United States District Court,
S.D. New York.

ENZO BIOCHEM, INC., et al,
Plaintiff(s).
v.
AMERSHAM PLC, et al,
Defendant(s).
Enzo Biochem, Inc., et al,
Plaintiff(s).
v.
Molecular Probes, Inc., et al,
Defendant(s).
Enzo Biochem, Inc., et al,
Plaintiff(s).
v.
Perkinelmer, Inc., et al,
Defendant(s).
Enzo Biochem, Inc., et al,
Plaintiff(s).
v.
Orchid Biosciences, Inc., et al,
Defendant(s).
Enzo Biochem, Inc., et al,
Plaintiff(s).
v.
Sigma-Aldrich Corporation, et al,
Defendant(s).
Affymetrix, Inc,
Plaintiff(s).
v.
Enzo Biochem, Inc., et al,
Defendant(s).
Enzo Life Sciences, Inc., et al,
Plaintiff(s).
v.
Affymetrix, Inc,
Defendant(s).
Roche Diagnostics GMBH, et al,
Plaintiff(s).
v.
Enzo Biochem, Inc., et al,
Defendant(s).

Nos. 02 Civ. 8448(JES), 03 Civ. 3819(JES), 04 Civ. 1555(JES), 03 Civ. 3816(JES), 03 Civ. 3820(JES), 04 Civ. 4046(JES), 03 Civ. 3817(JES), 03 Civ. 8907(JES)

July 10, 2006.

Background: Patentee filed infringement action against various alleged infringers of patents for the technology of labeling, hybridizing, and ultimately detecting nucleotides, and parties requested construction of patent claims.

Holding: The District Court, Sprizzo, J., held that court would construe patent claims.

So ordered.

4,707,440, 4,711,955, 4,994,373, 5,175,269, 5,241,060, 5,328,824, 5,449,767, 5,476,928. Construed.

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MEMORANDUM OPINION AND ORDER

SPRIZZO**, District Judge.**

At issue before the Court are the proper interpretations of fifteen claims covering eight different patents. Pursuant to this Court's function under Markman v. Westview Instruments, Inc., 517 U.S. 370, 372, 116

S.Ct. 1384, 134 L.Ed.2d 577 (1996), the following shall constitute the constructions of the relevant claims.

BACKGROUND

The patents at issue in this case involve the technology of labeling, hybridizing, and ultimately detecting nucleotides FN1-a processwhich is useful for, among other things, testing for the presence of diseases in a sample of blood. For the sake of ease, the eight patents can be conveniently divided into four groups.

FN1. A nucleotide is the basic building block of DNA and RNA. Naturally-occurring nucleotides are composed of a phosphate moiety, a pentose sugar moiety, and a nitrogenous base. There are four different bases in DNA-thymine, adenine, guanine, and cytosine. Nucleotides join together to form oligonucleotides (a few nucleotides) or polynucleotides (many nucleotides). To form the familiar double helix structure associated with DNA, each individual nucleotide binds with its complement, which is determined by the identity of the base. Thus, thymine binds with adenine, and guanine binds with cytosine. It is this unique sequence of complementary pairings which identifies, for instance, the genetic material found in an individual's blood or in a virus, such as the human immunodeficiency virus. As discussed *infra,* the ability to break open the double helix and introduce labeled complementary sequences makes the testing contemplated by the patents at issue in this case possible.

The "Ward patents," all of which share a common specification, are comprised of four patents the main purpose of which is to explain how to modify nucleotides by attaching a detectable label. *See, e.g.,* U.S. Patent No. 4,711,955 (filed May 23, 1983) col. 6, ll. 36-68, col. 7, ll. 1-17. Plaintiff, Enzo Biochem, Inc. and Enzo Life Sciences, Inc. ("Enzo" or "plaintiff"), FN2 has asserted claims 1 and 5 of the 4,711, 955 patent,FN3 claim 1 of the 5,328, 824 patent (filed Dec. 8, 1987), claim 42 of the 5,449, 767 patent (filed May 20, 1992), and claim 1 of the 5,476, 928 patent (filed Feb. 26, 1992) (collectively, "Ward patents").

FN2. Several of the actions considered here were brought as declaratory judgment actions against Enzo. For the sake of ease, however, Enzo will be referred to as "plaintiff," and all other parties, including declaratory judgment plaintiffs, will be referred to as "defendants."

FN3. After its initial citation, each individual patent will be referred to simply by the final three digits of its patent number.

The " '060 patent" is similar in technology and purpose to the Ward patents. *See* U.S. Patent No. 5,241,060 (filed June 4, 1990) col. 2, ll. 56-68, col. 3, ll. 1-64. Plaintiff has asserted claims 1, 2, and 3 of this patent.

The "formula patents," which share a common specification, are two patents which set forth a specific method of attaching a detectable signal to an oligo-or polynucleotide. *See, e.g.,* U.S. Patent No. 5,175,269 (filed Apr. 29, 1991) col. 3, ll. 21-40. Plaintiff has asserted claim 1 of the 4,707,440 patent (filed Jan. 30, 1984), and claims 1 and 4 of the 5,175,269 patent (collectively, "formula patents").

