

**United States Court of Appeals  
for the Federal Circuit**

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**ENZO BIOCHEM INC., ENZO LIFE SCIENCES,  
INC., YALE UNIVERSITY,**  
*Plaintiffs-Appellees*

v.

**APPLERA CORP., TROPIX, INC.,**  
*Defendants-Appellants*

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2014-1321

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Appeal from the United States District Court for the  
District of Connecticut in No. 3:04-CV-00929, Judge Janet  
Bond Arterton.

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Decided: March 16, 2015

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gued for plaintiffs-appellees. Also represented by  
MICHAEL HAWES.

CARTER GLASGOW PHILLIPS, Sidley Austin LLP, Wash-  
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Chicago, IL.

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Before PROST, *Chief Judge*, NEWMAN and LINN, *Circuit Judges*.

Opinion for the court filed by *Chief Judge* PROST.

Dissenting opinion filed by *Circuit Judge* NEWMAN.

PROST, *Chief Judge*.

This appeal arises from the judgment of the United States District Court for the District of Connecticut following a jury trial on issues of infringement and invalidity of U.S. Patent 5,449,767 (“767 patent”). The Plaintiffs, Enzo Biochem Inc., Enzo Life Sciences, Inc., and Yale University (collectively “Enzo”), asserted claims 1, 8, 67, 68, and 70 of the ’767 patent against the Defendant Applera Corp. and Tropix, Inc. (“Applera”). Relevant to this appeal, the jury returned a verdict for Enzo finding that Applera directly infringed all of the asserted claims, that Applera induced its customers to infringe all of the asserted claims, and that the claims at issue were not proven by clear and convincing evidence to lack enablement or written description. The district court denied Applera’s post-trial motions and granted Enzo’s motion for award of pre- and post-judgment interest, as modified. Applera appeals the district court’s claim construction, which construes the claims at issue to cover both direct and indirect detection of a signalling moiety, and in the alternative appeals the district court’s denial of Applera’s post-trial motion that the asserted claims were not enabled and lacked written description.

Because we agree with Applera that the district court erred in its claim construction by finding that the claims at issue covered direct detection, we reverse the district court’s claim construction, vacate the judgment of infringement, and remand for further findings under the claim construction articulated herein.

## BACKGROUND

This case involves the use of nucleotide probes that allow a scientist to detect, monitor, localize, or isolate nucleic acids when present in extremely small quantities, as is necessary for the sequencing of deoxyribonucleic acid (DNA).

As this court discussed extensively in a previous iteration of this case:

DNA and RNA are composed of a series of units, called "nucleotides." Each nucleotide is composed of a nitrogenous base, a pentose sugar, and a phosphate group. The phosphate group of one nucleotide forms a covalent bond with the pentose sugar of an adjacent nucleotide, thereby linking the nucleotides along a "sugar-phosphate backbone." Aside from linking the nucleotide units into a polynucleotide strand, the sugar-phosphate backbone provides structural support for the nitrogenous bases. The bases fall into two categories: pyrimidines and purines. Pyrimidines include cytosine ("C"), thymine ("T"), and uracil ("U"). Purines include adenine ("A") and guanine ("G"). DNA contains the bases adenine, thymine, cytosine, and guanine; RNA also includes adenine, cytosine, and guanine, but contains the base uracil in place of thymine. Two strands of DNA or RNA having complementary bases will bind, or "hybridize," to form a double-stranded complex, or "hybrid," which is held together by hydrogen bonds between complementary bases. In DNA, adenine on one strand binds to thymine on the other; in RNA, adenine binds to uracil; and in both DNA and RNA, cytosine binds to guanine. The process of forming a double-stranded hybrid is called "hybridization." The reverse process, re-

sulting in two separate strands, is called “denaturation.”

Because hybridization occurs in a predictable manner between complementary strands, it is possible to detect the presence of a nucleic acid of interest in a sample. For example, a chemical entity, called a “label,” can be attached to or incorporated into a nucleic acid strand of a known sequence, called a “probe,” which will hybridize with a complementary sequence of interest, called a “target.” Once the probe is hybridized with the target, a detectable signal is generated either from the label itself (referred to as “direct detection”) or from a secondary chemical agent that is bound to the label (referred to as “indirect detection”). If a signal is detected from the sample after all unhybridized probes have been removed, detection of the signal implies the presence of a target in that sample.

