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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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*Ex parte* MICHAEL BORNS

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Appeal 2011-010077  
Application 11/488,535  
Technology Center 1600

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Before DONALD E. ADAMS, DEMETRA J. MILLS, and  
FRANCISCO C. PRATS, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims to chimeric DNA polymerases. The Examiner entered a rejection for lack of written description.

We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

“One approach to modifying the property of a DNA polymerase is to generate chimeric DNA polymerases in which one or more protein domains having the requisite activity are combined with a DNA polymerase” (Spec. 1). The Specification discloses that one DNA-binding protein suitable for

fusion with a DNA polymerase is Sso7d, which is “a small, basic chromosomal protein from the hyperthermophilic archaeobacteria *Sulfolobus solfataricus*. . . . The wild-type protein sequence is set forth in SEQ ID NO:2” (*id.* at 11).

Thus, “fusion of . . . Sso7d or Sac7d from *Sulfolobus solfataricus* to a DNA polymerase, such as *Pfu* or *Taq* DNA polymerase, was shown to greatly increase the processivity of these DNA polymerases as disclosed in WO 01/92501 A1 and US2004/0081963 A1” (Spec. 1).

Along these lines, Appellant’s invention is directed to chimeric DNA polymerases in which mutated forms of Sso7d or Sso7d-like proteins are fused to a DNA polymerase domain (*see id.* at 11-13).

Claims 1-14, 16-22, 25, 29, and 31-33 stand rejected and appealed (App. Br. 6).<sup>1</sup> Claims 1, 5, 9, 13, and 18, the independent claims on appeal, illustrate the appealed subject matter and read as follows:

1. A chimeric DNA polymerase comprising a DNA binding domain and a polymerase domain, wherein said DNA binding domain has seven or more mutations, one mutation being present at seven, eight, or all nine of the following amino acid positions: 13, 16, 40, 41, 45, 55, 56, 61, and 63 of SEQ ID NO:2, or at a corresponding position in a wild-type Sso7d-like protein, wherein the wild-type Sso7d-like protein shows about 78% to about 98% sequence identity to the sequence of SEQ ID NO:2.

5. A chimeric DNA polymerase comprising a DNA binding domain and a polymerase domain, wherein said DNA binding domain has three or more mutations, one each at amino acid positions 40, 41, and 45 of SEQ ID NO:2, or at a corresponding position in a wild-type Sso7d-like protein, wherein the wild-type Sso7d-like protein shows

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<sup>1</sup> Appeal Brief entered November 22, 2010. Appellant presented a corrected copy of the appealed claims in a paper entered December 28, 2010.

about 78% to about 98% sequence identity to the sequence of SEQ ID NO:2.

9. A chimeric DNA polymerase comprising a DNA binding domain and a polymerase domain, wherein said DNA binding domain has six or more mutations, one each at amino acid positions 40, 41, 45, 55, 61, and 63 of SEQ ID NO:2, or at corresponding positions in a wild-type Sso7d-like protein, wherein the wild-type Sso7d-like protein shows about 78% to about 98% sequence identity to the sequence of SEQ ID NO:2.

13. A chimeric DNA polymerase comprising a DNA binding domain and a polymerase domain, wherein said DNA binding domain has mutations at amino acid positions 13, 16, 40, 45, 55, 56, and 63 of SEQ ID NO:2, or at corresponding positions in a wild-type Sso7d-like protein, wherein the wild-type Sso7d-like protein shows about 78% to about 98% sequence identity to the sequence of SEQ ID NO:2.

18. A chimeric DNA polymerase comprising a DNA binding domain and a polymerase domain, wherein said DNA binding domain has mutations at amino acid positions 13, 16, 40, 41, 45, 55, 56, 61 and 63 of SEQ ID NO:2, or at corresponding positions in wild-type Sso7d-like protein, wherein the wild-type Sso7d-like protein shows about 78% to about 98% sequence identity to the sequence of SEQ ID NO:2.

