United States District Court,
D. Connecticut.

PLANT GENETIC SYSTEMS, N.V. BIOGEN, INC,
v.
DEKALB GENETICS CORP.

No. 3:96CV2015 (DJS)

Sept. 7, 2001.

Patentee brought action against alleged infringer relating to patent on use of Agrobacterium to insert bar gene into both dicotyledons and monocotyledons. After a bench trial, the District Court, Squatrito, J., held that: (1) alleged infringer established by clear and convincing evidence that cell claims were invalid due to lack of enablement; (2) patent was not literally infringed by accused products; and (3) patent was not infringed under doctrine of equivalents.

Ordered accordingly.

5,561,236. Noninfringement.

Eric D. Daniels, Craig A. Raabe, Bradford S. Babbitt, Robinson & Cole, Hartford, CT, John F. Sylvia, Mintz, Levin, Cohn, Ferris, Glovsky & Popeo, P.C., Boston, MA, R. Danny Huntington, Eric H. Weisblatt, Regis E. Slutter, Barbara W. Walker, George A. Hovanec, Jr., Bruce Jeferson Boggs, Jr., H. Jonathan Redway, Susan M. Dadio, Burns, Doane, Swecker & Mathis, Alexandria, VA, for Plaintiffs.

John C. Yarvis, Jr., Francis J. Brady, Murtha Cullina LLP, Hartford, CT, Thomas A. Miller, Houston, TX, John F. Lynch, H. H. Kewalramani, Howrey Simon Arnold & White, LLP, Menlo Park, CA, Daniel T. Shvodian, Howrey Simon Arnold & White, LLP, Menlo Park, CA, for Defendant.

MEMORANDUM OF DECISION

SQUATRITO**, District Judge.**

In this action, the plaintiffs claim, *inter alia,* that the defendant's products infringe certain claims of United States Patent No. 5,561,236 (hereinafter 'the '236 patent'). After a thirteen day bench trial before the undersigned, the Court now articulates its findings of fact and conclusions of law. For the reasons that follow, the Court concludes that (1) Claims 1-5 and 10-11 (the cell claims) of the '236 patent are invalid for lack of enablement and that (2) the exclusivity of Claims 8-9 and 12-15 (the plant and seed claims) is limited to dicotyledonous plants and does not extend to monocotyledons such as the accused corn products. Accordingly, judgment is entered for the defendant on all counts.

I. Introduction

This case concerns the right to make, use, sell or offer for sale certain types of genetically engineered plants and seeds-- specifically corn. The defendant sells a variety of genetically engineered corn products. The central issues at trial were whether the defendant's sale of certain corn seeds or its research activities involving corn seeds and plants infringed the claims of the '236 patent.

A. Scientific Background

Since Neolithic man first began to cultivate crops, humans have had both economic and social incentives to create and enhance the properties of food plants. FN1 "The largest single step in the ascent of man is the change from [a] nomad[ic] lifestyle to village agriculture." Jacob Bronowski, *The Ascent of Man* 64 (1973). A civilization that could secure a reliable source of food was best equipped to become both a political and military power in its geographic region.

FN1. *See* William Langer, *An Encyclopedia of World History* 14 (5th ed.1972).

Scientists postulate that the shift of human societies from a nomadic existence toward more centralized, agrarian cultures was catalyzed by a natural act of genetic engineering. Wild wheat, a grassy plant of little agricultural value, naturally crossed with goat grass to produce, for the first time, a fertile wheat hybrid with a full head of grain that could be easily harvested. Id. at 65-67. FN2 The case at bar involves genetic engineering of a decidedly more deliberate nature.

FN2. The progeny of wild wheat and goat grass was called 'emmer,' a fertile species containing 28 chromosomes. Emmer subsequently crossed with another grass to produce 'bread wheat,' a more robust plant. Bread wheat served as an important source of food for developing civilizations in both the Middle East and Asia.

As man developed his agricultural skills, he began to use crude herbicides to enhance his efforts. The earliest farmers used sea salt, a strategy still employed by modern organic gardeners. Late in the 19th century, the selective control of broad leaf weeds became possible. A major development in modern weed control was the introduction in 1945 of the so-called 'organic' herbicides. These compounds were revolutionary because their high toxicity allowed for effective weed control at very low dosages. Id. Since modern herbicides were first employed, scientists have worked to increase their selectivity. The ideal herbicide kills only the undesirable plant, and has no adverse effects on either the desirable plants or the consumers of those plants.

There are conceptually at least two approaches to developing a useful herbicide. First, a herbicide could be developed that selectively kills only certain types of undesirable plants. In this model, the selectivity feature would be incorporated into the chemical structure of the herbicide. Alternatively, the selectivity feature could be incorporated into the plant itself so that it would be resistant to a non-selective herbicide. In this model, the herbicide would kill a broad spectrum of plant life except for certain genetically modified plants. This case involves the latter approach.

Plants create ammonia as a by-product of their biochemical processes. While the production of ammonia is a natural phenomenon, it presents the plant with a problem. High levels of ammonia are inevitably toxic to

plants. Plants remove the ammonia they produce via the action of an enzyme, glutamine synthetase. Glutamine synthetase, as its name plainly suggests, synthesizes glutamine by metabolizing the ammonia and another substance, glutamate. Unlike ammonia, glutamine is not toxic to plants.

In the early 1980's, researchers discovered that the biochemical action of glutamine synthetase could be inhibited-- that is the plant could be prevented from converting ammonia to glutamine-- by either bialaphos FN3 or glufosinate,FN4 two structurally related compounds isolated from certain species of *Streptomyces* bacteria. In the presence of either of these compounds, toxic levels of ammonia build up in the plant and it eventually dies. In light of the effect that these substances have on all plants, several different herbicides were developed.FN5 These herbicides are non-selective and indiscriminately kill most plants with which they come into contact.

FN3. Bialaphos is also known in the literature as SF-1293.

FN4. Glufosinate is also known as phosphinothricin or PPT.

FN5. For example, commercial herbicides that employ this non-selective approach include Liberty ™, Basta ™ and Ignite ™. Basta ™ is an Italian word meaning "enough" or "stop." As these names imply, the non-selective herbicide will kill all of the plants it contacts.

With the use of any non-selective herbicide, a commercial advantage can be obtained if a desirable food plant could be developed that would be resistant to the effect of the non-selective herbicide. The non-selective herbicide could then be indiscriminately applied to a field of crops. This would result in the destruction of all non-resistant plants, which in theory would only be the unmodified, non-food plants. Thus, after application of the non-selective herbicide, the only plants that would remain viable would be the desirable food plants. The plaintiffs in this case claim such an invention.