The final patent at issue is the " '373 patent." This patent "relates to a method for quantifiably detecting a targeted polynucleotide sequence in a sample of biological and/or nonbiological material employing a probe capable of generating a soluble signal." *See* U.S. Patent No. 4,994,373 (filed July 20, 1989) col. 1, ll. 15-18.

Plaintiff has asserted claims 1, 17, 18, and 25 of this patent.

After the parties briefed the issue of the proper construction of these claims, this Court held a five-day *Markman* Hearing that commenced on July 5, 2005. The Court heard testimony from plaintiff's expert, Dr. Gordon Hammes, and from defendants' experts, Dr. Michael Blackburn and Dr. George Stark. Following the Hearing, the Court accepted briefs and replies from all parties. The Court heard Oral Argument on September 30, 2005. On January 9, 2006, the parties submitted proposed claim construction orders.

DISCUSSION

[1] The interpretation of patent claims is a matter of law that is "exclusively within the province of the court" to decide. Markman, 517 U.S. at 372, 116 S.Ct. 1384. Recently, the en banc Federal Circuit, in Phillips v. AWH Corp., 415 F.3d 1303 (Fed.Cir.2005), offered definitive guidance to district courts as to how to carry out this function.

[2] [3] In *Phillips,* the Federal Circuit re-emphasized the principle that courts must interpret claim terms as having "the ordinary and customary meaning ... that the term would have to a person of ordinary skill in the art in question at the time of the invention." *Id.* at 1313. In making this determination, courts must consider claim terms "in the context of the entire patent," *id., see also id.* at 1314-15, and therefore should "focus [ ] at the outset on how the patentee used the claim term in the claims, specification, and prosecution history," *id.* at 1321, so as to avoid "unduly expansive" interpretations, *id.,* which encompass more than what the patentee actually invented, *id.* at 1316-17, 1321. At the same time, however, courts must be mindful not to "read[ ] limitations from the specification into the claim," *id.* at 1323, since the specification is designed to "provide [the] best mode" for using the invention but is not meant to cover every claimed embodiment, *id.*

[4] In addition, *Phillips* indicated that, while not as reliable, extrinsic evidence, including the testimony of experts, may be used by courts to provide a tutorial in the field of the invention and to "help the court determine what a person of ordinary skill in the art would understand claim terms to mean." *Id.* at 1317-19. Because claim construction is a matter for the court, however, the testimony of experts, as well as the arguments of parties and their counsel, can be completely ignored by the court in its discretion. *Id.; see also* Markman v. Westview Instruments, Inc., 52 F.3d 967, 983 (Fed.Cir.1995), *aff'd,* 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996).

The following shall constitute the Court's constructions of the claims at issue in these actions.FN4

FN4. Where possible, disputed terms in the asserted claims will be underlined.

A. Ward Patents

'955 Patent

As stated above, plaintiff has asserted claims 1 and 5 of the '955 patent.

Claim 1 provides:

A nucleotide or oligo- or polynucleotide sequence comprising at least one of a moiety having the structure - BA: FN5

FN5. Throughout this litigation, all parties have proceeded as if the term "-BA" in fact appears at the end of the preamble to claim 1 of the '955 patent. The preamble appearing in Plaintiff's Exhibit 1, a copy of which was provided to the Court, however, reads as follows: "A nucleotide or oligo- or polynucleotide sequence comprising at least one moiety having the structure:." Based on the assumptions made by the parties, and on the fact that no sense can be made of claim 1 without the inclusion of the term "-BA," this Court will assume that the omission was inadvertent and will proceed as if the term appeared in the preamble.

wherein B represents a 7-deazapurine or pyrimidine moiety;
wherein A represents a moiety selected from the group consisting of biotin and iminobiotin;

provided that if B is a 7-deazapurine, A is attached to the 7-position of the deazapurine, and if B is a pyrimidine, A is attached to the 5-position of the pyrimidine, A being attached to B directly or through a linkage group, *said linkage group not interfering substantially with the characteristic ability of A to form a detectable complex* with one of avidin, streptavidin or antibodies to biotin or iminobiotin.

[5] Although all parties agree that a naturally-occurring nucleotide is comprised of a phosphate group, a pentose sugar,FN6 and a nitrogenous base, *see* Hr'g Tr. at 385, 643, 786, plaintiff contends that claim 1 of the '955 patent does not require the presence of a pentose sugar (or for that matter a phosphate group) because the claim does not specifically call for the presence of those structures and because the patent as a whole is directed not to naturally-occurring nucleotides but rather to "modified nucleotides" or "nucleotide analogs," Pl.'s Proposed Order at 9.

FN6. A pentose sugar is a sugar molecule composed of five carbon atoms in a ring structure.

This Court cannot agree. Although the patent is concerned with modified nucleotides, when read as a whole it is clear that the modification contemplated is the addition of the "A" group, which serves as a label or probe,FN7 to the base of the nucleotide. *See, e.g.,* Hr'g Tr. at 169-70, 752. This is made abundantly clear by the "Detailed Description of the Invention." That segment of the patent lists several "essential criteria [that] must be satisfied in order for a modified nucleotide to be generally suitable as a substitute for a radioactively-labeled form of a naturally occurring nucleotide. " '955 patent col. 6, ll. 36-39. Each of those criteria concern "the probe," including its positioning, qualities, and characteristics. Id. at col. 6, ll. 39-68, col. 7, ll. 1-17. There is simply no support in the patent for any modifications other than the contemplated addition of a label to the base.

