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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte DIPANJAN CHOWDHURY and CHANDAN GUHA

Appeal 2025-002261
Application 17/005,548
Technology Center 1600

Before DEBORAH KATZ, RYAN H. FLAX, and
CYNTHIA M. HARDMAN, *Administrative Patent Judges*.

FLAX, *Administrative Patent Judge*.

DECISION ON APPEAL

Pursuant to 35 U.S.C. § 134(a), Appellant[1] appeals the Examiner's rejections of claims 60, 66, 67, 88, 90–95, and 101–104, which stand rejected as reciting improper *Markush* groupings.[2] We have jurisdiction under 35 U.S.C. § 6(b).

We reverse.

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[1] "Appellant" herein refers to the "applicant" as defined by 37 C.F.R. § 1.42. Appellant identifies "Dana-Farber Cancer Institute, Inc. and Albert Einstein College of Medicine, Inc.," as the real parties-in-interest. Appeal Br. 3 (we refer to the first Appeal Brief filed October 16, 2024, and the supplemental Appeal Brief filed October 30, 2024, interchangeably).

[2] A rejection under 35 U.S.C. § 101 was withdrawn. *See* Advisory Action (June 26, 2024); *see also* Answer 3 (listing grounds of rejection).

BACKGROUND AND CLAIMED SUBJECT MATTER

The Specification[3] states, "[m]icroRNAs (miRNAs) are small non-coding RNAs, typically about 19-22 nucleotides in size, that play important roles in the regulation of gene expression and various biological processes, such as cell cycle control. MiRNAs have been implicated in a number of diseases and are detected in biological fluids, such as serum." Spec. 2. The Specification further states that

> specific changes in the serum levels of specific miRNAs occur in subjects that have been exposed to total body irradiation, and that the changes in the levels of these specific miRNAs are radiation dose-dependent and correlate with a subject's risk of subsequent development of radiation disease, a subject's risk of poor prognosis from radiation exposure, and the efficacy of a treatment for reducing radiation-induced damage in a subject exposed to a significant dose of radiation (e.g., when the treatment for reducing radiation-induced damage in a subject is administered before or after total body irradiation).

Id. The Specification goes on to list dozens of miRNAs that fall into this category. *Id.* at 2–4.

The Specification describes that embodiments of the invention include the following basic steps, conducted using well-known techniques: (1) isolate and amplify miRNAs in a sample of biological fluid; (2) contact the amplified products to a substrate; and (3) detect the amplified miRNA products bound to the substrate. *Id.* at, *inter alia*, 43, 94–95, 102, 108, 114. The Specification explains that this miRNA assay and quantification allows the determining of a patient's exposure to and risk from radiation before the onset of symptoms. *Id.* at 66–68.

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[3] "Specification" or "Spec." refers to the application disclosure as filed.

Claim 60, reproduced below, is representative of the rejected claims:

60. A method of treating radiation-induced damage in a human subject in need thereof, the method comprising:

(a) determining at a first time point a first level of one or more miRNAs in a first serum sample obtained from the human subject, wherein the one or more miRNAs is selected from the group consisting of miR-130a-3p, miR-150-Sp, miR-142-Sp, miR-706, miR-342-3p, miR-136-Sp, miR-17-3p, miR-126-3p, miR-322-3p, miR-34b-3p, miR-187-3p, miR-194-Sp, miR-27a-3p, miR-30a-3p, and miR-30c-5p;

(b) after the first time point and before a second time point, administering a first treatment for reducing radiation-induced damage to the human subject, wherein the first treatment for reducing radiation-induced damage is selected from the group consisting of: a cytokine, potassium iodide, Prussian blue, diethylenetriamine pentaacetic acid, bone marrow transplantation, blood transfusion, and surgery to remove damaged tissues;

(c) determining a second level of the one or more miRNAs of step (a) in a second serum sample obtained from the human subject at the second time point; and

