

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT NO.: 5,322,938
ISSUED: Jun. 21, 1994
TO: McPherson et al.
FOR: DNA CONSTRUCT FOR ENHANCING THE
EFFICIENCY OF TRANSCRIPTION

ATTACHMENT TO FORM PTO-1465,
REQUEST FOR *EX PARTE* REEXAMINATION

SIR:

The Public Patent Foundation (“PUBPAT”), a not-for-profit public service organization that works to protect the public from the harms caused by undeserved patents and unsound patent policy, respectfully requests *ex parte* reexamination under 35 U.S.C. §§ 302 – 307 and 37 C.F.R. § 1.510 of every claim of United States Patent No. 5,322,938 issued June 21, 1994, to McPherson et al. and assigned to Monsanto Company (“the '938 patent”) because they are all invalid under 35 U.S.C. §§ 103 and their existence is causing significant public harm.¹

¹ A copy of the '938 patent is attached hereto as Appendix A.

THE '938 PATENT IS CAUSING SIGNIFICANT PUBLIC HARM

The '938 patent relates to genetic modification of plants. More specifically, the '938 patent claims chimeric transcriptional initiation regions for enhancing the efficiency of transcription. Monsanto is using the '938 patent – and three other patents for which requests for reexamination are being filed concurrently herewith – to harass and, in many instances, literally bankrupt countless numbers of American farmers. *See, e.g., Monsanto v. U.S. Farmers*, Center for Food Safety (2005). Monsanto's campaign of harassment has included the filing of dozens of infringement lawsuits against farmers, many of whom are financially unable to retain sufficient counsel to defend themselves in court.² Monsanto's aggressive assertion of its patents is not only obnoxious and offensive to the core fabric of American life and culture, it is also causing substantial public harm. As the Center for Food Safety found in its study of the matter:

Monsanto has used heavy-handed investigations and ruthless prosecutions that have fundamentally changed the way many American farmers farm. The result has been nothing less than an assault on the foundations of farming practices and traditions that have endured for centuries in this country and millennia around the world, including one of the oldest, the right to save and replant crop seed.

Id. Although these issues are not grounds to grant this request for reexamination, PUBPAT respectfully requests that they be considered when determining whether the validity of the '938 patent merits review by your office.

THE SUBSTANTIAL NEW QUESTION OF PATENTABILITY

The substantial new question of patentability raised by this request is whether claims 1 through 6 of the '938 patent were rendered obvious by U.S. Patent No. 4,407,956 issued

² Appendix C contains a listing of litigation involving the '938 patent.

to Howell on October 4, 1983 (“Howell”), in light of Guilley, et al., “Transcription of Cauliflower Mosaic Virus DNA: Detection of Promoter Sequences, and Characterization of Transcripts,” *Cell*, 30(3):763-773 (1982) (“Guilley”).³ A detailed explanation of the pertinency and manner of applying Howell and Guilley to each of claims 1 through 6 of the '938 patent is set forth below.

HOWELL AND GUILLEY RENDERED THE ‘938 PATENT OBVIOUS

The '938 patent claims priority through a string of applications, the first of which was filed on January 13, 1987. Although PUBPAT does not concede that the '938 patent can justifiably claim priority to January 13, 1987, we do not address that issue at this time because it is not material to the arguments made in this request. Since Howell issued on October 4, 1983, more than a year before January 13, 1987, Howell is prior art to the '938 patent under 35 U.S.C. § 102(b). Likewise, since Guilley was published in October 1982, more than a year before January 13, 1987, Guilley is also prior art to the '938 patent under 35 U.S.C. § 102(b).

One of ordinary skill in the art would have been motivated to combine the teachings of Howell and Guilley because they were both directed to the same exact subject matter, namely the use of cauliflower mosaic virus (“CaMV”) to introduce foreign genes into plants. Further, Guilley expressly cited two articles written by the sole named inventor of Howell and Howell expressly cited the journal *Cell* in which Guilley was published. Thus, there was more than sufficient suggestion and motivation in the art to combine the teachings of Howell and Guilley.

The chart below sets forth an element-by-element comparison of all 6 claims of

³ Appendix B contains a copy of Howell and Guilley.

the '938 patent to the combined teachings of Howell and Guilley. In essence, every element of each claim of the '938 patent was obvious in light of Howell and Guilley. As such, each claim of the '938 patent is invalid and should be canceled.

