

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 74

**UNITED STATES PATENT AND TRADEMARK OFFICE**

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

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Ex parte THOMAS E. WAGNER, and  
PETER C. HOPPE

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Appeal No. 2003-1126  
Application No. 08/449,285

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ON BRIEF

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Before SCHEINER, ADAMS, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

An oral hearing in this case was scheduled for January 20, 2004. Upon reviewing the case, however, we have determined that an oral hearing will not be necessary and we render the following decision based on the record. See 37 CFR § 1.194(c).

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 39, 41, 43, 50, 51, 55-79, 82, 83, 86-114, 116 and 119. Claims 39, 51, and 56 are representative of the subject matter on appeal, and read as follows:

39. A nonhuman transgenic mammal whose somatic and germ cells contain exogenous genetic material, wherein said material does not include any virus-specific DNA and includes at least one heterologous gene and a transcriptional control sequence operably associated therewith, wherein said gene is expressed at a detectable level in a plurality of said somatic cells or said germ cells, where said genetic material is selected so that the normal development of the embryo is not prevented by said material, where said mammal is selected from the group consisting of rodents, rabbits, goats, pigs, cattle, and sheep.
51. A nonhuman mammal characterized as having somatic and germ cells that contain exogenous material that does not include any virus-specific DNA, said material including at least one heterologous gene and a transcriptional control sequence operably associated therewith, said gene being expressible at a detectable level in a plurality of said somatic cells or said germ cells of said mammal under the control of said control sequence, said genetic material being selected so that the normal development of the embryo to term is not prevented by such material, said mammal having been obtained by the following steps:
- (a) introducing exogenous genetic material into a pronucleus of a mammalian zygote by microinjection, said genetic material including at least one heterologous gene and a control sequence operably associated therewith, thereby obtaining a genetically transformed zygote;
  - (b) transplanting an embryo derived from the genetically transformed zygote into a pseudopregnant female; and
  - (c) allowing the embryo to develop to term;
- or a mammal descended from a transgenic mammal so produced which retains the heterologous gene in expressible form, where said mammal is selected from the group consisting of rodents, rabbits, goats, pigs, cattle, and sheep.
56. A method of producing a polypeptide or protein which comprises:
- (a) producing a mammal capable of expressing said polypeptide or protein at a detectable level by a method which comprises
    - (i) introducing exogenous genetic material that does not include any virus-specific DNA into a pronucleus of a mammalian zygote by microinjection, said genetic material including at least one heterologous gene and a transcriptional control sequence operably associated

therewith, thereby obtaining a genetically transformed zygote;

(ii) transplanting an embryo from the genetically transformed zygote into a pseudopregnant female; and

(iii) allowing the embryo to develop to term; where said gene and control sequence are selected so that the gene is not activated in such a manner and degree as would prevent normal development of the embryo to term; and said polypeptide or protein is producible in a cell of said mammal which bears said gene, as a result of the expression of said gene under the control of said control sequence, and where said mammal, absent said exogenous genetic material is unable to produce said polypeptide or protein; and

(b) expressing said gene in said mammal, or progeny thereof which retain said gene in expressible form, thereby producing said polypeptide or protein at a detectable level, where said mammal is selected from the group consisting of rodents, rabbits, goats, pigs, cattle, and sheep.

The examiner relies upon the following references:

Strojek et al. (Strojek), "The use of transgenic animal techniques for livestock improvement," Genetic Engineering: Principles and methods, Vol. 10, pp. 221-246 (1988)

Kappel et al. (Kappel), "Regulating gene expression in transgenic animals," Current Opinion in Biotechnology, Vol. 3, pp. 548-553 (1992)

Houdebine, "Production of pharmaceutical proteins from transgenic animals," Journal of Biotechnology, Vol. 34, pp. 269-287 (1994)

Wall, "Transgenic livestock: Progress and prospects for the future," Theriogenology, Vol. 45, pp. 57-68 (1996)

Claims 39, 41, 43, 45, 50, 51, 55-79, 82, 83, 86-114, 116 and 119 stand rejected under the judicially created obviousness-type double-patenting as being unpatentable over claims 1-7 of U.S. Patent No. 4,873,191. Claims 39, 41, 43, 45, 50, 51, 55-79, 82, 83, 86-114, 116 and 119 also stand rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the specification fails to enable

the full scope of the claimed subject matter. After careful review of the record and consideration of the issues before us, we affirm the obviousness-type double patenting rejection, but reverse the rejection under 35 U.S.C. § 112, first paragraph.

### DISCUSSION

1. Rejection for Obviousness-type Double Patenting

Claims 39, 41, 43, 45, 50, 51, 55-79, 82, 83, 86-114, 116 and 119 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 4,873,191.

According to the rejection, “the nonhuman transgenic mammal and methods of producing a polypeptide or protein using the mammal of claims 39, 41, 43, 45, 50, 51, 55-79, 82, 83, 86-114, 116 and 119 are obvious over claims 1-7 of the '191 as the mammal of the claims is made by the method of [sic] claimed in '191.” Examiner’s Answer, page 3.

