

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SHANGHAI HONGENE BIOTECH CORPORATION,

Petitioner,

v.

CHEMGENES CORPORATION,

Patent Owner.

IPR2023-00875
U.S. Patent No. 8,309,707 B2

**PATENT OWNER'S MOTION TO AMEND CLAIMS
UNDER 37 C.F.R. § 42.121**

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I. INTRODUCTION

The challenged Claims of U.S. Patent No. 8,309,707 (“the ’707 Patent”) are directed to innovative compounds useful for synthesis of RNA in the reverse 5' → 3' direction. More specifically, the Claims are directed to new types of 3'-dimethoxytrityl (DMT)-5'-cyanoethyl (CE) ribonucleoside phosphoramidites, which can be used to synthesize high purity RNA in the reverse 5' → 3' direction. Independent Claims 1 and 2 each encompass a genus of compounds. This Motion to Amend proposes to narrow the scope of Claims 1 and 2 to delete species from the recited genera. Such narrowing amendments are fully supported by the ’707 Patent and its priority application and are not anticipated by or rendered obvious by Petitioner’s cited prior art.

II. STATEMENT OF RELIEF REQUESTED

Patent Owner respectfully requests that the Board grant this Motion to Amend and substitute challenged Claims 1 and 2 with the claims presented in **Appendix A**.

Further, Patent Owner requests that the Board issue preliminary guidance on this Motion. See Notice Regarding a New Pilot Program Concerning Motion to Amend Practice and Procedures in Trial Proceedings under the America Invents Act before the Patent Trial and Appeal Board, 84 Fed. Reg. 9,497 (Mar. 15, 2019) (providing a patent owner with the option to receive preliminary guidance from the

Board on its motion to amend) (“Notice”); *see also* 35 U.S.C. § 316(d) (2018); 37 C.F.R. § 42.121 (2019).

III. THE SUBSTITUTE CLAIMS SATISFY 37 C.F.R. § 42.121

Patent Owner hereby respectfully submits and requests admittance and entry of this Motion to Amend and “Substitute Claims” 4 and 5 are presented herewith under the provisions of 35 U.S.C. § 316(d) and 37 C.F.R. 42.121. Specifically, Patent Owner has submitted: (1) only a single respective Substitute Claim for each of the two claims (Claims 1 and 2) that were originally issued; (2) Substitute Claims that narrow the scope of the originally issued claims, and thus meet the requirement of not enlarging the scope of the claims; (3) proposed Substitute Claims that are fully supported by the original disclosure of the patent as shown herein; and (4) amended Substitute Claims responsive to grounds of unpatentability set forth by both the Petitioner in its Petition as well as the same or very similar grounds set forth by the Board in its Decision to Institute.

A. The Number of Substitute Claims is Reasonable.

Petitioner has challenged the patentability of issued Claims 1 and 2 in the ’707 Patent. Substitute Claims 4 and 5 correspond to issued Claims 1 and 2, respectively. Consequently, Patent Owner has satisfied the “presumption...that only one substitute claim would be needed to replace each challenged claim.” *See* 37 C.F.R. § 42.121 (a)(3).

B. The Substitute Claims Do Not Enlarge the Scope of the Claims.

Appendix A is a claim listing showing the amendments made to the originally-issued '707 Patent claims. As shown in Appendix A, Substitute Claim 4 retains all limitations of original independent Claim 1, but narrows the Claim by making the following amendments:

