Court was adjourned at 12:20 p.m.)
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C E R T I F I C A T E

I, J. ALLEN, RPR, United States District Court
Reporter for the Middle District of North Carolina, DO HEREBY
CERTIFY:

That the foregoing is a true and correct transcript of
the proceedings had in the above-entitled matter.

March 22, 2025

J. ALLEN

J. Allen, RPR
United States Court Reporter
324 W. Market Street
Greensboro, NC 27401