Labeling of nucleic acids has been accomplished using a variety of chemical entities. For example, with radioactive labels, an isotope of hydrogen ( $^3\text{H}$ ), phosphorous ( $^{32}\text{P}$ ), or carbon ( $^{14}\text{C}$ ) is substituted for a non-radioactive atom within the probe, and the isotope is then detected using a radiation detector. But radioactive labels have drawbacks. As explained in the . . . '767 . . . patent, radioactive labels are “potentially hazardous,” “expensive to purchase and use,” and “often very unstable.”

*Enzo Biochem, Inc. v. Applera Corp.*, 599 F.3d 1325, 1328 (Fed. Cir. 2010).

DNA sequencing relies on the aforementioned principles, except with the goal of determining the order of base pairs in an unknown DNA sequence rather than determining whether a known DNA sequence is present. Until

recently, the predominant method of DNA sequencing, and the method relevant to this case, was the Sanger method. The Sanger method requires that a sample of the DNA strand to be sequenced be placed in a solution that includes nucleotides, a primer (short piece of DNA), and a polymerase enzyme. Once combined, the primer hybridizes to a portion of the unknown DNA sequence. Then, starting at the primer, the polymerase enzyme attaches individual complementary nucleotides and covalently attaches them to the proceeding nucleotide in the strand.

The key to the Sanger method is that a small portion of the nucleotides added to solution are special nucleotides, capable of preventing the polymerase enzyme from adding any additional nucleotides to the DNA strand. These special nucleotides are called dideoxyterminators. The incorporation of the dideoxyterminators is random, and thus allows for the synthesized DNA strands to be of varying lengths. The newly synthesized complementary strands are then sorted from shortest to longest. One then identifies the dideoxyterminator for each strand length. By knowing strand length and the strand's dideoxyterminator, one can determine the nucleotide sequence of the unknown DNA strand.

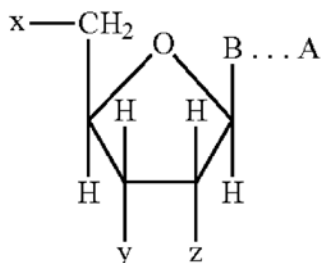
Just as with DNA probes, dideoxyterminators are detected either by direct or indirect detection. And just as when using DNA probes, detecting dideoxyterminators through direct detection, i.e., with radioactive isotopes, is potentially hazardous and expensive. To avoid these drawbacks, nucleotide probes that do not rely on traditional radioactive labels were developed. The '767 patent is directed toward these new nucleotide probes.

Claim 1 of the '767 patent is directed to a compound in which a nitrogenous base "B" is covalently attached, "directly" or through a "linkage group" (represented by the dotted line), to a chemical moiety "A." '767 patent col.

30 l. 59-col. 31 l. 11. The linkage group is not recited in the independent claim in structural terms, but is instead described as “not substantially interfer[ing] with the characteristic ability of the oligo- or polynucleotide to hybridize with a nucleic acid and . . . not substantially interfer[ing] with formation of the signalling moiety or detection of the detectable signal . . .” *Id.* at col. 31 ll. 1-7.

Claim 1 is representative and reads:

An oligo- or polynucleotide containing a nucleotide having the structure:



