UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/057,521	10/18/2013	Kelvin G. M. BROCKBANK	154260	6686

27049 7590 03/11/2020

OLIFF PLC
P.O. BOX 320850
ALEXANDRIA, VA 22320-4850

EXAMINER	
FAN, LYNN Y	

ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
03/11/2020	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

OfficeAction27049@oliff.com
jarmstrong@oliff.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte KELVIN G. M. BROCKBANK[1]

Appeal 2019-003724
Application 14/057,521
Technology Center 1600

Before ERIC B. GRIMES, DEBORAH KATZ, and
ULRIKE W. JENKS, *Administrative Patent Judges.*

GRIMES, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a biomaterial composition, which have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

STATEMENT OF THE CASE

The Specification states that "chondrocytes and cartilage tissue are preserved using various storage techniques, and . . . used as osteochondral

---

[1] Appellant identifies the real party in interest as LIFELINE SCIENTIFIC, INC. Appeal Br. 1. We use the word Appellant to refer to "applicant" as defined in 37 C.F.R. § 1.42(a).

allografts." Spec. ¶ 4. However, "[c]urrent preservation techniques do not acceptably maintain extracellular matrix integrity of cartilage, and in certain aspects, chondrocyte viability could be improved." *Id*. ¶ 5.

The Specification discloses "compositions and methods for storing biomaterials . . . in a manner that reduces or prevents the loss of biomaterial properties, such as extracellular matrix permeability and chondrocyte viability." *Id*. ¶ 8. "In certain aspects, the solutions described herein contain an agent that prevents or reduces the loss of biomaterial properties," which can be an enzyme inhibitor such as doxycycline. *Id*.

"After placing the biomaterial into any of the solutions . . . , this mixture can be stored at various temperatures," including hypothermic temperatures. *Id*. ¶ 34. "In certain aspects, hypothermic temperatures can include temperatures ranging -25°C from to +35°C. . . . For example, if chondrocytes and/or cartilage are the biomaterial, hypothermic temperatures rang[e] preferably from -25°C to +35°C." *Id*.

Claims 1, 3–5, 7–10, and 22–31 are on appeal. Claim 1, reproduced below, is illustrative:

1. A composition comprising a biomaterial and a solution that includes at least one agent that reduces or prevents a loss of biomaterial properties during storage of the biomaterial at hypothermic temperatures, wherein

a temperature of the composition is a hypothermic temperature,

the solution is an animal product-free solution,

the biomaterial comprises chondrocytes in an extracellular matrix or cartilage,

the at least one agent comprises doxycycline having a concentration of 10 μM, and

the biomaterial properties comprise:

cell viability; and

extracellular matrix integrity, which includes extracellular matrix permeability.

The claims stand rejected as follows:

Claims 1, 3–5, 7, 9, 22–25, 29, and 30 under 35 U.S.C. § 103(a) as obvious based on Cole[2] (Ans. 3);

Claims 8, 26–28, and 31 under 35 U.S.C. § 103(a) as obvious based on Cole and Brockbank[3] (Ans. 5); and

Claim 10 under 35 U.S.C. § 103(a) as obvious based on Cole and Nagase[4] (Ans. 6).

OPINION

Claims 1, 3–5, 7, 9, 22–25, 29, and 30 stand rejected as obvious based on Cole. The Examiner finds that "Cole teaches a culture (a composition) comprising tibias (a biomaterial comprises chondrocytes in an extracellular matrix and cartilage . . .) in serum-free media (an animal product-free solution) . . . and 5 μg/ml (11.25 μM) of doxycycline." Ans. 4.

The Examiner presents the calculations relied on for converting 5 μg/ml doxycycline to 11.25 μM. *Id*. at 8. The Examiner also notes that

[2] Ada A. Cole, et al., *Doxycycline Disrupts Chondrocyte Differentiation and Inhibits Cartilage Matrix Degradation*, Arthritis & Rheumatism 37:1727–1734 (1994).
[3] Kelvin G.M. Brockbank et al., *Tissue Preservation*, in Advances in Biopreservation, pages 157–196 (2006).
[4] Hideaki Nagase et al., *Aggrecanases and cartilage matrix degradation*, Arthritis Res Ther. 5:94–103 (2003).

