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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte YINGRU WU, DANNY JAMES LLEWELLYN, ADRIANE CRISTINE MACHADO, and ELIZABETH SALISBURY DENNIS

Appeal 2018-006530
Application 13/243,446
Technology Center 1600

Before DEMETRA J. MILLS, ROBERT A. POLLOCK, and ELIZABETH A. LAVIER, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected claims 104, 108, 111, 113–116, 118, 121, and 123–125 for lack of utility. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

NATURE OF THE INVENTION

The present invention generally relates to polypeptides, and polynucleotides encoding them, involved in the regulation of fibre initiation and/or elongation in fibre producing plants. Spec. 1. "In particular, the present invention provides methods of altering fibre initiation in cotton and products." *Id.*[1] "The invention also relates to the use of these polypeptides and polynucleotides as markers of fibre production in plants including cotton." *Id.* Pointing to "*Arabidopsis* leaf trichromes . . . as a model for elucidating the genetic mechanisms controlling cotton fibre initiation and differentiation," the Specification states that *Arabidopsis* trichome initiation is proposed to be controlled by a trichome promoting complex, and that "genes with similar functions [Myb family of transcription factors, and fibre initiation] in cotton have yet to be identified, and hence it remains speculative whether these two single celled epidermal hair systems share any common features." Spec. 2. Appellants specifically claim, however, a method of production of a polypeptide in a fibre producing plant by expressing the polypeptide having SEQ ID NO:1, which is a partial homeodomain like protein encoded by GhHDl cDNA (clone ON033M7), to produce the polypeptide. Spec. 17; Claim 104.

STATEMENT OF CASE

The following claim is representative.

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[1] Appellants' spelling of the word fibre (British English) is used throughout the Decision, unless quoted otherwise.

> 104. A method of production of a polypeptide in a fibre producing plant, the polypeptide comprising amino acids whose sequence is at least 95% identical to the sequence set forth as SEQ ID N0:1, the method comprising expressing in a cell of the fibre producing plant an exogenous polynucleotide encoding the polypeptide so as to produce the polypeptide.

Cited Reference

Walford et al., "Epidermal cell differentiation in cotton mediated by the homeodomain leucine zipper gene, GhHD-1." *The Plant Journal* 71.3 (2012): 464–478, (hereinafter, Walford).

Grounds of Rejection

1. Claims 104, 108, 111, 113-116, 118, 121 and 123–125 are rejected under 35 U.S.C. §101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well-established utility.

2. Claims 104, 108, 111, 113–116, 118, 121 and 123–125 are rejected under 35 U.S.C. § 112(a) or 35 U.S.C. § 112 (pre-AIA), first paragraph, as failing to comply with the enablement requirement.

FINDINGS OF FACT

The Examiner's findings of fact are set forth in the Answer at pages 4–21. The following facts are highlighted.

1. Appellants' GhHD1 protein of SEQ ID NO: 1 is 624 amino acids in length (see sequence listing).

2. The GhHD1 protein that Walford et al overexpressed in cotton plants is 725 amino acids in length (see page 465, right column, 1st paragraph under RESULTS).
3. SEQ ID NO: 1 is missing the first 100 amino acids from the N-terminal region of the GhHD1 protein of Walford et al (see attached Blast alignment).
4. The homeodomain of GhHD1 is located in the N-terminal region of the protein and Appellants' protein of SEQ ID NO: 1 is missing 42 of the 58 amino acids that comprise the homeodomain (see page 466 of Walford et al, Figure 1).
5. Walford determined that both cotton GhHD-1 proteins contain the four conserved domains that are common to all members of the HD-ZIP IV family (Figure **1a).** The homeodomain is at the **N** terminus (amino acids 58-1141 and the leucine zipper region !amino acids 117-181) is immediately downstream followed by a START domain (amino acids 247-466 and an adjacent conserved SAD domain (amino acids 467-725). Promoter sequences of both *GhHD-1* genes (Figure S1c) contain putative L 1 boxes (a cis-regulatory element required for epidermal L1 layer gene expression; Abe *et al.,* 2001), three putative MYBCORE and two putative MYBATRD22 recognition sequences (Urao *et al.,* 1993; Abe *et al.,* 1997). Walford, p. 465, col. 2.
6. "The homeodomain is believed to act as a DNA binding region, and therefore the Office contends Applicants' protein of SEQ ID NO: 1 does not bind to DNA, and therefore does not have the same activity/function as the GhHD1 protein of Walford et al." Ans. 6.