FN7. As discussed infra, because the polynucleotide sequences at issue are far too small to be visible, *see, e.g.,* Hr'g Tr. at 516, the addition of a label to the nucleotide is necessary in order to determine if hybridization with its complementary nucleic acid sequence has occurred.

Similarly, plaintiff's contention that the claim does not specifically call for a pentose sugar is unpersuasive. The claim is directed to a "nucleotide or oligo- or polynucleotide sequence," which is a structure that, absent clear indication otherwise, requires phosphate groups and pentose sugars. Although patentees can define terms in their patents as they wish, *see* Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed.Cir.1996), this patent offers no definitions that would supplant the ordinary meanings of these terms as

understood by a person of ordinary skill in this field at the time of the invention. *See, e.g.,* Hr'g Tr. at 391-92.FN8 Therefore, this claim requires that the "nucleotide or oligo- or polynucleotide sequence" at issue be comprised of otherwise naturally-occurring nucleotides which have been modified solely by the addition of at least one label "A" to a nitrogenous base "B." FN9

FN8. In addition, defendants point out that plaintiff, in prosecuting a patent with the same specification as the '955 patent and a claim similar to claim 1, told the Patent and Trademark Office that "[a]n oligo-or polynucleotide by definition has a defined sugar ring structure. Depiction of a ring structure in claim 190, it is respectfully submitted, is unnecessary and would be redundant." Defs.' Ex. 58, Tab 17, at 14. According to the Federal Circuit, these statements are relevant to the construction of the claim at issue, *see* Microsoft Corp. v. Multi-Tech Sys., Inc., 357 F.3d 1340, 1349-50 (Fed.Cir.2004), and they further support this Court's construction.

FN9. Plaintiff argues that this construction is foreclosed by the principle of claim differentiation, because, according to plaintiff, claim 5 of the '955 patent is identical to the Court's construction of claim 1. Claim 5, however, contains a series of elements, "X," "Y," and "Z" which must be attached to the pentose sugar moiety and which are not discussed in claim 1. As such, the pentose sugar moiety present in claim 1 need not contain these elements and therefore plaintiff's argument is unpersuasive.

[6] The second disputed term in claim 1 of the '955 patent is its restriction that the linkage group which can be used to link "A" to "B" "not interfer[e] substantially with the characteristic ability of A to form a detectable complex." Although the parties have argued extensively over the proper interpretation of this term, it is clear to the Court that the claim language contemplates that the linkage group can cause some interference, but that it cannot completely prevent the formation of a detectable complex or cause other considerable levels of interference. Having thoroughly considered the claim language in the context of the entire patent, the Court concludes that the only reasonable interpretation of the term is that the use of linkage groups which make it more likely than not that "a complex with one of avidin, streptavidin or antibodies to biotin or iminobiotin" will not form, or that, once formed, such a complex will not be "detectable" are not covered by the language of this claim.FN10

FN10. Avidin and streptavidin are polypeptides that form tight bonds with biotin and iminobiotin.

The only disputed language in claim 5,FN11 that "said linkage group not interfering substantially with the characteristic ability of A to form a detectable complex with one of avidin, streptavidin or antibodies to biotin or iminobiotin," is identical to the language in claim 1 and therefore is construed in the same fashion.

FN11. The parties also seemingly dispute whether the compound depicted in claim 5 of the '955 patent is necessarily limited to representing a monomer. In the proceedings before this Court, that issue was discussed in the context of claim 1 of the '928 patent. Since the resolution of that dispute is identical to both claims, the Court will discuss it infra during the discussion of the '928 patent.

'824 Patent

Plaintiff has asserted claim 1 of the '824 patent. In relevant part that claim provides:

A method of detecting the presence or absence of a nucleic acid in a sample which comprises the steps of ...

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

wherein B and A are covalently attached directly or indirectly through a linkage group, *said linkage group not interfering substantially with the characteristic ability of said compound to hybridize with said nucleic acid or of A to be detected....*

[7] The first area of disagreement with regard to claim 1 is whether "A" could, as plaintiff claims, be the sole component of the signaling moiety and therefore operate alone as a directly detectable signal.FN12 This Court agrees with defendants that the patent does not allow for such a construction.

FN12. In short, if "A" itself could be detected then it would comprise a directly detectable signal. An indirectly detectable signal would result where the component which later attached itself to "A" was responsible for the generation of the detectable signal. *See, e.g.,* Defs.' Post-Hr'g Brief at 21.

The claim language simply does not support plaintiff's position. "A" is described as "at least one component of a signalling moiety," indicating that the signaling moiety must be comprised of multiple constituent elements, of which "A" is one. In addition, the patent specification repeatedly describes "A" as "capable of forming a detectable complex with a polypeptide" such as avidin and streptavidin. *See, e.g.,* '824 patent col. 1, ll. 55-68, col. 3, ll. 1-28, 47-53, col. 5, ll. 32-37, 57-62, col. 7, ll. 26-31, col. 8, ll. 3-53, col. 18, ll. 1-57. Given the language of the claim and the description in the patent specification, it is clear to this Court that "A" is but one component of a multi-component signaling moiety capable of indirect detection via an attached polypeptide.

