UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte SERGEY VLADIMIROVICH BIRYUKOV,
PETER NIKOLAYEVICH SIMONENKO, ALENA SIMONENKO,
VLADIMIR ANATOLIEVICH SHIROKOV,
SERGEY GENNADIEVICH MAYOROV, and
ALEXANDER SERGEYEVICH SPIRIN

Appeal 2007-4324
Application 10/307,122
Technology Center 1600

Decided: November 27, 2007

Before ERIC GRIMES, NANCY J. LINCK, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of producing polypeptides using in vitro transcription translation reactions, which the Examiner has rejected on grounds of obviousness. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

BACKGROUND

"Several methods of polypeptide synthesis in [a] cell-free translation system are known" (Specification 1). There are "methods in which dialysis is used to add feed solution components to the reaction mixture and to remove low molecular weight components from the reaction mixture" (Specification 1); "methods in which continuous ultrafiltration is used for a simultaneous removing of low and high molecular weight components of products" (*id.*); and "methods in which periodic input of a feed solution into the reaction mixture and subsequent removing of low and high molecular weight components through the membrane are used" (*id.* at 2).

Appellants teach it is an "object of the present invention to describe a reactor which comprises at least one reactor volume, whose external surface contacts the external surface of the first and second porous barriers" (Specification 9). Appellants also note a "difference from the known designs is the formation of a two-layer construction with different cutoff sizes" (Specification 19).

STATEMENT OF THE CASE

The Claims

Claims 1-8, 22-30 and 32-34 are on appeal. The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). We will focus on claim 1, which is representative and reads as follows:

> 1. A method for obtaining a target polypeptide in a cell-free translation system, the method comprising
>
> providing a reaction mixture, and a feed solution wherein said reaction mixture comprises high molecular weight components, and said feed solution comprises low

molecular weight components, said high and low molecular weight components providing components for coupled transcription and translation,

providing a reactor module, said reactor module comprising a first and second porous barrier, wherein said barriers, optionally in combination with the reactor module walls, define a reactor volume, said first porous barrier having a molecular weight cutoff different from that of the second porous barrier,

introducing the reaction mixture into the reactor volume,

supplying the feed solution to the reactor module to mix with said reaction mixture to provide a reactor module mixture,

incubating the reactor module mixture at conditions that maintain the synthesis of the target polypeptide, and

removing the resulting products of synthesis from the reactor volume during synthesis of the target polypeptide, wherein said removal step comprises separating a first fraction and a second fraction from the reactor module mixture, wherein said first fraction comprises low molecular weight components, and said second fraction comprises high molecular weight components and the target polypeptide, said separation being accomplished by passage of the first fraction across the second porous barrier and passage of the second fraction across the first porous barrier.

The Examiner has rejected claims 1-8, 22-30 and 32-34 under 35 U.S.C. § 103(a) based on:

Alakhov et al., U.S. Patent 5,478,730, December 26, 1995 (hereafter "Alakhov"); and

Mozayeni et al., U.S. Patent 5,434,079, July 18, 1995 (hereafter "Mozayeni").

The Obviousness Issue

The Examiner's position is that Alakhov teaches a method of cell free peptide synthesis in a reactor with two porous barriers (Answer 5 (citing Alakhov, col. 6, ll. 14-24)). The Examiner states that Alakhov teaches barriers in which desired components can be retained in the reactor and other components may be removed from the reactor (Answer 5 (citing Alakhov, col. 2, ll. 5-15)). The Examiner recognizes that Alakhov does not teach two porous barriers with different molecular weight cutoffs (Answer 7). The Examiner relies upon Mozayeni for the teaching of two porous barriers with different molecular weight cutoffs in a cell free peptide synthesis method (Answer 7 (citing Mozayeni, col. 4, ll. 9-20)). According to the Examiner, it would have been obvious to substitute the two different molecular weight barriers of Mozayeni for the porous barriers in Alakhov (Answer 5-7).

Appellants respond that neither reference teaches or suggests the use of two porous barriers with different pore sizes in order to simultaneously separate both high and low molecular weight fractions from a cell-free transcription/translation reaction in a reactor (App. Br. 5).

In view of these conflicting positions, we frame the issue before us as follows:

Would the skilled artisan have been motivated or have had a reason to utilize two different size molecular weight barriers as taught by Mozayeni in the transcription/translation reactor of Alakhov?

FINDINGS OF FACT

1. Alakhov teaches a cell-free translation system with a reaction mixture that comprises a range of sizes of molecular weight components from 0.1 kD to 100 kD (*see* Alakhov, col. 4, ll. 38-52).

2. Alakhov teaches a reactor module with two separate stages, with circulation of both high and low molecular weight components, where the high molecular weight components are retained behind a porous barrier (*see* Alakhov, col. 6, ll. 51-57).

3. Alakhov teaches exchange of both the high and low molecular weight streams (Alakhov, col. 6, ll. 28-34 ("one could have two flow streams, a relatively slow stream which is in contact with the ribosomes and continuously but slowly exchanges various of the higher molecular weight components of the reaction system, while also removing product from the reaction region, and a somewhat faster stream which provides for the exchange of the lower molecular weight materials")).

4. Mozayeni teaches bioreactors with parallel porous barriers to form a lumen for use in cell-free translation systems (*see* Mozayeni, col. 2, ll. 18-36).

5. Mozayeni teaches "By using membranes having different cutoffs for molecular weight in each of upper housing 110 and lower housing 111, membrane cutoff size can be readily optimized" (Mozayeni, col. 4, ll. 54-57).