(d) (i) determining that the first treatment administered in step (b) was effective and administering one or more additional doses of the first treatment for reducing radiation-induced damage to the human subject; or

(d) (ii) determining that the first treatment administered in step (b) was not effective and administering a second treatment for reducing radiation-induced damage to the human subject, wherein the first treatment for reducing radiation-induced damage is not the same as the second treatment for reducing radiation-induced damage;

wherein one or more of:

(i) an elevation in the second level of one or more miRNAs selected from the group consisting of miR-136-Sp,

> miR-322-3p, miR-142-Sp, miR-706, miR-150-Sp, miR-342-3p, miR-17-3p, miR-187-3p, miR-194-Sp, and miR-27a-3p, and
>
> (ii) a decrease in the second level of one or more miRNAs selected from the group consisting of miR-130a-3p, miR-126-3p, miR-34b-3p, miR-30a-3p, and miR-30c-Sp,
>
> as compared to the first level(s) of one or more miRNAs selected from the group consisting of miR-136-Sp, miR-322-3p, miR-142-Sp, miR-706, miR-150-Sp, miR-342-3p, miR-17-3p, miR-187-3p, miR-194-Sp, miR-27a-3p, miR-130a-3p, miR-126-3p, miR-34b-3p, miR-30a-3p, and miR-30c-5p, indicates that the treatment for reducing radiation-induced damage administered to the human subject was effective.

Appeal Br. 28 (Claims App'x).

REJECTION

Claims 60, 66, 67, 88, 90–95, and 101–104 stand rejected as containing improper *Markush* groupings.[4] Final Action 6–10.

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[4] Appellant states:

> the Examiner does not list claim 97 or claim 98 among the rejected claims in the body of the Final Office Action or in the body of the Advisory Action. *See* January 2024 Final Office Action, page 6, and June 2024 Advisory Action, page 2.
>
> Therefore, Appellant assumes that claims 97, 98, and 105-107 are allowed and that claims 60, 66-67, 88, 90-95, and 101-104 are the subject of this appeal (*see* Claims Appendix).

Appeal Br. 5; *see also* Answer 3 (confirming rejected claims) and Advisory Action summary sheet, item 15 (listing allowed and rejected claims).

OPINION

I. LEGAL STANDARDS

A. BURDEN & STANDARD OF REVIEW

"[T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability. If that burden is met, the burden of coming forward with evidence or argument shifts to the applicant." *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992). Arguments made by Appellant in the Appeal Brief and properly presented in the Reply Brief (dated April 18, 2025) have been considered. *See* 37 C.F.R. § 41.37(c)(1)(iv) (2021). We review the record, per Appellant's arguments, for (reversible) examiner error.

B. MARKUSH GROUPS

According to the Office's Manual of Patent Examination Procedure ("MPEP") § 2117.I, "[a] 'Markush' claim recites a list of alternatively useable members. *In re Harnisch*, 631 F.2d 716, 719 . . . (CCPA 1980)." Furthermore, according to MPEP § 2117.II:

> A Markush claim may be rejected under judicially approved "improper Markush grouping" principles when the claim contains an improper grouping of alternatively useable members. A Markush claim contains an "improper Markush grouping" if either: (1) the members of the Markush group do not share a "single structural similarity" or (2) the members do not share a common use. *Supplementary Guidelines* at 7166 (citing *In re Harnisch*, 631 F.2d 716, 721–22[)] . . . .
>
> Where a Markush grouping describes part of a combination or process, the members following "selected from the group consisting of" (or a similar introductory phrase) must be ***substitutable***, one for the other, with the ***expectation that the same intended result would be achieved***. *Multilayer Stretch Cling Film Holdings, Inc. v. Berry Plastics Corp.*, 831 F.3d 1350, 1357 . . . (Fed. Cir. 2016)("It is generally understood that

> . . . the members of the Markush group . . . are alternatively ***usable for the purposes of the invention*** . . . .")(citations omitted).