> Cole does teach a dosage of 10 μM doxycycline is used in the study (p.1732 col right - para 1). Hence, Cole discloses a composition comprising the claimed biomaterial and the claimed solution including doxycycline, and the disclosed 10 μM of doxycycline of Cole would reduce or prevent a loss of biomaterial properties . . . , since doxycycline of Cole appears to be the same as claimed.

Id.

The Examiner notes that claim 1 recites a "hypothermic temperature," and some dependent claims recite specific temperature ranges, but considers these "intended use limitations." *Id*. at 4–5. The Examiner reasons that "[t]he intended use of the claimed composition does not patentably distinguish the composition, per se. . . In order to be limiting, the intended use must create a structural difference between the claimed composition and the composition of the prior art. In the instant case, the intended use fails to create a structural difference." *Id*. at 5.

We agree with the Examiner that claim 1 is unpatentable based on Cole. Claim 1 is directed to a composition that comprises "a biomaterial"; specifically, a biomaterial comprising "chondrocytes in an extracellular matrix or cartilage." Cole discloses cultures comprising "[t]ibias from 12-day chick embryos." Cole 1728, right col. "[A]t 12 days of embryonic development . . . the tibia consists of a thin bony collar, a marrow cavity, and 2 tibial cartilages." *Id*. at 1727–1728.

Cole's cultures also include "serum-free media containing Dulbecco's modified Eagle's medium" supplemented with ascorbate, glucose, and penicillin/streptavidin. *Id*. at 1728, right col. Cole's serum-free medium reasonably appears to be free of animal products. *See* Spec. ¶ 27 (Suitable solutions include "Dulbecco's Modified Eagle Medium"; animal product-

free solutions do not contain "fetal bovine serum (FBS) or any other product derived from an animal.").

Cole states that "treated tibias were incubated in the presence of doxycycline at 5 μg/ml, 20 μg/ml, or 40 μg/ml." Cole 1728, right col. Cole also states "[t]he dosage of doxycycline used in this study (83 μM, 41 μM, and 10 μM) is comparable with the drug concentrations reported by other investigators to inhibit enzyme activity of neutrophil collagenase but not fibroblast collagenase." *Id*. at 1732. This statement is reasonably interpreted to be Cole's conversion of the μg/ml units used in its experiments ("in this study") to units of μM, to make them directly comparable to the doxycycline concentrations used "by other investigators" in their own studies. Thus, Cole's disclosure supports the Examiner's finding (Ans. 8) that Cole's composition comprises 10 μM doxycycline.

Claim 1 recites an "agent that reduces or prevents a loss of biomaterial properties during storage of the biomaterial at hypothermic temperatures, wherein . . . the biomaterial properties comprise: cell viability; and extracellular matrix integrity, which includes extracellular matrix permeability." Claim 1 also recites the agent that meets this functional requirement: 10 μM doxycycline. Because Cole's composition comprises 10 μM doxycycline, it would inherently possess the functional properties that result from including 10 μM doxycycline in a composition. Cole's composition therefore meets the functional limitation recited in claim 1.

Finally, claim 1 states that "a temperature of the composition is a hypothermic temperature." Cole discloses that "[t]he tibias were maintained in culture . . . at 37°C." Cole 1728, right col. The Specification states that

"hypothermic temperatures can include temperatures ranging -25°C from to +35°C." Spec. ¶ 34. This statement, however, does not purport to define the term "hypothermic temperature," nor does it limit hypothermic temperatures to those between -25°C and +35°C; it only states that "hypothermic temperatures can include" that range. Thus, the broadest reasonable interpretation of "a hypothermic temperature," read in light of the Specification, includes some temperatures below -25°C and some temperatures above +35°C, possibly including +37°C, the temperature of Cole's composition.

Even assuming that the broadest reasonable interpretation of "a hypothermic temperature" does not include +37°C, however, we conclude that the temperature limitation of claim 1 does not result in a structural difference. Cole's composition comprises the same biomaterial, the same solution, and the same doxycycline concentration as the claimed composition. Cole's composition therefore appears to be identical to the claimed composition, even though it might have a different temperature.

