UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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*Ex parte* RONALD STEWART HILL,
RICHARD CHRIS KLANN, and FRANCIS V. LAMBERTI

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Appeal 2008-4207
Application 10/971,544
Technology Center 1600

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Decided: November 20, 2008

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Before LORA M. GREEN, RICHARD M. LEBOVITZ, and
JEFFREY N. FREDMAN, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal from the final rejection of claims 1-3, 5, 7, 9, 10, 12, 14, 20, 24, 26-29, 34-38, 46-52, and 121-126. Jurisdiction is under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

The claims are directed to methods of regenerating connective tissue involving administration of a bioactive hydrogel matrix. Claims 1-3, 5, 7, 9,

10, 12, 14, 20, 24, 26-29, 34-38, 46-52, and 121-126 are pending (App. Br. 2) and stand finally rejected by the Examiner as follows:

1) Claims 1-3, 5, 7, 9, 10, 12, 14, 20, 24, 26-29, 34, 35, 38, 52, and 126 under 35 U.S.C. § 103(a) as obvious over Usala (US 6,261,587 B1, Jul. 17, 2001) and Liu (US 5,972,385, Oct. 26, 1999) (Ans. 4);

2) Claims 36, 46, 49, 50, and 51 under 35 U.S.C. § 103(a) as obvious over Usala, Liu, and Rhee (US 5,470,911, Nov. 28, 1995) (Ans. 6-7);

3) Claims 36, 37, and 46-51 under 35 U.S.C. § 103(a) as obvious over Usala, Liu, and Lin (US 2004/0091462 A1, May 13, 2004) (Ans. 9); and

4) Claims 36, 37, and 121-125 under 35 U.S.C. § 103(a) as obvious over Usala, Liu, and Young (US 2003/0032098 A1, Feb. 13, 2003) (Ans. 11).

Claim 1 is representative of the claimed subject matter and reads as follows:

> 1. A method for regenerating connective tissue comprising administering a bioactive hydrogel matrix to a site in need of connective tissue regeneration, thereby effecting regeneration of connective tissue selected from the group consisting of bone, cartilage, ligament, and tendon,
>
> wherein the bioactive hydrogel matrix comprises a polypeptide, a long chain carbohydrate, and one or more components selected from the group consisting of polar amino acids, polar amino acid analogs or derivatives, divalent cation chelators, and combinations thereof.

## OBVIOUSNESS OVER USALA AND LIU

Claims 1-3, 5, 7, 9, 10, 12, 14, 20, 24, 26-29, 34, 35, 38, 52, and 126 stand rejected under 35 U.S.C. § 103(a) as obvious over Usala and Liu (Ans. 4).

*Issue*

The issue in this rejection is as follows: Does Usala teach a method of administering a hydrogel matrix to a joint which would achieve the claimed result of "effecting regeneration of connective tissue selected from the group consisting of bone, cartilage, ligament, and tendon"?

*Scope and content of the prior art*

In making an obviousness determination, we must first determine the scope and content of the prior art. Thus, we begin our analysis with the Usala and Liu patents, which form the basis of the obviousness rejection.

THE USALA PATENT

1. Usala describes a hydrogel matrix useful for promoting vascularization (Usala, at col. 2, ll. 23-24).

2. The matrix comprises denatured collagen protein fragments loosely bound to dextran (Usala, at col. 2, ll. 40-41).

3. The matrix can further comprise additional components, including:

4. ● a nitric oxide scavenger, such as L-cysteine, or a nitric oxide inhibitor, such as an L-arginine analogue (Usala, at col. 2, ll. 43-54; at col. 5, ll. 1-15);

5. ● a divalent chelator to increase matrix rigidity (Usala, at col. 3, l. 65 to col. 4, l. 10; at col. 5, ll. 1-15); and

6. ● effective amounts of polar amino acids to increase the rigidity of the matrix and enhance collagen binding to the basement membrane (Usala, at col. 4, ll. 24-50; at col. 5, ll. 1-15).