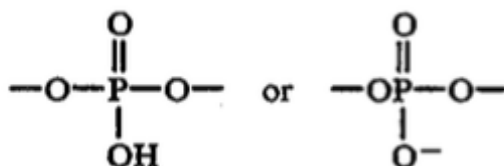
wherein B represents a 7-deazapurine or a pyrimidine moiety covalently bonded to the C<sup>1'</sup>-position of the sugar moiety, provided that whenever B is a 7-deazapurine, the sugar moiety is attached at the N<sup>9</sup>-position of the 7-deazapurine, and whenever B is a pyrimidine, the sugar moiety is attached at the N<sup>1</sup>-position of the pyrimidine;

wherein A comprises at least three carbon atoms and represents at least one component of a signaling moiety capable of producing a detectable signal;

wherein B and A are covalently attached directly or through a linkage group that does not substantially interfere with the characteristic ability of the oligo- or polynucleotide to hybridize with a nucleic acid and does not substantially interfere with

formation of the signalling moiety or detection of the detectable signal, provided also that if B is 7-deazapurine, A or the linkage group is attached to the 7-position of the deazapurine, and if B is pyrimidine, A or the linkage group is attached to the 5-position of the pyrimidine;

wherein one of x and y represents



and the other of x and y is absent or represents  $\text{---OH}$  or  $\text{---H}$ ; and wherein z represents  $\text{H---}$  or  $\text{HO---}$ .

At a *Markman* hearing, the district court construed disputed claim terms for several patents, including the '767 patent. Of significance here, the district court construed two phrases of claim 1 of the '767 patent. First, the district court construed the phrase "A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing a detectable signal" as "A comprises at least three carbon atoms and is one or more parts of a signalling moiety, which includes, in some instances, the whole signalling moiety." *Enzo Biochem, Inc. v. Applera Corp.*, No. 3:04-CV-929, 2006 WL 2927500, at \*2, \*4 (D. Conn. Oct. 12, 2006). Second, the district court construed the phrase "signalling moiety" as "a chemical entity capable of producing a detectable signal." *Id.* Because the district court's construction does not require that any additional components be attached to "A" to form the signalling moiety, and that a "signalling moiety" may itself produce a detectable signal, the district court's claim construction allows for direct detection. In other words, because the claim was construed in such a manner that no additional

steps are required to detect the compound, it can be directly detected. This is in contrast with a claim construction that would limit the claim to indirect detection by requiring that another compound be added to “A” in order for it to be detectable. Thus, the district court’s construction allowed for both direct and indirect detection of the claimed compound.

The case then proceeded to a jury trial, where the jury found that the asserted claims were infringed and that the ’767 patent was not invalid for lack of written description and enablement. The district court then denied Applera’s post-trial motions.

Applera timely appealed to this court, arguing that the district court erred in its claim construction or in the alternative that the asserted claims were invalid for lack of written description or enablement. This court has jurisdiction over this case under 28 U.S.C. § 1295(a)(1).

#### DISCUSSION

While the ultimate construction of a claim term is a legal question reviewed de novo, underlying factual determinations made by the district court are reviewed for clear error. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, No. 13-854, 2015 WL 232131, at \*11 (U.S. Jan. 20, 2015). Specifically, “when the district court reviews only evidence intrinsic to the patent (the patent claims and specifications, along with the patent’s prosecution history), the judge’s determination will amount solely to a determination of law, and the Court of Appeals will review that construction de novo.” *Id.* at \*10. However, when the district court looks beyond the intrinsic evidence and consults extrinsic evidence, for example to understand the relevant science, these subsidiary fact findings are reviewed for clear error. *Id.*

To the extent possible, “the words of a claim are generally given their ordinary and customary meaning.”



*Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) (internal quotation marks omitted). The “ordinary and customary meaning of a claim term” is that meaning that a person of ordinary skill in the art in question, at the time of the invention, would have understood the claim to mean. *Id.* at 1313. “Because the meaning of a claim term as understood by persons of skill in the art is often not immediately apparent, and because patentees frequently use terms idiosyncratically,” the court also looks to “the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art.” *Id.* However, when doing so the court must stay ever vigilant to avoid reading limitations from the specification into the claim. *Id.*

It is with these tenets in mind that the court now reviews the district court’s *Markman* order.