> Where . . . the claimed and prior art products are identical or substantially identical . . . the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. Whether the rejection is based on "inherency" under 35 U.S.C. § 102, on "prima facie obviousness" under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products.

In re Best, 562 F.2d 1252, 1255 (CCPA 1977) (citations and footnote omitted).

Appellant has not provided evidence that a composition comprising the components recited in claim 1, at a temperature of +37°C, differs from an otherwise identical composition at a "hypothermic" temperature of +35°C, or even that it differs from one at +5°C, as recited in some dependent claims.

Appellant argues, however, that "even if . . . Cole can be interpreted as teaching that a dosage of 10 μM doxycycline is used in Cole . . . , the composition of Cole is not the same as the claimed composition." Reply Br. 4. Specifically, Appellant argues that

> the "structural difference" brought about by the expressly recited . . . **hypothermic temperature** . . . is that—unlike [Cole] in which [doxycycline] is used at 37°C where the chondrocytes proliferate (i.e., the cartilage should grow) —the hypothermic temperature requirement of the claims effectively holds the recited biomaterial comprising chondrocytes in stasis in the cold, i.e., there is no proliferation and/or even any expectation of proliferation at the recited hypothermic temperatures.

Id. at 4–5. Appellant thus argues that the recited hypothermic temperature "creates a structural difference at least in terms of chondrocyte proliferation in the composition." *Id*. at 5.

This argument is unpersuasive. First, the Specification does not describe "a hypothermic temperature" as one that "holds . . . chondrocytes in stasis in the cold," as Appellants argue. Reply Br. 5. The Specification states, rather, that "hypothermic temperatures can include . . . +35°C," Spec. ¶ 34, which is equivalent to about 95°F.

In addition, we are not persuaded that the effect of the temperature of a composition on its components (including living components such as

chondrocytes) is a change in its structure. Neither the identity nor the amounts of the components of Cole's composition—Dulbecco's modified Eagle's medium, animal product-free supplements, 10 μM doxycycline, and embryonic chick tibias—change when the temperature of the composition is lowered from 37°C to 35°C, or even to 5°C.

Rather, a change in the temperature of a composition affects its functional properties by changing the rate of movement of the molecules making up that composition, which affects the rate of chemical reactions, including the chemical reactions taking place in living cells. Although cells may grow more slowly, or not at all, in compositions that are colder, Appellant does not direct us to evidence to support the argument that any change is due to a change in the composition, rather than a change in the environment in which the composition is placed, which determines its temperature.

A similar issue was addressed in *SmithKline Beecham Corp. v. Copley Pharm., Inc.*, 45 Fed. Appx. 915 (Fed. Cir. 2002). The issue presented was whether a prior art reference "anticipates claims 2 and 4 . . . directed to nabumetone, an anti-inflammatory drug." *Id*. at 916. "The only difference is that claim 2 claims the chemical in its solid form, and claim 4 recites the compound in an oil form." *Id*. at 917. The court concluded that, "[b]ecause expert testimony confirmed that nabumetone when made is in an oil form and always solidifies at room temperature, . . . the solid form is an inherent property of the compound. Thus claim 2 is inherently anticipated by" the prior art. *Id*.

Just as the compound in *Copley* did not change its structure when it solidified at room temperature, Appellant's claimed composition does not change its structural make-up when its temperature is changed from 37°C to 35°C, or 5°C. Thus, whatever effect the claimed composition has on chondrocytes at a given temperature is inherent in the composition, and therefore also inherent in the structurally identical composition disclosed by Cole.

In the Appeal Brief, Appellant argued that Cole's teachings would not have led a skilled artisan to modify its doxycycline concentration to the claimed 10 μM. Appeal Br. 8–9, 11–12, 15. These arguments are unpersuasive in view of Cole's own conversion of its 5 μg/ml doxycycline concentration to 10 μM. Cole 1728, right col. ("doxycycline at 5 μg/ml, 20 μg/ml, or 40 μg/ml") and 1732, right col. ("[t]he dosage of doxycycline used in this study (83 μM, 41 μM, and 10 μM)"). Thus, no modification of Cole's doxycycline concentration is required to meet the relevant claim limitation.