<i>'938 Patent</i>	<i>Howell and Guilley</i>
1. A chimeric transcriptional initiation region comprising:	Howell taught that “[t]he DNA of certain viruses such as cauliflower mosaic virus which infect plants may serve as 'vehicles' for the introduction of 'exogenous' or 'foreign' DNA into plant cells.” 1:54-57. The terms exogenous and foreign DNA are synonymous with DNA construct. Howell further taught DNA constructs having regions that include transcription initiation sites. 5:33-36.
as operably joined components	Howell taught that “[t]he various genes may be introduced simultaneously with or sequentially with regulatory signals,” which one of ordinary skill in the art would have understood to mean that the genes were functionally linked between the affecting sequences. 5:48-50. Thus, Howell taught operably linked components.

<i>'938 Patent</i>	<i>Howell and Guilley</i>
(i) a tandemly duplicated CaMV 35S enhancer sequence comprising	<p>Howell taught that (i) “[r]egulatory elements would be inserted [into the viral DNA vehicles, including specifically CaMV] to insure the appropriate or <i>enhanced</i> 'expression' of the foreign structural gene in the infected plant,” (ii) that “[r]egulatory elements may be derived from a variety of donors, eucaryotic promoter sites from plants, etc. or the elements may be <i>duplicate copies</i> of elements already resident within the viral DNA,” and (iii) “the term, regulatory element, is also taken to include coding signals – signals for transcription initiation and termination, capping sites, ribosome binding, translation initiation start and stop signals, etc..” 5:14-36 (emphasis added). Thus, Howell taught duplicate copies of regulatory elements, including signals for transcription initiation, within the viral DNA construct. It would have been obvious to place these duplicate regulatory elements in tandem and one of ordinary skill in the art would have understood Howell's broad definition of regulatory elements to also include enhancer sequences generally and, since CaMV was Howell's primary example, CaMV enhancer sequences specifically.</p> <p>Guilley specifically taught that the CaMV 35S region was much more active than other CaMV regions. 770. Thus, one of ordinary skill in the art would have been motivated to make DNA constructs according to Howell's teaching using the 35S region of CaMV as taught by Guilley, because Howell recognized that “it may be desirable to increase the copy number of a gene endogenous to the plant to enhance production of the gene product in the plant.” 3:40-44.</p>
an AluI-EcoRV fragment of a CaMV 35S upstream region;	<p>Howell taught that, “[o]ne linker insertion at an Alu I site near a Bgl I site between region I and region VI described as an intergenic region was found to retain infectivity, being in the Eco RI b restriction fragment adjacent to the Eco RI c restriction fragment.” 7:26-31. Thus, Howell taught a CaMV DNA vector having a fragment containing an Alu I restriction site linker. Guilley also taught various Eco RI fragments of the CaMV 35S promoter region, which is inherently upstream. 764-65.</p>
and (ii) a promoter comprising an RNA polymerase binding site and an mRNA initiation site,	<p>Howell taught regulatory elements including ribosome binding sites and transcription initiation sites. 5:33-36. Promoters inherently have a RNA polymerase binding site and an initiation site. Thus, Howell taught a promoter with RNA polymerase binding and mRNA initiation sites. Further, Guilley expressly disclosed promoters with RNA polymerase transcription sites and RNA initiation sites. 770-71.</p>

'938 Patent	<i>Howell and Guilley</i>
wherein when a nucleotide sequence of interest is transcribed under the regulatory control of said chimeric transcriptional initiation region,	Howell taught that generally “[a] wide variety of genes are of interest for insertion into the virus, particularly, genes which modify the existing properties of the plant or endow the plant with the ability to produce new substances.” More specifically, Howell taught that “modified CaMV DNA has been prepared with insertion of an oligonucleotide into an active region, with retention of infectivity and movement of the product.” 5:37-40; 7:46-49.
the amount of transcription product is enhanced as compared to the amount of transcription obtained with a chimeric transcriptional initiation region comprising a single copy of said CaMV enhancer sequence and said promoter.	Howell taught that (i) “[r]egulatory elements would be inserted [into the viral DNA vehicles, including specifically CaMV] to insure ... <u>enhanced</u> 'expression' of the foreign structural gene in the infected plant,” (ii) that “[r]egulatory elements ... may be <u>duplicate copies</u> of elements already resident within the viral DNA,” and (iii) “the term, regulatory element, is also taken to include ... signals for <u>transcription initiation</u> .” 5:14-36 (emphasis added). Thus, Howell taught duplicate copies of regulatory elements, including signals for transcription initiation, within the viral DNA construct. One of ordinary skill in the art would have understood Howell's broad definition of regulatory elements to include enhancer sequences generally and, since CaMV was Howell's primary example, CaMV enhancer sequences specifically. As such, Howell taught the use of multiple CaMV enhancer sequences within its DNA construct to increase the amount of transcription obtained.
2. The chimeric transcriptional initiation region according to claim 1, wherein said promoter is obtainable from the upstream region of a plant virus gene.	Both Howell and Guilley taught a promoter upstream of a CaMV virus. Further, promoters are inherently upstream of the gene of interest.