We begin with the language of the claims.<sup>1</sup> Claim 1 of the ’767 patent states that “A” “comprises at least three carbon atoms and represents *at least one component of a signaling moiety* capable of producing a detectable signal” and is attached to “B” so that it “does not substantially interfere with formation of the signalling moiety.” ’767 patent col. 30 l. 66-col. 31 l. 6 (emphasis added). First, the phrase “at least one component of a signalling moiety” indicates that the signalling moiety is composed of multiple parts as the term “component” in and of itself indicates a multipart system. Thus, construing the phrase to allow for a single-component system, as the district court did here, would read out the phrase “component of a signalling moiety” and would thus impermissibly broaden

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<sup>1</sup> The court finds that Enzo’s argument that Applera waived its ability to appeal the district court’s claim construction meritless given the posture of the previous appeal.

the claim. See *Bicon, Inc. v. Straumann Co.*, 441 F.3d 945, 950 (Fed. Cir. 2006) (“Claims are interpreted with an eye toward giving effect to all terms in the claim.”).

Second, the claim language requires that “A” be attached either directly or through a linkage group that “does not substantially interfere with formation of the signalling moiety.” ’767 patent col. 31 ll. 5-6. The plain reading of this phrase is that “A” cannot be the whole signalling moiety, as the claimed compound does not include a *formed* signalling moiety. In other words, if “A” alone could be the signalling moiety, as the district court found, the requirement that “A” not interfere with the formation of the signalling moiety would be read out of the claim, as the signalling moiety would be formed by the sole presence of “A.”

Enzo urges that we should hold that the inventors’ inclusion of the term “at least one of” allows for both direct and indirect detection. Enzo cites to *Howmedica Osteonics Corp. v. Wright Medical Technology, Inc.*, 540 F.3d 1337 (Fed. Cir. 2008), to support this argument. Specifically, Enzo argues that *Howmedica* illustrates that patentees use open-ended language, such as “at least one,” to encompass multiple embodiments. *Howmedica* dealt with a patent for a prosthetic knee with a tibular and femoral component. 540 F.3d at 1340. At issue was the correct construction for a claim reciting “the femoral component including at least one condylar element” conforming to the geometric limitations specified in the claim. *Id.* at 1344. There was no dispute that the claim could cover a unicondylar prosthesis, but the parties disagreed as to whether both condyles of a bicondylar femoral component must meet the geometric limitations of the claim. *Id.* We agreed with the district court that the phrase “at least one” in the claim language means “one or more” condylar elements are required, but held that the claim does not require both condyles of a bicondylar femoral component to conform to the geometric limita-

tions of the claim, noting that the claim says that “the condylar element” must have the specified geometry, instead of “both” or “each” condylar element. *Id.*

*Howmedica* is inapposite. Here, the dispute is whether “A” can comprise the entirety of “a signalling moiety” despite the claim language that “A” is a “component of a signalling moiety.” *Howmedica* was not concerned with whether “the femoral component” could be comprised solely of a condylar element, but whether the femoral component could *include* one or more condylar elements, and whether each must conform to the geometric limitations. Thus, unlike in *Howmedica* where the claim did not require the prosthetic knee to have more than one condylar element, here the plain reading of the disputed claim term requires that a signalling moiety be composed of components, of which at least one is “A.”

The specification provides additional support that claim 1 covers only indirect detection. First, throughout the specification, “A” is described as being capable of forming a signalling moiety only in conjunction with other chemicals, never that “A” alone can be a signalling moiety. *See* ’767 patent (Abstract), col. 3 ll. 47-53, col. 5 ll. 33-35, col. 7 ll. 28-30, col. 8 ll. 4-8, col. 11 ll. 5-7, col. 16 ll. 63-65. Second, the background portion of the specification further describes the invention as a “series of novel nucleotide derivatives that contain biotin, iminobiotin, lipoic acid, and other determinants attached covalently to the pyrimidine or purine ring” and explains that these nucleotides “will interact specifically and uniquely with proteins such as avidin or antibodies.” *Id.* at col. 3 ll. 2-3. The specification then goes on to describe this interaction as being used “for the detection and localization of nucleic acid components in many of the procedures currently used in biomedical and recombinant-DNA technologies.” *Id.* at col. 3 ll. 3-9. In other words, the patent describes how “A,” a biotin, iminobiotin, or lipoic acid, forms a detectable unit, i.e., a signalling moiety, upon interaction with avidin

or antibodies. Third, the specification's only discussion of direct detection, here radioactive labeling, was exclusively in the context of discussing how indirect detection is a superior method. The specification not only discusses the limitations and drawbacks of using radioactive labeling, but states that the claimed compounds can be used "as an alternative to radioisotopes for detection and localization" and that these compounds have "detection capacities equal to or greater than products which utilize radioisotopes and often can be performed more rapidly and with greater resolving power." *Id.* at col. 3 ll. 5-13.