The second area of dispute in claim 1 of the '824 patent is the "interfering substantially" language that was at issue in claims 1 and 5 of the '955 patent. The Court adopts the same construction for this claim as it did for those.

'767 Patent

Plaintiff has asserted claim 42 of this patent. Claim 42 provides:

An *oligo- or polynucleotide sequence comprising at least one of a moiety having the structure:*

-BA

wherein B represents a 7-deazapurine or a pyrimidine moiety suitable for incorporation into a polynucleotide and;

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

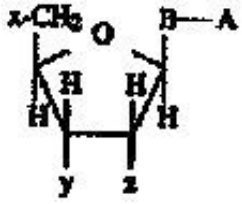
wherein B and A are covalently attached directly or through a linkage group *that does not substantially interfere with the characteristic ability of the sequence to hybridize with a nucleic acid and does not substantially interfere with formation of the signalling moiety or detection of the detectable 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.

The three disputed elements of this claim are interpreted identically to their counterparts in claim 1 of the '955 patent and claim 1 of the '824 patent.

'928 Patent

Claim 1 of this patent has been asserted in this case. Claim 1 provides:

A compound useful as a probe for detecting the presence or absence of a nucleic acid, *said compound having the structure:*

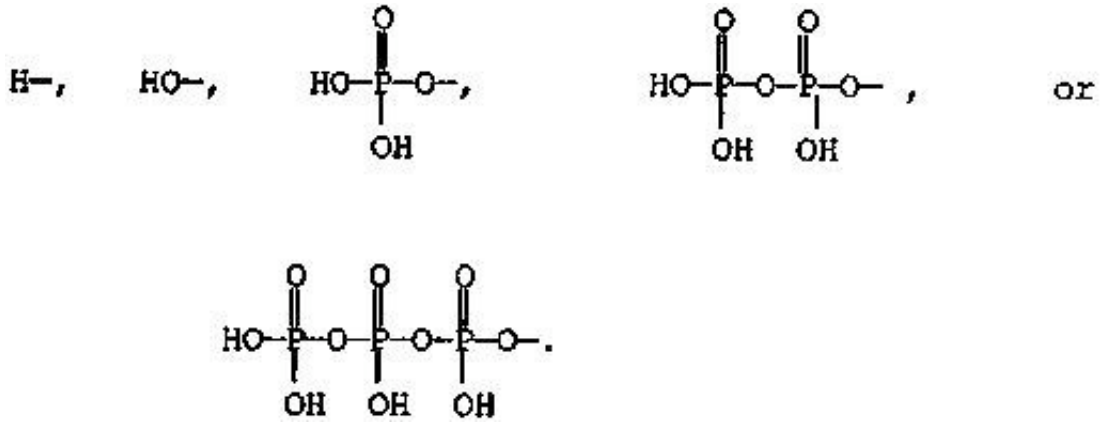


wherein B represents a purine, 7-deazapurine, or pyrimidine moiety suitable for incorporation into a polynucleotide and covalently bonded to the C^1-position of the sugar moiety, provided that when B is a purine or 7-deazapurine, the sugar moiety is attached at the N^9-position of the purine or deazapurine, and when B is pyrimidine, the sugar moiety is attached at the N^1 position of the pyrimidine;
wherein A represents at least three carbon atoms and an indicator molecule selected from the group consisting of fluorescent dyes, electron-dense reagents, enzymes which can be reacted with a substrate to produce a visually detectable reaction product, and radioisotopes;

wherein B and A are covalently attached directly or through a linkage group, *said linkage group not interfering substantially with detection of A;*

wherein if B is purine, A is attached to the 8-position of the purine, if B is a 7-deazapurine, A is attached to the 7-position of the deazapurine, and if B is pyrimidine, A is attached to the 5-position of the pyrimidine; and

wherein each of x, y, and z represents:



[8] The parties dispute whether the compound depicted in claim 1 is necessarily a monomer FN13 and whether such compound is capable of being linked together with other such compounds to form an oligoor polynucleotide sequence. As can be seen by looking at the diagram for the "x," "y," and "z" components of the compound, each possibility has only one dash that is not already linked to another atom.FN14 These dashes, which represent the number of valences (or electrons) that each atom has available to share, dictate the number of bonds that can be formed by each grouping. Since each of "x," "y," and "z" have only one open valence remaining, it follows that each can link to the compound at the positions depicted in the claim but they cannot link to any additional compounds. *See, e.g.,* Hr'g Tr. at 241, 676.FN15

FN13. A monomer is a "stand-alone molecule." *See, e.g.,* Hr'g Tr. at 676.

FN14. The unattached dash is located at the end of each compound given as a possibility for "x," "y," or "z."

FN15. That is, the "x" compound has one open valence available with which to bind to "CH_2" at the position shown, and the "y" and "z" compounds each have one open valence to bind to their respective positions on the pentose sugar moiety depicted in the claim. Without additional open valences, however, it would be impossible for the entire compound to bind with other compounds.

Plaintiff argues that, despite the unambiguous language of the claim terms, the claim nonetheless contemplates "opening up" some of the valences to allow the compound to be incorporated into a polynucleotide. *See, e.g.,* id. at 242. To support this assertion plaintiff argues that the compound's usefulness as a probe would be frustrated if it were construed as a monomer, *see* Pl.'s Post-Hr'g Brief at 19-20, and points to the language in the claim that element "B" is "suitable for incorporation into a polynucleotide."

