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Paper 13
Entered: August 30, 2017

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BIOEQ IP AG,
Petitioner,

v.

GENENTECH, INC.,
Patent Owner.

Case IPR2016-01608
Patent 6,716,602 B2

Before TONI R. SCHEINER, ERICA A. FRANKLIN, and MICHELLE N. ANKENBRAND, *Administrative Patent Judges*.

FRANKLIN, *Administrative Patent Judge*.

DECISION
Denying Petitioner's Request for Rehearing
37 C.F.R. § 42.71

I. INTRODUCTION

bioeq IP AG ("Petitioner") requests a rehearing of the Decision Denying Institution of an *inter partes* review of claims 1, 3–4, 6–16, 18, 20, 22–25, 27–28, and 30–39 of U.S. Patent No. 6,716,602 B2 (Ex. 1001, "the '602 patent") entered on February 22, 2017 (Paper 11, "Dec."). Paper 12 ("Reh'g Req."). In the Petition (Paper 3; "Pet."), Petitioner raised the following challenges to the claims:

Reference(s)	**Basis**	**Claim(s) challenged**
Seeger[1]	§ 102(b)	1, 3–4, 6, 9, 15–16, 20–22, 24–25, 27–28, 30, 33, 39
Seeger	§ 103(a)	7–8, 31–32
Seeger and Markie's[2]	§ 103(a)	10, 12, 23, 34, 36
Seeger and Cabilly[3]	§ 103(a)	11, 13–14, 18, 35, 37–38

Petitioner also relied on the declaration of Dr. Morris Z. Rosenberg, DSc. (Ex. 1002). Genentech, Inc. ("Patent Owner") filed a Preliminary Response to the Petition. Paper 9 ("Prelim. Resp."). We authorized Petitioner to file a Reply to Patent Owner's Preliminary Response, Paper 10 ("Reply"), to

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[1] Anke Seeger et al., *Comparison of temperature- and isopropyl-ß-D-thiogalacto-pyranoside-induced synthesis of basic fibroblast growth factor in high-cell-density cultures of recombinant Escherichia coli*, 17 ENZYME & MICROBIAL TECH. 947–53 (1995) (Ex. 1010).
[2] Savvas C. Makrides, *Strategies for Achieving High-Level Expression of Genes in Escherichia coli*, 60 MICROBIOLOGICAL REVIEWS 512–38 (1996) (Ex. 1023).
[3] Shmuel Cabilly, *Growth at sub-optimal temperatures allows the production of functional, antigen-binding Fab fragments in Escherichia coli*, 85 GENE 553–57 (1989) (Ex. 1032).

address corrections to the '602 patent claims requested by Patent Owner in its Request for Certificate of Correction submitted to the Director of the Patent Office after the filing of the Petition.

Upon consideration of the Petition, Preliminary Response, Reply, and evidence of record, we determined that Petitioner failed to demonstrate a reasonable likelihood that it would prevail in showing the unpatentability of at least one challenged claim. Dec. 2. In the Rehearing Request, Petitioner seeks reconsideration of that determination. Reh'g Req. 1.

II. ANALYSIS

"When rehearing a decision on petition, a panel will review the decision for an abuse of discretion." 37 C.F.R. § 42.71(c). "The burden of showing a decision should be modified lies with the party challenging the decision. The request must specifically identify all matters the party believes the Board misapprehended or overlooked, and the place where each matter was previously addressed in a motion, an opposition, or a reply." *Id.* § 42.71(d). Because Petitioner has not met its burden, as discussed below, the Rehearing Request is *denied*.