Substitute Claim 4		'707 Patent (Ex. 1001)
W	Removes “N-H” diradical from the options of W.	33:66; 34:49-52
B	Removes “9-(N ⁶ -isopropyl phenoxyacetyladeninyl)-,” “1-(N ⁴ —(N,N-dimethylformamidinyl)cytosinyl)-,” “1-(N ⁴ -isopropyl phenoxyacetylcytosinyl)-,” “9-(N ² -isopropylphenoxyacetylguaninyl)-N ⁴ -phenoxyacetylcytosinyl)-,” “1-(N ⁴ -tertbutylphenoxyacetylcytosinyl)-,” “1-(N ⁴ -isopropyl phenoxyacetylcytosinyl)-,” “1-(N ⁴ -benzoyl-5-methylcytosinyl)-,” “1-(N ⁴ —(N,N-dimethylformamidinyl)-5-methylcytosinyl)-,” “1-(N ⁴ -acetyl-5-methylcytosinyl)-,” “1-(N ⁴ -benzoyl-5-fluorocytosinyl)-,” “9-(N ⁶ -benzoyl-7-deazaadeninyl)-,” “9-(N ⁶ —(N,N-dimethylformamidinyl)-7-	34:57-35:9

	deazaadeninyl)-”, “9-(N ² -isobutyryl-7-deazaguaninyl)-”, and “9-(N ² —(N,N dimethylformamidinyl)-7- deazaguaninyl)-” from the options of B.	
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As shown in Appendix A, Substitute Claim 5 retains all limitations of original independent Claim 2, but narrows the Claim by making the following amendments:

Substitute Claim 5		'707 Patent (Ex. 1001)
W	Removes “N-H” diradical from the options of W.	35:44, 49-52
B	Removes “9-(N ⁶ -isopropyl phenoxyacetyladeninyl)-”, “1-(N ⁴ —(N,N-dimethylformamidinyl)cytosinyl)-”, “1-(N ⁴ -isopropyl phenoxyacetylcytosinyl)-”, “9-(N ² -isopropylphenoxyacetylguaninyl)-N ⁴ -phenoxyacetylcytosinyl)-”, “1-(N ⁴ -tertbutylphenoxyacetylcytosinyl)-”, “1-(N ⁴ -isopropyl phenoxyacetylcytosinyl)-”, “1-(N ⁴ -benzoyl-5-methylcytosinyl)-”, “1-(N ⁴ —(N,N-dimethylformamidinyl)-5-methylcytosinyl)-”, “1-(N ⁴ -acetyl-5-methylcytosinyl)-”, “1-(N ⁴ -benzoyl-5-fluorocytosinyl)-”, “9-(N ⁶ -benzoyl-7-deazaadeninyl)-”, “9-(N ⁶ —(N,N-dimethylformamidinyl)-7-	35:57-36:11

	deazaadeninyl)-”, “9-(N ² -isobutyryl-7-deazaguaninyl)-”, and “9-(N ² —(N,N dimethylformamidinyl)-7- deazaguaninyl)-” from the options of B.	
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In view of these amendments, each of Substitute Claims 4 and 5 is narrower in scope than corresponding Claims 1 and 2. *See* 37 C.F.R. § 42.121 (a)(2)(ii).

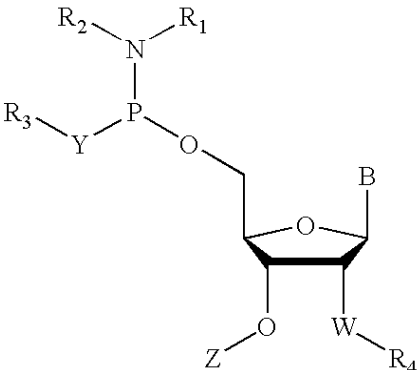
C. The Substitute Claims Are Supported by the ’707 Patent and the Supporting Applications.

The ’707 Patent issued from U.S. Application No. 12/584,625 (“the ’625 Application”) (Ex. 1002, 5-71), and claims priority to U.S. provisional Appl. No. 61/191,065 (“the ’065 Provisional”) (Ex. 2002).

Patent Owner identifies the following portions of the ’625 Application, and the ’065 Provisional (collectively “the Supporting Applications”), that provide 35 U.S.C. § 112 support for the proposed Substituted Claims. As demonstrated below, a person of ordinary skill in the art (“POSA”) would have understood that the Substitute Claims are fully described by the Supporting Applications. *See* 37 C.F.R. §§ 42.121(a)(2)(ii), 42.121(b). Ex. 2001, ¶¶76-77, 84-85.