> See also, https://www.merriam-webster.com/medical/homeodomain (a domain in a protein that is encoded for by a homeobox, that consists of about 60 amino acid residues which are usually similar from one such domain to another, and that recognizes and binds to specific DNA sequences in genes regulated by the homeotic gene).

PRINCIPLES OF LAW

In making our determination, we apply the preponderance of the evidence standard. *See, e.g., Ethicon, Inc. v. Quigg*, 849 F.2d 1422, 1427 (Fed. Cir. 1988) (explaining the general evidentiary standard for proceedings before the Office).

An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible. If an invention has a well-established utility, rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, based on lack of utility should not be imposed. *In re Folkers*, 344 F.2d 970, 52 CCPA 1269 (1965).

Section 35 U.S.C. § 101 requires a utility that is both substantial and specific. A substantial utility requires

> show[ing] that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research. Simply put, to satisfy the "substantial" utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public.

In re Fisher, 421 F.3d 1365, 1371, 76 USPQ2d 1225, 1230 (Fed. Cir. 2005). A specific utility is "a use which is not so vague as to be meaningless." *Id.* In other words, "in addition to providing a 'substantial' utility, an asserted use must also show that that *claimed invention* can be used to provide a well-defined and particular benefit to the public." *Id.* (emphasis added).

35 U.S.C. 101 - Utility Rejection

> The Examiner states that Appellants'
>
> SEQ ID NO: 1 is a partial homeodomain like protein encoded by the coding region of GhHD1 cDNA clone ON033M7, the coding region sequence set forth in SEQ ID NO: 18 (page 17, key to sequence listing). … Applicants disclose that GhHD1 is only 43% and 42% identical to the other cotton homeodomain proteins that are present in Genebank, GhHOX1 (AAM97321) and GhHOX2 (AAM97322), respectively (page 50, lines, 5–7). … GhHD1 exhibited fiber initial enriched expression being more than twofold enhanced in fiber initial cells relative to non-fiber epidermal cells (page 57, lines 29–31). … *Applicants do not disclose results from cotton plants transformed with said construct [SEQ ID NO:1].*

Final Act. 5 (emphasis added).

Appellants contend that, "Without any actual evidence, the Examiner contends that 'Appellants' protein of SEQ ID NO: 1 does not bind to DNA' and then in turn contends that it 'therefore does not have the **same activity/function** as the GhHDl protein of Walford et al.'" Reply Br. 8. Appellants contend that

> expressing a polypeptide *comprising* amino acids of SEQ ID NO: 1 in a fibre-producing plant, <u>including the longer full sequence that is readily determined,</u> was well within the reach of a POSA [person of ordinary skill in the art] without undue

> experimentation and Walford confirms that such a plant does, in fact, have altered fibre characteristics.

App. Br. 11. Appellants argue that

> Understanding that the subject specification described partial cDNA and polypeptide sequences (624 amino acids of about 700), the inventors in Example 10, on pages 55–56 of the subject application, outlined two different approaches for determining the full-length sequence of partial cDNA clones. As explained in the Declaration of Danny Llewellyn under 37 C.F.R. §1.132, filed October 25, 2016 (hereinafter "Llewellyn Declaration", . . .) such approaches were in fact used to produce a full-length cDNA sequence of GhHD1, as described in appellants' post-filing publication: "Walford, et al (2012). Epidermal cell differentiation in cotton mediated by the homeodomain leucine zipper gene, GhHD-1. The Plant Journal, 71 (3), 464–478" (hereinafter "Walford", . . .).

Id. at 11.

> Appellants argue that
>
> Walford describes successfully determining the full-length GhHD1 coding region using a technique described in Example 10 of the subject application. Walford also describes overexpressing this full-length GhHD1 coding region in cotton plants, which comprises the amino acids of SEQ ID NO: 1, to test the effects of the expressed polypeptide on the plant's fibre characteristics (i.e. fibre number, fibre length, fuzz fibre length, cellulose content, and dry weight) as described in Example 13 and pages 36–37 of the subject application. This testing confirmed that such cotton plants have an increased number of fibre initials at 0 dpa relative to their wild type counterparts.

Id. at 11. Finally, Appellants argue that the pending claims are also directed to an assay to determine the effect of the expressed polypeptide on fibre characteristics. App. Br. 13.

The issue is: whether the preponderance of the evidence supports the Examiner's rejection of the claims for lack of utility.