It was discovered that a certain species of bacteria from the *Streptomyces* genus possess a gene (called either the *bar* or *pat* gene) that encodes for the production of a protein that inactivates the herbicidal substance, such as bialaphos, from inhibiting the action of glutamine synthetase.FN6 This is the biochemical equivalent of a linguistic double negative. The *bar* gene produces a substance that prevents the active ingredient in the non-selective herbicide from itself inhibiting the plant's ability to metabolize ammonia. The plaintiffs claim that they could genetically modify desirable food plants so that these plants would now contain a foreign gene that would render the transformed plant impervious to the effects of certain glufosinate-based herbicides. Thus, the modified plants would now be able to fend off the biochemical attack of the non-selective herbicide and would survive while their less genetically robust compatriots (i.e., the non-desirable weeds) would perish.FN7

FN6. Another gene that putatively has the same action is the "slr" gene.

FN7. Environmental groups have generally questioned the wisdom of these type of gene alterations to food plants. As reported in a front page story in The New York Times, Semintis, Inc. was experimenting in Idaho with the development of glyphosate-resistant pea plants (as opposed to glufosinate resistant corn plants

which are the subject of this case). The test plots were destroyed by environmentalists, who later explained that "[t]hese peas weren't normal.... [t]hey had their genes changed to make the plants stay alive when sprayed with glyphosate herbicide. These gene-altered plants can cross-breed with regular plants, and we don't know what they will do to people, animals, the soil, or anything." *S.U.V.'s, Golf and Even Peas Join the Growing Hit List of Eco-Vandals,* The New York Times, 7/1/01, at p. 1. (internal quotes omitted).

The key issue at trial was a dispute concerning the scope of the patent claims. The defendant does not contest that the plaintiffs possess patent rights with respect to the modification of certain types of plants and plant cells. For example, modified tomato, potato and tobacco plants are undisputedly covered by the '236 patent. The defendant contends, however, that the plaintiffs' patent rights extend only to this general category of plants.

Flowering plants are phenotypically broken down into two broad categories: monocotyledons and dicotyledons, commonly called monocots and dicots. The distinction is based on whether the cotyledon, or the initial growth produced by the seed, contains one leaf (monocot) or two leaves (dicot). The seedlings of other plants, such as pine trees and many gymnosperms, can produce more than two leaves and are called polycotyledons or polycots. As is discussed in greater detail below, the working examples in the '236 patent are all dicots, while the accused product in this case is corn-- undisputedly a monocot.

In addition to endowing transformed plants with resistance to certain herbicides, the *bar* gene is also widely used as a selectable marker. A selectable marker is a gene that allows researchers to determine whether other genes have also been incorporated into a plant. Thus researchers who have identified a gene that confers another desirable trant to plants, for example the ability to resist certain species of harmful insects, will link that new gene to the *bar* gene, and then attempt to incorporate this entire gene construct into the target plant. They can determine whether their efforts have been successful by testing for the presence of the selectable marker. If the *bar* gene is used as the selectable marker, simply spraying the plants with glufosinate will kill those plants that do not possess the selectable marker. Those plants that survive are likely to contain both the *bar* gene and the target gene of interest which in this example is a gene for insect resistance.

B. The '236 Patent

In general, the owners of the '236 patent claim the legal ability to exclude others from making, using, selling or offering for sale modified plants, seeds and plant cells containing the *bar* gene. The defendant sells various corn products and conducts research in which the corn plant cells contain the *bar* gene, in some cases serving in the capacity as a selectable marker. Specifically, the plaintiffs allege that the defendant's products infringe claims 1-5, 8-9, and 10-15 of the '236 patent. This group of claims break down into two subsets. First, claims 1-5 and 10-11 comprise what the Parties call the cell, tissue and culture claims (hereinafter 'the cell claims'). This group is controlled by Claim 1, the lone independent claim in this grouping. It reads:

A plant cell having a heterologous DNA stably integrated into its genome; said DNA comprising a heterologous DNA fragment encoding a protein having an acetyl transferase activity which inactivates a glutamine synthetase inhibitor in said cell.

The Parties refer to the second group of claims as the "plant and seed" claims.FN8 This group includes

Claims 8-9 and 12-15. Claim 8, which is representative of claims 12-15, reads:

FN8. For the purposes of this decision, the Court assumes that the plants and seeds are proper subject matter for patent protection under 35 U.S.C. s. 101. The Court notes, however, that at the time this decision was issued, the United States Supreme Court had granted a writ of certiorari in J.E.M. Ag Supply Inc. v. Pioneer Hi-Bred International, 531 U.S. 1143, 121 S.Ct. 1077, 148 L.Ed.2d 954 (2001). In the case below, the Federal Circuit affirmed a district court ruling that seeds and seed grown plants are patentable subject matter under 35 U.S.C. s. 101. See Pioneer Hi-Bred International v. J.E.M. Ag Supply Inc., 200 F.3d 1374, 1378 (Fed.Cir.2000).

"A plant which consists of the cells of claim 1 and which is susceptible to infection and transformation by Agrobacterium and capable of regeneration thereafter."
Likewise, claims 12-15 require that the cells of claims 2-5, respectively, be susceptible to infection by *Agrobacterium* and regeneration thereafter. The reference in claims 8 and 12-15 to "transformation by *Agrobacterium* " refers to a method by which the *bar* gene is introduced into the plant cell. As this methodology forms one of the most extensively litigated issues in this case, it is discussed at length below.FN9
FN9. Claim 9 claims "a seed of the plant of Claim 8."

Because the two sets of claims present different legal issues with respect to claim construction and enablement, the Court will discuss them separately. The Court first turns to Claims 1-5 and 10-11, labeled the 'cell claims' by the Parties.

II. Cell Claims [Claims 1-5, 10,11]

A. The Meaning of the Cell Claims

[1] The Parties agree as to the scope and meaning of this set of claims. Specifically, they agree that the term 'plant cell' "do[es] not contain any limitation regarding the type of cell or type of plant species [covered]." Defendant's Post-Trial Reply Brief at 2. The Parties agree that these claims cover every type of plant cell, including cells from both monocots and dicots. *Id., see also* Plaintiffs' Proposed Findings of Facts, at 70. Thus, for example, if Claim 1 is valid it would cover any plant cell having the *bar* gene stably integrated into its genome.