<i>'938 Patent</i>	<i>Howell and Guilley</i>
3. The chimeric transcriptional initiation region according to claim 2, wherein said plant virus gene is a CaMV 35S gene.	Howell taught the use of CaMV, including inherently CaMV promoter, and Guilley expressly taught CaMV 35S.
4. The chimeric transcriptional initiation region according to claim 1, wherein said promoter is obtainable from the upstream region of a gene indigenous to a plant cell genome.	Both Howell and Guilley taught a promoter upstream of a CaMV virus, which is a “gene indigenous to a plant cell genome.” Further, promoters are inherently upstream of the gene of interest.
5. The chimeric transcriptional initiation region according to claim 1, wherein said promoter is a T-DNA promoter.	Howell taught that “in the case of the tumor inducing (Ti) plasmid in the bacterium Agrobacterium[, a] portion of the Ti plasmid is transferred from bacterium to plant when Agrobacterium infects plants.” 1:44-47 (the “portion of the Ti plasmid [that] is transferred” is commonly referred to as the T-DNA). Howell continued to teach that “[t]hat type of DNA transfer has been [] utilized in certain genetic modification experiments involving plants.” 1:47-50. In order to achieve this genetic modification, the T-DNA must inherently contain a promoter because a promoter is required to achieve expression in the plant cell.
6. The chimeric transcriptional initiation region according to claim 5, wherein said promoter is a T-DAN gene 7 or gene 5 promoter.	Howell taught that “in the case of the tumor inducing (Ti) plasmid in the bacterium Agrobacterium[, a] portion of the Ti plasmid is transferred from bacterium to plant when Agrobacterium infects plants.” 1:44-47 (the “portion of the Ti plasmid [that] is transferred” is commonly referred to as the T-DNA). Howell continued to teach that “[t]hat type of DNA transfer has been [] utilized in certain genetic modification experiments involving plants.” 1:47-50. In order to achieve this genetic modification, the T-DNA must inherently contain a promoter, such as gene 7 or gene 5, because a promoter is required to achieve expression in the plant cell.

CONCLUSION

For the reasons set forth above, each of the claims of the '938 patent are invalid for being obvious in light of Howell and Guilley. As such, PUBPAT respectfully requests that they be reexamined *ex parte* and ultimately canceled.

September 29, 2006

/s/

Date

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CERTIFICATE OF SERVICE

The undersigned certifies that a copy of this Request for *Ex Parte* Reexamination in its entirety, including all accompanying documents, is being deposited with the U.S. Postal Service as Priority Mail with Delivery Confirmation on the date of the signature below in an envelope addressed to the attorney of record for the assignee of U.S. Patent No. 5,322,938 as provided for in 37 C.F.R. § 1.33(c):

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APPENDIX A

U.S. PATENT NO. 5,322,938

APPENDIX B

HOWELL AND GUILLEY

APPENDIX C

COPENDING LITIGATION

U.S. Patent No. 5,322,938 is or has been the subject of the following litigation:

1. Monsanto Company v. Agmax, LLC, Filed December 23, 2005, D.C. S.D. Illinois, Doc. No. 4:05cv4223
2. Monsanto Company v. Anderson & Jones Inc, et al, Filed November 19, 1999, D.C. E.D. Missouri, Doc. No. 4:99cv1805
3. Monsanto Company v. Dewayne Hendrix, et al, Filed Apr. 6, 2001, D.C. E.D. Missouri, Doc. No. 4:01cv523ERW
4. Monsanto Company v. Norman Kelly, et al, Filed Sep. 14, 2001, D.C. E.D. Missouri, Doc. No. 4:01cv1484CEJ
5. Monsanto Company, et al v. Olvey, et al, Filed November 23, 2004, D.C. Arizona, Doc. No. 2:04cv2667
6. Monsanto Company v. Kem Ralph individually, et al, Filed Jan. 28, 2000, D.C. E.D. Missouri, Doc. No. 4:00cv135
7. Monsanto Company v. Mitchell Scruggs, et al, Filed Sep. 7, 2000, D.C. N.D. Mississippi, Doc. No. 3:00CV161-B-A
8. Monsanto Company v. Hal Swann (d/b/a Howell Everett Swann), et al, Filed Sep. 14, 2000, D.C. E.D. Missouri, Doc. No. 4:00CV01481CEJ