

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ROBERT R. GRANADOS

Appeal No. 1997-3116
Application 08/294,953

ON BRIEF

Before WINTERS, WILLIAM F. SMITH, and GRIMES, Administrative Patent Judges.

GRIMES, 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 1-10, all of the claims pending in the application. Claim 1 is representative of the claims on appeal and reads as follows:

1. An insect cell line established in a serum free medium from Trichoplusia ni egg cells which supports replication of virus in serum free medium, supports expression of protein after infection by a recombinant virus in said serum free medium, grows in said serum free medium, and retains said ability to support replication of virus and to support expression of protein.

The examiner relies on the following references:

Granados	5,298,418	Mar. 29, 1994
Granados	5,300,435	Apr. 05, 1994

Wickham et al. (Wickham), "Screening of Insect Cell Lines for the Production of Recombinant Proteins and Infectious Virus in the Baculovirus Expression System," Biotechnol. Prog., Vol. 8, pp 391-396 (1992)

Stiles et al. (Stiles), "Initiation and Characterization of Five Embryonic Cell Lines From The Cotton Boll Weevil Anthonomus Grandis In a Commercial Serum-Free Medium," In Vitro Cell. Dev. Biol., Vol. 28A, pp 355-363 (1992)

Claims 1-8 stand rejected under 35 U.S.C. § 103 over the combination of Stiles and Granados ('435).

Claims 9 and 10 stand rejected under 35 U.S.C. § 103 over the combination of Granados ('418) and Wickham.

We reverse the rejection of claims 1-8, affirm the rejection of claims 9 and 10, and enter a new ground of rejection under 37 CFR § 1.196(b).

Background

As disclosed by Appellant's specification, insect cell lines have been used to produce many different recombinant products. See pages 1-2. The specification also discloses that use of serum-free medium is important for large-scale production using insect cells because it is cheaper and contains fewer extraneous proteins to get rid of during later purification steps. Page 2. Finally, the specification discloses that an insect cell line had been established in serum-free medium but asserts that those skilled in the art believed that other insect cell lines had to be established in serum-containing medium and later adapted to

serum-free medium. Page 3. The specification discloses establishment of Trichoplusia ni cell lines in serum-free medium.

Discussion

The pending claims are drawn to cell lines derived from Trichoplusia ni eggs, which are established in a serum-free medium, and which have various recited properties. The examiner rejected all of the claims over the prior art.

1. The rejection of claims 1-8.

The examiner rejected claims 1-8 as obvious over Stiles in view of Granados ('435). According to the examiner, Stiles teaches establishing cell lines derived from insect eggs in a serum-free medium but does not teach Trichoplusia ni cell lines. Granados ('435) teaches establishing cell lines derived from Trichoplusia ni eggs but does not teach establishing such cell lines in serum-free medium. The examiner concluded that, in view of the combined references, it would have been obvious to a person of ordinary skill in the art to use the methods taught by Stiles to establish cell lines derived from T. ni eggs in serum-free medium. The examiner states that the skilled artisan would have been motivated to use serum-free medium to establish T. ni cell lines because Granados ('435) adapted the disclosed T. ni cell lines to serum-free medium after they had been established in serum-containing medium.

Appellant argues that at the time of the present invention, those skilled in the art did not believe that it was possible to establish T. ni cell lines in serum-free medium. Appellant argues that the insect cell lines taught by Stiles were derived from a different species of insect (cotton boll weevil), which belongs to a

different Order within the family Insecta, and that the references provide no basis on which the skilled artisan would expect T. ni cells to behave similarly.

Appellant also argues that Granados ('435) actually teaches away from the claimed cell lines, in that Granados ('435) teaches that established T. ni cell lines were adapted to serum-free medium, "as is commonly practiced in the art."

Thus, Appellant concludes that the cited references would not have provided a person of ordinary skill in the art with an expectation that Stiles' method would be successful if applied to T. ni cells.

Although the prior art need not provide absolute predictability of success, it must provide those skilled in the art with a reasonable expectation of success.

In re O'Farrell, 853 F.2d 894, 903-04, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art. Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure.

In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988) (citations omitted).

We have carefully considered the evidence and reasoning presented by Appellant and the examiner, and we find ourselves in agreement with Appellant—the cited prior art would not have provided those of ordinary skill in the art with an adequate basis to expect that the method taught by Stiles would succeed when applied to Trichoplusia ni. Stiles successfully established cell lines from cotton boll weevil cells in serum-free medium but made no prediction

that the disclosed method would be likely to succeed with cells from other insect species. On the contrary, Stiles stated that their cell lines were “apparently the first invertebrate cells to have been both isolated and continuously subcultured in a serum-free tissue culture medium.” Page 355.