Appellant also argues that the claimed composition

> results in superior properties. . . . [T]he electrical conductivity data of Figure 6 (which takes into account the proteoglycan content) reflects that 10 μM achieved the best results for retention of electrical conductivity and permeability, in the presence of viable cells (even regarding viability, as further shown in Figure 5, the 10 μM group was significantly higher than all other groups), which is not suggested by the results described in Cole.

Appeal Br. 16. Appellant argues that

> there is no evidence of record, suggesting that one skilled in the art would have thought that the recited agent (including doxycycline having a concentration of 10 μM) could or should be effective to reduce or prevent the loss of the recited

> biomaterial properties (including cell viability and extracellular matrix integrity, which includes extracellular matrix permeability) at hypothermic temperatures (i.e., refrigeration temperatures) where metabolism is very low.

Id. at 17.

These arguments are unpersuasive. The data shown in Appellant's Figures 5 and 6 compares samples having 0, 10, 30, 100, or 300 μM doxycycline. Appellant argues that the 10 μM sample "achieved the best results," including "significantly higher" viability. Appeal Br. 16. However, Cole's composition also comprises 10 μM doxycycline. Cole 1728, right col. Thus, whatever properties are conferred on the claimed composition based on 10 μM doxycycline cannot be the basis for showing a difference, let alone an unexpected difference, from Cole's composition. *Cf. Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1347 (Fed. Cir. 1999) ("[T]he discovery of a previously unappreciated property of a prior art composition . . . does not render the old composition patentably new to the discoverer.").

With regard to claim 22, Appellant argues that "[t]he record lacks any articulation of a finding that the prior art included the features as recited in claim 22, which requires the composition is without ice nucleation (at hypothermic temperatures)." Appeal Br. 18.

We are not persuaded. Claim 22 reads: "The composition of claim 1, wherein at the hypothermic temperatures the composition is without ice nucleation." Appeal Br. A-2. Claim 22 does not require any additional components (e.g., an antifreeze agent) compared to claim 1, and any composition is "without ice nucleation" when it is entirely liquid. Claim 22 therefore reads on the composition of claim 1 in a liquid condition; e.g., at a

hypothermic temperature of 35°C or 5°C. Thus, claim 22 is unpatentable over Cole for the reasons discussed above with respect to claim 1.

With regard to claims 29 and 30, Appellant argues:

> Nowhere does Cole or the other applied references suggest a hypothermic temperature composition including the claimed ingredients, much less one in which the temperature of the composition (including all the ingredients therein) is specifically set in the range from -5°C to +10°C, or in the range from -0°C to +5°C.

Appeal Br. 20.

This argument is also unpersuasive, for the reasons discussed above with respect to claim 1. To reiterate, the temperature of a composition does not change what the composition is made of; the temperature only changes the rate at which molecules in the composition move. Appellant fails to direct us to evidence showing that the identity and amount of the components in Cole's composition are the same at 5°C as they are at 37°C. Thus, the temperature ranges recited in claims 29 and 30 do not structurally distinguish the claimed compositions from Cole's composition.

Appellant has waived arguments directed specifically to the rejections based on Cole combined with Brockbank or Nagase. *See* Appeal Br. 5 ("For the reasons detailed below, Appellant requests the reversal of the Examiner's rejections [collectively]."). For the reasons set out in the Answer and above, therefore, we affirm the rejection of claims 8, 26–28, and 31 under 35 U.S.C. § 103(a) based on Cole and Brockbank, and the rejection of claim 10 under 35 U.S.C. § 103(a) based on Cole and Nagase.

DECISION SUMMARY

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1, 3–5, 7, 9, 22–25, 29, 30	103(a)	Cole	1, 3–5, 7, 9, 22–25, 29, 30	
8, 26–28, 31	103(a)	Cole, Brockbank	8, 26–28, 31	
10	103(a)	Cole, Nagase	10	
Overall Outcome			1, 3–5, 7–10, 22–31	

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a). *See* 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED