

The opinion in support of the decision being entered today
is not binding precedent of the Board.

Paper No. 31

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte JITKA FORSTOVA,
BEVERLY E. GRIFFIN, and
NINA S. KRAUZEWICZ

Appeal No. 1998-0667
Application No. 08/280,306

HEARD: April 11, 2002

Before WILLIAM F. SMITH, SCHEINER, and MILLS, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision in an appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 9, 13, 18 through 22, 25, 26, and 28 through 32. Subsequent to the final rejection, the examiner determined that claim 26 is free of rejection and has only objected to that claim. In addition, claim 27 is pending and is also objected to by the examiner.

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AND INTERFERENCES**

Claims 1, 2, 6, 18, and 29 are representative of the subject matter on appeal and read as follows:

1. A method of transferring material into a host cell comprising:

providing a pseudocapsid formed from a papovavirus major capsid antigen and excluding minor capsid antigens, which pseudocapsid has exogenous material associated therewith; and

treating the host cell with the pseudocapsid so that the material is taken up by the cell and is biologically functional in that cell.

2. A method as claimed in claim 1 wherein the biological functioning of the exogenous material in the host cell has a therapeutic effect on a multi-cellular organism containing that cell.

6. A pseudocapsid formed from papovavirus major capsid antigen and excluding minor capsid antigens, which pseudocapsid has exogenous material associated therewith; but excluding pseudocapsids associated with exogenous genetic material and no other exogenous material when the pseudocapsid is formed from only the mouse polyoma virus major capsid antigen VP1.

18. A method of making a pseudocapsid comprising providing an empty pseudocapsid formed from papovavirus major capsid antigen and excluding minor capsid antigens; providing exogenous material; and mixing the empty pseudocapsid and exogenous material whereby the exogenous material becomes associated with the empty pseudocapsids; but excluding a method in which exogenous genetic material is associated with an empty pseudocapsid formed from only the mouse polyoma virus major capsid antigen, VP1.

29. A pseudocapsid formed from papovavirus major capsid antigen and excluding minor capsid antigens, which pseudocapsid has exogenous material associated therewith, wherein the pseudocapsid transfers the exogenous material into a host cell so that the material is taken up by the cell and is biologically functional in the cell.

The references relied upon by the examiner are:

Lowy et al. (Lowy) 5,437,951 Aug. 1, 1995

Slilaty et al. (Slilaty), "Gene Transfer of Polyoma-Like Particles Assembled in a Cell-Free System," Science, Vol. 220, pp. 725-727 (May 13, 1983)

Hanvey et al. (Hanvey), "Antisense and Antigene Properties of Peptide Nucleic Acids," Science, Vol. 258, pp. 1481-1485 (November 27, 1992)

Sandig et al. (Sandig), "Generation of DNA-Packaging Proteins by Overexpression in the Baculovirus/Insect Cell System," 12th Meeting of the European Society for Animal Cell Technology (May 17-21, 1993)

Haynes et al. (Haynes), "Mutations in the Putative Calcium-Binding Domain of Polyomavirus VP1 Affect Capsid Assembly," Journal of Virology, Vol. 67, No. 5, pp. 2486-2495 (1993)

Culver et al. (Culver), "Gene Therapy for Cancer," Trends in Genetics, Vol. 10, No. 5, pp. 174-178 (May 1994)

Wu-Pong, "Oligonucleotides: Opportunities for Drug Therapy and Research," Pharmaceutical Technology, Vol. 18, pp. 102, 104, 106, 108, 110-112, 114 (October 1994)

Wagner, "Gene Inhibition Using Antisense Oligodeoxynucleotides," Nature, Vol. 372, pp. 333-335 (November 24, 1994)

Miller et al. (Miller 1994), "Gene Transfer and Antisense Nucleic Acid Techniques," Parasitology Today, Vol. 10, No. 3, pp. 92-97 (1994)

Hodgson, "Advances in Vector Systems for Gene Therapy," Expert Opinion in Therapeutic Patents, Vol. 5, No. 5, pp. 459-468 (May 1995)

Marshall, "Gene Therapy's Growing Pains," Science, Vol. 269, pp. 1050-1055 (August 25, 1995)

Miller et al. (Miller 1995), "Targeted Vectors for Gene Therapy," FASEB Journal, Vol. 9, pp. 190-199 (February 1995)

Stull et al. (Stull), "Antigene, Ribozyme and Aptamer Nucleic Acid Drugs: Progress and Prospects," Pharmaceutical Research, Vol. 12, No. 4, pp. 465-483 (1995)

The claims stand rejected as follows:

Claims 2 through 5 under 35 U.S.C. § 112, first paragraph (enablement);

Claims 29 through 32 under 35 U.S.C. § 102(b) as anticipated Sandig;

Claims 1, 25, and 28 under 35 U.S.C. § 103 with the examiner relying upon Slilaty and Lowy as evidence of obviousness;

Claims 6 through 9 and 18 through 21 under 35 U.S.C. § 103 with the examiner relying upon Sandig and Lowy again as evidence of obviousness;

Claim 13 under 35 U.S.C. § 103 with the examiner relying upon Sandig, Lowy, and Hanvey as evidence of obviousness; and,

Claim 22 under 35 U.S.C. § 103 with the examiner relying upon Sandig, Lowy, and Haynes as evidence of obviousness.