6. Mozayeni teaches that identical membranes are used in production runs (*see* Mozayeni, col. 4, ll. 57-60).

DISCUSSION

The disputed difference between the Alakhov method and the claim 1 method is the use of two different porous barriers which have different molecular weight cutoffs, and the resulting fractionation in which different size components are separated by the different porous barriers (*see supra*, at p. 4).

In analyzing this difference, we first interpret the claim. Other than requiring that the porous barriers have different molecular weight cutoffs, no specific difference in the molecular weight cutoffs is required by claim 1. Consonant with that, no specific requirement for the terms "high molecular weight components" and "low molecular weight components" is found in claim 1. Turning to the Specification, we find that no specific definition of either of these terms is present.

In the absence of a specific definition in the Specification for "high" and "low" molecular weight components, we give these terms their broadest reasonable interpretation. *See, e.g., In re Hyatt,* 211 F.3d 1367, 1372 (Fed. Cir. 2000) ("During examination proceedings, claims are given their broadest reasonable interpretation consistent with the specification.").

A larger component will be a "high" molecular weight component and a smaller component will be a "low" molecular weight component, dependent upon the specific molecular weight cutoffs of the porous barrier(s) selected. Applying this interpretation to claim 1, Alakhov teaches a reactor in which low molecular weight compounds can pass through a porous barrier (*see* FF 1-3). Mozayeni teaches the use of two different porous barriers in a single reactor for the purpose of optimizing the molecular weight cutoff size (*see* FF 5). Combining these teachings results in a reactor with two porous barriers with different molecular weight cutoffs.

When two different porous barriers are used in a reactor, the first porous barrier with a lower molecular weight cutoff will necessarily permit egress of compounds with lower molecular weights and retain those with higher molecular weights. Similarly, the second porous barrier with a higher molecular weight cutoff will necessarily permit egress of some compounds with molecular weights intermediate between the molecular weight cutoffs of the first and second barriers.

The Examiner has identified at least one specific reason to use the two molecular weight cutoffs of Mozayeni in the reactor of Alakhov, which is to optimize membrane cutoff size (*see* FF 5; Answer 7-8). *See KSR Int'l v. Teleflex Inc.,* 127 S. Ct. 1727, 1741 (2007) ("it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.").

In our opinion, the Alakhov and Mozayeni combination would have suggested the structural limitation of the reactor module in the second step of the claim. The combination of Alakhov and Mozayeni would therefore necessarily have resulted in a method of differential separation of some "high" and some "low" molecular weight components during the cell-free transcription/translation method in the reactor.

Based on the above, we conclude the Examiner has made a prima facie case of obviousness under 35 U.S.C. § 103(a) (FF 1-6).

Appellants argue that the "present claims specifically require that the feed solution is mixed with the reaction mixture and then two streams are isolated from that mixture (i.e., the 'reactor module mixture') by the use of two porous barriers that differ from one another based on their molecular weight cutoff" (App. Br. 7). We reject this argument, as it imputes limitations regarding the use of two different streams in the reactor that are not found in the claim. We decline to read this limitation into the claim. *See In re Van Geuns*, 988 F.2d 1181, 1184 (Fed. Cir. 1993) ("limitations are not to be read into the claims from the specification").

Appellants also argue they have found that the use of two porous barriers permits simultaneous addition and removal of high and low molecular weight components and that the prior art did not recognize this reason for using two porous barriers (*see* App. Br. 9). While Appellants may have a different reason for using two different porous barriers than the prior art, this difference is not reflected in a claim limitation and therefore does not impart patentability to the claims. *See In re Beattie,* 974 F.2d 1309, 1312 (Fed. Cir. 1992) ("As long as some motivation or suggestion to combine the references is provided by the prior art taken as a whole, the law does not require that the references be combined for the reasons contemplated by the inventor").

We also reject Appellants' argument that "Mozayeni is devoid of any suggestion that a reaction chamber can be formed that has two different pore-sized porous barriers forming the chamber walls, wherein the two barriers differ *substantially from one another*" (App. Br. 8 (emphasis in original)). This argument is inconsistent with the logic of Mozayeni. In Mozayeni, the reason for using two different porous barriers was to determine which barrier was optimal (*see* FF 5). If the porous barriers did not differ "substantially" from one another, no optimization could occur. Therefore, the skilled artisan would have recognized that Mozayeni is suggesting porous barriers that must differ from one another enough to permit differences in their properties as they affect the transcription/translation reaction. In any case, no such limitation appears in claim 1.

We also reject Appellants' argument that "'obvious to try' is not the standard for obviousness under 35 USC § 103. The use of two separate and distinct porous barriers in the orientation as claimed is but one of many ways the procedure disclosed by Alakhov and Mozayeni could be modified" (App. Br. 10). As we discussed above, there is a specific reason to use the two porous barriers of Mozayeni in the reactor of Alakhov, i.e., to optimize the Alakhov reactor. Also, under *KSR*, it's now apparent "obvious to try" may be an appropriate test in more situations than we previously contemplated. When there is motivation

> to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

KSR Int'lv. Teleflex Inc., 127 S. Ct. 1727, 1742 (2007). This reasoning is applicable here. The "problem" facing the skilled artisan is how to optimize a transcription/translation reaction in a reactor. The skilled artisan would have had reason to apply the solution of Mozayeni in optimizing reactors because using two different porous barriers is a predictable way to identify optimal reaction conditions (*see* FF 5).

CONCLUSION

In summary, we affirm the rejection of claim 1 under § 103(a). Pursuant to 37 C.F.R. § 41.37(c)(1)(vii)(2006), we also affirm the rejection of claims 2-8, 22-30 and 32-34 under § 103(a), as these claims were not argued separately.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

<u>AFFIRMED</u>

APJ initials:

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