B. Enablement of the Cell Claims

1. Requirements of 35 U.S.C. s. 112

[2] As a threshold issue, when determining whether a patent is enabled under s. 112, courts should be mindful that, once examined and issued, all United States patents enjoy a presumption of validity. *See* 35 U.S.C. s. 282 ("A patent shall be presumed valid."); *see also* Jamesbury Corp. v. Litton Indus. Prods. Inc., 756 F.2d 1556, 1559 (Fed.Cir.1985), *cert. den'd,* 488 U.S. 828, 109 S.Ct. 80, 102 L.Ed.2d 57 (1988). Such presumption, however, is in no way dispositive. "The courts are the final arbiter of patent validity and, although courts may take cognizance of, and benefit from, the proceedings before the patent examiner, the question is ultimately for the courts to decide, without deference to the rulings of the patent examiner." Quad Envtl. Techs. Corp. v. Union Sanitary Dist., 946 F.2d 870, 876 (Fed.Cir.1991).

[3] Further, the burden of proving that the '236 patent is not enabled rests squarely with Dekalb. *See* Lear Siegler Inc. v. Aeroquip Corp., 733 F.2d 881, 885 (Fed.Cir.1984). For Dekalb to overcome the presumption of validity attached to the '236 patent, it bears the burden of presenting clear and convincing evidence that the cell claims were not enabled as of March 11, 1987, the effective filing date of the '236 patent.FN10 Id., *see also* Enzo Biochem Inc. v. Calgene Inc., 188 F.3d 1362, 1367 (Fed.Cir.1999)("Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application is first filed."). With this background in mind, the Court turns to a discussion of the requirements for enablement under 35 U.S.C. s. 112.

FN10. The plaintiffs initially argued that either one of three dates should be used, but later conceded during trial that March 11, 1987 was the controlling date. "The relevant time for determining enablement is the plaintiffs' effective filing date, namely March 11, 1987 ...." Plaintiffs' Post-Trial Reply Brief at 18. The defendant now contends in its briefs that the effective filing date was March 11, 1986, but agrees that the "patent is invalid regardless of which date ... is the effective filing date." *See* Defendant's Initial Post-Trial Brief at p. 15, n. 2. For the purposes of its analysis, the Court will use March 11, 1987 as the effective filing date. Using this date, the conclusion that certain claims are invalid due to lack of enablement would also apply with equal force had the 1986 date been used.

The statutory basis for the enablement requirement is found in 35 U.S.C. s. 112, which reads in its relevant part:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same ....

[4] To pass muster under s. 112, a patent must describe the claimed invention in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the claimed invention. *See* Hybritech Inc. v. Monoclonal Antibodies Inc., 802 F.2d 1367, 1384 (Fed.Cir.1986), *cert. den'd,* 480 U.S. 947, 107 S.Ct. 1606, 94 L.Ed.2d 792 (1987). "[T]here must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed." In re Vaeck, 947 F.2d 488, 496 (Fed.Cir.1991).

[5] [6] [7] While the specification need not disclose what is well known in the art, "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out a mere germ of an idea does not constitute enabling disclosure." Genentech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1365-66 (Fed.Cir.1997). Rather, "[t]o be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " Genentech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1365 (Fed.Cir.1997), *quoting* In re Wright, 999 F.2d 1557, 1561 (Fed.Cir.1993). "Enablement is not precluded by the necessity for some experimentation .... However, experimentation needed to practice the invention must not be undue experimentation. The key word is undue, not experimentation." In re Wands, 858 F.2d 731, 737 (Fed.Cir.1988) (footnotes, citations and internal quotes omitted). "[W]hen there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art." Genentech

Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366 (Fed.Cir.1997).

[8] [9] The oft-cited *Wands* decision sets forth a number of factors that a court should consider in determining whether a disclosure is sufficient or requires undue experimentation to practice the claimed invention. *See* In re Wands, 858 F.2d 731, 737 (Fed.Cir.1988). These include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id*. The *Wands* factors are "illustrative, not mandatory" and all eight factors need not be reviewed in determining whether a disclosure is enabling. Amgen Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1213 (Fed.Cir.1991). "What is relevant depends on the facts." *Id*.

In this case, a logical starting point is to determine what the '236 patent does and does not claim. In general terms, the inventions claimed by the '236 patent are plants and plant cells that have stably integrated the *bar* gene into their genetic structure. The specific scientific methodology used to insert the bar gene is not part of the claimed invention.

[10] [11] If the gene insertion methodology was well known to those skilled in the art, there may be no need to include it in the specification. "[T]he omission of minor details [from the specification] does not cause a specification to fail to meet the enablement requirement." Genentech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1365 (Fed.Cir.1997). If, however, the failure to include the methodology needed to practice the invention requires persons attempting to practice the '236 patent to engage in undue experimentation, the enablement requirement is not met. Id. Further, it is axiomatic that if no methodology existed by which the invention could be practiced, the claims are not enabled. If, as the Parties agree, the cell claims cover all plant cells, including both monocots and dicots, then to satisfy the enablement requirement methodology must have existed as of March 11, 1987 by which the bar gene could be inserted into both types of plant cells. In this case, one of the central questions addressed at trial was whether any methodology existed as of this date by which the *bar* gene could be stably integrated into monocots. PGS argues that, as of this date, the known methods for transforming plant cells include *Agrobacterium*-mediated transformation, electroporation, and microprojectile bombardment using what is commonly known as the "gene gun." See Plaintiffs' Reply Brief at 20. Each of these techniques will be discussed individually.

2. *Agrobacterium*-mediated Transformation

A significant amount of evidence concerning the scope and limitations of the *Agrobacterium*-mediated transformation of plant cells was presented at trial. The attention given to this process by the Parties is understandable, as it is relevant to the enablement of the cell claims and also is a specific limitation of the plant and seed claims. With respect to the cell claims, the plaintiffs contend that foreign DNA could be stably integrated into monocots such as corn by *Agrobacterium* at least by the time the patent was filed in March of 1987. The defendant responded, *inter alia,* by presenting testimony that the plaintiffs' first *Agrobacterium*-mediated transformation of corn did not occur until 1990, over three years after the '236 patent was filed.

(a) General Background for the *Agrobacterium*-mediated Transformation of Plant Cells

Agrobacterium tumefaciens is a gram-negative soil bacterium that causes crown gall disease in a variety of plants, especially members of the rose family, such as apple, pear, cherry, almond, raspberry and roses. A separate strain can cause the formation of crown galls on grapevines. A crown gall is a large tumor-like

swelling (a gall) that typically occurs at just above the soil level. Although it can look formidable, the growth of a gall is not inevitably fatal to the plant.