ANALYSIS

We find that the Examiner has provided evidence to support a prima facie case of lack of utility and lack of enablement. We provide the following additional comment to the Examiner's argument set forth in the Final Rejection and Answer.

Claim Scope

Claim 104 is directed to

> A method of production of a polypeptide in a fibre producing plant, the polypeptide comprising amino acids whose sequence is at least 95% identical to the sequence set forth as SEQ ID NO:1, the method comprising expressing in a cell of the fibre producing plant an exogenous polynucleotide encoding the polypeptide so as to produce the polypeptide.

In order for the claimed method to have a utility, there must be a useful reason to insert the polypeptide having SEQ ID NO:1 into a fibre producing plant, and the product of SEQ ID NO:1, produced by the process, must be useful. Where the invention is a process, the product resulting from that process must have utility in order for the process to have utility. *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966). In the present case, we do not find that Appellants' Specification discloses that the product

of the claimed process (expressing in a cell of the fibre producing plant an exogenous polynucleotide (having SEQ ID NO:1) encoding the polypeptide so as to produce the polypeptide)), has a specific and substantial utility.

The Examiner argues that the full sequence of the fiber initiation gene GhHD1 (a partial homeodomain like protein encoded by the coding region of GhHD1 cDNA clone ON033M7; SEQ ID NO: 1), from cotton ovules, was not known or disclosed in the application, as filed. Ans. 7. The Examiner further argues that

> Appellants' polypeptide of SEQ ID NO: 1 is missing an essential region as compared to the full-length protein reported in Walford et al, and therefore the polypeptide is nonfunctional. Neither Appellants nor the prior art have provided any direct evidence that overexpressing the polypeptide of SEQ ID NO: 1 will have any affect on the plant, in particular, any affect on fiber initiation and/or elongation. It is apparent that extensive further research, not considered to be routine experimentation, would be required before one skilled in the art would know how to use the claimed invention.

Ans. 7.

We find that the Examiner has provided evidence to support a prima facie case of lack of utility. We agree with the Examiner that neither the Appellants nor the prior art have provided any direct evidence that overexpressing the polypeptide having the specific sequence of SEQ ID NO: 1 will have any effect on the plant, in particular, any effect on fibre initiation and/or elongation. The Specification admits that genes controlling leaf trichomes in *Arabidopsis* were known, however, states that "genes with similar functions in cotton have yet to be identified, and hence it remains speculative whether these two single celled epidermal hair systems share any

common features." Spec. 2. Furthermore, Appellants' protein of SEQ ID NO: 1 is missing the first 100 amino acids from the N-terminal region of the GhHD1 protein of Walford et al (see attached Blast alignment). The homeodomain is located in the N-terminal region of the protein and Applicants' protein of SEQ ID NO: 1 is missing 42 of the 58 amino acids that comprise the homeodomain (see page 466 of Walford et al, Figure 1). As indicated by the Examiner, it is well known in the art that a homeodomain is a DNA binding region. FF6. Appellants' protein of SEQ ID NO: 1 is missing 42 of the 58 amino acids that comprise the important homeodomain (see page 466 of Walford et al, Figure 1). Accordingly, the Examiner finds that the protein encoded by SEQ ID NO: 1 "does not bind to DNA, and therefore does not have the same activity/function as the GhDH1 protein of Walford." Ans. 6.

The Examiner has provided a reasonable, technical and scientific basis to believe that the method of claim 104 lacks utility. The burden of proof shifts to Appellants to rebut the Examiner's prima facie case of lack of utility.

In rebuttal of the Examiner's prima facie case of lack of utility, Appellants put forth the Declaration under 37 C.F.R. § 1.132 of Dr. Llewellyn, an inventor of the claimed subject matter and a co-author of the Walford publication, cited above and of record.

According to Dr. Llewellyn, the Walford publication "describes the protocol we used to isolate the full-length GhHD-1 gene." Decl. ¶ 6. Dr. Llewellyn states that, "The protocols described in Walford et al. were conducted substantially as described in Example 10 of the subject application and were routine in the art at the time the application was filed."

Decl. ¶ 8. Appellants also contend the Examiner has not provided adequate evidence or reasoning why a polypeptide consisting of the amino acid sequence set forth as SEQ ID NO: 1 would have no activity or function. App. Br. 14.