7. The matrix is also useful "for conditions that may benefit from directed suppression of the immune response at a particular site" (Usala, at col. 6, ll. 18-21).

8. "Because the matrix is beneficial in preventing or reducing the inflammatory response, it may be used to treat chronic inflammatory diseases, including rheumatoid arthritis . . . For example, to reduce arthritis, the matrix may be injected into a joint in need thereof" (Usala, at col. 7, ll. 1-9).

THE LIU PATENT

9. Liu describes a crosslinked collagen-polysaccharide matrix for the repair of bone, cartilage, and soft tissues (Liu, at col. 2, ll. 19-22).

10. "The collagen may be purified, native or modified collagen of any type" (Liu, at col. 2, ll. 22-24).

11. The polysaccharide may be a long chain polysaccharide, such as dextran (Liu, at col. 2, ll. 26-29).

12. Liu teaches that growth of cartilage tissue is "desired" in "disease-induced cartilage damage such as in . . . rheumatoid arthritis" (Liu, at col. 8, ll. 58-62).

*The differences between the claimed invention and the prior art*

Because Appellants did not separately address the patentability of any individual claim, we have selected claim 1 as representative for the purpose of deciding this rejection. *See* 37 C.F.R. § 41.31(c)(1)(vii). Therefore, it is only necessary for us to address the differences between claim 1 and the prior art.

13. Claim 1 is directed to a "method of regenerating connective tissues comprising administering a bioactive hydrogel matrix to a site in need of connective tissue regeneration . . . thereby effecting regeneration of connective tissue."

14. The connective tissue recited in claim 1 is selected from bone, cartilage, ligament, and tendon.

15. The claimed hydrogel matrix comprises: (1) a polypeptide; (2) a long chain carbohydrate; and (3) a component which is (a) a polar amino acid; (b) a polar amino acid analog or derivative; or (c) a divalent cation chelator.

16. Usala describes a "hydrogel matrix" (FF1) as recited in claim 1.

17. Usala's matrix comprises:

18. ● denatured collagen protein which meets the claimed limitation of (1) a "polypeptide" (FF2, 15);

19. ● dextran which is (2) a long chain carbohydrate as in claim 1 (FF2, 11, 15); and

20. ● polar amino acids and chelators as in (3) (a) and (c) of claim 1 (FF4-6, 15).

21. In sum, Usala describes a hydrogel matrix that meets all the limitations of the hydrogel matrix recited in claim 1.

22. Usala does not teach that its matrix is for regenerating connective tissue as required by claim 1 (FF13).

23. However, Usala states that its matrix can be injected into the joint to treat rheumatoid arthritis (FF8).

24. Liu teaches that cartilage regeneration is "desired" in "disease-induced cartilage damage such as in . . . rheumatoid arthritis" (FF12).

## ANALYSIS

The claims are directed to administering a hydrogel matrix to a connective tissue in order to achieve its regeneration (FF13). Usala teaches a hydrogel matrix that meets all the limitations of claim 1 (FF16-21), but does not state that its matrix is for "regenerating connective tissues" as

additionally required by the claim (FF22). However, Usala discloses that its matrix can be administered to a joint afflicted by rheumatoid arthritis (FF8, 23) which would have been known to be a site in need of cartilage regeneration (FF12, 24). Thus, Usala teaches administering a hydrogel matrix "to a site in need of connective tissue regeneration" – i.e., cartilage – as required by the claimed invention. Because Usala's hydrogel matrix meets all the limitations of the claimed hydrogel matrix, persons of ordinary skill in the art would have reasonably expected it to possess the same characteristics, i.e., to achieve cartilage regeneration once injected ("administered") to a rheumatoid joint.[1] In sum, while Usala does not explicitly teach the claimed limitation of "effecting regeneration of connective tissue", it would have reasonably been expected to occur upon injection of Usala's hydrogel. We conclude that such evidence is sufficient to establish prima facie obviousness of the claimed subject matter.