Appellants state that they intend to file a terminal disclaimer upon the indication of allowable subject matter. As appellants do not argue the rejection and as a terminal disclaimer has not been filed, this rejection is affirmed.

2. Rejection under 35 U.S.C. § 112, first paragraph

Claims 39, 41, 43, 45, 50, 51, 55-79, 82, 86-114, 116 and 119 stand rejected under 35 U.S.C. § 112, first paragraph. According to the rejection,

the specification, while being enabling for a transgenic mouse whose somatic and germ cells contain a DNA sequence encoding a protein of interest under the control of a transcriptional control sequence and methods of using the mouse to produce the protein in its blood and isolating the protein from the blood, does not

reasonably provide enablement for the breadth of the claims to transgenic rodents, rabbits, goats, pigs, cattle or sheep expressing any genetic material of interest under obtainable conditions, and methods of producing a polypeptide of interest in the above listed transgenic mammals. . . . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Examiner's Answer, pages 3-4.

The rejection addresses the relevant Wands factors. See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1403 (Fed. Cir. 1988). Factors that should be considered in determining whether a specification is enabling, or if it would require an undue amount of experimentation to practice the invention include: (1) the quantity of experimentation necessary to practice the invention, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. See id.

With respect to the nature of the invention, the examiner comments that the claimed invention is drawn

to a transgenic nonhuman mammal whose genome contains at least one heterologous gene and a transcriptional control sequence operatively associated where the mammal expresses the gene at a detectable level in a plurality of the mammal's cells, and the methods of producing a polypeptide or protein in the transgenic mammal or progeny of the transgenic mammal. The mammal can be anyone of a rodent, rabbit, goat, pig, cattle and sheep. The protein can be any polypeptide or protein.

Examiner's Answer, page 4. According to the rejection, "[a] compelling feature of a transgenic mammal is that the heterologous genetic material is present in all, or

at least almost all, somatic and germ cells of the mammals. In this regard, the transgenic mammal can pass the heterologous gene to its progeny through either the female or male germ cells.

With respect to the state of the art at the time of filing, the examiner observes that the earliest filing date is June 12, 1981. The rejection contends that at that time, “the production of transgenic rabbits, goats, pigs, cattle or sheep was neither routine nor well known,” but “was an emerging endeavor of scientific research.” Id. at 5.

With respect to the amount of guidance presented by the specification and the working examples, the last factors discussed by the rejection, the rejection asserts that “the specification does not provide any teachings as to transgenic mice, other rodent [sic], rabbits, goats, pigs, cattle or sheep where expression of the transgene provides anything short of a phenotypic change that benefits the art,” i.e., “there is no disclosed use for a transgenic mammal that expresses the transgene at a detectable level in some cells.” Id. at 6.

The rejection contends that when the claims are read in light of the specification, “the artisan would see that the use for the claimed mammals and methods of producing a polypeptide or protein is to increase feed utilization and growth rate in food mammals, to increase feed utilization and milk production in mammals, to produce of [sic] meats of altered flavor, to serve as developmental models and to eliminate or diminish genetic diseases.” Id. at 7-8. According to the rejection, those uses require expression of specific genetic material, but that at the time of filing, “the ability to specifically produce desired phenotypes in a

transgenic mammal was unpredictable.” Id. at 8. Moreover, the rejection notes further that the specification “does not teach nor provide guidance as to the nucleic acid constructs or nucleic acid vectors to be employed in the production of transgenic nonhuman mammals that exhibit any of the above discussed, disclosed phenotypes.” Id.

The specification further contends that “[t]ransgenic mammals and methods of polypeptide or protein production, to meet any of the disclosed uses, require more than an outline of making the mammal. It requires very specific guidance as to the promoters or expression regulatory sequences, the genetic material or DNA sequences encoding a particular protein, and in some cases, the tissues in which expression is to be achieved to produce a mammal with a phenotype of the disclosure.” Id.

The rejection argues that the only guidance provided by the specification is the production of a mouse that expresses a rabbit  $\beta$ -globin gene, and that example “does not provide guidance for the production of transgenic mammals for their entire breadth as the expression of rabbit  $\beta$ -globin does not fall within the disclosed uses for the transgenic mammal.” Id. at 10. The rejection thus concludes “that the skilled artisan would need to engage in an undue amount of experimentation without a predictable degree of success to reach the invention as claimed. Id. at 12.

Appellants argue that, by trying to limit the claims to the one exemplified embodiment, the examiner is penalizing them for filing “when they had only

transgenically expressed one gene under the control of the promoter in one species of mammal.” Substitute Appeal Brief, page 12.

“[E]nablement requires that the specification teach those in the art to make and use the invention without ‘undue experimentation.’ That some experimentation may be required is not fatal; the issue is whether the amount of experimentation required is not ‘undue.’” In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991) (citation omitted, emphasis in original). “Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations.” In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). “[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.” In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971) (emphasis in original). “[I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.” Id. at 224, 169 USPQ at 370.