We are not persuaded by Appellants' Declaration or argument that the Examiner has not provided evidence that SEQ ID NO:1 would have no activity or function. First, the Declaration of Dr. Llewellyn does not provide evidence that the polypeptide with the specific sequence of SEQ ID NO:1, when expressed in the cell of a fibre producing plant, would have a specific and substantial utility or is functional. The Examiner has provided a technical or scientific reason that the polypeptide of SEQ ID NO:1 is missing 42 of the 58 amino acids that comprise the homeodomain, and would likely have difficulty with DNA binding. *See generally Ex parte Sudilovsky*, 21 USPQ2d 1702 (BPAI 1992 (explaining that scientific reasoning alone can be sufficient to support rejection for undue experimentation under § 112, but noting that reliance on "either or both" § 101 and § 112, first paragraph, "has been judicially approved").

The Examiner presented a scientific or technical reason why one of ordinary skill in the art would not believe SEQ NO:1 has a specific and substantial utility, because the sequence is missing a large portion of a critical homeodomain region, as compared to the Wolford sequence. Both the Wolford publication and the Llewellyn Declaration fail to support or provide evidence that SEQ NO:1, the partial homeodomain like protein encoded by GhHDl cDNA (clone ON033M7), has the asserted utility of being expressed in a cell of the fibre producing plant, wherein the plant product has a readily recognized utility.

In sum, the Declaration of Dr. Llewellyn does not provide evidence that the expression product of SEQ ID NO:1 provides an immediate benefit to the public or is functional.

Appellants argue that they need only establish one utility, and that the claimed a method has a specific and substantial utility in an assay for effect on fibre characteristics, even if some polypeptides comprising the sequence of SEQ ID NO: 1 have a greater effect and others have a lesser effect on plant fiber characteristics. App. Br. 13; Reply Br. 7. Consistent with the holding in *In re Fisher*, we find that Claim 104 is directed to a method, and not an assay per se. Even if claim 104's method steps could somehow be construed to be an assay, we conclude that the claimed method steps provide no immediate benefit to the public, as the function of SEQ ID NO:1 was unclear to those of ordinary skill in the art at the time of filing of the present application.

Enablement Rejection

Claims 104, 108, 111, 113–116, 118, 121 and 123–125 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the enablement requirement.

The Examiner contends that "The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)." Ans. 15. The Examiner argues that, "Appellants do not disclose results from cotton plants transformed with" the construct/clone expressing the polypeptide of SEQ ID NO:1. Ans. 16. The Examiner further argues that

> Applicants contend enablement of the claimed invention is confirmed by Walford et al, (2012, The Plant Journal 71:464–478 … . Walford et al disclose overexpression of [full length] GhHD1 in fiber producing plants result in an increase in the number of fiber initiations compared to wild type plants (summarized by Applicants on page 14 of Remarks filed 6/24/2015, 2nd paragraph). The Office contends the GhHD1 protein that Walford et al overexpressed in cotton plants is 725 amino acids in length (see page 465, right column, 1st paragraph under RESULTS), whereas Applicants' GhHD1 protein of SEQ ID NO: 1 is 624 amino acids in length (see sequence listing). ***The Office contends the two GhHD1 proteins are not the same.*** Applicants' protein of SEQ ID NO: 1 is missing the first 100 amino acids from the N-terminal region of the GhHD1 protein of Walford et al (see attached Blast alignment). The homeodomain is located in the N-terminal region of the protein and Applicants' protein of SEQ ID NO: 1 is missing 42 of the 58 amino acids that comprise the homeodomain (see page 466 of Walford et al, Figure 1). The homeodomain is believed to act as a DNA binding region, and therefore the Office contends Applicants' protein of SEQ ID NO: 1 does not bind to DNA, and therefore does not have the same activity/function as the GhHD1 protein of Walford et al. The Office contends there is no evidence showing that increasing the expression of Applicants' GhHD1 protein of SEQ ID NO: 1 in a plant will have any affect on fiber initiation and/or elongation when expressed at any time or around the time of anthesis.

Final Act. 6.

Appellants contend that "A person of ordinary skill could have readily expressed the exogenous polynucleotide recited in claims based on what is described in subject specification coupled with what was well known in the art." App. Br. 21. Appellants argue that, "As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. *In* re *Fisher,* 427 F.2d

833, 839, 166 USPQ 18, 24 (CCPA 1970) (emphasis added)." Appellants argue that the specification teaches those in the art enough that they can make and use the invention without 'undue experimentation.'" App. Br. 21–22.

Appellants argue that enablement of the claimed invention is confirmed by the Llewellyn Declaration and Walford publication. Reply Br. 11-12.