Biologically, *Agrobacterium tumefaceiens* acts as a parasite. It possesses the biological weaponry to insert a portion of its own DNA, called either the transfer DNA or T-DNA,FN11 into the plant's genome.FN12 After accepting the bacterium's T-DNA into its own genetic structure, the plant is forever biologically enslaved to produce a class of compounds called opines, which serve as a source of organte nutriments for the invading colony of *Agrobacterium*.

FN11. The plasmid that contains the T-DNA in *Agrobacterium* is often called the Ti plasmid (for tumor inducing plasmid).

FN12. This technique is also used by many viruses.

Owing to *Agrobacterium's* natural abilities, scientists developed methods to use if as a vehicle for inserting other portions of foreign DNA into unsuspecting plant hosts. By creating techniques to replace *Agrobacterium's* natural T-DNA with other sequences, scientists can use *Agrobacterium* to insert foreign genes into plants. In this case, the plaintiffs claim that they could have used this method to insert the *bar* gene into various types of plants. While it is undisputed that they succeeded in using *Agrobacterium* to insert the *bar* gene into certain dicots, it is disputed whether the same procedures worked with monocots.

(b) Impact of *In re Goodman*

The appropriate starting point for the Court's analysis is provided by the Federal Circuit's decision in In re Goodman, 11 F.3d 1046 (Fed.Cir.1993). In that case, the applicant claimed a method for manufacturing mammalian peptides in plant cells. *Id*. at 1049. In his patent, which had an effective filing date of July 29, 1985, he described the claimed invention in general terms, but provided only a single working example: the infection and transformation of a tobacco plant with *Agrobacterium*. *Id*. The patent examiner rejected a set of claims that purported to cover the production of mammalian proteins in any modified plant cell because such claims were not enabled. *Id*. On appeal, the Board of Patent Examiners upheld this decision, finding that the "specification taught only the *Agrobacterium*-mediated transformation method of plant transformation. This method works only with dicotyledonous plant cells, not all 'plant cells.' " *Id*. The Federal Circuit, in reviewing the Board's decision, conducted a review of the methods for gene transformation in monocol plants, including *Agrobacterium,* direct DNA transfer to protoplasts, microinjection, and viral-mediated gene transfer. It concluded that

[O]n [the applicant's] 1985 filing date, the record shows no reliable gene transformationmethod for use with monocot plants. Each of the methods for monocot plants was fraught with unreliability. The teachings in the specification do not cure this unpredictability. The record shows that practicing a gene transformation method for all monocot plants, if possible at all in 1985, would have required extensive experimentation that would preclude patentability .... Goodman's specification does not enable one skilled in biotechnology in 1985 to practice the method for all 'plant cells' as [the claims] require.FN13 *Id*. at 1052.

FN13. The Court notes that the Federal Circuit considered several publications which were mentioned during the course of trial in this case. Specifically, in reaching its conclusion that disclosure of the

Agrobacterium-mediated transformation of a dicot was not enabling for a claim that also included monocots, the circuit court discussed (1) J.P. Hernalsteens et al., *An Agrobacterium Transformed Cell Culture from the Monocot Asparagus officinalis,* J. EMBO, 3039-41 (1984); (2) Hooykaas-Van Slogteren et al., *Expression of Ti Plasmid Genes in Monocotyledonous Plants Infected with Agrobacterium tumefaciens,* 311 Nature 763 (1984); (3) Potrykus et al., *Direct Gene Transfer to Cells of a Graminaceous Monocot,* 199 Mol. Gen. Genet. 183 (1985) and (4) Goodman et al., *Gene Transfer in Crop Improvement,* 236 Science 48 (1987).

Thus, the *Goodman* decision creates a clear point of embarkation for this Court's analysis. Similar to the applicant in *Goodman,* the plaintiffs in this case assert broad claims for the transformation of all 'plant cells,' while disclosing only the *Agrobacterium*-mediated transformation of certain dicots. Pursuant to the holding in *Goodman,* as of July 29, 1985, such a disclosure was not enabling for a claim that purported to cover all plant cells, including both monocots and dicots. *Id*. The question remains, however, whether advances in the relevant art between July 29, 1985 and March 11, 1987 would alter the conclusion reached by the *Goodman* court. *See id*. at 1052.

(c) Specific Teachings of the '236 Patent

The specification of the '236 patent teaches two methods to transform dicots such as tobacco, potato and tomato: namely the leaf disc and tuber disc methods. Both of these methods employ *Agrobacterium* to deliver the new genetic material to the plant. As a threshold issue, the plaintiffs' witnesses conceded at trial that neither of these methods could be used to transform a monocot such as corn at the time the patent was filed. For example, Dr. Leemans, a scientist at PGS, testified as follows:

Q: ... [U]sing the methods disclosed in the '236 patent, and exercising ordinary skill, could anyone have made transgenic corn, transgenic rice or transgenic wheat as of March 11, 1987?

A: With the method described in the examples of the '236 patent, no.

See Transcript of trial testimony at 441:24-442.4.FN14

FN14. Similar testimony was also given by Dr. Botterman, another of the plaintiffs' experts. *See* Transcript of Trial Testimony at 964:11-965:2.

Thus, the plaintiffs' own scientist concedes that the specification of the '236 patent does not include any working examples that would allow a person skilled in the art to insert the *bar* gene into any of the listed monocots. This admission is not fatal, however, if the defendant fails to prove that insertion of foreign DNA into plant cells other than dicots would require undue experimentation by practitioners skilled in the art in 1987. To this end, extensive testimony was presented at trial concerning the state of art for the transformation of plant cells in early 1987. The Court next turns to the most extensively litigated issue in this case: the post- *Goodman* ability to transform monocots with *Agrobacterium*.

(d) Post-1985 Developments in *Agrobacterium*-mediated Transformation

As discussed above, the Federal Circuit concluded that practicing a gene transformation method for all monocot plants, if possible at all in 1985, "would have required extensive experimentation that would

preclude patentability." In re Goodman, 11 F.3d at 1052 (Fed.Cir.1993). Subsequent to this decision, in August 1986, Stephen Goldman and Anne Graves published an article describing a method by which corn seedlings can be infected with *Agrobacterium*. After infection, the seedlings are allowed to grow and are then observed in most of the cases to produce opines, the natural proteins encoded by the wild-type *Agrobacterium*. *See* A. Graves & S. Goldman, *The Transformation of Zea mays Seedlings with Agrobacterium tumefaciens,* 7 Plant Molecular Biology 43-50 (1986). The plaintiffs claim that this paper is evidence that a person of ordinary skill in the art could transform monocots in early 1987. For the reasons that follow, the Court disagrees.