We reverse.

Background

The claimed invention involves pseudocapsids formed from a papovavirus major capsid antigen. As explained in the paragraph bridging pages 4-5 of the specification:

The term "papovavirus" defines a general family of viruses including polyoma virus (a mouse virus), simian virus 40 (SV40), human variants (such as BK and JC) and papillomaviruses including human and bovine variants and other members. In each case, there is a major capsid antigen and one or more minor capsid antigens. For example, in papillomavirus the major antigen is L1 and the minor antigen is L2. In the present invention, the "pseudocapsids" are formed from the major capsid antigen and not the minor antigen(s).

Reference is made to Montross¹ for further information in regard to pseudocapsids of polyoma virus.

¹ Montross et al. (Montross), "Nuclear Assembly of Polyomavirus Capsids in Insect Cells Expressing the Major Capsid Protein VP1," Journal of Virology, Vol. 65, No. 9, pp. 4991-4998 (September 1991) (Copy of record).

As explained at page 8, lines 8-10 of the specification, “[t]he term ‘exogenous material’ as used herein means material other than wild type papovavirus nucleic acid. Preferably, the material is genetic material, for example DNA.” The exogenous material may be a protein or other polypeptide, or any pharmacologically active compound. See, e.g., page 8, lines 21-23 of the specification. The phrase “associated with” as used in the claimed invention is defined at page 5 of the specification as follows:

By the exogenous material being ‘associated with’ the pseudocapsid, we mean that the material is protected thereby. For example, exogenous DNA will be protected from degradation by DNases such as DNaseI, and exogenous protein will be protected from proteases. The exogenous material can be enclosed within an empty pseudocapsid or otherwise wrapped up with the capsid antigen.

As seen from claim 2 on appeal, one embodiment of the present invention involves the situation where the exogenous material functions in the host cell to the extent that it has a “therapeutic effect” on a multi-cellular organism containing that cell. In other words, one embodiment of the present invention involves the art area known as “gene therapy.” See, e.g., specification, page 13, lines 4-34.

Discussion

1. Enablement.

We first express our concern about the anomalous situation confronting us where dependent claims 2-5 are rejected as being non-enabled while claim 1, the independent claim from which these claims directly or indirectly depend, is not rejected. It has long been held that a claim must be enabled throughout its scope. In re Vaeck,

947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991); In re Wands, 858 F.2d 731, 736-37, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). As a matter of logic, assuming claims 2-5 are proper dependent claims and we see no reason why they are not, the examiner's decision that claims 2-5 are non-enabled necessarily means that claim 1 is non-enabled. We find no explanation on the record as to the examiner's reasoning behind the decision not to reject claim 1 as being non-enabled. In view of our disposition of the rejection of claims 2-5 under this section of the statute, we view this as harmless error on the examiner's part.

In reviewing the facts and reasoning relied upon by the examiner in stating the rejection on pages 5-8 of the Examiner's Answer and amplified in the examiner's response to the appellants' arguments on appeal appearing at pages 12-15 of the Answer, it appears that the examiner's concern is directed more to his belief that the field of gene therapy itself is non-enabled as opposed to the use of the present pseudocapsid technology in the field of gene therapy being non-enabled. We reach this conclusion on the basis that the references relied upon by the examiner in support of the enablement rejection are directed to gene therapy in general or gene therapy as implemented by other therapeutics besides pseudocapsids. Our review of the examiner's evidence in light of the correct legal standards leads us to conclude that the evidence does not support the broad proposition that gene therapy is non-enabled. Since we have no separate stated position specific to the present pseudocapsid technology, the examiner's rejection cannot be sustained.

The portions of the references relied upon by the examiner in the Answer in support of his case for the most part express concerns regarding possible problems which may have to be overcome in order for gene therapy to be useful in a clinical setting. For example, the examiner states at page 5 of the Answer, "Wagner states that while oligos [oligonucleotides] 'show great promise', development of delivery systems is essential. Wagner concludes that 'critical evaluation of antisense [oligos] in vivo...should eventually lead to the development of improved methods in antisense therapy for human diseases.[']" In like manner, the examiner relies upon Stull at page 5 of the Answer for the proposition that "[n]ucleic acid drugs must overcome several formidable obstacles before they can be widely applied as therapeutics."