This Court cannot agree. Although confining the compound in claim 1 to a monomer may well limit its use, *but see* Hr'g Tr. at 422-23, this Court is constrained by the clear import of the claim language. According to Dr. Blackburn, in order to convert the monomer represented in claim 1 into a compound capable of being incorporated into a polynucleotide sequence, it would need "to be changed in a very significant way" and approximately thirty percent of the atoms depicted would need to be removed-something clearly not

contemplated by the language of the claim. *See* Hr'g Tr. at 677-78. Furthermore, when claim 1 is contrasted with claim 2 of the patent it becomes clear that if the claim was meant to cover a compound that could be incorporated into a polynucleotide sequence, the claim language itself would reflect this. In claim 2, the "x" and "y" elements are depicted with two open valences, thus allowing the entire compound to be incorporated into a polynucleotide sequence.FN16 Finally, plaintiff's reliance on the "suitable for incorporation into a polynucleotide" language is misplaced, as that language refers to "B" and not the entire compound at issue.

FN16. In relevant part, claim 2 of the '928 patent states that "one of x and y represents:



and the other of x and y is absent or represents -OH or -H." As can be seen, these compounds have two open valences-one at the beginning and one at the end of the depictions.
The second area of dispute in this claim is the familiar "interfering substantially" term which this Court has already addressed in previous claims.

B. '060 Patent

Plaintiff has asserted claims 1, 2, and 3 of this patent.FN17 Claim 1 provides:

FN17. Claims 2 and 3 of the '060 patent require no construction independent of the construction given to claim 1.

A nucleotide having the formula PM-SM-BASE-Sig wherein PM is a phosphate moiety, *SM is a sugar moiety,* BASE is a pyrimidine, purine or 7-deazapurine moiety, PM being attached at the 3' or the 5' position of SM when the nucleotide is a deoxyribonucleotide and at the 2', 3' or 5' when the nucleotide is a ribonucleotide, BASE being attached to the 1' position of SM from the N^1 position when BASE is a pyrimidine or the N^9 position when BASE is a purine or a 7-deazapurine, and Sig is covalently attached to BASE at a position other than the C^5 position when BASE is a pyrimidine, at a position other than the C^8 position when BASE is a purine and at a position other than the C^7 position when BASE is a 7-deazapurine and wherein Sig represents a detectable moiety.
[9] As discussed above, all parties agree that naturally-occurring nucleotides require a phosphate moiety, a pentose sugar, and a nitrogenous base. The question before the Court is whether claim 1 of the '060 patent similarly requires the presence of a pentose sugar moiety. This Court finds that it does not.

Although defendants presented no testimony at the *Markman* Hearing regarding this patent and have essentially contended that the same analysis applies to this patent as to the Ward patents, *see, e.g.,* Defs.'

Proposed Order at 20, this Court cannot agree. While the specification of the Ward patents made it clear that its understanding of "modified nucleotides" was limited to modifications attaching a label to the base of the nucleotide, the specification of the '060 patent teaches that "derivatives of mono, oligo and polysaccharides are also useful in the preparation of the special nucleotides of this invention" and can be used as either "the sugar S(SM) or as the Sig moiety thereof." '060 patent col. 30, ll. 40-58. In addition, the specification provides a unique definition of the term nucleotide: "[t]he special nucleotides of this invention include a phosphoric acid P moiety ..., a sugar *or* monosaccharide S moiety ..., a base B moiety ..., a purine or a pyrimidine and a signalling chemical moiety Sig covalently attached thereto ..." Id. at col. 20, ll. 45-51 (emphasis added). Therefore, this Court finds that a person of ordinary skill in the art would have understood the "sugar moiety" called for in claim 1 to encompass "mono, oligo and polysaccharides" and "derivatives" thereof so long as those moieties had the structures necessary to make the required connections specified by the claim.

C. Formula Patents

'440 Patent

Plaintiff has asserted claim 1 of the '440 patent. In relevant part, claim 1 provides:

A detectable molecule of the formula

A^3-(-X-R^1-E-Det^b)$_m$

where

A^3 is an *oligo- or polynucleotide* having at least one modifiable reactive group consisting of amino, hydroxy, cis OH, halide, aryl, imidazoyl, carbonyl, carboxyl, thiol or a residue comprising an activated carbon;

-Xis selected from the group consisting of

-NH-CO-, -NH-C(NH)-, -N=N-, -NHSO$_2$-, -OSO$_2$-, -NH-N =N-, -NH-CH$_2$(O)-NH-, -CH$_2$-NH, -O-CO-, -NH-CO-CH$_2$-S-, -NH-CH$_2$-, -O-CO-CH$_2$-, -O-CO-NH-, and -S-CH$_2$-; ... FN18

FN18. Claim 1 of the '440 patent contains a more accurate recitation of the "X" structures which includes the spatial orientation and location of double bonds. Regrettably, the parties did not provide the Court with electronic versions of these depictions for use in this Opinion.