Persuasive evidence of the significance of this work comes from the article itself. In the article, the authors reported that they detected opines in the corn plants after exposing corn seedlings to *Agrobacterium*. As discussed previously, opine production in plants is one characteristic of infection by wild-type *Agrobacterium,* because the bacteria conscript the plants to produce opines. In the article, however, the authors expressly state that the detection of opines was not unambiguous proof that they had transformed the corn plants. "While the presence of T-DNA directed enzyme activities can be unambiguously detected in these corn plants, the actual presence of any Ti sequences within the putative hosts remains to be demonstrated." *Id*. at 49. This viewpoint was reaffirmed at the deposition of Anne Graves during a discussion of her work

Q: So you never ruled out the possibility of transient expression, correct FN15

FN15. This question is not worded in the clearest manner. Because the questioner asks the deponent to agree with his question, the affirmative answer given by Graves indicates that it is correct that she never ruled out the possibility of transient expression, a conclusion that is supported by her answer to the later question. In other words, Graves is responding to the question "Is it correct that you never ruled out the possibility of transient expression?"

Graves: Yes.
[question omitted]

Q: ... Did anyone to your knowledge ever rule out the possibility of transient expression as what you where seeing in corn using your Plant Molecular Biology technique? [...]

Graves: Not that I'm aware of,

Graves Depo. Tr., Nov. 12 1998 at 188: 17-18.

Thus, the authors themselves recognized that testing the corn plants for the presence of opines was not conclusive evidence that they had stably incorporated a heterologous DNA sequence into the plant's genome.

Additionally, other researchers in the field came to have reservations about the Goldman and Graves work. In 1985, working with the authors, a group of scientists at Eli Lilly & Company (hereinafter 'Lilly') attempted to repeat and expand upon the published work. In an attempt to supplement the reported evidence, the Lilly team looked for confirmation that *Agrobacterium's* natural T-DNA had been incorporated into the corn's genome. One method by which this could be confirmed is through either a Southern or Northern blot

analysis. These techniques, commonly used for years in biotechnology research, allow scientists to visualize the genetic constituents of the plant to look for the presence of specific DNA or RNA constructs. Additionally, the Lilly group wanted to reconfirm the published reports concerning the authors' detection of opines. At trial, the evidence clearly and convincingly indicated that the Lilly group could neither confirm the authors' original observations concerning opines produced by infected plants nor detect presence of any foreign DNA in either a Southern blot or a Northern blot experiment. When blind control opine samples were submitted to Anne Graves herself, the Lilly group found that her results "included *every kind* of wrong answer." FN16 (emphasis in original). Further, the Northern and Southern blot tests provided "no positive evidence for the presence of DNA or RNA encoding the opine synthase phenotypic marker ...." After further testing, on June 30, 1987, the Lilly team concluded, *inter alia,* that "our failure to corroborate the results of the opine synthase assays with other assays tends to discredit the opine synthase work." Thus, the Lilly team, working with Goldman and Graves, were unable to confirm the findings of the 1986 paper.FN17

FN16. Opines are a category of organic compounds that include two substances named octopine and nopaline. Tests to confirm the presence of opines specifically look for octopine and nopaline and detection methods allow researchers to distinguish between the two. According to the Lilly scientists, Graves detected octopine in the nopaline plants, nopaline in the octopine plants, and both octopine and nopaline in the control plants.

FN17. As additional evidence in support of this conclusion, the defendant argued that opines can be detected in non-transformed plants. As evidence for this conclusion, it cited the work of Paul Christou et al., *Opine Synthesis in Wild-Type Plant Tissue,* 82 Plant Physiology 218-221 (1986). In this paper, Christou reports that non-transformed plant tissue or callus grown in an arginine enriched media for 3-5 days exhibited detectible levels of opines. This result does not necessarily lead to the conclusion proposed by the defendant. The Christou paper is devoid of any evidence that plant tissue not exposed to artificially high levels of arginine would produce detectable levels of opines. Further, there was no evidence that Goldman and Graves exposed their plants to such artificially high levels of arginine.

While the limitations of Goldman and Graves' work were apparently recognized by both the authors and other scientists in the field, there was also substantial evidence presented at trial that the plaintiffs themselves recognized the limitations of both the published technique and the feasibility of transforming monocots with *Agrobacterium* in general. First, when asked about the meaning of Goldman and Graves' paper, Anne-Marie Bouckaert, the witness designated by the plaintiffs under Fed. R. Civ. Pro. 30(b)(6), responded in the following manner

Q: Well, am I correct Goldman and Graves purport to describe the successful transformation of Zea mays seedlings with Agrobacterium?

A: No you're not correct. They report that upon infection of Zea mays seedlings with Agrobacterium, that they could detect opine synthesis, which is the first indication that there is an interaction between Agrobacterium and the plants so--

Q: So you did not take this work as evidencing successful transformation of Zea mays with Agrobacterium?

A: No.

Additionally, the defendant presented credible evidence that even after the publication of the Goldman and Graves paper, PGS itself could not transform corn with *Agrobacterium* until many years after the effective filing date of the '236 patent. In September 1987, PGS held a Product Policy Steering Meeting and concluded that corn represented a strategic opportunity for the company to create a commercially successful product. Shortly thereafter, Leemans received a memo indicating that the PGS Board of Directors had approved a budget overrun to accelerate the corn transformation program. The memo specifically indicated "Don't spare the horses," a phrase that Leemans' testimony indicated meant that the transformation of corn was an important scientific priority at PGS.

In response to these priorities, Leemans placed Dr. Kathleen D'Halluin in charge of PGS's corn transformation efforts. She began to experiment with both *Agrobacterium* and electroporation FN18 methods, but was unsuccessful. Although she was aware of the Goldman and Graves method, she did not attempt to employ this methodology.

FN18. For a discussion of electroporation, *see* infra, Section 11(B)(3).

Throughout 1988, PGS's efforts failed to produce any evidence that *Agrobacterium* could be used to stably integrate foreign DNA into corn cells, or any other monocotylenous plant cells for that matter. In 1988, D'Halluin wrote that she had conducted experiments "to understand why cereal transformation by *Agrobacterium* has been so less successful." PGS continued its efforts.

The next year, on June 26, 1989, D'Halluin wrote a memo stating:

Our attempts to use *Agobacterium*-mediated transformation have been unsuccessful until now ....The main problems in corn transformation seems to be the stable integration of the foreign DNA in the plant DNA. It is possible to get DNA in corn cells and to get TRANSIENT expression, but stable transformation seems to be very difficult. (Emphasis in original).