Claim 1 is representative of the challenged claims and is reproduced below:

> 1. A method for increasing the product yield of a properly folded polypeptide of interest produced by recombinant host cells, wherein expression of the polype[]ptide by the recombinant host cells is regulated by an inducible system, which method comprises
>
> (a) culturing the recombinant host cells under conditions of high metabolic growth rate; and
>
> (b) reducing the metabolic rate of the cultured recombinant host cells at the time of induction of polypeptide expression, wherein reducing the metabolic rate comprises reducing the feed

> rate of a carbon/energy source, or reducing the amount of available oxygen, or both, and wherein the reduction in metabolic rate result in increase yield of properly folded polypeptide.

Ex. 1001, 18:11–24.

In the Rehearing Request, Reh'g Req. 1, Petitioner challenges our determination that "Petitioner has not shown persuasively that a person of skill in the art would have understood Seeger's method to have included reducing the metabolic rate of the cultured recombinant host cells at the time of expression induction," Dec. 11. Petitioner asserts that we "(i) misapprehended the science underlying the claimed methods; and (ii) overlooked that Dr. Rosenberg's GUR calculation in fact accounted for the change in temperature at induction in Seeger, and conclusively showed a reduction in metabolic rate." Reh'g Req 1. In particular, Petitioner asserts that we "failed to appreciate that GUR provides a direct read-out of metabolism in Seeger, such that any variable that may affect metabolism is accounted for," including temperature. *Id*. at 2.

In the Reply to Patent Owner's Preliminary Response, Petitioner addressed Patent Owner's argument distinguishing Seeger's method from the method of the challenged claims and critiquing Dr. Rosenberg's GUR calculation. *See*, e.g., Reply 2–3. We presented that argument in the Decision as follows:

> In the Reply, Petitioner acknowledges that temperature is one of the "external factors that influence[s] the metabolic rate," along with amount of glucose and oxygen supplied. Reply 2. According to Petitioner, Dr. Rosenberg's GUR calculation is a "'read-out' of the cells' metabolic rate," and accounts for each of those external factors, including temperature. *Id*. In support of that contention, Petitioner states, "Dr. Rosenberg calculated GUR throughout Seeger's fed-batch phases, i.e., before and after

> temperature change induced bFGF expression, thus accounting for temperature." *Id*. at 2–3 (citing Ex. 1002 ¶ 56) (emphasis omitted).

Dec. 12. Petitioner reiterates that argument in the Rehearing Request. Reh'g Req. 6–10. As we explained in the Decision, Petitioner's argument is unpersuasive because it is not supported by evidence. Dec. 12–13. Specifically, we stated,

> Petitioner's assertion is not supported by the evidence of record. Dr. Rosenberg's discussion of his calculation for the GUR in the paragraph cited by Petitioner explains only that Seeger increased the temperature, without describing or suggesting that he considered that temperature increase in his calculation or conclusions. Ex. 1002 ¶ 56. Moreover, as Patent Owner has asserted, Dr. [Rosenberg's] calculation set forth in Appendix A does not include a variable accounting for the temperature shift. Ex. 1002, App. A. Thus, Petitioner has not shown persuasively that a person of skill in the art would have understood Seeger's method to have included reducing the metabolic rate of the cultured recombinant host cells at the time of expression induction. *See MEHL/Biophile Int'l. Corp.*, 192 F.3d at 1365.

Id.[4] Thus, Petitioner has not established that we overlooked or misapprehended its argument as to this issue.

With regard to the claim recitation "wherein the reduction in metabolic rate results in increased yield of properly folded polypeptide," Petitioner argued in the Petition that such reduction is an intended result of

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[4] Contrary to Petitioner's assertion in the Rehearing Request, the rationale set forth in the Decision does not rely upon "Herendeen" teaching anything about "the effect of temperature on metabolic rate." *See* Reh'g Req. 3–6 (citing Sherrie L. Herendeen et al., *Levels of Major Proteins of Escherichia coli During Growth at Different Temperatures*, 139 J. BACTERIOLOGY 185–94 (1979) (Ex. 2002). Rather, the Decision is appropriately based upon the insufficient showing of Dr. Rosenberg relied upon by Petitioner.

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