1. Substitute Claim 4 is Fully Supported.

Substitute Claim 4 is directed to:

Substitute Claim 4
A phosphoramidite having formula (1), Formula (1)  where,
Y is an oxygen atom or a sulfur atom;
W is selected from the group consisting of an oxygen diradical and a fluorine radical, and R₄ is selected so that, if W is an oxygen diradical, then R₄ is tert butyl dimethyl silyl (TBDMS) or triisopropylsilyloxymethylene (TOM); and if W is a fluorine radical, then R₄ is not present;
B is selected from the group of nucleoside base radicals consisting of -9-(N⁶-benzoyladeninyl)-, 9-(N⁶-acetyladeninyl)-, 9-(N⁶-tert butyl phenoxyacetyladeninyl)-, 9-(N⁶-phenoxyacetyladeninyl)-, 1-(N⁴-benzoylcytosinyl)-, 1-(N⁴-acetylcytosinyl)-, 1-(N⁴-phenoxyacetylcytosinyl)-, 1-

(N ⁴ -tertbutylphenoxyacetylcytosinyl)-, 9-(N ² -isobutyrylguaninyl)-, 9-(N ² -tertbutylphenoxyacetylguaninyl)-, and 1-uracilyl-; or, B is a modified nucleoside base radical selected from the group consisting of 1-(5-methyl-uracilyl)-, and -(5-fluoro-uracilyl)-;
Z is a protecting group selected from the group consisting of dimethoxytriphenylmethyl (DMT), monomethoxytriphenylmethyl (MMT) and trimethoxytriphenylmethyl (TMT);
R ₁ is an alkyl or aryl radical;
R ₂ is an alkyl or aryl radical; and,
R ₃ is a cyanoethyl radical, alkyl radical or aryl radical.

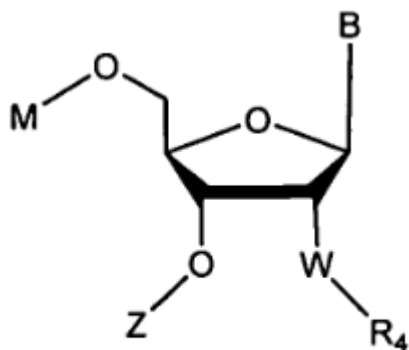
Each of these elements is recited in original Claim 1 of the '707 Patent (Ex. 1001, 33:47-35:17), and is supported by, *inter alia*, pages 20:30-23:15, 37:11-38:9, 40:10-43:10, 45:4-23 (Claim 1) of the '625 Application. Ex. 1002, 23:30-26:15, 39:11-40:9, 42:10-45:10, 47:4-23 (Claim 1); Ex. 2001, ¶77. Each of these elements is also supported by, *inter alia*, pages 14-16, 24, and 26-27 of the '065 Provisional. Ex. 2002, 21-23, 31, 33-34; Ex. 2001, ¶77.

2. Substitute Claim 5 is Fully Supported.

Substitute Claim 5 is directed to:

Substitute Claim 5

A derivatized nucleoside having a structure of formula 2,



Formula (2)

where,

M is a hydrogen radical or a linker;

if M is a linker, then it is represented by the formula $Y-C(O)$ and, optionally, connected to a solid support suitable for oligonucleotide synthesis, wherein

Y is a chain of between 2 and 20 carbons, selected from the group consisting of alkyl, alkenyl, cycloalkyl, aryl, and aralkyl, in a hydrocarbyldiradical moiety, optionally comprising intervening $-O-$, $-S-$, $-S(O)_2-$, $-C(O)-$, and $-NR_6-$, where R_6 is a hydrogen radical, or a substituted C_1 to C_{20} alkyl or a substituted aralkyl;

