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Judge Connolly (D. Del.) Overturns $96 Million Molecular Diagnostics Jury Verdict, Finds Patents Invalid Under § 112

Synopsis:

In a case with implications for the litigious molecular diagnostics space and written description law, Chief Judge Connolly of the District of Delaware reversed a $96 million jury verdict in favor of Natera, Inc. (Natera) against its competitor CareDx, Inc. (CareDx).[1] In January 2024, a jury found that two of CareDx's cell-free DNA (cfDNA) blood tests (AlluSure and AlloSeq) infringed two of Natera's patents and awarded Natera damages of approximately $96 million.[2] CareDx filed a motion for judgment as a matter of law, asking Chief Judge Connolly to find the asserted patents invalid for lack of written description under 35 U.S.C. § 112. On February 24, 2025, Judge Connolly granted CareDx's motion and found the asserted claims of Natera's patents invalid for lack of written description.[3]

1. Patent Dispute Between CareDx and Natera: Background and Claims

CareDx sells AlloSure and AlloSeq—blood tests that are used to assess whether a transplanted kidney is being rejected by the recipient's body. Specifically, AlloSure and AlloSeq are used to detect cfDNA, which "is fragmented DNA in the bloodstream that originates from cells undergoing cell injury and death."[4] When a transplanted kidney is being rejected, "donor-derived cell-free DNA (dd-cfDNA) increases in the blood" of the transplant recipient.[5] AlloSure and AlloSeq allow for the detection of dd-cfDNA in a transplant recipient's blood.

Natera asserted two patents, U.S. Patent Nos. 10,655,180 (the '180 patent) and 11,111,544 (the '544 patent) (collectively, the "asserted patents"), related to methods for preparing, amplifying and detecting cfDNA.[6] Relying on the insight that dd-cfDNA will be present in different fractions depending on whether the transplanted kidney is being accepted or rejected by the recipient, Natera's patent claims were directed to extracting and amplifying cfDNA from a patient at given locations on the genome:

21. A method for preparing a preparation of amplified DNA derived from a biological sample of a second individual useful for determining genetic data for DNA from a first

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individual in the biological sample, the method comprising:

- Extracting cell-free DNA from the biological sample;
- Preparing a preparation of amplified DNA by amplifying a plurality of target loci on the cell-free DNA extracted from the biological sample to generate amplified DNA;
- Analyzing the preparation of amplified DNA by sequencing the amplified DNA using sequencing-by-synthesis to obtain genetic data of the plurality of target loci, and determining the most likely genetic data for DNA from the first individual based on allele frequencies in the genetic data at the plurality of target loci.

Asserted claim 14 of the ’180 patent recites a similar method, directed to identifying SNPs (Single Nucleotide Polymorphisms), as a way of assessing the relative amount of DNA in each sample:

14. A method for measuring an amount of DNA in a biological sample, the method comprising:

- Performing a targeted PCR amplification for more than 100 SNP loci on one or more chromosomes expected to be disomic in a single reaction mixture using more than 100 PCR primer pairs, wherein the reaction mixture comprises cell-free DNA extracted from a biological sample of a subject comprising DNA of mixed origin, wherein the DNA of mixed origin comprises DNA from the subject and DNA from a genetically distinct individual, wherein neither the subject nor the genetically distinct individual is a fetus, wherein the DNA of mixed origin comprises DNA from a transplant, and wherein the amplified SNP loci comprise SNP loci on at least chromosome 1, 2, or 3;
- Measuring a quantity of each allele at a plurality of amplified SNP loci that comprise an allele present in the genetically distinct individual but not the subject, wherein the quantity of each allele at a plurality of amplified SNP loci are measured by high-throughput sequencing;
- Measuring an amount of the DNA from the genetically distinct individual in the biological sample using the quantity of each allele at the SNP loci and an expected quantity of each allele at the SNP loci for different DNA fractions,
- Wherein the method is performed without prior knowledge of genotypes of the genetically distinct individual.

At trial, CareDx argued, among other things, that the asserted claims were invalid for lack of written description under 35 U.S.C. § 112. The jury disagreed and found that the asserted patents were not invalid.

CareDx filed a motion for judgment as a matter of law under FRCP 50(b), arguing that no reasonable jury could find that the specifications of the asserted patents satisfy the written description requirement in view of the evidence presented at trial.