Similarly, Granados ('435) disclosed that it was the “commonly practice[] in the art” to establish T. ni cell lines in serum-containing medium, and later adapt them to serum-free medium. The examiner argues that this teaching shows that Granados appreciated the advantages of serum-free medium for insect tissue culture, and therefore it would have been obvious to establish T. ni cell lines in serum-free medium from the start. The examiner’s argument, however, proves too much. The fact that Granados knew of the advantages of serum-free medium suggests that Granados ('435) would have taught establishing T. ni cell lines in serum-free medium, if such an approach had been considered likely to succeed. The fact that Granados ('435) teaches establishing T. ni cell lines in serum-containing medium, then adapting the cells to serum-free medium, suggests that those skilled in the art believed that T. ni cell lines could only be established in media that contained serum.

Although “[f]or obviousness under § 103, all that is required is a reasonable expectation of success,” In re O’Farrell, 853 F.2d at 904, 7 USPQ2d at 1681, that “expectation of success must be founded in the prior art, not in the applicant’s disclosure.” In re Dow Chemical Co., 837 F.2d at 473, 5 USPQ2d at 1531. The prior art relied on by the examiner here would not have provided a person of ordinary skill in the art with a reasonable expectation that the method

disclosed by Stiles would be successful if applied to the T. ni cell lines disclosed by Granados ('435). The rejection of claims 1-8 under 35 U.S.C. § 103 is therefore reversed.

2. The rejection of claims 9 and 10.

The examiner rejected claims 9 and 10 as obvious over Granados ('418) and Wickham. According to the examiner, "Granados and Wickham et al disclose an insect cell line derived from the eggs of *Trichoplusia ni*. Granados also discloses that the cell line is susceptible to various baculoviruses." Office Action (Paper No. 3), page 8. The examiner considered these similarities sufficient to shift the burden to Appellant to show that the claimed cells differ from the prior art cells.

Appellant argues that "[t]he references relied upon by the Examiner merely teach other *T. ni* cell lines established in media including serum. This rejection should be reversed for all of the reasons for [sic] stated above for the reversal of the rejection of claim 1." Appeal Brief, page 7.

"[W]hen the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 708, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See also In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

In responding to the examiner's rejection of claims 9 and 10, Appellant relies on the same "expectation of success" argument that he makes in regard to

claims 1-8. The rationale underlying the two rejections differs, however, in a way that makes Appellant's argument unpersuasive here.

The examiner rejected claims 9 and 10 on the basis that the claimed, deposited cell lines were the same as or not patentably distinct from cell lines disclosed by the prior art. That is, the examiner considered the similarities between the T. ni egg-derived cell lines disclosed by the prior art to be sufficient to shift the burden to Appellant to show evidence that the claimed cell lines differ from the prior art cell lines. Appellant has neither argued that the similarities are insufficient to justify shifting the burden of proof nor come forward with evidence of dissimilarity to show that claims 9 and 10 do not encompass the prior art cell lines.

Appellant's only basis for arguing that the claimed cell lines differ from those in the prior art is that the prior art cell lines were established in medium containing serum, while the claimed cell lines were established in serum-free medium. This difference, however, is not in the properties of the claimed products, but rather in the method by which the product was made. Claims 9 and 10 are not drawn to a method of making a cell line by establishing it in serum-free medium; the claims are to a product. "[The] patentability of a claim to a product does not rest merely on a difference in the method by which that product is made. Rather, it is the product itself which must be new and unobvious." In re Pilkington, 411 F.2d 1345, 1348, 162 USPQ 145, 147 (CCPA 1969) (emphasis in original). Appellant is arguing that the product is different because the manner in which it is made is different. The patentability of the product, however, must be

based on the properties of the product itself. Appellant's argument is therefore unpersuasive and we affirm the rejection.

New Ground of Rejection

Under the provisions of 37 CFR § 1.196(b), we make the following new ground of rejection: Claims 1 -3, 7, and 8 are rejected under 35 U.S.C. § 102(b) over Granados ('435). Claim 1 is drawn to a cell line derived from Trichoplusia ni eggs, which (1) supports replication of virus in serum-free medium; (2) supports expression of protein after infection by a recombinant virus in serum-free medium; (3) grows in serum-free medium; and (4) retains the ability to support replication of virus and expression of protein. The dependent claims recite additional properties of the claimed cell lines.

As we noted above, the recitation in claim 1 that the claimed cell lines are "established in a serum free medium" is merely a limitation on the method by which the claimed product is made and does not distinguish the claimed product from the prior art. "[The] patentability of a claim to a product does not rest merely on a difference in the method by which that product is made. Rather, it is the product itself which must be new and unobvious." In re Pilkington, 411 F.2d at 1348, 162 USPQ at 147.