In the summer of 1990, the efforts of D'Halluin and her research group finally bore fruit. They were able to use an electroporation-based method to create a fully transformed corn plant. In 1993, they transformed corn by employing a particle gun. However, they still had not yet been able to employ any *Agrobacterium*-based method for transforming corn.

In early 1996, D'Halluin wrote that "[a]t the beginning of 1995, the T-DNA transformation of corn was still a complete black box." Defendant's Exhibit 83. The team continued to work on the problem. Later in 1995, PGS reported its first successful transformation of corn with *Agrobacterium*.FN19

FN19. In their briefs, the plaintiffs contend that, until late 1994, they devoted minimal resources to developing a workable *Agobacterium*-based method for the transformation of corn. They argue that, in late 1994, D'Halluin received a new technician to work on the problem and was permitted to spend 80% of her own time on the problem. *See* Plaintiffs' Proposed Finding of Fact at para. 503. Even with these resources, it took D'Halluin over seven months to report the first transformed corn plant to PGS management. Id. at para. 505. Further, PGS admits that the "Japan Tobacco publications from 1994 ... suggested to D'Halluin to add an extra virulence gene ... [to] increase the efficiency of her transformation." Id. at para. 506.

Thus, in 1995, many years after the filing date of the '236 patent, it required a full time research scientist and a Ph.D. scientist devoting the majority of their time to the project over seven months to produce transformed corn plants. Also, technology that post-dated the '236 patent apparently 'suggested' to them how to modify their approach. Evidence for the non-enablement of the cell claims of '236 patent comes from the plaintiffs' own statements.

The plaintiffs argued at trial that all of the elements required for the successful use of *Agrobacterium* existed in the art in 1987. Even assuming *arguendo* that this is correct, the testimony at trial plainly revealed that no one-including PGS-was able to put those elements together to create a successful transformation method until many years after the effective filing date of the '236 patent. Scientific research involves attempting to understand why and how things-in this case biological processes-work. In science, the existence of constituent elements does not necessarily equate with the understanding of how to apply those elements to create a useful methodology. This case is an example of that principle. Starting in late 1987, with a stated corporate desire to transform corn, D'Halluin invested at least a portion of both her and her group's time experimenting with *Agrobacterium*. In 1989, she wrote that "[o]ur attempts to use *Agrobacterium*-mediated transformation have been unsuccessful until now." D'Halluin's resume, her testimony and her demeanor on the stand convinced this Court that she is a well-qualified scientist. The defendant does not suggest otherwise. Yet, even in light of PGS's high priority to develop a method for transforming corn, it took her and her research group a significant period of time to develop a methodology which would allow for the *Agrobacterium*-mediated transformation of corn. It is clear that the process of constructing a workable *Agrobacterium* methodology was a complicated, labor-intensive process that far exceeded the sum of its constituent parts. To successfully practice this technique on monocots in 1987 would have required undue experimentation.

Articles published by others in respected journals well after the effective filing date for the '236 patent also reflect this viewpoint. In the summer of 1990-over three years after the effective filing date of the '236 patent-the successful transformation of corn by microprojectile technology was reported in the journal Science. Summarizing the development of technology to that date, the article stated:

First, researchers had to find a way to get novel genes into plant cells, and then, using cell culture techniques, they had to coax the transformed cells into regenerating into whole, fertile plants. In 1983, they appeared to be well on their way when [certain research groups] ... showed that a modified plasmid from the pathogen *Agrobacterium tumefaciens* could act as a vector, transferring foreign DNA into plants. However, they still faced a monocot barrier: the *Agrobacterium* vector that easily transferred DNA into dicotyledonous plants, such as tobacco and petunia, failed to work with the monocots, which include all of the valuable cereals. A. Moffat, *Corn Transformed,* 249 Science 630 (1990).

At trial, the defendant presented clear and convincing evidence that the so-called 'monocot barrier' was still firmly in place in March of 1987. At that time, *Agrobacterium*-mediated transformation of monocots-if possible at all-would have required extensive experimentation that would preclude patentability.FN20 As such, no *Agrobacterium*-based methods existed that would allow a person skilled in the art to use this technique to practice the entire scope of Claim 1 of the '236 patent without undue experimentation. The Court next turns to another technique cited by the plaintiffs: electroporation.

FN20. The plaintiffs also argue in their post trial brief that a paper published in 1987 by Nigel Grimsley confirms the work of Goldman and Graves. *See* Plaintiffs' Exhibit 335. The Court disagrees. The Grimsley publication describes a method for agroinfection, not transformation. Agroinfection involves the placement of foreign DNA anywhere in a host cell, without the need for stable integration into the host cell's genome.

As Claim 1 of the '236 patent is specifically limited to plant cell having a heterologous DNA stably integrated into its genome, the mere fact that maize cells can be can be infected by *Agrobacterium* does little toward enabling a claim that requires stable integration.

3. Electroporation

Next, the plaintiffs argue that in 1987 a person skilled in the art could use a technique called 'electroporation' as a means of achieving the stable integration of heterologous DNA in plant cells. Electroporation is a technique in which researchers essentially use electrical pulses to force foreign DNA into the cells. In early 1986, Fromm and do authors published a paper that disclosed a method that used electroporation to transform Black Mexican Sweet thereinafter (BMS') corn protoplasts FN21 with a foreign selectable marker gene. The BMS protoplasts would then regenerate their cell wall and successively divide to form a cell culture. These BMS cultures were never able to form plants. The plaintiffs claim that this methodology indicates that one skilled in the art could transform plant cells other than dicots in March, 1987 and that "[t]o this day, Dekalb has ignored the devastating impact of the Fromm work ...." Plaintiffs' Reply Brief at p. 21.

FN21. Plant cells have a cell wall, unlike mammalian cells that are surrounded by a cell membrane. A protoplast is a plant cell that is devoid of its normal cell wall. *See* Bruce Alperts et al., *Molecular Biology of the Cell* 1143 (2d ed.1989).

The author's interpretation of his own work indicates that the plaintiffs' argument is misplaced. Fromm testified at the trial and indicated that the electroporation technique described in his paper worked only on BMS protoplasts and could not be extended to either other varieties of corn or other dicots in general. For example, he stated that he was unable to use this method to transform a non-BMS corn cell because protoplasts from ordinary corn cells would not reform the cell walls, and thus were not amenable to his technique.