The panel agrees that the examiner has failed to meet the burden of establishing a prima facie case that the specification fails to enable the full scope of the claimed subject matter. The rejection focuses on uses disclosed by the specification, such as increasing feed utilization and growth rate in food mammals; increasing feed utilization and milk production in mammals, the production of meats of altered flavor; and the development of developmental models to eliminate or diminish genetic diseases. A product, however, need only enable a single use to enable the product, see MPEP § \_\_\_\_, and as pointed out by appellants, one of the uses disclosed by the specification is production of a protein product, see Supplemental Appeal Brief, page 17. The examiner has not provided evidence to demonstrate that one skilled in the art would not expect the method to work with mammals other than mice or genes other than the rabbit  $\beta$ -globin gene.

Moreover, Appellants argue that:

Interestingly, the claims of the '191 patent are not limited to methods for making transgenic mice, nor are the claims limited to making transgenic animals that express a particular gene under the control of a particular promoter. Therefore, the Office has previously concluded that Applicants' specification was enabling for methods for making transgenic animals much more broadly than those for which experimental results are provided in the specification. It is inconsistent for the Office now to assert that transgenic animals that are made using these methods are not enabled by the same specification.

Supplemental Appeal Brief, page 16.

In the response to this argument, the examiner contends that:

The key to appellants' argument . . . is that they have developed a method of making transgenic mammals, and they have received broad claims to this aspect of the invention. However, what they have not taught are the mammals themselves. While the broad method may be enabled, the broad products are not so enabled. Appellants are enabled for mammals expressing a heterologous protein in their blood and methods of producing the protein and isolating it from their blood. However, it is the breadth of the mammals for which appellants are not enabled. The bridge appellants have found, and patented, is to the method of making the mammals. This may seem [sic] counter intuitive at first, but the method's use as disclosed in the making of transgenic nonhuman mammals. The product uses are defined [sic] in the specification as increased growth rate and efficiency of feed utilization in animals used to produce meat, such as the transfer of genes relating to growth and feed utilization from a buffalo into beef cattle to create a new species; an increase in milk production and efficiency of feed utilization by transferring exogenous genetic material from species or breeds of the same species which have either or both traits; the alteration of meat flavor such as in lamb; the transfer of genes for an in vivo analysis of gene expressing during differentiation and the transgenic mammals can be used in the elimination or diminution of genetic diseases. The skilled artisan reading the specification would see that the method is enabled as transgenic nonhuman animals can be made by the specification. However, the uses of the mammals and method require much more exacting phenotypes. The specification never contemplates mere expression of a transgenic for the mammals or the methods of producing a polypeptide or protein in the mammals. There is no use for such a mammal or method that is even readily apparent. If the genetic material is only expressed but not sufficiently so as to isolate from blood or if the expression does not meaningfully alter the phenotype of the mammal in an art useful way, then there is no use for either the mammal or the method of producing a polypeptide or protein. None is disclosed and none is readily apparent.

Examiner's Answer, pages 28-29 (emphasis added).

Claims 1 of the '191 patent, which is not limited to any specific mammal or any specific gene, reads as follows:

1. A method of obtaining a mammal characterizes as having a plurality of cells containing exogenous genetic material, said material including at least one gene and a control sequence operably associated therewith, which, under predetermined conditions, express said gene under the control of said control sequence in a cell of said mammal, which comprises:

(a) introducing exogenous material into a pronucleus of a mammalian zygote by microinjection, said zygote being capable of development into a mammal, said genetic material including at least one gene and a control sequence associated therewith, thereby obtaining a genetically transformed zygote;

(b) transplanting an embryo derived from the genetically transformed zygote into a pseudopregnant female capable of bearing an embryo to term;

(c) allowing the embryo to develop to term;

where said gene and control sequence are selected so that the gene is not activated in such manner and degree as would prevent normal development of the embryo to term.

What we understand the examiner's argument to be is that, while the specification is enabling for a broad method of producing the claimed transgenic material, it does not teach one skilled in the art how to use the product. The panel does not agree that this is a proper distinction, however, i.e., that the amount of disclosure required to enable a product is higher than that required to

enable the method of producing the product. The method of making the product has a use beyond that of merely the production of the product; it also encompasses the use of the product itself. Therefore, if the method of making the product is enabled, the product itself is enabled. Because the examiner does not question that the method of making the product as claimed in the '191 patent is not enabled to the full scope of the claims, she cannot reasonably assert that the instantly pending product claims, which are more limited in scope than the allowed claims, are not enabled by the instant specification, and the rejection is reversible on those grounds alone.

#### CONCLUSION

Because the examiner failed to establish a prima facie case that the specification fails to enable the full scope of the claimed subject matter, the rejection under 35 U.S.C. § 112, first paragraph, is reversed. The obviousness-type double patenting rejection of the pending claims, in the absence of a terminal disclaimer, is affirmed

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

AFFIRMED

Toni R. Scheiner	)	
Administrative Patent Judge	)	
	)	
	)	
	)	BOARD OF PATENT
Donald E. Adams	)	
Administrative Patent Judge	)	APPEALS AND
	)	
	)	INTERFERENCES
	)	
Lora M. Green	)	
Administrative Patent Judge	)	

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Charles K. Sholtz  
Xenogen Corporation  
860 Atlantic Avenue  
Alameda, CA 94501