Granados ('435) discloses the Trichoplusia ni egg-derived cell line BTI-Tn-5B1-4. This cell line is disclosed to grow in serum-free medium (col. 9, lines 25-45); to support replication of virus in serum-free medium (col. 9, line 50 to col. 10, line 45); and to be useful for production of proteins encoded by recombinant viruses (col. 8, lines 34-40). Granados ('435) does not indicate that these

properties were unstable (i.e., Granados ('435) implicitly discloses that the cells retained the ability to support replication of virus and expression of protein).

In addition, the specification of the application on appeal shows that the Tn-5B1-4 cell line "is known to express recombinant proteins at high levels" (page 3, line 27). Thus, the evidence of record in this application shows that the prior art Tn-5B1-4 cell line meets the limitations of claim 1.

Claims 2 and 3 add the limitations that the cell line produces at least 30 or 50 occlusion bodies, respectively, per cell when it is infected by Autographa californica multiple nuclear polyhedrosis virus (ACMNPV) and cultured under specific conditions. Granados ('435) discloses that the Tn-5B1-4 cell line meets these limitations. See col. 10, line 45 to col. 11, line 13 (when cultured under the recited conditions, Tn-5B1-4 cells produced 6.5×10^7 occlusion bodies per 10^6 cells, or 65 occlusion bodies per cell).

Claim 7 adds the limitation that the cell line expresses at least 175 IU/ml of β -galactosidase when infected by recombinant ACMNPV expressing a β -galactosidase gene,¹ under specific culture conditions. The instant specification provides evidence that the Tn-5B1-4 cell line meets this limitation. See pages 11-12 and Figure 2 (showing β -galactosidase expression of approx. 200 IU/ml for cell line Tn-5B1-4).

Claim 8 adds the limitation that the cell line expresses at least 2 IU/ml of alkaline phosphatase when infected by recombinant ACMNPV expressing a

¹ Claim 7 contains an apparent typographical error that should be corrected if this case is subject to further examination. Claim 7 recites an insect cell line which expresses β -galactosidase "after

secreted alkaline phosphatase gene, under specific culture conditions.² The instant specification provides evidence that the Tn-5B1-4 cell line meets this limitation. See pages 12-13 and Table 3 (showing alkaline phosphatase expression at an average of 2.29 IU/ml in cell line Tn-5B1-4).

Summary

We reverse the rejection of claims 1-8 and affirm the rejection of claims 9 and 10. We also enter a new ground of rejection of claims 1-3, 7, and 8, based on anticipation. As a result, claims 4-6 are free of rejection.

In addition to affirming the examiner's rejection of one or more claims, this decision contains a new ground of rejection pursuant to 37 CFR ' 1.196(b) (amended effective Dec. 1, 1997, by final rule notice, 62 Fed. Reg. 53,131, 53,197 (Oct. 10, 1997), 1203 Off. Gaz. Pat. & Trademark Office 63, 122 (Oct. 21, 1997)). 37 CFR ' 1.196(b) provides, AA new ground of rejection shall not be considered final for purposes of judicial review.@

TIME PERIOD FOR RESPONSE

Regarding any affirmed rejection, 37 CFR ' 1.197(b) provides:

(b) Appellant may file a single request for rehearing within two months from the date of the original decision

infection by a recombinant . . . virus expressing secreted alkaline phosphatase." The claim obviously should recite a recombinant virus expressing β -galactosidase.

² Claim 8 also contains an apparent typographical error that should be corrected if this case is subject to further examination. Claim 8 is drawn to cells expressing a specific level of alkaline phosphatase but recites measuring, in step (i), " β -galactosidase production at six days post infection." The enzyme measured should obviously be alkaline phosphatase.

37 CFR ' 1.196(b) also provides that appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of proceedings (37 CFR ' 1.197(c)) as to the rejected claims:

(1) Submit an appropriate amendment of the claims so rejected or a showing of facts relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the application will be remanded to the examiner. . . .

(2) Request that the application be reheard under ' 1.197(b) by the Board of Patent Appeals and Interferences upon the same record. . . .

Should appellant elect to prosecute further before the Primary Examiner pursuant to 37 CFR ' 1.196(b)(1), in order to preserve the right to seek review under 35 U.S.C. ' ' 141 or 145 with respect to the affirmed rejection, the effective date of the affirmance is deferred until conclusion of the prosecution before the examiner unless, as a mere incident to the limited prosecution, the affirmed rejection is overcome.

If appellant elects prosecution before the examiner and this does not result in allowance of the application, abandonment or a second appeal, this case should be returned to the Board of Patent Appeals and Interferences for final action on the affirmed rejection, including any timely request for rehearing thereof.

Appeal No. 1997-3116
Application 08/294,953

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

REVERSED IN PART, AFFIRMED IN PART
37 CFR ' 1.196(b)

Sherman D. Winters)	
Administrative Patent Judge)	
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)	
)	BOARD OF PATENT
William F. Smith)	
Administrative Patent Judge)	APPEALS AND
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Appeal No. 1997-3116
Application 08/294,953

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