ANALYSIS

We are not persuaded by Appellants' arguments. Appellants do not claim a polypeptide having the full length putative homeodomain leucine zipper (HD-ZIP) transcription factor, *GhHD-1*, expressed in trichomes and early fibres, as disclosed in Walford. Appellants claim a method of production of a polypeptide in a fibre producing plant, the polypeptide comprising amino acids whose sequence is at least 95% identical to the sequence set forth as **SEQ ID NO:1**, so as to produce the polypeptide of **SEQ ID NO:1**. Appellants have not shown that the product of this method [polypeptide of SEQ ID NO:1] is a functional fibre producing product.

If a claim fails to meet the utility requirement of 35 U.S.C. § 101 because it is shown to be nonuseful or inoperative, then it necessarily fails to meet the how-to-use aspect of the enablement requirement of 35 U.S.C. § 112(a) or pre-AIA 35 U.S.C. § 112, first paragraph. As noted in *In re Fouche*, 439 F.2d 1237 (CCPA 1971), if "compositions are in fact useless, appellant's specification cannot have taught how to use them." 439 F.2d at 1243; *see* MPEP § 2164.07.

Notwithstanding the above well-settled principle that an invention with no utility does not meet the enablement requirement, Appellants argue that,

> even without amino acids of the putative GhHDl homeodomain, appellants submit that it is **plausible** that a polypeptide *consisting* of the amino acids set forth as SEQ ID N0:1 would have some effect on plant fibre characteristics by virtue of the activity of domains, other than the putative homeodomain, that are present in the 624-amino acid sequence set forth as SEQ ID NO: 1.

App. Br. 14–15 (emphasis added).

We are not persuaded by Appellants' argument that "even without amino acids of the putative GhHDl homeodomain, appellants submit that it is **plausible** that a polypeptide *consisting* of the amino acids set forth as SEQ ID NO:1 would have some effect on plant fibre characteristics." This is merely attorney argument that is unsupported by evidence. *See In re Pearson*, 494 F.2d 1399, 1405 (CCPA 1974) ("Attorney's argument in a brief cannot take the place of evidence."). Absent any evidence that SEQ ID NO:1 would have some effect on plant fibre characteristics, the contrary also remains plausible, that a polypeptide consisting of the amino acids set forth as SEQ ID NO:1 would have no effect on plant fibre characteristics, especially in view of the fact that the sequence is missing a large portion of the homeodomain. A plausible effect is neither a specific nor substantial utility or an indication that one of ordinary skill in the art would have been able to make and use the invention without undue experimentation.

Information needed to satisfy 35 U.S.C. § 112, first paragraph, must be disclosed in the specification, not in a later-filed declaration. "§ 112 requires that, unless the information is well known in the art, the application

itself must contain this information; it is not sufficient to provide it only through an expert's declaration." *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991). "Enablement, or utility, is determined as of the application filing date." *In re Brana*, 51 F.3d 1560, 1567 n.19 (Fed. Cir. 1995). Application sufficiency must be judged as of the filing date; later issuing patents or publications may not be relied on to establish that the specification is enabling. Applicants cannot rely on publications published after the effective filing date to rebut a *prima facie* case of non-enablement. *Ex parte Hitzeman*, 9 USPQ2d 1821, 1823 (BPAI 1988). A post-filing declaration may be used to show the accuracy of a statement in the specification, but not to "render an insufficient disclosure enabling." *Brana*, 51 F.3d at 1567 n.19.

Appellants argue that enablement of the claimed invention is confirmed by the Llewellyn Declaration and Walford publication. Reply Br. 11–12. But the Declaration of Dr. Llewellyn does not provide evidence that the polypeptide with the specific sequence of SEQ ID NO:1, missing a large portion of the homeodomain, when expressed in the cell of a fibre producing plant, would have a specific and substantial utility or is functional. To the contrary, the Examiner has provided a reasoned, technical or scientific argument that the polypeptide of SEQ ID NO:1 is missing 42 of the 58 amino acids that comprise the homeodomain, and would likely have difficulty with DNA binding. *See Sudilovsky*, 21 USPQ2d 1702.

For similar reasons, the Examiner's enablement rejection is also affirmed.

DECISON

The cited references support the Examiner's utility and enablement rejections, which are affirmed for the reasons of record. All pending, rejected claims 104, 108, 111, 113–116, 118, 121 and 123–125 fall.

AFFIRMED