W is selected from the group consisting of an oxygen diradical, and a fluorine radical, and R₄ is selected so that, if W is an oxygen diradical, then R₄ is tert butyl dimethyl silyl (TBDMS) or triisopropylsilyloxymethylene (TOM); and if W is a fluorine radical, then R₄ is not present;
B is selected from the group of nucleoside base radicals consisting of -9-(N⁶-benzoyladeninyl)-, 9-(N⁶-acetyladeninyl)-, 9-(N⁶-tert butyl phenoxyacetyladeninyl)-, 9-(N⁶-phenoxyacetyladeninyl)-, 1-(N⁴-benzoylcytosinyl)-, 1-(N⁴-acetylcytosinyl)-, 1-(N⁴-phenoxyacetylcytosinyl)-, 1-(N⁴-tertbutylphenoxyacetylcytosinyl)-, 9-(N²-isobutyrylguaninyl)-, 9-(N²tertbutylphenoxyacetylguaninyl)-, and 1-uracilyl-; or B is selected from the group of modified nucleoside base radicals selected from the group consisting of 1-(5-methyl-uracilyl)-, and -(5-fluoro-uracilyl)-; and,
Z is a protecting group selected from the group consisting of dimethoxytriphenylmethyl (DMT), monomethoxytriphenylmethyl (MMT) and trimethoxytriphenylmethyl (TMT).

Each of these elements is recited in original Claim 2 of the '707 Patent (Ex. 1001, 35:18-36:15), and is supported by, *inter alia*, pages 20:30-23:15, 38:11-26, 40:10-43:10, 45:25-46:15 (Claim 2) of the '625 Application. Ex. 1002, 23:30-26:15, 40:11-26, 42:10-45:10, 47:25-48:15 (Claim 2); Ex. 2001, ¶85.

Each of these elements is supported by, *inter alia*, pages 15-16, 24, and 26-27 of the '065 Provisional. Ex. 2002, 22-23, 31, 33-34; Ex. 2001, ¶85. The shading in the depicted chemical formula image in Substitute Claim 5 has been corrected as noted on pages 9-10 of the Institution Decision and is also supported by the cited support in the '625 Application and the '065 Provisional. Ex. 2001, ¶85.

D. The Substitute Claims Are Responsive to the Instituted Grounds.

The proposed Substitute Claims are responsive to the Grounds at issue in this IPR because they each respond to a ground of unpatentability involved in the trial. Specifically, proposed Substitute Claim 4 deletes the species in Claim 1 that Petitioner alleged was anticipated in Ground I, and proposed Substitute Claim 5 deletes the species in Claim 2 that Petitioner alleged was anticipated in Ground II. For at least these reasons, and as further explained in Section IV below, the Substitute Claims are patentable over the instituted Grounds. *See* 37 C.F.R. §42.121(a)(2)(i).

IV. THE SUBSTITUTE CLAIMS ARE PATENTABLE OVER THE INSTITUTED GROUNDS

Patent Owner does not bear the burden of proving the patentability of Substitute Claims 4 and 5. *See Lectrosonics, Inc. v. Zaxcom, Inc.*, IPR2018-01129, Paper 15 at 3-4 (PTAB Feb. 25, 2019); *Aqua Prods., Inc. v. Matal*, 872 F. 3d 1290, 1295-96, 1327 (Fed. Cir. 2017) (*en banc*). Rather, Petitioner must prove

unpatentability by a preponderance of the evidence. *See Lectrosonics*, Paper 15 at 4. However, Patent Owner provides the following comments regarding Substitute Claims 4 and 5.