From these and other statements in the Answer, it is our belief that the examiner is of the opinion that gene therapy will not be enabled until it is clinically available to humans. However, this is not the legal standard to be applied.

As explained in In re Brana, 51 F.3d 1560, 1567, 34 USPQ2d 1436, 1442 (Fed. Cir. 1995), the USPTO should not confuse "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption," citing Scott v. Finney, 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120 (Fed. Cir. 1994). The rejection before the court for review in Brana was under 35 U.S.C. § 112, first paragraph (enablement). However, the court discussed the issues raised in the appeal in the context of both enablement and the utility requirement of 35 U.S.C. § 101. The court went on to state in Brana, 51 F.3d at 1568, 34 USPQ2d at 1442-43:

On the basis of animal studies, and controlled testing in a limited number of humans (referred to as Phase I testing), the Food and Drug Administration may authorize Phase II clinical studies. See 21 U.S.C. § 355(i)(1); 21 C.F.R. § 312.23(a)(5), (a)(8) (1994). Authorization for a Phase II study means that the drug may be administered to a larger number of humans, but still under strictly supervised conditions. The purpose of the Phase II study is to determine primarily the safety of the drug when administered to a larger human population, as well as its potential efficacy under different dosage regimes. See 21 C.F.R. § 312.21(b).

FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Scott, 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

While the claims involved in Brana were directed to chemical compounds taught to be useful in treating cancer, we believe these principles can be applied to the claims at hand directed to methods of gene therapy, especially in light of the examiner's apparent holding that gene therapy in general is non-enabled.

The references relied upon by the examiner themselves document various clinical trials of gene therapy techniques. One example is found in Wagner which states "[c]linical trials are now in progress to evaluate the therapeutic potential of antisense [oligodeoxynucleotides] in several human diseases . . ." Wagner, page 333, first full paragraph. Miller states at page 197, right-hand column, "[o]f the gene therapy protocols that have so far entered clinical trials . . ." Marshall sets forth a table at page

1055 listing "U.S. GENE THERAPY TRIALS SPONSORED BY INDUSTRY." The table contains 14 entries. Culver states at page 175, left-hand column, "[o]n the basis of these studies, several gene therapy trials in humans have been approved" Table 1 of Marshall lists a number of trials of gene therapy for cancer.

While not explicitly stated, we believe the examiner's position is based in large part upon the possibility or perhaps even the probability that many of the protocols used in the documented clinical trials may never be approved for clinical use in humans. Indeed, a number of the quotes relied upon by the examiner from the references refer to problems or obstacles in delivering the therapeutic to the target in a clinical setting. However, as stated in Brana, that is not the standard for enablement and/or utility.

Absent a fact-based statement from the examiner which focuses on the claimed subject matter instead of gene therapy as a general field, we hold that the examiner has failed to establish that the subject matter of claims 2-5 on appeal is non-enabled.

2. Sandig.

The sole reason set forth at page 8 of the Examiner's Answer in support of this rejection is "Sandig et al. disclose pseudocapsids formed from only the polyoma virus major capsid antigen, VP1, and having exogenous DNA associated therewith." Missing from the examiner's statement of the rejection is any acknowledgment that claim 29 requires that the "pseudocapsid transfers the exogenous material into a host cell so that the material is taken up by the cell and is biologically functional in the cell."

Appellants' position focuses on this latter requirement of claim 29. Appellants argue that the pseudocapsids of Sandig consisting of VP1 only were not able to transfer

the exogenous material, i.e., DNA, into a host cell so that the DNA was taken up by the cell and was biologically functional in the cell. The examiner agrees with appellants that the results reported in Sandig indicate that the pseudocapsids formed of VP1 were unable to transfer the associated DNA into a host cell so that the DNA was biologically functional. The examiner argues in the paragraph bridging pages 15-16 of the Examiner's Answer in responding to appellants' arguments:

There are two possible explanations for the difference in the results obtained by Sandig et al. and Appellants. One explanation is that Appellants discovered how to use the particles of Sandig et al. to transfer and express DNA in cells. But 'discovery of an unobvious property and use does not overcome the statutory restraint of section 102 when the claimed composition is known' (In re Spada, p. 1658). The second possible explanation is that Appellants discovered a new method for making pseudocapsids and/or associating DNA therewith, which somehow changes the physical properties of the composition. If this is the case, the claim does not incorporate whatever process of manufacture might distinguish the claimed composition from that disclosed by Sandig et al.