At oral argument, Enzo was repeatedly asked to point the court to a location in the specification that supports its proposed claim construction. In response, Enzo cited to column 14 line 63 to column 15 line 12 and column 8. Oral Arg. at 14:27-14:52, 19:15-19:42, <http://oralarguments.cafc.uscourts.gov/default.aspx?fl=2014-1321.mp3>. The first cited section of the specification, however, refers to experimentation conducted to determine whether biotin may be successfully attached to nucleotides, i.e., whether the invention may be synthesized, not whether the claimed invention may utilize direct detection. The second citation also provides no support for Enzo's argument. The section reads that "A may be any moiety which has at least three carbon atoms and is capable of *forming a detectable* complex with a polypeptide when the modified nucleotide is incorporated into a double stranded duplex containing either deoxyribonucleic or ribonucleic acid." '767 patent col. 8 ll. 4-8 (emphasis added). The section continues to discuss how "A" may be ligands that interact with appropriate antibodies. *See id.* at col. 8 ll. 9-45. Thus, the section does not discuss direct detection, but instead discusses indirect detection. In fact, at oral argument Enzo agreed that nowhere in the specification—including the sections it had cited—were ligands described as being directly detectable. Instead, Enzo argued that extrinsic expert

testimony indicated that the described ligands could be detected through various methods, such as proton NMR spectroscopy. However, the expert testimony cited by Enzo does not discuss whether ligands, such as biotin, as attached to the dideoxyterminator, could be directly detected, but instead whether one could directly detect a “clean pure solution of biotin” in a test tube, a fundamentally different question. J.A. 11290-91. Thus, neither section of the ’767 patent specification cited by Enzo supports the inclusion of direct detection, even when extrinsic expert testimony is considered.

We have long recognized the “distinction between using the specification to interpret the meaning of a claim and importing limitations from the specification into the claim can be a difficult one to apply in practice.” *Phillips*, 415 F.3d at 1323 (citing *Comark Commc’ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1186-87 (Fed. Cir. 1998)). Here, we are using the specification to more fully understand what the patentee claimed. *See id.* at 1315 (“[T]he best source for understanding a technical term is the specification from which it arose, informed, as needed, by the prosecution history.” (internal brackets and quotation marks omitted)). Throughout the ’767 patent, the inventors repeatedly emphasized that “A” in combination with other chemicals, forms a signalling moiety not that “A” itself can be a signalling moiety. Therefore, we are persuaded that the inventors were claiming only indirect detection.

The district court concluded, based on expert testimony, that example 9 in the specification was an example of direct detection; however, this argument was not raised by Enzo either in its briefing on appeal or during oral argument. Nevertheless, even if we were to consider the district court’s finding, which would be subject to review for clear error under *Teva*, this sole factual finding does not override our analysis of the totality of the specification, which clearly indicates that the purpose of this

invention was directed towards indirect detection, not direct detection.

The district court additionally relied upon claim differentiation to support its finding that the claims at issue cover both direct and indirect detection. *Enzo*, 2006 WL 2927500, at \*3. The district court found that dependent claims 67, 68, and 70 of the '767 patent involved direct detection and therefore independent claim 1 must not be limited to indirect detection. *Id.* However, dependent claims cannot broaden an independent claim from which they depend. *Curtiss-Wright Flow Control Corp. v. Velan, Inc.*, 438 F.3d 1374, 1381 (Fed. Cir. 2006) (“In the most specific sense, claim differentiation refers to the presumption that an independent claim should not be construed as requiring a limitation added by a dependent claim.” (citing *Nazomi Commc’ns, Inc. v. Arm Holdings, PLC*, 403 F.3d 1364, 1370 (Fed. Cir. 2005)) (internal quotation marks omitted)). Thus, as claim 1 is limited to indirect detection by its own plain meaning, it would be inappropriate to use the doctrine of claim differentiation to broaden claim 1 to include a limitation imported from a dependent claim, such as direct detection.