A. Level of Ordinary Skill in the Art.

Patent Owner notes that the Institution Decision adopted the following definition of a POSA:

an ordinarily skilled artisan would have had a Ph.D. (or equivalent degree) in organic or medicinal chemistry, and two to three years of post-graduate work experience in medicinal chemistry, synthetic organic chemistry, and nucleic acid chemistry, including the development of oligonucleotide therapeutics, diagnostics, or building blocks. Alternatively, . . . an individual holding a Bachelor's or Master's degree in organic chemistry or medicinal chemistry, who had extensive work experience in these fields, and who had gained a thorough understanding of the development of nucleic acid-based materials, would also have qualified as an ordinarily skilled artisan.

Paper 6, at 5 (internal citation omitted).

For the reasons explained in Section V of the Patent Owner's Response, Patent Owner disagrees and proposes the following definition of a POSA:

a POSA would have had a Ph.D. (or equivalent degree) in organic chemistry, and at least 2 to 3 years of post-graduate work experience in the development and syntheses of nucleosides, nucleotides, and nucleic acids, including, but not limited to, the syntheses of oligonucleotides

through solid phase oligonucleotide synthesis (“SPOS”) pursuant to P(III) chemistry.

Alternatively, someone with a Ph.D. (or equivalent degree) in organic chemistry, and who focused on the development and syntheses of nucleosides, nucleotides, and nucleic acids, including, but not limited to, the syntheses of oligonucleotides through SPOS during his or her Ph.D. studies.

Alternatively, someone with a Bachelor’s or Master’s degree in organic chemistry who had at least 5 years of extensive work experience in these fields, and who had gained a thorough understanding of the syntheses of nucleic acid-based materials pursuant to P(III) chemistry, would also have qualified as a POSA.

Ex. 2001, ¶64. This definition would not exclude medicinal chemists so long as the medicinal chemist in question met the above requirements. *Id.* ¶65.

Patent Owner contends that the amended claims are patentable over the instituted grounds under either definition of a POSA. *Id.*

B. Claim Construction.

The proposed Substitute Claims should be construed in accordance with “the ordinary and customary meaning of such claim[s] as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent.” 37 C.F.R. § 42.100.

C. Petitioner's References Do Not Anticipate or Render Substitute Claim 4 Obvious.

Petitioner's cited references do not disclose the limitations of Substitute Claim 4 (shown above in § III.C.1). Ex. 2001, ¶¶69-75.

Petitioner cites U.S. Patent No. 5,869,696 ("the '696 Patent") (Ex. 1014) as anticipating Claim 1, alleging that the '696 Patent's Example 3 is a species of Claim 1 where in formula (1), Y is an oxygen atom, **W is a N—H diradical**, R₄ is trifluoroacetyl, B is 1-uracilyl- nucleoside base radical, Z is a DMT protecting group, R₁ is an alkyl radical (specifically an isopropyl radical), R₂ is an alkyl radical (specifically an isopropyl radical), and R₃ is a cyanoethyl radical, and the Institution Decision adopted this position. Paper 6, at 7; Ex. 2001, ¶¶71-72. Substitute Claim 4 limits "W" such that it excludes "N—H diradical" from the group "consisting of an oxygen diradical and a fluorine radical." Ex. 2001, ¶73. The '696 Patent does not disclose a compound with any of the "W" and "R₄" species recited in Substitute Claim 4 and therefore does not anticipate Substitute Claim 4. *Id.*, ¶73.

The '696 Patent does not disclose or suggest any phosphoramidites having a group at "W" selected from the group consisting of an oxygen diradical and a fluorine radical, where if W is an oxygen diradical, then R₄ is tert butyl dimethyl silyl (TBDMS) or triisopropylsilyloxymethylene (TOM); or if W is a fluorine radical, then R₄ is not present. *Id.*, ¶74. The '696 Patent also does not disclose the

amended definition of “W” in combination with the other structural features of Claim 1. *Id.*

Nothing in the ’696 Patent alone or in combination with any other references of record in this IPR would have provided a POSA with a reason or motivation to modify the N—H (at a position corresponding to “W” in Substitute Claim 4) and trifluoroacetyl (at a position corresponding to “R₄” in Substitute Claim 4) of the ’696 Patent in such a way so as to arrive at the claimed compound with a reasonable expectation of success. *Id.*, ¶75.