[10] The first issue to be addressed is the familiar question of whether a pentose sugar moiety is required in the "oligo- or polynucleotide" of claim 1. Plaintiff argues that the definitions of the terms "polynucleotide" and "polysaccharide" contained in the specification compel the conclusion that claim 1 does not require the presence of a pentose sugar moiety. *See* Pl.'s Proposed Order at 18. The specification provides that "[b]y 'polynucleotide' is meant to include both polyribonucleotides, polydeoxyribonucleotides, or anypolypurine [sic], poly-pyrimidine or analogue, or combinations thereof, " '440 patent col. 6, ll. 27-30, and that "[b]y 'polysaccharide' is meant to include any polysaccharide either naturally or non-naturally occurring, linear, non-linear or crosslinked ...," id. col. 6, ll. 38-40.

This Court finds that insofar as "polypurines" or "poly-pyrimidines" have pentose sugars that can be modified in forming an "analogue" of those structures, there is no pentose sugar requirement when these structures are used as the "polynucleotide" at issue in claim 1. However, there is no support for the proposition that the pentose sugar moieties present in "polyribonucleotides" or "polydeoxyribonucleotides" can be altered in any way. Rather, the standard understanding of those terms, which include pentose sugar moieties, applies to this claim. Finally, the Court finds that plaintiff's reliance on the definition of "polysaccharide" in the patent is misplaced. While that term, as defined by the patent, explicitly includes "non-naturally occurring" sugar moieties, it is never used in connection with the sugar moiety element of "polynucleotide" but rather is used to describe an alternative structure that can serve as A^3. *See* id. at col. 7, ll. 25-29, 60-66.

[11] The second dispute regarding this claim is the orientation of the chemical groups provided for as "X." A related issue is the nature of the bonds between the various components that comprise the molecule "A^3-(-X-R^1-E-Det^b)$_m$." FN19

FN19. There was also much discussion at the *Markman* Hearing about whether intervening structures could be placed between the various components, despite plaintiff and its expert repeatedly indicating that this was not an issue. *See* Hr'g Tr. at 278-79; Pl.'s Post-Hr'g Brief at 22 n. 22. Regardless, for the record, the Court finds that the claim does not allow intervening structures since allowing such structures would undermine the claim language and infinitely expand the scope of the claim.

Given the plain language of the claim, this Court finds that the chemical groups provided for as "X" must be oriented as pictured in the claim, with the left-most element attached to "A^3" and the right-most element attached to "R^1." This conclusion is supported by the claim's listing of one of the groups-"-NH-CH_2-"-in both directions. Additional support is provided by Dr. Blackburn's testimony stating that flipping the orientation of the groups would lead to compounds with "quite different" chemical properties. *See* Hr'g Tr. at 617.

[12] The last remaining issue is the nature of the bonds between the components, as represented by the solid lines between "A^3," "X," "R^1," "E," and "Det^b." The Court heard testimony from both experts explaining that outside the realm of chemical formulas, a solid line need not necessarily represent only covalent bonds.FN20 *See, e.g., id.* at 277-80, 704-07, 711-26. Here, both experts agreed that the formula represented by "A^3-(-X-R^1-E-Det^b)$_m$" is not a standard chemical formula but rather a "descriptive" or "modular" formula. *See id.* at 277, 706. Because the patent itself never restricts the solid lines to the representation of covalent bonds, and because dependent claim 3, which specifically calls for "covalent coupling," teaches that the solid lines are not inherently limited to representing covalent bonds, *see* Phillips, 415 F.3d at 1324-25, this Court finds that the solid lines may include covalent as well as non-covalent bonds, including, for example, hydrogen bonds, *see, e.g.,* Hr'g Tr. at 278.

FN20. A covalent bond is formed when two atoms share electrons. *See, e.g.,* Hr'g Tr. at 278. Hydrogen bonding, which is a form of non-covalent bonding, tends to result in a weaker bond. *See id.*

'269 Patent

Claims 1 and 4 of the '269 patent have been asserted by plaintiff. Claim 1 provides, in relevant part:

A compound of the formula

A^3-(-X-R^1-E-)$_m$

where

A^3 is an *oligo- or polynucleotide* having at least one modifiable reactive group consisting of amino, hydroxy, cis OH, halide, aryl, imidazoyl, carbonyl, carboxyl, thiol or a residue comprising an activated carbon where the modifiable group is contained within or attached to a sugar or a phosphate moiety;

-Xis selected from the group consisting of:

-NH-CO-, -NH-C(NH)-, -N=N-, -NH-SO_2-, -OSO_2-, -NH-N=N-, -NH-CH_2-, -CH_2-NH-, -O-CO-, -NH-CO-CH_2-NH-, -O-CO-CH_2-, -S-CH_2-, -O-CO-NH-; ...

For purposes of this claim construction, the relevant portions of claim 4 of the '269 patent are identical to claim 1, with the exception that the subject of claim 4 is "[a] detectable molecule of the formula A^3-(-X-R^1-E-Det^b)$_m$."

For the reasons stated above, the disputed terms of claims 1 and 4 of the '269 patent are given the same interpretations as those terms are given in claim 1 of the '440 patent.

D. '373 Patent

Plaintiff has asserted claims 1, 17, 18, and 25 of this patent.FN21 Claim 1 provides:

FN21. Claims 17, 18, and 25 require no claim constructions independent of that given to claim 1.

