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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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*Ex parte* DOUGLAS J. DELLINGER, ZOLTAN TIMAR,  
AGNIESZKA SIERZCHALA, GERALDINE DELLINGER,  
MARVIN H. CARUTHERS, and JOEL MYERSON

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Appeal 2012-001897  
Application 11/387,269  
Technology Center 1600

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Before ERIC GRIMES, LORA M. GREEN, and  
SHERIDAN K. SNEDDEN, *Administrative Patent Judges*.

SNEDDEN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of performing post-synthesis deprotection of a synthetic precursor of a nucleic acid. The Examiner has rejected the claims under the judicially created doctrine of obviousness-type double patenting. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

### STATEMENT OF THE CASE

Claims 1-35 are on appeal. Claim 1 is representative and reads as follows (emphasis added):

1. A method of performing post-synthesis deprotection of a synthetic precursor of a nucleic acid, comprising:
  - providing a synthetic precursor of a nucleic acid comprising at least one protecting group selected from the group consisting of: *a base protecting group, a 2'-hydroxyl protecting group*, and a combination thereof, and
  - deprotecting at least one of the protecting groups* of said synthetic precursor of a nucleic acid by contacting said precursor with a solution comprising an  $\alpha$ -effect nucleophile, wherein the solution is at a pH of about 4 to 11, and wherein the  $\alpha$ -effect nucleophile has a pKa of about 4 to 13.

The claims stand rejected as follows:

- I. Claims 1-35 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4-11, 13-20 and 30-32 of US 7,585,970 (hereinafter “the ‘970 patent”).
- II. Claims 1-35 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of US 7,101,986 (hereinafter “the ‘986 patent”).

The Examiner withdrew, on appeal, rejections of claims 1, 16, 21, 26 and 31 under 35 U.S.C. § 112, first paragraph, and rejections of claims 1-35 under the judicially created doctrine of obviousness-type double patenting over various claims of US 6,630,581, US 7,271,258, US 7,385,050, US 7,135,565, US 7,585,970, US 7,101,986, US 7,572,908 and US 7,572,290

and US Applications 11/899,828, 11/949,667, 12/118,655, 11/387,388 and 11/389,326.

I.

*Issue*

The Examiner has rejected claims 1-35 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4-11, 13-20 and 30-32 of the '970 patent.

The Examiner finds that

the '970 patent at claim 1, step "(b)," the 2' -ribosyl moiety substituent, variable "R<sub>1</sub>," is defined in part as "protected hydroxyl," an essential limitation in the process step wherein the oligomer chain is extended by one monomer unit. In the same claim, step "(c)" provides for: "contacting the result of step (b) with a reagent comprising a nucleophilic ion or a salt thereof that exhibits an alpha effect at neutral to mildly basic pH to concurrently remove the hydroxyl protecting group from the result of step (b) and oxidize the internucleotide linking moiety wherein said reagent comprises a peroxide."

(Ans. 6.)

Appellants contend that claim 1 "requires post-synthesis deprotection of a 2'-hydroxyl and/or nucleobase protecting group" and, in contrast, the claims of the '970 patent "describe deprotection of **3' or 5' -hydroxyl** protecting group and **simultaneous** phosphite triester **oxidation**, which is not the same as deprotection of a **2' hydroxyl** and/or **nucleobase** protecting group." (App. Br. 28-29.) Appellants further contend that claim 1 of the '970 patent

recites two types of hydroxyl protecting groups, a "hydroxyl protecting group" (which is present at the R<sub>2</sub> or R<sub>3</sub> position), and a "protected hydroxyl" that may be present at the R<sub>1</sub>

position. Antecedent basis for the “hydroxyl protecting group” recited in step (c) is only found in the phrase “R<sub>2</sub> or R<sub>3</sub> is a hydroxyl protecting group”. Thus, the language of the cited claim makes it clear that only the 3' or 5' group (and *not* the 2' group) is deprotected by the  $\alpha$ -effect nucleophile.

