The opinion in support of the decision being entered today was not written
for publication and is not binding precedent of the Board.

Paper No. 18

# UNITED STATES PATENT AND TRADEMARK OFFICE

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## BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

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Ex parte ARTHUR DALE ERICSSON, DANIEL HRNA
and THOMAS J. MALONEY

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Appeal No. 2002-1562
Application No. 09/183,454

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ON BRIEF

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Before ADAMS, MILLS and GRIMES, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

## DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. §134 from the examiner's final rejection of claims 25-30, 32-38 and 42-44,[1] which are all of the claims pending in this application.

Claims 25 and 42 are illustrative of the claims on appeal and read as follows:

25. A composition of matter comprising,
a living pathogen-targeting organic moiety conjugated to a radioisotope which has a half-life of less than 100 days,

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[1] The Answer indicates that the rejected claims are claims 25-30, 32-38 and 42-43. Answer, page 3. We note, however, the Final Rejection rejected claims 25-30, 32-38 and 42-44, and Appellants acknowledge this in the Brief, page 2. We find the failure to reject claim 44 in the Answer to be an inadvertent error on the part of the examiner. For purposes of this appeal we include claim 44 with the rejected claims, and note no prejudice to appellants in doing so.

wherein the living pathogen-targeting organic moiety is covalently linked to a complexing agent which binds the radioisotope, and

the living pathogen-targeting organic moiety is linked to the radioisotope via a bifunctional complexing agent.

42. A method for treating an infectious disease caused by living pathogens in a mammal, wherein said mammal produces antibodies in response to said living pathogens, said method comprising

obtaining antibodies from said mammal;

replicating said antibodies to produce replicated antibodies,

conjugating said replicated antibodies with a radioisotope which emits Auger electrons and has a half-life of less than 100 days to produce a therapeutic composition, and

administering said therapeutic composition to said mammal in a manner to bring said therapeutic composition into contact with said living pathogens,

wherein said antibodies are conjugated with the radioisotope with a complexing agent.

The prior art references relied upon by the examiner are:

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| Osther et al (Osther) | 5,529,776 | June 25, 1996 |

Li, M. et al (Li), "Labeling Monoclonal Antibodies with $^{90}$-Yttrium and $^{111}$-Indium-DOTA Chelates: A Simple and Efficient Method," Bioconjugate Chemistry, Vol. 5, No. 5, pp. 101-103 (1994)

Lewis, M.R. et al., (Lewis), "A Facile, Water-Soluble Method for Modification of Proteins with DOTA. Use of Elevated Temperature and Optimized pH to Achieve High Specific Activity and High Chelate Stability in Radiolabeled Immunoconjugates," Bioconjugate Chemistry, Vol. 5, No. 6, pp. 565-576 (1994)

Grounds of Rejection

Claims 25-30, 32-38 and 42-44 stand rejected under 35 U.S.C. § 103(a) for obviousness over Osther in view of Li and Lewis.

We reverse this rejection.

## DISCUSSION

In reaching our decision in this appeal, we have given consideration to the appellants' specification and claims, to the applied references, and to the respective positions articulated by the appellants and the examiner.

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellants regarding the noted rejections, we make reference to the examiner's Answer for the examiner's reasoning in support of the rejection, and to the appellants' Brief for the appellants' arguments thereagainst. As a consequence of our review, we make the determinations which follow.

### 35 U.S.C. § 103

Claims 25-30, 32-38 and 42-44 stand rejected under 35 U.S.C. § 103(a) for obviousness over Osther in view of Li and Lewis.

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. See In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). It is well-established that the conclusion that the claimed subject matter is prima facie obvious must be supported by evidence, as shown by some objective teaching in the prior art or by knowledge

generally available to one of ordinary skill in the art that would have led that individual to combine the relevant teachings of the references to arrive at the claimed invention. See In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988).