For at least these reasons, Substitute Claim 4 is patentable over the ’696 Patent and this Motion is responsive to the Petition’s Ground I.

D. Petitioner’s References Do Not Anticipate or Render Substitute Claim 5 Obvious.

Petitioner’s cited references do not disclose the limitations of Substitute Claim 5 (shown above in § III.C.2). Ex. 2001, ¶¶78-83.

Petitioner alleges the ’696 Patent anticipates Claim 2 because the ’696 Patent’s Example 2 is a species of Claim 2 where in formula (2), M is a succinate linker represented by the formula Y—C(O) in a hydrocarbyl diradical, wherein Y is an alkyl chain having 2 carbons, i.e., ethyl . . . and further comprises an intervening —C(O)—, W is a N—H diradical, R₄ is trifluoroacetyl, B is 1-uracilyl- nucleoside

base radical, and Z is a DMT protecting group, and the Institution Decision adopted this position. Paper 6, at 10; Ex. 2001, ¶¶80-81.

Substitute Claim 5 limits “W” such that it excludes “N—H diradical” from the group “consisting of an oxygen diradical and a fluorine radical.” Ex. 2001, ¶82. The ’696 Patent does not disclose or suggest any derivatized nucleosides having a group at “W” selected from the group consisting of an oxygen diradical, and a fluorine radical, and R₄ is selected so that, if W is an oxygen diradical, then R₄ is tert butyl dimethyl silyl (TBDMS) or triisopropylsilyloxymethylene (TOM); and if W is a fluorine radical, then R₄ is not present. *Id.* The ’696 Patent also does not disclose the amended definition of “W” in combination with the other structural features of Substitute Claim 5. *Id.*

Nothing in the ’696 Patent alone or in combination with any other references of record in this IPR would have provided a POSA with a reason or motivation to modify the N—H (at a position corresponding to “W” in Substitute Claim 5) and trifluoroacetyl (at a position corresponding to “R₄” in Substitute Claim 5) of the ’696 Patent in such a way so as to arrive at the claimed compound with a reasonable expectation of success. *Id.*, ¶83.

For at least these reasons, Substitute Claim 5 is patentable over the ’696 Patent and this Motion is responsive to the Petition’s Ground II.

V. INFORMATION DISCLOSURE

With the submission of this Motion to Amend, Patent Owner is submitting an Information Disclosure Statement in **Appendix B** disclosing a ChemGenes catalog.

VI. CONCLUSION

For at least all the above and foregoing reasons, Patent Owner respectfully submits that Substitute Claims 4 and 5 are patentable, and respectfully requests a Final Written Decision confirming the patentability of these claims.

Dated: February 5, 2024

Respectfully submitted,

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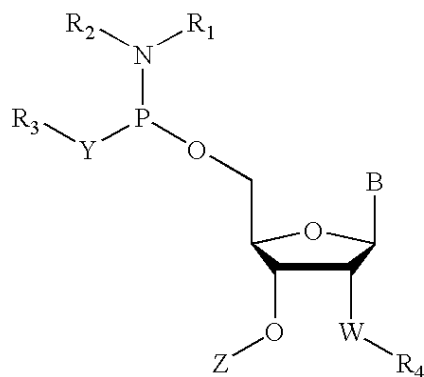
APPENDIX A

CLAIM LISTING

Proposed amended claims are shown in marked-up form below.