Once a prima facie case is established, the burden shifts to the applicants to show that the prior art does not necessarily or inherently possess the characteristics of the claimed hydrogel matrix.[2]

Appellants state "Usala nowhere discloses or suggests a method of repairing connective tissue" (App. Br. 5). They contend that the Examiner is "confusing the teaching of Usala around application of its matrix to sites in

[1] *In re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990), the Federal Circuit held it was reasonable to presume that structurally similar chemical compounds have similar properties. In our opinion, this presumption would also hold true for composition of matters which, as here, are identical in their composition.
[2] *In re Fitzgerald*, 619 F.2d 67, 70 (CCPA 1980); *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977).

need of 'repair', particularly in relation to arthritic joints . . . In particular, the Examiner is improperly assuming that 'repair' means regeneration or formation of new connective tissue" (Reply Br. 3).

This argument is not persuasive. While Usala does not expressly teach regenerating "bone, cartilage, ligament, and tendon" as recited in claim 1, this limitation would have been met by carrying out Usala's method. That is, Usala explicitly teaches administering its hydrogel matrix to a joint to treat rheumatoid arthritis (FF8) with a composition that meets all the limitations of claim 1 (FF21) – and thus would have reasonably been expected to achieve the claimed result of connective tissue regeneration. It is unnecessary for Usala to expressly teach connective regeneration since this outcome would have been accomplished inherently by following Usala's method for treating arthritic joints. When inherency is based on 35 U.S.C. § 103, Appellants bear the burden of proving that the claimed product is not the same as the prior art product. *In re Best*, 562 F.2d at 1255. Appellants have not met that burden here.

The claim recites that the method is "for regenerating connective tissue" and that administering the claimed hydrogel "thereby" effects "regeneration of connective tissue selected from the group consisting of bone, cartilage, ligament, and tendon." We do not consider these limitations to distinguish the claimed method over Usala. In each of these cases, the claim language asserts a result of administering the hydrogel matrix. Generally, a limitation which only states the result of what is recited in the claims does not constitute a limitation of the claim scope. *Texas Instruments Inc. v. U.S. Intern. Trade Com'n*, 988 F.2d 1165, 1172 (Fed. Cir. 1993).

Appellants also argue that "the Examiner is isolating individual sentences from their context in an attempt to link Usala with the presently claimed invention. In doing so, the Examiner is improperly broadening the actual teaching of Usala" (App. Br. 6).

We are not persuaded by this argument that the Examiner erred in applying Usala to the claimed invention. As discussed above, Usala has explicit disclosure directing the ordinary skilled artisan to inject its hydrogel matrix into a joint (FF8). That Usala may teach other uses for its matrix – as argued by Appellants (App. Br. 6-9) – does not detract from its explicit teaching about treating joints. It is well settled that all disclosures in a reference must be considered. *See Merck & Co. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989).

Appellants also contend that the methods of Usala and Liu can not be combined because their compositions are different (App. Br. 10). Appellants state that Usala's matrix is based on gelatin, a highly denatured form of collagen, while Liu teaches collagen which is a distinct material (*id*. at 10-11) and not recognized as equivalent (*id*. at 11-15).

We acknowledge that the Examiner relied upon Liu in setting forth the basis of the rejection. However, upon consideration of the record as a whole, we find Liu unnecessary to reach all the limitations the subject matter of claim 1. Thus, we do not need to consider the differences between Liu's collagen composition and Usala's hydrogel.[3]

[3] We note Appellants' arguments that Liu teaches collagen, not a gel as taught by Usala; however, Liu's teaching is not restricted to native collagen, but also extends to "modified collagen" (FF10) which would include collagen modified by denaturation as taught by Usala.