Q: Now at this same time, if you wanted to take a corn cell, a corn cell from a regular corn plant, make protoplasts out of it, what about, I mean, and make protoplasts, what about getting that kind of a protoplast back to a ordinary corn cell?

A: We were not able to do that.

Q: So when you tried to take non-BMS protoplast[s] and do the experiment with non-BMS protoplasts and get them into corn cells so you can regenerate a plant, you couldn't do that"

A: We could not do that

[. . . . .]

Q: When you tried to move this work with electroporation to ordinary corn cells and transform them, you didn't have the same success, I mean, ordinary corn protoplasts and transform them?

A: In our hands, we took corn cells that were capable of reforming plants. We could establish what we

called regenerable cultures, which is a corn cell culture that makes plants again, and we could make protoplasts from that. The problem is our protoplasts would die and would never, in our hands, never divide and form plants again. So we had a couple pieces, but no one system that went all the way from protoplasts back to plants.

Fromm testified that his electroporation method was successful with BMS cells, but not others. He could take the BMS cells, make protoplasts, and introduce foreign DNA. These protoplasts would regenerate their cell walls and divide to form a cell culture. However, when he experimented with corn cells other than BMS, he obtained different results. Protoplasts derived from non-BMS cell lines were not able to reform their cell walls and would die. Fromm's method required protoplasts capable of regenerating their cell walls after electroporation. Thus, he could not apply his technique to any cell line other than BMS. The testimony at trial established that Fromm's electroporation method was not a general technique applicable to even other types of corn cells, much less any other monocots.

Thus, the evidence clearly indicated that Fromm's method was limited to the introduction of foreign DNA into BMS corn cells. Simply put, the electroporation technique published by Fromm in 1986 did not allow anyone-including even the author himself-to transform any monocot other than one special cell line of corn cells. Fromm himself testified that he was unable to apply his own work to non BMS corn cells.FN22 As such the electroporation method disclosed by Fromm in his 1986 paper does not provide a general method by which a person skilled in the art could transform a variety of plant cells and in no way serves to enable the full scope of the cell claims in the '236 patent.FN23

FN22. The defendant makes much of the fact that Fromm could never regenerate transformed plants by his method. Such criticism is misplaced in a discussion of whether Fromm's technique enabled the cell claims of the '236 patent, which only require that a plant cell have heterologous DNA (i.e. the *bar* gene) stably integrated into its genome. In today's decision, the Court concludes that the defendant proved by clear and convincing evidence that the electroporation method published by Fromm in 1986 was not a generalized method for use with monocotylenous plant cells. The fact that Fromm could only transform BMS corn and not other varieties (i.e. because the protoplasts required by his method from other corn cell lines would die) is the dispositive fact, not that plants could not be generated.

FN23. As noted in the previous section, the method D'Halluin employed in the summer of 1990 used electroporation. This technique was different than the one Fromm published in 1986, in that it used immature plant embryos and a Type I callus. D'Halluin and coworkers published their new method in 1992. *See,* D'Halluin et al., *Transgenic Maize by Tissue Electroporation* 4 The Plant Cell 1495-1505 (1992).

4. Microprojectile Bombardment

Finally, the plaintiffs argue that the cell claims of the '236 patent are enabled because a technique called microprojectile bombardment was available for the transformation of monocots in 1987. The defendant proved otherwise at trial.

In 1990-over three years after the effective filing date of the '236 patent-a team of Dekalb researchers reported the first transformation of corn via microprojectile bombardment, commonly called the 'gene gun' in biotechnology circles. A gene gun propels genes directly into whole plant cells by shooting them through

the cell wall. It uses metallic microprojectiles coated with DNA that encode for an enzyme that endows the target cell with herbicide resistance. On August 10, 1990, an article appeared in Science announcing the team's success and characterizing their work as "the capstone of almost a decade's efforts to genetically engineer this country's most important crop." FN24 *See* A. Moffat.*Corn Transformed,* 249 Science 630 (1990). In the summer of 1990, microprojectile technology "appear[ed] to be the only satisfactory technique for transforming whole cells of monocots and these transformed cells are amenable to cell culture." *Id.*

FN24. The first publication of the work was in July, 1990. *See* W. Gordon-Kamm et al., *Transformation of Maize Cells and Regeneration of Fertile Transgenic Plants,* 2 The Plant Cell 603 (1990).

In light of the substantial evidence presented by the defendant at trial, the Court concludes that, as of March 11, 1987, a person skilled in the art who attempted to transform monocots with microprojectile technology would have to engage in undue experimentation. As such, this method does not provide a basis upon which the full scope of the cell claims of the '236 patent could be practiced.

5. Application of the *Wands* Factors

[12] With this discussion of the evidence presented at trial as a backdrop, the Court now turns to an analysis of the factors outlined in *Wands*. First, as of March, 1987, it is readily apparent that to practice the inventions covered by the cell claims of the '236 patent, a person skilled in the art would have to engage in an undue amount of experimentation. In the late 1980's, hoping to be the first to realize the potentially huge commercial rewards of producing a transformed corn product, the management at PGS directed their scientists not to "spare the horses" when it came to developing a transformed corn product. Even under these circumstances, the plaintiffs' scientists testified that they could not transform corn until years after the effective filing date of the '236 patent. This fact indicates that a significant amount of work was required to realize the broad reach of the cell claims. It would not be until 1995-even years after filing the '236 patent-that D'Hulluin would develop a workable methodology using *Agrobacterium*.FN25 The plain import of such evidence is that a significant amount of experimentation was necessary to be able to stably insert a heterologous DNA fragment into a monocotylenous plant cell in early 1987.

FN25. Further, even viewing the plaintiffs' claims in the best light possible, PGS admits that it took at least seven months to obtain a workable *Agrobacterium*-based method when they started such work in about 1995.

Second, the patent itself provided little guidance to others who want to practice the full scope of its inventions. The only methods disclosed were based on *Agrobacterium,* which as stated above is a technique that the plaintiffs were not able to reduce to practice with monocots until many years after the patent was filed. The specification lacked working examples for the transformation of any types of plants other than dicots. This lack of a monocot-based example is telling because the evidence at trial plainly revealed that plant transformation in the late 1980's was a highly unpredictable art. Indeed, the plaintiffs' own scientists admitted at trial that, as of the filing date of the '236 patent, no one had the ability to transform either rice or wheat, other examples of commercially important monocots.