2. Judge Connolly’s Opinion

Beginning with the ’544 patent, Judge Connolly explained that claim 21 recites “a method by which (1) cell-free DNA is extracted from a biological sample of one individual (i.e., the ‘second individual’); (2) target loci on the extracted cell-free DNA is ‘amplified’ and ‘sequenc[ed by] synthesis to obtain genetic data’; and (3) ‘the most likely genetic data’ for DNA from another individual (i.e., the ‘first individual’) in the obtained genetic data is ‘determin[ed]’ from that data ‘based on allele frequencies.’”[7] Thus, to satisfy the written description requirement, the specification must show that the inventors possessed the full scope of this claim, including the individual claim elements and all three claim elements “as an integrated whole.”[8]

Judge Connolly first focused on whether the specification “adequately describes the combination of the claimed steps as an integrated whole.”[9] CareDx’s expert, Dr. Brian Van Ness, testified that the specification does not describe all three of the claimed steps being performed in combination. Dr. Van Ness’s testimony was largely unrebutted—Natera cited only two passages from the specification, admitted that the specification lacked working examples, and otherwise relied on the testimony of its expert, Dr. John Quackenbush.

Judge Connolly found Dr. Quackenbush’s testimony “conclusory” and “‘far too general’” to support the jury’s decision.[10] Specifically, Dr. Quackenbush “never pointed to any text in the patent’s written description that would lead an artisan of ordinary skill to know that the inventor had invented a combination of those different pieces.”[11] And Judge Connolly explained that the Federal Circuit has held that “pointing to an ‘amalgam of disclosures’ from which an artisan could have created the claimed invention does not satisfy” the written description requirement.[12]

Judge Connolly also explained that after CareDx introduced evidence that supports its written description position, it was Natera’s burden to produce evidence to rebut that position. But Natera did not produce any evidence beyond Dr. Quackenbush’s conclusory testimony. Because there was “no substantial evidence to support the jury’s finding of adequate written description,” Judge Connolly held that “judgment of invalidity of the asserted claims of the ’544 patent as a matter of law is warranted.”[13]

Likewise, Judge Connolly held that “[t]he ’180 patent’s written description… is inadequate as a matter of law for the same reason the ’544 patent’s written description is inadequate—i.e., Natera did not adduce at trial substantial evidence that the patent’s text shows that the inventor possessed the combination of the elements of the claimed methods.”[14]

3. Conclusion and Takeaways

In the competitive and litigious field of molecular genomics, where new applications (e.g., new computational approaches) for the underlying technology of high-throughput screening are being developed and patented, Judge Connolly’s decision suggests that placing all elements into a specification in piecing them together later may be insufficient. Instead, Judge Connolly’s decision underscores the importance of tying the individual components of an invention together in a patent specification, and that providing working examples of the inventions may be critical.

For patent litigators, Judge Connolly’s decision highlights several important points to be mindful of at trial. Judge Connolly held, consistent with Federal Circuit precedent, that if a patent broadly claims several components of an invention, the specification must disclose those elements “as an integrated whole” to satisfy the written description requirement. Pointing to disparate portions of the specification will not suffice if nothing is tying those elements together.

Judge Connolly’s opinion also underscores the importance of lawyers minding their burdens and ensuring that they have supported their arguments (including their expert’s testimony) with reliable evidence. This is especially true, and can be easy to overlook, where burdens shift from one party to the other, as was the case here.

Finally, this case shows that even after an adverse jury decision, it is still possible to prevail—but understanding how to proceed, and what issues to focus on, are critical. Here, CareDx chose to focus on a select number of issues in its motion rather than attempting to relitigate the full spectrum of issues the jury considered. In doing so, CareDx successfully invalidated the patents and avoided the $96 million in damages for which it was otherwise liable.

[1] *Natera, Inc.* v. *CareDx, Inc.*, No. 20-38-CFC-CJB (D. Del.).

[2] *Id*., D.I. 460.

[3] *Id*., D.I. 558.

[4] https://labproducts.caredx.com/products/alloseq-cfdna

[5] *Id*.

[6] Natera asserted three claims of the ’544 patent (claims 21, 26, and 27) and two claims of the ’180 patent (claims 14 and 15) against CareDx.

[7] D.I. 558 at 8-9.

[8] *Id*. at 9.

[9] *Id. at 10.*

[10] *Id*. at 11 (quoting *Juno Therapeutics, Inc. v. Kite Pharma, Inc.*, 10 F.4th 1330, 1336-37 (Fed. Cir. 2021)).

[11] *Id*.

[12] *Id*. (quoting *Flash-Control*, 2021 WL 2944592, at *3).

[13] *Id*. at 13.

[14] *Id*. at 14.