For the foregoing reasons, we affirm the rejection of claim 1. Claims 2, 3, 5, 7, 9, 10, 12, 14, 20, 24, 26-29, 34, 35, 38, 52, and 126 fall with claim 1 because separate arguments for their patentability were not provided. 37 C.F.R § 41.37(c)(vii)(1).

OBVIOUSNESS OVER USALA, LIU, AND RHEE

Claims 36, 46, 49, 50, and 51 stand rejected under 35 U.S.C. § 103(a) as obvious over Usala, Liu, and Rhee (Ans. 6-7).

Appellants do not separately argue the claims. We select claim 46 to decide the issues in this rejection. Claim 46 is to the method of claim 1, but further recites that "the bioactive hydrogel matrix is administered in dehydrated form such that body fluids rehydrate" it. The Examiner states that Rhee teaches administering dehydrated matrix that is rehydrated after injection into a patient (Ans. 7-8) as in claim 46. The Examiner finds that persons of ordinary skill in the art would have been motivated to administer Usala's as a dehydrated matrix for its expected benefits as taught by Rhee (*id*. at 8). As we agree with the Examiner's findings and conclusion, and Appellants do not provide arguments or evidence to rebut it, we affirm the rejection of claim 46. Claims 36, 49, 50, and 51 fall with claim 46 as separate arguments for their patentability were not provided. 37 C.F.R § 41.37(c)(vii)(1).

OBVIOUSNESS OVER USALA, LIU, AND LIN

Claims 36, 37, and 46-51 stand rejected under 35 U.S.C. § 103(a) as obvious over Usala, Liu, and Lin (Ans. 9).

Appellants do not separately argue the claims. We select claim 37 to decide the issues in this rejection. Claim 37 is to the method of claim 1, but where the bioactive hydrogel matrix further comprises an osteoconductive material which is demineralized bone matrix. The Examiner finds that Lin teaches demineralized bone matrix in a gel and that therefore persons of ordinary skill in the art would have had reason to incorporate it into Usala's hydrogel matrix (Ans. 9-10). As we agree with the Examiner's findings and conclusion, and Appellants do not provide arguments or evidence to rebut it, we affirm the rejection of claim 37. Claims 36 and 49-51 fall with claim 37 as separate arguments for their patentability were not provided. 37 C.F.R § 41.37(c)(vii)(1).

OBVIOUSNESS OVER USALA, LIU, AND LIN

Claims 36, 37, and 121-125 stand rejected under 35 U.S.C. § 103(a) as obvious over Usala, Liu, and Young (Ans. 6-7).

Appellants do not separately argue the claims. We select claim 121 to decide the issues in this rejection. Claims 121 "is drawn to a method for attaching a first and second connective tissue using a hydrogel matrix comprising a polypeptide and long chain carbohydrate to coat a portion of the tissues, contacting and suturing the tissues" (Ans. 11). The Examiner finds such limitations are taught by Young and that persons of ordinary skill in the art would have been motivated to have combined Young's teachings with Usala and Liu "because Young et al. teach that these modifications are desirable for bone and cartilage repair" (*id*. at 12). As we agree with the Examiner's findings and conclusion, and Appellants do not provide arguments or evidence to rebut it, we affirm the rejection of claim 121.

Claims 36, 37, and 122-125 fall with claim 121 as separate arguments for their patentability were not provided. 37 C.F.R § 41.37(c)(vii)(1).

## CONCLUSIONS OF LAW

As we conclude that Usala teaches a method of administering a hydrogel matrix to a joint which would achieve the claimed result of "effecting regeneration of connective tissue selected from the group consisting of bone, cartilage, ligament, and tendon", we affirm the rejection of claims 1-3, 5, 7, 9, 10, 12, 14, 20, 24, 26-29, 34, 35, 38, 52, and 126 as obvious over Usala and Liu.

We also affirm the rejections of claims 36, 37 46-51, and 121-125 for the reasons stated above.

## TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

## AFFIRMED

Ssc:

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