This issue can be readily resolved by simple reference to Sandig and the present specification. In reporting the results concerning the pseudocapsids consisting of VP1, Sandig states that the results are "consistent with electron microscopy data showing only particles adsorbed to the cell surface." In other words, the pseudocapsids described in Sandig and relied upon by the examiner in support of this rejection had the exogenous DNA adsorbed to the pseudocapsid surface and not contained therein. In contrast to this description of the particles of Sandig, the present specification states:

By the exogenous material being 'associated with' the pseudocapsid, we mean that the material is protected thereby. For example, exogenous DNA will be protected from degradation by DNases such as DNaseI, and exogenous protein will be protected from proteases. The exogenous

material can be enclosed within an empty pseudocapsid or otherwise wrapped up with the capsid antigen.

Specification, page 5.

These two passages provide a clear objective distinction between the work described in Sandig and the present invention. As defined by appellants, the exogenous material associated with the pseudocapsid of claim 29 is protected by the pseudocapsid, i.e., "enclosed within an empty pseudocapsid or otherwise wrapped up with the capsid antigen," while that of Sandig was adsorbed to the pseudocapsid surfaces.

On this record, it is clear that the pseudocapsids described in Sandig relied upon by the examiner do not allow for the transfer of the exogenous material into a host cell so that the materials taken up by the cell is biologically functional in the cell as required by the rejected claims.

The rejection under 35 U.S.C. § 102(b) based upon Sandig is reversed.

3. Obviousness rejections.

The first obviousness rejection is premised upon the disclosures of Slilaty and Lowy. At page 8 of the Answer, the examiner states that Slilaty describes a method of using polyoma virus pseudocapsids to transfer DNA in the cultured rat cells. However, the pseudocapsids of Slilaty are not composed entirely of major capsid antigen. The examiner makes note of the teaching in Slilaty that a limitation of the polyoma virus pseudocapsid as a gene transfer agent is its small size which limits the amount of DNA which can be packaged.

The examiner relies upon Lowy for its teaching that human papilloma virus capsid is larger in size than polyoma virus capsid. The examiner relies upon Lowy's teaching of a method for producing empty human papilloma virus capsids composed entirely of a major capsid antigen. However, the examiner does not assert and it does not appear that Lowy teaches that the empty human papilloma virus capsids which are composed entirely of the major capsid antigen are described as being useful for transferring exogenous materials into cells.

The examiner reasons it would have been obvious to one of ordinary skill in the art to modify the method of Slilaty by replacing the polyoma pseudocapsid with the human papilloma virus pseudocapsid composed entirely of the major capsid antigen since "one would have expected that more DNA could be packaged in the [human papilloma virus] pseudocapsid" (Examiner's Answer, page 9). However, what is missing from the examiner's position is an explanation why one of ordinary skill in the art would have expected pseudocapsids composed entirely of the major capsid antigen associated with exogenous material would permit the exogenous material to be taken up by a cell and be biologically functional in that cell. Viewing the two references relied upon by the examiner, only Slilaty is directed to a method of transferring material into a host cell. However, the pseudocapsids of Slilaty are not composed entirely of major capsid antigens required by the claims on appeal. While one perhaps would assume that the larger capsid of Lowy may be able to "package" more DNA, it is unclear from the record why one would expect the larger Lowy capsid to be able to deliver such DNA so that it is biologically functional in a cell. From these two references, it is only capsids

which contain major and minor antigens which can deliver functional biological material (Slilaty), not capsids formed only from the major capsid antigen as required by the claims. Absent a fact-based explanation from the examiner, we do not find that one of ordinary skill in the art would have had a reasonable expectation of success in achieving the claimed invention based upon the teachings of Slilaty and Lowy.

The remaining § 103 rejections are premised upon Sandig. As explained above, Sandig expressly teaches that polyoma virus pseudocapsids formed from the major capsid antigen did not permit the exogenous DNA to be taken up by a cell and be biologically functional in that cell. The examiner relies upon the disclosure of Lowy of empty human papilloma virus capsids composed entirely of the major capsid antigen. But again, Lowy does not describe the use of those capsids for transferring exogenous materials into a cell. Accordingly, we do not find that the combination of Sandig and Lowy establishes the requisite reasonable expectation of success needed in order to arrive at a proper conclusion of prima facie obviousness.

The rejections under 35 U.S.C. § 103(a) are reversed.

Other Issue

We make of record U.S. Patent Number 6,046,173 which issued from an application stated to be a continuation of the present application. Upon return of the application, the examiner should review the claims of U.S. Patent Number 6,046,173 and determine whether double patenting issues arise.

The decision of the examiner is reversed.

REVERSED

William F. Smith
William F. Smith
Administrative Patent Judge

Demetra J. Mills
Demetra J. Mills
Administrative Patent Judge

Toni R. Scheiner
Toni R. Scheiner
Administrative Patent Judge

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Application No. 08/280,306

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