(Reply Br. 4.)

The issue presented is:

Does the evidence of record support the Examiner’s findings that the subject matter of claim 1 is not patentably distinct from the claims of the ‘970 patent?

*Findings of Fact*

FF1. The ‘970 patent relates to “[a] method for synthesizing a polynucleotide.” (Abstract.)

FF2. The method of the ‘970 patent involves forming an internucleotide bond and then “exposing the result of the forming an internucleotide bond step to a composition which concurrently oxidizes the internucleotide bond and removes a hydroxylprotecting group from the Sugar group.” (The ‘970 patent, col. 3, ll. 14-37.)

FF3. Step “(b)” of claim 1 of the ‘970 patent provides the structure of the Sugar group (formula IVd), where “one of R<sub>2</sub> or R<sub>3</sub> is a *hydroxyl protecting group*.” (*Id.* at col. 53, l. 66.) (Emphasis added.) The structure of the sugar group shows a substituent R<sub>1</sub> at the 2' position, where “R<sub>1</sub> is “hydrido, hydroxyl, protected hydroxyl, lower alkyl, substituted lower alkyl, or alkoxy” (*id.* at col. 53, ll. 55-60, 64-65).

FF4. Step “(c)” of claim 1 of the ‘970 patent requires contacting the result of step (b) with a reagent comprising a

nucleophilic ion or a salt thereof that exhibits an alpha effect at neutral to mildly basic pH to concurrently remove the *hydroxyl protecting group* from the result of step (b) and oxidize the internucleotide linking moiety wherein said reagent comprises a peroxide.

(*Id.* at col. 54, ll. 8-14.) (Emphasis added.)

FF5. The '970 patent discloses as follows:

“It will be apparent from the description herein given ordinary knowledge in the art that the hydroxylprotecting group and the reactive group designated by R2 and R3 may occupy either the 5'-O or 3'-O positions.” (*Id.* at col. 14, ll. 46-50.)

#### *Principles of Law*

“Obviousness-type double patenting is a judge-made doctrine that prevents an extension of the patent right beyond the statutory time limit. It requires rejection of an application claim when the claimed subject matter is not patentably distinct from the subject matter claimed in a commonly owned patent.” *In re Berg*, 140 F.3d 1428, 1431 (Fed. Cir. 1998).

#### *Analysis*

We agree with Appellants that the claims of the '970 patent relate to the removal of the “hydroxyl protecting group” at the R2 or R3 positions, which occupy the 5'-O or 3'-O positions of the sugar group of formula IVd. This claim construction is supported by the plain reading of claim 1 (FF3 and FF4) and by the disclosure of the '970 patent (FF5). We thus find that the '970 patent claims are not directed to the post-synthesis deprotection of a 2'-hydroxyl and/or nucleobase protecting group as required by claim 1 on appeal. We find that the Examiner does not adequately explain how the

disclosure of the '970 patent supports his interpretation of the claims to the contrary.

### *Conclusion of Law*

We conclude that the preponderance of the evidence of record does not support the Examiner's conclusion that the subject matter of claim 1 is not patentably distinct from the claims of the '970 patent. We thus reverse the rejection of claim 1 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over various claims of the '970 patent. As claims 2-35 are dependent on claim 1 or otherwise directed to substantially the same subject matter, we reverse the rejection as to those claims as well.

## II.

### *Issue*

The Examiner has rejected claims 1-35 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of the '986 patent. The Examiner finds that

step (a) in claim *I* of the '986 patent must be read as if it states that both 2' -hydroxyl and 5' -hydroxyl protecting groups are present. If this claim is not read this way, then the claimed process cannot make RNA precursors because the absence of a 2'-hydroxyl protecting group requires that a free 2'-hydroxyl group must be present.

(Ans. 10.)