The sole rejection before us for review is the Examiner's rejection of claims 1-14, 16-22, 25, 29, and 31-33 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

#### DISCUSSION

The Examiner initially noted that, while the claims recite mutations at specific locations of the Sso7d amino acid sequence, the mutations "include but are not limited to one or more point mutations, N- and/or C-truncations, internal deletion or insertion . . . or any additional type of post-translational

modification at these referred to amino acid positions” (Ans. 4 (citing Spec. 22, 24)). The Examiner reasoned, therefore, that the claimed DNA polymerases “have no required structure for either the DNA binding domain or the polymerase domain” (*id.*).

While contending that the genus of chimeric DNA polymerases encompassed by the claims is thus limited only “by the number and position of mutations of the DNA binding domain relative to SEQ ID NO:2[,]” the Examiner also noted the claims’ separate recitation of mutations not only “relative to SEQ ID NO:2, but also those mutation positions which are a corresponding mutation in an Sso-7d-like protein” (*id.*).

In contrast to this claim breadth, the Examiner found that the Specification “only provides the representative species of [a] chimeric DNA polymerase comprising the amino acid sequence of SEQ ID NO: 20, encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the disclosed species” (*id.* at 5).

The Examiner also found that the Specification “fails to describe additional representative species of these enzymes by any identifying structural characteristics or properties other than DNA polymerase activity and corresponding mutation positions recited in claim 1, for which no predictability of structure is apparent” (*id.*). The Examiner further reasoned that given the “lack of additional representative species as encompassed by the claims, Appellant[] ha[s] failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Appellant[] w[as] in possession of the claimed invention” (*id.*).

Appellant contends that a sufficient correlation between the structure and function of the claimed polymerases is provided by the fact that, in addition to being known in the art, the Specification provides the amino acid sequence of the Sso7d protein as well as a number of examples of Sso7d-like proteins, and the claims recite the specific positions within that sequence of the mutations required by the claims (*see* App. Br. 15). Thus, Appellant urges, a skilled artisan

could readily identify each of the mutated residues in the known sequences of the DNA binding proteins encompassed by the claims with reference to SEQ ID NO:2 and Sso7d-like proteins because the recited mutated residues are specifically disclosed in SEQ ID NO:2 and are easily identifiable from the alignment presented in Figure 1.

(*Id.* at 16; *see also id.* at 25, 27, 29, 31.) In other words, Appellant argues, “the claims specifically recite the mutant polymerases by way of defined alterations to the amino acid sequences of *known* DNA binding proteins (*i.e.*, by complete structural information) described in the specification” (*id.* at 16).

Appellant further contends that, although the claims encompass chimeric polymerases with any number of mutations in addition to those specifically recited, that fact does not demonstrate that the claims lack descriptive support (*id.* at 17 (citing *Ex parte Anderson*, Appeal No. 2005-0908); *see also id.* at 25, 27, 29, 31-32).

In particular, Appellant urges, SEQ ID NO:2 provides “a starting point for one of skill in the art to identify corresponding residues in other DNA polymerases having homologous structures to SEQ ID NO:2” (App. Br. 18). Similarly, Appellant argues, the six wild-type Sso7d-like proteins

provided in Appellant’s disclosure would allow a skilled artisan to “readily identify all chimeric DNA polymerases covered by the claims” (*id.*).

As stated in *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992):

[T]he examiner bears the initial burden . . . of presenting a *prima facie* case of unpatentability. . . .

After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument.

Appellant’s arguments do not persuade us that a preponderance of the evidence fails to support the Examiner’s position.

As to the Board’s previous decision in *Ex parte Anderson*, we note the decision’s express statement that it is not binding precedent (*see* App. Br., Appendix 4).

Moreover, as our reviewing court has more recently pointed out, the written description requirement “ensures that when a patent claims a genus by its function or result, the specification recites sufficient materials to accomplish that function - a problem that is particularly acute in the biological arts.” *Ariad Pharms., Inc. v. Eli Lilly and Co.*, 598 F.3d 1336, 1352-53 (Fed. Cir. 2010) (en banc).

Thus, a “sufficient description of a genus . . . requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can ‘visualize or recognize’ the members of the genus.” *Id.* at 1350 (quoting *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568-69 (Fed. Cir. 1997)).