A method for *detecting a polynucleotide sequence* which comprises:
fixing said polynucleotide sequence to a solid support which comprises or is contained within a transparent or translucent, non-porous system, such that a single-strand of the polynucleotide is capable of hybridizing to complementary nucleic acid sequences;

forming an entity comprising said polynucleotide sequence hybridized to a polynucleotide or oligonucleotide probe, said probe having attached thereto a chemical label further comprising a signalling moiety capable of generating a *soluble signal;* and *generating and detecting said soluble signal*.

[13] In brief, the technology at issue in this patent involves the determination of whether substances, described as "analytes," are present in biological or non-biological samples, such as "blood[,] urine, feces, saliva, pus, semen, serum, other tissue samples, fermentation broths, culture media, and the like." '373 patent col. 5, ll. 22-27. Detection of these substances is accomplished by "denaturing" strands of DNA or

RNA found in the sample, such that these normally two-stranded molecules are separated into single-stranded form. *See* id. at col. 5, ll. 37-41. The single-stranded DNA or RNA of the sample is then attached to a solid surface, and a probe, which is single-stranded DNA or RNA sequence complementary to the analyte, is introduced. If the analyte is present in the sample, then the probe will bind, or hybridize, to the sample. Detection is accomplished by washing away unhybridized probes and then searching for the presence of the labeled probe using a variety of techniques. *See* id. at col. 5, ll. 58-68, col. 6, ll. 1-8.

All parties agree that it is possible for the test just described to be conducted by attaching unlabeled single-stranded probes to the solid surface and then introducing labeled strands of the sample. If the sample contains DNA or RNA complementary to the probe (that is, if the analyte is present in the sample), then hybridization will occur and the same steps will be taken to detect the presence of the label. *See, e.g.,* Hr'g Tr. at 308, 520-21.

The question before the Court is whether claim 1 of the '373 patent contemplates conducting the test using the latter process described, i.e., attaching the probe to the solid surface. This Court finds that it does not.

The language of claim 1 indicates that "a polynucleotide sequence" is fixed to a "solid support" and "hybridized to a polynucleotide or oligonucleotide probe." Although plaintiff is correct that this language is theoretically broad enough to encompass conducting the test in either of the above fashions, FN22 the patent specificationcontains definitions which necessarily limit the claim to the method whereby the sample, and not the analyte's complementary sequence, is fixed to the solid support. The patent defines "probe" as "[a] *labelled* polynucleotide or oligonucleotide sequence which is complementary to a polynucleotide or oligonucleotide sequence *of a particular analyte* and which hybridizes *to said analyte sequence*." '373 patent col. 1, ll. 42-45 (emphasis added). "Analyte," which is defined as "[a] substance or substances, either alone or in admixtures, whose presence is to be detected," id. at col. 1, ll. 28-30, is described as possibly being present in "any biological or non-biological sample" including blood, urine, and saliva, id. at col. 5, ll. 22-26. It is thus clear from these descriptions that the "probe" in claim 1 cannot be the sample, but, rather, is the sequence complementary to the analyte. In addition, because the patent requires that the probe be labeled, it would be impossible to conduct this test with the probe fixed to the solid support, since to do so would result in false positives. *See, e.g.,* Hr'g Tr. at 520, 539-40. Therefore, this Court finds that claim 1 of the '373 patent requires that the sample, which is the substance within which one is looking for the presence of the analyte, must be fixed to the solid support, and that the probe, which is a labeled sequence complementary to the analyte, is not so fixed.FN23

FN22. The reason for this is, quite simply, that the labeled sample could be thought of as acting as a "probe" when the sequence complementary to the analyte is fixed to the solid support. In effect, the labeled sample would look for its complementary sequence and hybridization (and later detection) would reveal the analyte's presence.

FN23. Plaintiff's argument that example 5 compels a contrary construction is unpersuasive. Although that example indicates that "[t]he advantages of this invention are also obtainable when the probe is immobilized on a non-porous plastic surface," as explained above, the language of the patent places that setup for the test outside the scope of claim 1.

[14] The second dispute regarding this claim is the meaning of the term "soluble signal." Plaintiff claims

that the patent's description of "insoluble 'signals' " as "precipitates, certain fluorescers, and the like, " '373 patent col. 4, ll. 40-42, as well as its references to prior art, *see* id. at col. 4, ll. 45-64, compel the conclusion that the term "soluble signal," as used in claim 1 of the '373 patent, "is any signal, including light, that does not form a precipitate," Pl.'s Proposed Order at 24.

This Court cannot agree. First, the definition relied on by plaintiff is ambiguous, since it defines "insoluble signals" to include "*certain fluorescers, and the like*." '373 patent col. 4, ll. 40-42 (emphasis added); *see* Hr'g Tr. at 340-43. Second, even if this definition provided definitive guidance as to the scope of the term "insoluble signal" as used in the patent, it is nonetheless not a definition of what the patentee meant by the term at issue in this case-"soluble signal." Given that the patent does not provide a unique definition for "soluble signal," the Court must look to the patent as a whole, which supports the conclusion that this term was meant to have its ordinary meaning to a person skilled in the art.FN24

FN24. As Dr. Stark pointed out, the term itself is something of a non sequitur, because "solubility is a property of compounds, and a signal, particularly in the context of this patent, is light, and it does not make any sense whatsoever to talk about whether light is soluble." Hr'g Tr. at 541-42.