It is the examiner's position that (Answer, page 4),

> Osther et al disclose anti-HIV neutralizing antibodies useful in vaccine preparations, immunotherapeutic preparations, and assays for HIV-1 (abstract). In addition, Osther et al disclose the following: (1) HIV-1 encoded protein can be purified from a lysate of HIV-1 infected cells or it can be produced by recombinant methods for administration as an immunotherapeutic to humans infected by HIV-1 or related viruses (column 2, lines 22-35, columns 3-4, lines 50-68 and 1-25, respectively, column 5, lines 19-61; columns 7-8,lines 64-68 and 1-40, respectively); and (2) in Example 2, a sandwich radioimmunoassay was performed by attaching recombinant HIV-1 antigen to wells.

The examiner acknowledges that Osther fails to disclose a bifunctional chelating agent such as DOTA conjugated to the radioisotope and targeting moiety antibody. Answer, page 4.

Li is relied on by the examiner for the disclosure of monoclonal antibodies labeled with $^{90}$Yttrium- and $^{111}$Indium-DOTA chelates. Id. Monoclonal antibodies so labeled are indicated by Li to be "medically useful". Li, page 102, column 1. A reason for using the DOTA-peptide is to reduce the accumulation of the radioactivity in the liver by introducing a cleavable linker between the chelate and the monoclonal antibody. Li, page 103, column 2. Li particularly discloses the use of such antibody conjugates for cancer diagnosis and therapy in vivo. Li, page 103, column 1. Particularly described in Li is the uptake of such antibody conjugates by tumors in nude mice. Li, page 103, column 2.

Lewis discloses the modification of proteins with DOTA at an elevated temperature and optimized pH to achieve a high specific activity and high chelate stability in radiolabeled immunoconjugates. Answer, page 5. The antibodies are useful for tumor imaging and to reduce radiation damage and toxicity to normal organs and tissues. Answer, page 6. Lewis discloses the use of such antibodies for diagnosis and therapy in vivo. Lewis, p. 565, column 1.

The examiner summarizes (Answer, page 6):

> It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Osther et al using the teachings of Lewis et al and Li et al and generate an antibody-radioisotope composition conjugated to a chelating agent because both Lewis et al and Li et al disclose that it was well known in the art to generate compositions comprising an antibody conjugated to a radioisotope through a bifunctional chelating agent, such as DOTA.

The appellants respond, arguing, "there is not the slightest hint in the cited references of making a pathogen targeting antibody which contains a radioisotope." [Emphasis added.] Brief, page 3. Appellants also argue there is no motivation to conjugate radioisotopes to pathogen antibodies in the cited references. Brief, page 4.

According to the specification (page 4) the living pathogen-targeting moiety is in the form of an antiviral, antifungal or antibacterial antibody, although fragments of such antibodies or antibiotics which function to selectively carry the radioisotope into or onto a targeted pathogen are also considered suitable. Viruses, fungi, bacteria or prions

may be selected as targets by appropriate selection of the organic moiety.

Upon review of the prior art references, we do not find the examiner has provided sufficient evidence to support a prima facie case of obviousness. When the claims are read in view of the specification, they require the treatment of living pathogens, such as viruses, fungi, bacteria or prions.

While Osther discloses the use of labeled monoclonal antibodies as an in vitro diagnostic for HIV infection (Osther, column 4, line 54 to column 5, line 60), Osther does not disclose or enable the use of radiolabelled monoclonal antibodies for the treatment of HIV infection in vivo. Moreover, while Osther does disclose that antibodies described therein may be used as an immunotherapeutic (Osther, column 6, line 20 to column 11, line 20), there is no disclosure that the antibodies used in immunotherapy are radiolabeled.

Nor do we find that Li or Lewis make up for the deficiencies of Osther. What is missing from the examiner's analysis is why one of ordinary skill in the art with knowledge of radiopharmaceuticals for the treatment of tumors and cancer in vivo, would have been motivated to substitute the radiolabel of such radiopharmaceuticals, for the radiolabel of a composition for the in vitro diagnosis of HIV infection as described in Osther. Nor is there evidence of record of an expectation of success that radiolabeled conjugates for the treatment of tumors can be substituted with a pathogen-targeting organic moiety and successfully used for the treatment of pathogens, as

defined in the specification and as claimed.

