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The opinion in support of the decision being entered today  
(1) was not written for publication in a law journal and  
(2) is not binding precedent of the Board.

Paper No. 32

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES  
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Ex parte ARUN SRIVASTAVA

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Appeal No. 1996-2009  
Application No. 07/982,193  
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Heard: March 23, 2000  
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Before WINTERS, GRON, and LORIN, Administrative Patent  
Judges.

LORIN, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. ' 134 from the final rejection of claims 1-3, 7-12, and 14-19. On consideration of the record, we affirm the examiner's decision rejecting these claims under the judicially



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judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of Srivastava.

Claims 11 and 14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 or 9 of Srivastava.

Claims 1-3, 7, 8, 15, 17 and 18 are rejected under 35 U.S.C. ' 103 as being unpatentable over Lebkowski in view of Izban.

Claims 10, 11 and 14 are rejected under 35 U.S.C. ' 103 as being unpatentable over Lebkowski in view of Izban as applied to claims 1-3, 7, 8, 15, 17 and 18 and further in view of appellant's admissions.

Claims 9 and 12 are rejected under 35 U.S.C. ' 103 as being unpatentable over Lebkowski in view of Izban as applied to claims 1-3, 7, 8, 15, 17 and 18 and further in view of Kim.

Claims 16 and 19 are rejected under 35 U.S.C. ' 103 as being unpatentable over Lebkowski in view of Izban as applied to claims 1-3, 7, 8, 15, 17 and 18 and further in view of Lu.

### Decision

#### *Obviousness-Type Double Patenting Rejections*

All the claims on appeal have been rejected under the judicially created doctrine of obviousness-type double patenting. Appellants do not address the merits of these rejections except to say that they have agreed to file the

appropriate terminal disclaimer upon indication of allowable subject matter.<sup>1</sup> Accordingly we affirm the rejections.

*Rejections Under 35 U.S.C. ' 103*

Examiner has made four rejections under 35 U.S.C. ' 103 covering all the claims on appeal. In all four statements of the rejections the same primary and secondary references are cited: Lebkowski and Izban, respectively. Only the tertiary references are different.

Consequently, the linch pin of all these rejections is the art combination: Lebkowski in view of Izban.

The examiner has the initial burden of establishing a prima facie case of obviousness. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). We have carefully reviewed examiner's position but, for the following reasons, the PTO's burden of establishing a prima facie case of obviousness has not been met.

As we interpret representative claim 1, the claimed invention is directed to an expression vector comprising

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<sup>1</sup> "Appellant has indicated on this record that upon indication of allowable subject matter, Appellant will file the appropriate terminal disclaimer to overcome the obviousness-type double patenting rejection. Accordingly, the only rejection maintained for consideration on appeal is the rejection of Claims 1-3, 7-12 and 14-19 under 35 U.S.C. ' 103." Brief, p. 2.

two inverted terminal repeats [ITRs] of adeno-associated virus [AAV] between which resides at least one cassette comprising a promoter operably linked to a heterologous gene. Importantly, the promoter is capable of affecting cell-specific expression of the heterologous gene (see Specification, p. 17, lines 1-2).

According to the examiner (Examiner's Answer, p. 4), the primary reference, Lebkowski, discloses expression vectors for site-specific integration comprising two inverted terminal repeats of adeno-associated virus (AAV) and a cassette comprising a promoter (CMV or MSV promoter) operably linked to a heterologous gene (cat or neo), and wherein the cassette resides between the [ITRs] (see Abstract and Figure 1, for example).

Lebkowski's expression vector differs from the claimed expression vector only in that Lebkowski does not disclose a promoter capable of effecting cell-specific expression of the heterologous gene. Lebkowski teaches p40 instead, which is a promoter for AAV.

Recognizing that appellant's "invention differs from [Lebkowski] in that appellant uses a cell specific promoter to provide cell-specific gene expression" (Examiner's

Answer, p.4), the examiner relies on Izban for its disclosure of a known cell-specific promoter. Based on this evidence, the examiner concludes that  
It would have been obvious to include a cell-specific vector, such as the one taught by Izban, in an AAV expression vector, such as those taught by Lebkowski, in order to achieve expression of a gene only in those cells in which its expression is desired.

Examiner's Answer, p. 5.

Although the examiner concludes, based on the art combination, that it would have been obvious to "include" the Izban promoter in Lebkowski's AAV expression vector, and thereby achieve the claimed invention, how this inclusion is to be accomplished is not explained. We consider two scenarios reflected in the arguments of the parties: 1) the Izban promoter is incorporated along with p40 in Lebkowski's AAV expression vector, and 2) the Izban promoter is substituted for p40 in Lebkowski's AAV expression vector. Either way we are not persuaded that the examiner has made out a prima facie case of obviousness for the claimed expression vector.

Under the first scenario, even if we were to find that the combination of Lebkowski and Izban would have suggested to those of ordinary skill in the art that they should make the claimed expression vector by including both the p40 and an Izban promoter in the AAV expression

vector, to establish the prima facie case of obviousness, the prior art would have to also reveal that, in so including the promoter, those of ordinary skill would have had a reasonable expectation of success in obtaining an AAV vector with cell-specific gene expression. "Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).<sup>2</sup> The burden rests on the examiner to support the prima facie case of obviousness with a showing that in combining the promoters there would have been a reasonable expectation of success in obtaining the claimed vector. Here that has not been done.

Whether the combination of the p40 and an Izban promoter in the AAV expression vector would yield "an

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<sup>2</sup> "Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under ' 103 requires, inter alia, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. See In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. Id."

expression vector for site-specific integration and cell-specific gene expression" as the claims require is unclear. The examiner does not explained why one would have expected the Izban promoter to predominate or otherwise disregard Lebkowski's p40. Neither reference involves combining promoters, and neither discusses the consequences related to such a combination.