Accordingly, “merely drawing a fence around the outer limits of a purported genus is not an adequate substitute for describing a variety of materials constituting the genus and showing that one has invented a genus and not just a species.” *Id.*

Nonetheless, “the written description requirement does not demand either examples or an actual reduction to practice; a constructive reduction to practice that in a definite way identifies the claimed invention can satisfy the written description requirement.” *Id.* at 1352 (citing *Falkner v. Inglis*, 448 F.3d at 1366-67 (Fed. Cir. 2006)).

Specifically, the Federal Circuit has “set forth a number of factors for evaluating the adequacy of the disclosure [supporting generic claims], including ‘the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue.’” *Id.* at 1351 (quoting *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005)).

Here, the genera encompassed by Appellant’s claims are relatively broad, as the claims have very little limitation as to structure. For example, contrary to Appellant’s seeming suggestion, claim 1 *does not* recite a chimeric DNA polymerase having a DNA binding domain with the amino acid sequence of SEQ ID NO:2, or having 78% to about 98% sequence identity to the sequence of SEQ ID NO:2, with at least seven mutations at the positions recited in the claim.

Rather, because of its concededly open language (*see* App. Br. 17, n. 2), claim 1 encompasses any DNA polymerase that also has a DNA binding domain, as long as the binding domain has something other than the amino acids naturally present at positions 13, 16, 40, 41, 45, 55, 56, 61, and 63 of

SEQ ID NO:2, or at the corresponding positions in a wild-type Sso7d-like protein that has about 78% to about 98% sequence identity to the sequence of SEQ ID NO:2. While they recite slightly different required mutations, independent claims 5, 9, 13, and 18, reproduced above, are similarly broad as to the structures encompassed.

Moreover, rather than being simple one-for-one amino acid substitutions, the many changes to SEQ ID NO:2 or its similar sequences can include N-terminal, internal, or C-terminal truncations (*see* Spec. 25). Thus, we detect no error in the Examiner's conclusion, stated in the Final Rejection, that claims 1, 5, 9, 13, and 18, encompass structures which "may be 'mutated' an unlimited number of times such that [they] in no way resemble[] anything that would ever be construed as being associated with SEQ ID NO:2" (Final Rejection 4).

Turning to the Specification, in contrast to the wide variation in structures encompassed by the claims, the only expressly described functional chimeric DNA polymerases having mutated DNA binding domains are constructs having the Sso7d protein as the binding domain, with specific single amino acid substitutions at specific positions in the protein's sequence (*see* Spec. 12-13, 39-42; *see also* Fig. 2). While a number of amino acid substitutions were tested, the "results indicated that only a limited number of amino acids could be changed without causing a loss of Sso7d functionality in the DNA polymerase chimera" (Spec. 41).

Other than those specific single amino acid substitutions in the Sso7d sequence, however, Appellant does not direct us to, nor do we see, any specific guidance correlating protein sequence, i.e. structure, to enzymatic

function. To the contrary, the Specification suggests that modifying these proteins is unpredictable:

It was observed that many amino acids that vary between the Sso7d-like polypeptides could not be changed without negatively effecting the Sso7d-chimeric DNA polymerases. In addition, some of the amino acids which did not vary between the Sso7d like proteins could be changed without causing a loss of Sso7d-chimeric DNA polymerase functionality.

(*Id.* at 12; *see also id.* at 42 (“Amino acids L and A are structurally very similar to I and yet all changes resulted in a functionally deficient chimera when compared to the wild-type construct.”)).

Thus, given the unpredictability in modifying these proteins, and given the fact that each of independent claims 1, 5, 9, 13, and 18 encompasses a broad genus of chimeric DNA polymerases that includes significantly modified molecules which need not have any particular similarity with the Sso7d protein (SEQ ID NO:2) or an Sso7d-like protein, and further given the fact that the Specification describes only certain specific amino acid substitutions to the Sso7d sequence which provide a functional DNA polymerase, Appellant’s arguments do not persuade us that the Examiner erred in finding that the Specification failed to adequately describe the full scope of the subject matter recited in claims 1, 5, 9, 13, and 18. We therefore affirm the Examiner’s rejection of those claims, and their dependents, for failing to comply with the written description requirement of 35 U.S.C. § 112, first paragraph.

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**TIME PERIOD**

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

**AFFIRMED**

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