Likewise, we do not find that the combination of the in vitro diagnostic disclosed in Osther with Li and Lewis is sufficient to meet the requirements of composition claim 25. In particular, it would reasonably appear that the secondary references, Li and Lewis, provide a radiolabeled linker to improve the in vivo clearance of the radiolabel by the liver when administered to treat cancer or tumors. We do not find that the secondary references provide reason, suggestion or motivation to substitute an radiolabeled linker for use in vivo, for a conventional radiolabel in an in vitro diagnostic sandwich assay for HIV infection, as described in Osther. Thus, we find no reason to modify the in vitro diagnostic assay described in the primary reference, Osther, to include the bifunctional linkers of Li and Lewis. Without motivation to combine the cited references for the treatment of pathogens, and with no evidence of other motivation to combine the cited references to arrive at the claimed composition, we do not find the examiner has provided sufficient evidence to support the rejection of the method of treatment or composition claims.

The rejection of the claims 35 U.S.C. 103(a) for obviousness over Osther in view of Li and Lewis is reversed.

Other issues

1. Upon return of the application to the examiner, we recommend that the examiner carefully revisit the issue of enablement under 35 U.S.C. § 112, first paragraph, with respect to the pending claims. The record reflects that the examiner previously made and withdrew a rejection of the claims for lack of enablement, based upon an argument that the specification failed to teach how to make specific chelated forms of the bioconjugate. See Paper No. 5, pages 3-5.

In reconsidering the issue of enablement, the examiner should begin by determining the scope of the pending claims and determine whether the specification supports and teaches how to use the claimed invention within the full scope of the claimed invention. In particular, the examiner should review the specification to determine whether the specification supports the full scope of the claimed method of treatment. In this regard, the examiner should carefully consider the holding in Enzo Biochem Inc. v. Calgene Inc., 188 F.2d 1362, 1371, 52 USPQ2d 1129, 1136 (Fed. Cir. 1999). In Enzo, the Federal Circuit concluded, based on the evidence before the district court in that case at that time, that antisense technology was highly unpredictable. In such unpredictable art areas, the Federal Circuit has refused to find broad generic claims enabled by specifications that demonstrate the enablement of only one or a few embodiments and do not demonstrate with reasonable specificity how

to make and use other potential embodiments across the full scope of the claim. See, e.g., In re Goodman, 11 F.3d 1046, 1050-52, 29 USPQ2d 2010, 2013-15 (Fed. Cir. 1993). The pending claims would appear to encompass the treatment of pathogens including viruses, fungi, bacteria or prions.

If the examiner should determine that the specification does not enable the entire scope of the pending claims, we recommend that the examiner provide evidence of lack of enablement to support any such rejection. Any further communication from the examiner which contains a rejection of the claims should provide appellants with a full and fair opportunity to respond.

2. We also direct the examiner's attention to copending application 09/938,884, entitled “Extracorporal System for Treating Disease with Radionucleotides “. We recommend that the examiner review the disclosure and claims of copending application 09/938,884 to determine if there may be obviousness-type double patenting issues present related to the claims of the present application.

## CONCLUSION

The rejection of claims 25-30, 32-38 and 42-44 under 35 U.S.C. § 103(a) for obviousness over Osther in view of Li and Lewis is reversed. Prior to further prosecution, it is recommended that the examiner consider the issue of enablement of the claims under 35 U.S.C. § 112, first paragraph to ensure that the specification

supports the full scope of the claims, and the issue of obviousness-type double patenting.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED

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| DONALD E. ADAMS<br>Administrative Patent Judge | ) |
| DEMETRA J. MILLS<br>Administrative Patent Judge | ) BOARD OF PATENT<br>) APPEALS AND<br>) INTERFERENCES |
| ERIC GRIMES<br>Administrative Patent Judge | ) |

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