Claim 4 (proposed substitute for Claim 1). A phosphoramidite having formula (1),

Formula (1)



where,

Y is an oxygen atom or a sulfur atom;

W is selected from the group consisting of an oxygen diradical, ~~a N-H diradical~~ and a fluorine radical, and R₄ is selected so that,

if W is an oxygen diradical, then R₄ is tert butyl dimethyl silyl (TBDMS) or triisopropylsilyloxymethylene (TOM);

~~if W is a N-H diradical, then R₄ is of the form R₅^{*} where x is selected from the group consisting of fluorenylmethyloxycarbonyl (Fmoc), trifluoroacetyl, acetyl, alkanoyl, and aroyl; and~~

if W is a fluorine radical, then R₄ is not present;

B is selected from the group of nucleoside base radicals consisting of -9-(N⁶-benzoyladeninyl)-, 9-(N⁶-acetyladeninyl)-, 9-(N⁶-tert butyl phenoxyacetyladeninyl)-, 9-(N⁶-phenoxyacetyladeninyl)-, ~~9-(N⁶-isopropyl phenoxyacetyladeninyl)-~~, 1-(N⁴-benzoylcytosinyl)-, 1-(N⁴-acetylcytosinyl)-, ~~1-(N⁴—(N,N-dimethylformamidinyl)cytosinyl)-~~, 1-(N⁴-phenoxyacetylcytosinyl)-, 1-(N⁴-tertbutylphenoxyacetylcytosinyl)-, ~~1-(N⁴-isopropyl phenoxyacetylcytosinyl)-~~, 9-(N²-isobutyrylguaninyl)-, 9-(N²-tertbutylphenoxyacetylguaninyl)-, ~~9-(N²-isopropylphenoxyacetylguaninyl)-~~ N⁴-phenoxyacetylcytosinyl)-, ~~1-(N⁴-tertbutylphenoxyacetylcytosinyl)-~~, ~~1-(N⁴-isopropyl phenoxyacetylcytosinyl)-~~, and 1-uracilyl-;

or, B is a modified nucleoside base radical selected from the group consisting of ~~1-(N⁴-benzoyl-5-methyleytosinyl)-~~, ~~1-(N⁴—(N,N-dimethylformamidinyl)-5-methyleytosinyl)-~~, ~~1-(N⁴-acetyl-5-methyleytosinyl)-~~, ~~1-(5-methyl-uracilyl)-~~, and ~~-(5-fluoro-uracilyl)-~~, ~~1-(N⁴-benzoyl-5-fluorocytosinyl)-~~, ~~9-(N⁶-benzoyl-7-deazaadeninyl)-~~, ~~9-(N⁶—(N,N-dimethylformamidinyl)-7-deazaadeninyl)-~~, ~~9-(N²-isobutyryl-7-deazaguaninyl)-~~, and ~~9-(N²—(N,N-dimethylformamidinyl)-7-deazaguaninyl)-~~;

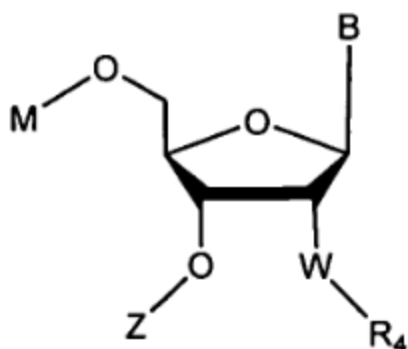
Z is a protecting group selected from the group consisting of dimethoxytriphenylmethyl (DMT), monomethoxytriphenylmethyl (MMT) and trimethoxytriphenylmethyl (TMT);

R₁ is an alkyl or aryl radical;

R₂ is an alkyl or aryl radical; and,

R₃ is a cyanoethyl radical, alkyl radical or aryl radical.