(emphasis added). Per the quoted MPEP text above, the Office cites *Multilayer Stretch* as explaining the law, in particular, quoting that a *Markush* group's members must be "alternatively usable *for the purposes of the invention*." *Multilayer Stretch*, 831 F.3d at 1357 (emphasis added). *Multilayer Stretch* also phrases this another way: the "listed group of species . . . are useful for the purposes of the claim." *Id.* (in the cited case, the claim listed resin materials that were usable in an inner, strong and stretchable, layer of a multilayer film). Thus, when considering the propriety of the members of a recited *Markush* group, the context of the claimed invention is of paramount importance.

II. ANALYSIS OF THE REJECTION

The Examiner determines that the claims' listings of miRNAs (the lists are extensive and we will not reproduce them here, *but see* quoted independent claim 60 above as an example) constitute improper *Markush* groups. Final Action 7. The Examiner determines that the recited lists of miRNAs "do not share a single structural similarity, as each miRNA has a different chemical structure in that it consists of a different nucleotide sequence. The only structural similarity present is that all of the miRNAs comprise nucleotides." *Id.* at 9. The Examiner continues, "the recited miRNAs do not belong to a chemical or art-recognized class because there is no expectation from the knowledge in the prior art that the miRNAs behave in the same manner and can be substituted for one another with the same intended result achieved." *Id.*

The Examiner states that, "while the different miRNAs are asserted to have the property of being correlated with radiation exposure, they do not share a substantial structural similarity essential to this activity." *Id.* Thus, the Examiner concludes that "the recited miRNAs are not members of the same recognized physical or chemical class or the same art-recognized class," and, therefore, the recited lists of miRNAs are improper *Markush* groups per the MPEP § 706.07 (now MPEP § 2117)[5]. *Id.* at 12.

Appellant argues that "when the Markush group occurs in a claim reciting a process or a combination (not a single compound), it is sufficient if the members of the group are disclosed in the specification to possess at least one property in common which is mainly responsible for their function in the claimed relationship, and it is clear from their very nature or from the prior art that all of them possess this property." Appeal Br. 17 (citing *In re Harnisch*, 631 F.2d at 724). Appellant argues that, "[t]he instant claims are not drawn to the members of the Markush group as compounds per se, i.e., the claims are not compound or composition of matter claims reciting a Markush group of miRNA molecules. Rather, the claims are directed to methods of treating that use a cellular state or miRNA signature that is present after exposure to radiation." *Id.* at 20.

Moreover, as argued by Appellant, "[t]he miRNAs recited in the claim[s] are markers, i.e., whose presence or relative amount(s) trigger (or not) the steps of the claimed method of treatment." *Id.* at 21. As markers, argues Appellant, the miRNAs of the claims are substitutable for one another and they are structurally similar enough to be classified as a unified

[5] *See* Appeal Br. 18 n.3 (identifying this modification to the MPEP).

class in the context of the claimed methods, thus, the recited *Markush* groups are proper. *See id.* at 21–24.

We find Appellant's arguments persuasive.

The seminal case regarding claims reciting a *Markush* group is, as cited by the MPEP (above), *In re Harnisch*, 631 F.2d 716. In *Harnisch*, the invention related to compounds useful as dyes and claimed a group of such that were actual dyes or intermediates of dyes, which the court found to be of "a single structural similarity" in this claimed objective so as to be considered to "belong to a subgenus, as defined by appellant, which is not repugnant to scientific classification." *Id.* at 722. The court called this a "unity of invention," similar to the facts of prior case *In re Jones*, 162 F.2d 479 (CCPA 1947), where "the court found all of the [claimed *Markush* group] compounds included in the claims were plant growth stimulants, thus having a common function," therefore, the court reversed a rejection for an improper *Markush* group. *Harnisch*, 631 F.2d at 722.