Consequently, based on the information in these references, one can only speculate as to the result of the combination. We agree with appellant's argument that "in the absence of the requisite teaching of the present invention there could not be a reasonable expectation that the inclusion of a cell-specific promoter such as that disclosed by Izban et al. in the vector of Lebkowski et al. can achieve the present invention, especially since the vectors of Lebkowski et al. contain a strong promoter capable of overriding a cell-specific promoter [appellant's emphasis]." Brief, sentence bridging pp. 5-6. The examiner has therefore not established that, based on the prior art disclosures, those of ordinary skill would have had a reasonable expectation of success in obtaining "an expression vector for site-specific integration and cell-specific gene expression."

Accordingly, under this scenario, the examiner has not

made out a prima facie case of obviousness.

We now turn to the second scenario, whereby the prima facie case of obviousness is predicated on substituting Izban's cell-specific promoter for, rather than including it with, Lebkowski's p40. Here also the examiner has not shown that there would have been a reasonable expectation of success in obtaining the claimed vector by replacing p40 with Izban's promoter.

To reinforce the prima facie case of obviousness under the second scenario, the examiner (Examiner's Answer, p. 7) relies on this passage in Lebkowski (p. 3991):

Theoretically, all sequences between the two AAV inverted repeats can be deleted and replaced by exogenous DNA. In this case, 3,500 to 4,000 bases of DNA could be accommodated, allowing for the potential introduction of two genes into a given cell by a single AAV vector.

As we understand it, the examiner reasons that this passage would have suggested to those of ordinary skill to delete the entire sequence between the ITRs in the AAV expression vector, which would include p40, resulting in an open section, and to insert therein not only exogenous DNA but Izban's cell-specific promoter in place of the deleted p40.

The difficulty with the examiner's reasoning is that rather than supporting the prima facie case of

obviousness, in our view it supports appellant's position that the result of replacing p40 with another promoter is speculative and therefore there can be no reasonable expectation of success. As with the first scenario, here too examiner has not shown that there would have been a reasonable expectation of success in obtaining the claimed invention by incorporating the Izban promoter between the ITRs of Lebkowski's AAV expression vector. Lebkowski's disclosure that "theoretically" all sequences between the ITRs can be deleted or replaced indicates that the results from manipulating this area of the AAV expression vector are a matter of speculation. To then also insert Izban's promoter in the deleted section only adds to the speculative nature of the result. Absent knowledge gained from appellant's specification, there is no reasonable expectation of success in obtaining the claimed expression vector from such a deletion/insertion.

We therefore agree with appellant:

Lebkowski et al. states that "theoretically, all sequences between the two AAV inverted terminal repeats can be deleted and replaced with endogenous DNA" [appellant's emphasis]. Lebkowski et al., however, does not teach, or even suggest, that all sequences between the two AAV terminal repeats can be deleted and replaced by endogenous DNA to construct a vector capable of site-specific integration and cell-specific expression [appellant's emphasis]. It is only with the benefit of the present specification that the Examiner establishes a nexus between the claimed invention and the cited prior art teaching.

Brief, p. 6.

Another difficulty with examiner's reasoning is that, even if we agreed that the above-mentioned Lebkowski passage expressly suggests deleting the entire sequence between the ITRs, the prior art would not have suggested to those of ordinary skill in the art to insert a promoter other than p40. Neither Lebkowski nor Izban suggest replacing p40 with another promoter in an AAV expression vector. The examiner admits that none of Lebkowski's vectors are without p40 (Examiner's Answer, p. 7), and Lebkowski provides no reason, and the examiner does not point to any, for substituting a different promoter for p40. Similarly, there is no suggestion in Izban that would have led one to select Izban's murine albumin promoter as an alternative promoter in the AAV expression vector. Aside from inserting exogenous DNA, Lebkowski does not provide any direction as to which or what type of promoter could be successfully inserted. Given that Izban does not suggest inserting its promoter in an AAV expression vector, the only reason for doing so is provided by appellant's disclosure. Therein appellant describes the advantages and problems associated with AAV-based vectors with general promoters for gene therapy

purposes<sup>3</sup> and how these problems are overcome by incorporating a cell-specific promoter instead.<sup>4</sup> Nevertheless, one cannot rely on appellant's disclosure to support a case of obviousness. "Obviousness can not be established by hindsight combination to produce the claimed invention," In re Dance, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998).

Not only is there no reasonable expectation of success that the substitution examiner argues would achieve the claimed result, but there is no suggestion in the cited prior art to making that substitution. Accordingly, examiner has not established a prima facie case of obviousness under the second scenario.

Since the examiner has not met the burden of establishing a prima facie case of obviousness under either the first or second scenario, the rejections under 35 U.S.C. ' 103 are reversed.

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<sup>3</sup> "While AAV-based vectors allow stable, site-specific integration of the transferred gene, the indiscriminate expression of the transferred gene in all cell lineages presents significant problems. Thus, a need exists for AAV vectors which effect tissue-specific expression of the transferred gene." Specification, p. 5.

<sup>4</sup> "The vectors of the present invention contain a promoter which directs tissue-specific expression. For example, the wild-type parvovirus B19 has a limited host range and exhibits a remarkable tissue tropism for the erythroid elements of bone marrow" Specification, p. 12.

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

AFFIRMED

SHERMAN D. WINTERS	)	
Administrative Patent Judge	)	
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	)	
	)	
	)	BOARD OF PATENT
TEDDY S. GRON	)	APPEALS
Administrative Patent Judge	)	AND
	)	INTERFERENCES
	)	
	)	
	)	
HUBERT C. LORIN	)	
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