Claim 5 (proposed substitute for Claim 2). A derivatized nucleoside having a structure of formula 2,



Formula (2)

where,

M is a hydrogen radical or a linker;

if M is a linker, then it is represented by the formula Y—C(O) and, optionally, connected to a solid support suitable for oligonucleotide synthesis, wherein

Y is a chain of between 2 and 20 carbons, selected from the group consisting of alkyl, alkenyl, cycloalkyl, aryl, and aralkyl, in a hydrocarbyldiradical moiety, optionally comprising intervening —O—, —S—, —S(O)₂—, —C(O)—, and —NR₆—, where R₆ is a hydrogen radical, or a substituted C₁ to C₂₀ alkyl or a substituted aralkyl;

W is selected from the group consisting of an oxygen diradical, ~~a N—H diradical~~ and a fluorine radical, and R₄ is selected so that,

if W is an oxygen diradical, then R₄ is tert butyl dimethyl silyl (TBDMS) or triisopropylsilyloxymethylene (TOM);

~~if W is a N—H diradical, then R₄ is of the form R₅^x where x is selected from the group consisting of fluorenylmethyloxycarbonyl (Fmoc), trifluoroacetyl, acetyl, alkanoyl, and aroyl; and~~

if W is a fluorine radical, then R₄ is not present;

B is selected from the group of nucleoside base radicals consisting of -9-(N⁶-benzoyladeninyl)-, 9-(N⁶-acetyladeninyl)-, 9-(N⁶-tert butyl phenoxyacetyladeninyl)-, 9-(N⁶-phenoxyacetyladeninyl)-, ~~9-(N⁶-isopropyl phenoxyacetyladeninyl)-~~, 1-(N⁴-benzoylcytosinyl)-, 1-(N⁴-acetylcytosinyl)-, ~~1-(N⁴-phenoxyacetyladeninyl)-~~, 1-(N⁴-benzoylcytosinyl)-, 1-(N⁴-acetylcytosinyl)-, ~~1-(N⁴—(N,N-dimethylformamidinyl)cytosinyl)-~~, 1-(N⁴-phenoxyacetylcytosinyl)-, 1-(N⁴-tertbutylphenoxyacetylcytosinyl)-, ~~1-(N⁴-isopropyl phenoxyacetylcytosinyl)-~~,

9-(N²-isobutyrylguaninyl)-, 9-(N²-tertbutylphenoxyacetylguaninyl)-, 9-(N²-isopropylphenoxyacetylguaninyl)-, N⁴-phenoxyacetyleytosinyl-, 1-(N⁴-tertbutylphenoxyacetyleytosinyl)-, 1-(N⁴-isopropylphenoxyacetyleytosinyl)-, and 1-uracilyl-;

or B is selected from the group of modified nucleoside base radicals selected from the group consisting of

~~1-(N⁴-benzoyl-5-methyleytosinyl)-, 1-(N⁴-(N,N-dimethylformamidinyl)-5-methyleytosinyl)-, 1-(N⁴-acetyl-5-methyleytosinyl)-, 1-(5-methyl-uracilyl)-, and -(5-fluoro-uracilyl)-, 1-(N⁴-benzoyl-5-fluorocytosinyl)-, 9-(N⁶-benzoyl-7-deazaadeninyl)-, 9-(N⁶-(N,N-dimethylformamidinyl)-7-deazaadeninyl)-, 9-(N²-isobutyryl-7-deazaguaninyl)-, and 9-(N²-(N,N-dimethylformamidinyl)-7-deazaguaninyl)-; and,~~

Z is a protecting group selected from the group consisting of dimethoxytriphenylmethyl (DMT), monomethoxytriphenylmethyl (MMT) and trimethoxytriphenylmethyl (TMT).

APPENDIX B

INFORMATION DISCLOSURE STATEMENT

Patent Owner submits the following exhibit which is also listed on the Exhibit List in Patent Owner's Response being filed contemporaneously herewith.

Ex. No.	Description
2005	ChemGenes Corporation Catalog, Bio Technology Products & Manufacturer of DNA-RNA Intermediates (1999)

CERTIFICATE OF SERVICE

The undersigned certifies that a copy of the foregoing PATENT OWNER'S MOTION TO AMEND CLAIMS UNDER 37 C.F.R. § 42.121 was served on February 5, 2024, to the following counsel for Petitioner via electronic mail at Hongene@procopio.com:

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