What both of these cases make clear, particularly in view of the Federal Circuit's holding in *Multilayer Stretch*, quoted above, is that, if a recited *Markush* group lists a set of things that the inventor describes as a subgenus, and those things are described in the specification as <u>useful for the function of the invention</u> because of their similarities, then their inclusion in a *Markush* group is not improper.

This concept is also illustrated by the language of MPEP § 2117.II.A:

> A recognized physical class, a recognized chemical class, or an art-recognized class is a class wherein there is an expectation from the knowledge in the art that ***members of the class will behave in the same way in the context of the claimed invention***. In other words, each member could be substituted one for the other, with the expectation that ***the same intended***

> ***result would be achieved***. For example, in the context of a claim covering a disposable diaper, a limitation "the fastener selected from the group consisting of a pressure sensitive adhesive and complementary release material, a complementary hook and loop structure, a snap, and a buckle" would likely be considered an art recognized class because a review of the prior art would establish that it was well known that each member could be substituted for each other with the expectation that the intended result (repositionable and refastenable) would occur.

(emphasis added). As shown by the diaper claim example, a *Markush* group's species may be structurally divergent, i.e., a buckle is very different than a hook and loop structure, but if they would be expected to perform the same function in the context of the invention, they are properly grouped.

The Examiner states, "[t]he examiner agrees that the claimed miRNAs are all disclosed in the specification to be correlated with the radiation exposure." Final Action 10. "[T]he Examiner acknowledges that . . . the miRNAs are transcribed and processed the same way." Answer 8. Thus, the Examiner acknowledges some structural and functional similarity amongst the recited group of miRNAs, in the context of the invention. The Examiner, however, then asserts that "it is essential to study the function of each miRNA singularly and in a specific cellular context in order to understand its precise function." *Id.* at 9 (emphasis omitted) (quoting "Oliveto (WJBC Feb 26, 2017 Vol 8 Issue 1 pages 45-56)"). The Examiner's position is that the claimed lists of miRNAs must perform their biological miRNA functions in some way, in relation to the claimed invention, but the Examiner misinterprets or overlooks the claimed invention. Individual miRNA functionality is not contemplated in the context of the claimed invention.

Here, as acknowledged by the Examiner, the Specification identifies the claimed miRNA species as representative of a patient's exposure to radiation, as they are quantifiable and can be observed to either increase or decrease in quantity as a patient's reaction to such exposure. *See, e.g.*, Spec. 2–4. The listed miRNA species need not function as miRNAs, in the same way, to the same end, or at all, for the invention to work. The listed miRNA species need only be quantifiable to achieve the invention's purpose and this function is not disputed here. The Examiner does not suggest that this functionality is not common amongst the claimed group.[6] Like the diversity of diaper fasteners listed by the MPEP text above, the diversity of miRNA species may be structurally different (in that they are composed of different nucleotide sequences and potentially perform differently as biomolecules), but they are the same in that they all reportedly function as quantitatively representative of patient radiation exposure and, so, they are substitutable for this purpose and are common members of an art recognized class.

Here, what matters in the context of the invention is whether the claimed miRNAs are produced in response to radiation exposure, and at what level they are produced. Therefore, as argued by Appellant, per the explanation in the Specification (*see supra* Background and Claimed Subject Matter), we find that the recited miRNAs *are* interchangeable in the context of the invention and we do not agree with the Examiner that the recited *Markush* groups are improper. For the reasons above, we are persuaded by Appellant's arguments and we reverse the Examiner's rejection.

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[6] In fact, the Examiner might even concede it: "The examiner agrees that the claimed miRNAs are all disclosed in the specification to be correlated with the radiation exposure." Final Action 10.

CONCLUSION

Based on the foregoing, we reverse the Examiner's rejection.

DECISION SUMMARY

Claim(s) Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
60, 66, 67, 88, 90–95, 101–104		Improper Markush Group		60, 66, 67, 88, 90–95, 101–104

REVERSED