Appellants contend that

The cited claims are different in part from the current claims because they do not explicitly recite a 2'-hydroxyl protecting group. In addition, [claim 1 of the '986 patent] recites "contacting the coupled nucleoside monomer with an

alpha effect nucleophile to simultaneously (i) irreversibly remove the carbonate protecting group, and (ii) oxidize the phosphite triester linkage.” As such, the [claims of the ‘986 patent] do not explicitly recite post-synthesis deprotection of a 2'-hydroxyl or nucleobase protecting group.

The rejected claim requires post-synthesis deprotection of a 2'-hydroxyl or nucleobase protecting group. Nowhere is this element taught in the cited claims. Rather, at best [claim 1 of the ‘986 patent] describes deprotection and phosphite triester oxidation *during synthesis, which is not the same as post-synthesis deprotection of a 2'-hydroxyl or nucleobase protecting group.*

(App. Br. 37.) (Emphasis added.)

The issue presented is:

Does the evidence of record support the Examiner’s findings that the subject matter of claim 1 is not patentably distinct from the claims of the ‘986 patent?

*Additional Findings of Fact*

FF6. The ‘986 patent relates to “methods for synthesizing oligonucleotides using nucleoside monomers having carbonate protected hydroxyl groups that are deprotected with  $\alpha$ -effect nucleophiles,” where the “ $\alpha$ -effect nucleophile[s] irreversibly cleave the *carbonate protecting groups* while simultaneously oxidizing the internucleotide phosphite triester linkage to a phosphodiester linkage.” (The ‘986 patent, Abst.)

FF7. Claim 1 of the ‘986 patent provides as follows:

A method of synthesizing an oligonucleotide on a solid support comprising:

(a) coupling a nucleoside monomer having a protected hydroxyl group to a free hydroxyl group on a support-bound nucleoside monomer, *wherein the hydroxyl group on the coupled nucleoside monomer is protected with a carbonate*

*protecting group* and the coupling reaction gives rise to a phosphite triester bond between the support-bound nucleoside monomer and the coupled nucleoside monomer; and

(b) contacting the coupled nucleoside monomer with an alpha-effect nucleophile to simultaneously (i) *irreversibly remove the carbonate protecting group*, and (ii) oxidize the phosphite triester linkage to a phosphotriester linkage.

(*Id.* at col. 27.)

FF8. The '986 patent discloses that "it has now been discovered that rapid and selective deprotection can be achieved under such conditions by employing carbonate groups for 5'-OH or 3'-OH protection." (*Id.* at col. 4, ll. 29-32.)

#### *Analysis*

We agree with Appellants that the claims of the '986 patent describe a process for synthesizing an oligonucleotide that is not the same as the method of the instant claim 1, directed to a method involving the post-synthesis deprotection of a 2'-hydroxyl or nucleobase protecting group. (*See* App. Br. 37.) The claims of the '986 patent require "contacting the coupled nucleoside monomer with an alpha-effect nucleophile to simultaneously (i) irreversibly remove the carbonate protecting group, and (ii) oxidize the phosphite triester linkage to a phosphotriester linkage." (FF7.) The '986 patent describes that elements (i) and (ii) are achieved under conditions employing carbonate groups for 5'-OH or 3'-OH protection (*see e.g.*, FF8). After reviewing the evidence on this record, we are not persuaded by the Examiner's arguments that the method described by the claims of the '986 patent necessarily requires deprotection of a 2'-hydroxyl or nucleobase protecting group as recited in claim 1.

*Conclusion of Law*

We conclude that the preponderance of the evidence of record does not support the Examiner's conclusion that the subject matter of claim 1 is not patentably distinct from the claims of the '986 patent. We thus reverse the rejection of claim 1 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over various claims of the '986 patent. As claims 2-35 are dependent on claim 1 or otherwise directed to substantially the same subject matter, we reverse the rejection as to those claims as well.

SUMMARY

We reverse all rejections on appeal.

REVERSED

cdc