#### CONCLUSION

The district court erred in construing the disputed claims of the patent-in-suit to cover both direct and indirect detection. Accordingly, we reverse the district court’s claim construction, vacate the district court’s finding of infringement, and remand to the district court with instruction to determine, consistent with the analysis in this opinion, whether the accused product infringes.

#### **REVERSED-IN-PART, VACATED-IN-PART, AND REMANDED**

#### COSTS

Costs are awarded to Applera.

# United States Court of Appeals for the Federal Circuit

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INC., AND YALE UNIVERSITY,  
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v.

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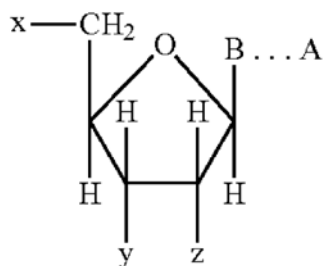
Appeal from the United States District Court for the  
District of Connecticut in No. 3:04-cv-00929-JBA, Judge  
Janet Bond Arterton.

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NEWMAN, *Circuit Judge*, dissenting.

The principal issue discussed by the panel majority is the construction of claim terms that determine whether Patent No. 5,449,767 covers direct detection of the signaling moiety, or only indirect detection. The distinction between direct and indirect detection is stated to be material to whether Applera infringes the '767 patent. The principal disputed term concerns the signaling structure represented by "A" in claim 1, and the meaning of "at least one component," here shown in boldface:

1. An oligo- or polynucleotide containing a nucleotide having the structure:

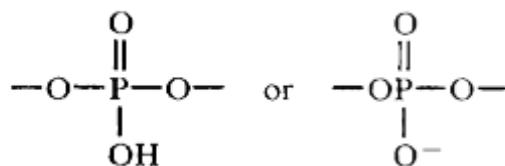


wherein B represents a 7-deazapurine or a pyrimidine moiety covalently bonded to the C1'-position of the sugar moiety, provided that whenever B is a 7-deazapurine, the sugar moiety is attached at the N<sup>9</sup>-position of the 7-deazapurine, and whenever B is a pyrimidine, the sugar moiety is attached at the N<sup>1</sup>-position of the pyrimidine;

wherein A comprises at least three carbon atoms and represents **at least one component** of a signaling moiety capable of producing a detectable signal;

wherein B and A are covalently attached directly or through a linkage group that does not substantially interfere with the characteristic ability of the oligo- or polynucleotide to hybridize with a nucleic acid and does not substantially interfere with formation of the signalling moiety or detection of the detectable signal, provided also that if B is 7-deazapurine, A or the linkage group is attached to the 7-position of the deazapurine, and if B is pyrimidine, A or the linkage group is attached to the 5-position of the pyrimidine;

wherein one of x and y represents





and the other of x and y is absent or represents –OH or –H; and wherein z represents H– or HO–.

'767 Patent col. 30 l. 48 to col 31 l. 21 (emphases added). The description of **A** in the specification includes the following introduction:

**A** may be any moiety which has at least three carbon atoms and is capable of forming a detectable complex with a polypeptide when the modified nucleotide is incorporated into a double-stranded duplex containing either deoxyribonucleic or ribonucleic acid.

**A** therefore may be any ligand which possesses these properties, including haptens which are only immunogenic when attached to a suitable carrier, but are capable of interacting with appropriate antibodies to produce complexes.

'767 Patent col. 8 ll. 4-14. The specification includes further detail and several specific examples.