"Soluble" is generally understood to mean dissolved, or uniformly dispersed, in solution. *See, e.g.,* Hr'g Tr. at 542; *Merriam-Webster Dictionary* 655 (1974). The language of the '373 patent embraces this definition, as it describes a system whereby an enzyme or other reagent reacts with a chromogen or substrate to produce a product dissolved in solution that makes its presence known by fluorescing or creating a color change which can be "measured by a spectrophotometer or the like." *See* '373 patent col. 6, ll. 4-65, col. 7, ll. 7-36, col. 8, ll. 50-56. Contrary to the position of plaintiff and its expert, a fluorescent signal that originated from a tethered molecule within the solution simply would not meet this definition.FN25 Such a signal would not result from a soluble product, as the origin of the signal would not be uniformly dispersed throughout the solution.FN26

FN25. The prior art references cited in the patent do not teach to the contrary. *See, e.g.,* Hr'g Tr. at 335-36, 553-57.

FN26. The Court found particularly unpersuasive Dr. Hammes' testimony stating that a tethered signal could be considered uniformly distributed if one re-defined the "solution" to include only that area directly surrounding the tethered molecule. *See* Hr'g Tr. at 367-69. Such a definition finds no support in the patent, and it is certainly inconsistent with the ordinary understanding of "solubility."

The Court's conclusion finds further support in representations made to the Patent and Trademark Office by plaintiff while prosecuting a patent with the same specification as the '373 patent. At that time, plaintiff represented that "[w]ith soluble signals as set forth in the instant invention, the signal is not localized....Indeed, with the generation of a soluble signal, a dispersed or scattered signal is obtained." Decl. of Sandy Choi, dated June 17, 2005, Ex. O at 36-37. As discussed above, such representations are relevant to the construction of the claim at issue, *see* Microsoft Corp. v. Multi-Tech Sys., Inc., 357 F.3d 1340, 1349-50 (Fed.Cir.2004), and they further support this Court's construction.FN27 Therefore, as discussed above, this Court finds that "soluble signal" as used in claim 1 of the '373 patent requires a soluble product which generates a detectable signal. As such, tethered fluorescent molecules and other signals generated by non-

dissolved molecules are outside the scope of this claim.

FN27. Contrary to defendants' repeated representations to this Court that plaintiff's statements on related patents are "binding," *see* Defs.' Post-Hr'g Brief at 10; Defs.' Post-Hr'g Reply at 3, the Court in *Microsoft Corp*. clearly held that such statements are "relevant" but are not binding, *see* Microsoft Corp., 357 F.3d at 1349-50.

CONCLUSION

In sum, the Court finds that:

Claim 1 of the '955 patent and claim 42 of the '767 patent require that the "nucleotide or oligo- or polynucleotide sequence" at issue be comprised of otherwise naturally-occurring nucleotides which have been modified solely by the addition of at least one label "A" to a nitrogenous base "B";

Claims 1 and 5 of the '955 patent, claim 1 of the '824 patent, claim 42 of the '767 patent, and claim 1 of the '928 patent exclude the use of linkage groups which make it more likely than not that "a complex with one of avidin, streptavidin or antibodies to biotin or iminobiotin" will not form, or that, once formed, such a complex will not be "detectable";

Claim 1 of the '824 patent and claim 42 of the '767 patent require that "A" be one component of a multi-component signaling moiety capable of indirect detection via an attached polypeptide;

Claim 1 of the '928 patent and claim 5 of the '955 patent specify a compound which is necessarily limited to being a monomer;

Claims 1, 2, and 3 of the '060 patent encompass nucleotides whose sugar moiety can be "mono, oligo and polysaccharides" and "derivatives" thereof so long as those moieties have the structures necessary to make the required connections specified by the claims;

Claim 1 of the '440 patent and claims 1 and 4 of the '269 patent allow for "analogues" of "polypurines" and "polypyrimidines," including, for example, the modification of any pentose sugar moieties present in those compounds, but do not allow for any such modification to "polyribonucleotides" or "polydeoxyribonucleotides";

Claim 1 of the '440 patent and claims 1 and 4 of the '269 patent require that the chemical groups provided for as "X" be oriented as pictured in the claims, with the left-most element attached to "A^3" and the right-most element attached to "R^1";

Claim 1 of the '440 patent and claims 1 and 4 of the '269 patent allow for covalent as well as for non-covalent bonds between the components in the "descriptive" or "modular" formulas "A^3-(-X-R^1-E-Det^b)$_m$" and "A^3-(-X-R^1-E-)$_m$";

Claims 1, 17, 18, and 25 of the '373 patent require that the sample, which is the substance within which one is looking for the presence of the analyte, must be fixed to the solid support, and that the probe, which is a

labeled sequence complementary to the analyte, cannot be so fixed; and

Claims 1, 17, 18, and 25 of the '373 patent require, in their use of "soluble signal," the creation of a soluble, or uniformly dispersed, product which generates a detectable signal.

It is SO ORDERED.

S.D.N.Y.,2006.
Enzo Biochem, Inc. v. Amersham PLC

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