#### DISCUSSION

The construction of the '767 claims is not new to this court. In the prior appeal, *Enzo Biochem Inc. v. Applera Corp.*, 599 F.3d 1325 (Fed. Cir. 2010), Applera had argued that **A** is not the whole signaling moiety, but only part of a multi-component signaling moiety. The district court had found that: “**A** . . . is one or more parts of a signaling moiety, which includes, in some instances, the whole signaling moiety.” *Id.* at 1330 (quoting *Enzo Biochem, Inc. v. Applera Corp.*, No. 3:04cv929, 2006 WL 2927500, at \*3 (D. Conn. Oct. 12, 2006)). My colleagues now hold that the district court’s claim construction is incorrect, now concluding that **A** cannot be the whole signaling moiety, as a matter of grammatical construction of the claim clause.

My colleagues hold that the clause “at least one component of a signaling moiety” requires, as a matter of linguistics, “that the signalling moiety is composed of multiple parts as the term ‘component’ in and of itself indicates a multipart system.” Maj. Op. at 11 (emphasis added). Thus the panel majority concludes that A can never “include[], in some instances, the whole signaling moiety,” contrary to the district court’s holding.

My colleagues err. The rules of grammar and linguistics, even in legal documents, do not establish that “at least one” means two or more. Also, precedent has spoken on this point and is directly contrary. See *Howmedica Osteonics Corp. v. Wright Med. Tech., Inc.*, 540 F.3d 1337, 1344 (Fed. Cir. 2008) (stating that “at least one” means “one or more”).

The district court construed “at least one” in accordance with not only grammatical logic, but also with the intrinsic record and the extrinsic evidence. The district court found that the specification includes a specific example of direct detection, citing the expert evidence:

[T]he expert evidence indicates that Example 9 could involve direct detection. See Reply Expert Report of Richard R. Sinden, Def. Ex. 13, ¶¶ 56, 57 (citing Kricka Report, Def. Ex. 10, ¶ 30). Thus, importing into Claim 1 only the examples of indirect detection from the specification would skew the full illustrative range of all examples, resulting in utilization of the specifications as “limitations” on Claim 1 rather than as aids for understanding technical terms.

*Enzo Biochem*, 2006 WL 2927500, at \*3. The district court also found that claims 67, 68 and 70 of the ’767 patent “teach direct detection, with ‘A compris[ing] an indicator molecule.’” *Id.* The district court observed that claim 67 of the ’767 patent “teaches that ‘A comprises an indicator molecule,’ and Claims 68 and 70 teach that ‘An

oligo- or polynucleotide of claim 67 where said indicator *is* fluorescent, electron dense, or an enzyme capable of depositing insoluble reaction products,' or '*is* selected from the group consisting of fluorescein and rhodamine.'" *Id.* at \*4. The district court stated that "in the context of all the dependent claims taken together, the Court sees no basis for inferring from the word 'comprise' in certain claims that A *must* have more than one component, as opposed to suggesting that A *may* have more than one component." *Id.* Applera's expert Dr. Kricka had so conceded on cross-examination, and the district court summarized, "the jury was entitled to credit Dr. Kricka's testimony that several parts of the original application disclosed compounds that allowed for direct detection." *Enzo Biochem, Inc. v. Applera Corp.*, No. 3:04cv929, 2013 WL 3965305, at \*8 (D. Conn. Aug. 1, 2013). These factual findings are entitled to deference, in accordance with the Court's instruction in *Teva Pharmaceuticals USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831 (2015).

My colleagues on this appeal do not point to any contrary evidence; they simply rule that grammar requires that if the signaling moiety is "at least one component" then there must be at least two components. From this, my colleagues rule that "claim 1 covers only indirect detection," Maj. Op. at 11, ignoring the testimony and the district court's findings and the jury verdict based on the evidence at trial.

In *Teva*, the Court established that, when construing claims, appropriate deference must be given to the findings of the district court. The district court received some conflicting testimony, along with concessions on cross-examination, from which the court concluded that "at least one component" may include "the whole signaling moiety." My colleagues show error of neither fact nor law in the court's findings and conclusions.

Grounds for reversal of the court's construction that the claims include direct as well as indirect detection have not been shown. From the panel majority's contrary ruling, I respectfully dissent.