[13] "It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. However, there must be a significant disclosure, either through

illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed." In re Vaeck, 947 F.2d 488, 496 & n. 23 (Fed.Cir.1991). In this case, the teachings of the '236 patent, even when read in the broad context of general ability of scientists to carry out plant cell transformationin 1987, are only an invitation to practice the transformation of non dicotyledonous plant cells. See Enzo Biochem Inc. v. Calgene Inc., 188 F.3d 1362, 1370 (Fed.Cir.1999), *citing* Fiers v. Revel, 984 F.2d 1164, 1171 (Fed.Cir.1993). What is "glaringly missing" from the specification is the disclosure of how the idea of stably integrating heterologous DNA into the genome of any plant cell might be implemented in cellular hosts other than dicots. *Id*. at 1375 (concluding that a specification disclosing only how to practice an invention in *E. coli* was not enabling for a claim that covered all cells).

C. Conclusion: Enablement of the Cell Claims

[14] After considering the extensive testimony presented on this issue during the course of the trial, as well as the Parties' post-trial briefs, the Court concludes the defendant has shown by clear and convincing evidence that the cell claims of the '236 patent were not enabled. "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out a mere germ of an idea does not constitute enabling disclosure." Genentech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1365-66 (Fed.Cir.1997). In March of 1987, a person skilled in the art who attempted to stably integrate the *bar* gene into plants cell other than dicots would have had to engage in undue experimentation-assuming that they could have successfully completed the task at all. Further, this deficiency is not cured by the specification. Therefore, patentability is precluded and the cell claims are invalid due to lack of enablement.FN26

FN26. Because the Court concludes that the cell claims were not enabled, it need not reach the defendant's additional argument that claims are invalid because they lack an adequate written description.

The Court now turns to the plant and seed claims

III. Plant and Seed Claims [Claims 8-9, 12-15]

A. Legal Standards for Claim Construction

[15] [16] [17] "The construction of a patent, including the terms of art within its claim, is exclusively within the province of the court." Markman v. Westview Instruments, Inc., 517 U.S. 370, 116 S.Ct. 1384, 1386, 134 L.Ed.2d 577 (1996). In determining the meaning of a claim, the court first examines the intrinsic evidence of the record, including the claims, specification, and the prosecution history. *See* Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed.Cir.1996). Intrinsic evidence is "the most significant source of the legally operative meaning of the disputed claim language." *Id*. at 1582. "Even within the intrinsic evidence, however, there is a hierarchy of analytical tools." Digital Biometrics, Inc. v. Identix, Inc., 149 F.3d 1335, 1344 (Fed.Cir.1998). First, "the actual words of the claim are the controlling focus." *Id.; see also* Thermalloy, Inc. v. Aavid Engineering, Inc., 121 F.3d 691, 693 (Fed.Cir.1997). Second, the specification (also called the written description) should be considered, in particular to determine if the patentee acted as his own lexicographer. *See* York Prods. Inc. v. Central Tractor Farm and Family Ctr., 99 F.3d 1568, 1572 (Fed.Cir.1996). Finally, the prosecution history is relevant "because it may contain contemporaneous exchanges between the patent applicant and the PTO about what the claims mean." Digital Biometrics, Inc., 149 F.3d 1335, 1344 (Fed.Cir.1998).

[18] [19] If the intrinsic evidence does not sufficiently resolve ambiguities, then the court may consider extrinsic evidence, including expert and inventor testimony, in order to arrive at a "proper understanding of the claims." Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed.Cir.1996). "It is entirely appropriate, perhaps even preferable, for a court to consult trustworthy extrinsic evidence to ensure that the claim construction ... is not inconsistent with clearly expressed, plainly, apposite and widely held understandings in the pertinent technical field." Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1308 (Fed.Cir.1999) "Although the patent file may often be sufficient to permit the judge to interpret the technical aspects of the patent properly, consultation of extrinsic evidence is particularly appropriate to ensure that his or her understanding of the technical aspects of the patent is not entirely at variance with the understanding of one skilled in the art." *Id.;see also* Mantech Envtl. Corp. v. Hudson Envtl. Servs., Inc., 152 F.3d 1368, 1373 (Fed.Cir.1998).

[20] [21] In ascertaining the meaning of a claim, the court should construe claims in a manner designed to preserve their validity. Digital Biometrics, Inc. v. Identix, Inc., 149 F.3d 1335, 1344 (Fed.Cir.1998). As discussed *supra,* 35 U.S.C. s. 112 requires patentees to provide a written description of the invention, "in such full, clear, concise and exact terms as to enable any person skilled in the art ... to make and use the [invention]." "Because the applicant has the burden to particularly point out and distinctly claim the subject matter which the applicant regards as his invention, if the claim is susceptible to a broader and a narrower meaning, and the narrower one is clearly supported by the intrinsic evidence while the broader one raises questions of enablement under s. 112 para. 1, [the court] will adopt the narrower of the two." Digital Biometrics, Inc. v. Identix, Inc., 149 F.3d 1335, 1344 (Fed.Cir.1998)(internal quotations omitted); *see also* Athletic Alternatives, Inc. v. Prince Mfg., Inc., 73 F.3d 1573, 1581 (Fed.Cir.1996); Ethicon Endo-Surgery, Inc. v. United States Surgical Corp., 93 F.3d 1572, 1581 (Fed.Cir.1996).

B. Intrinsic Evidence

1. Language of the Claims

The plant and seed claims of the '236 patent consist of Claims 8-9 and 12-15 (Claim 8) which is representative of claims 12-15, reads: FN27

FN27. Claim 9 claims "a seed of the plant of Claim 8."

A plant which consists of the cells of claim 1 and which is susceptible to infection and transformation by Agrobacterium and capable of generation thereafter.
The wording of this claim is straightforward and precise. Simply put, Claim 8 purports to cover a plant which consists of the cells of Claim 1, subject to three further limitations. Specifically, the covered plants must be (1) susceptible to infection by *Agrobacterium;* and (2) susceptible to transformation by *Agrobacterium* and, after both of these events have occurred, (3) capable of regeneration. Given the agreement that the cells of Claim 1 include all plant cells-including both monocots and dicots-the plain language of Claim 8 means that the patentee is entitled to coverage of any plant that can be infected and transformed by *Agrobacterium* and is still capable of regeneration after these events have occurred. This construction, however, sheds little light on the true scope of these claims. It simply posits the followingquestion: As of March 11, 1987,FN28 which types of plants were susceptible to the specified biological manipulations by *Agrobacterium* and subsequently were still capable of regeneration? In an attempt to resolve this issue, the Court turns next to the written description.

FN28. The plaintiffs filed the PCT application designating the United States on this date. At trial, PGS conceded in open court that it is the effective filing date for the '236 patent.

2. Written Description

[22] Unfortunately, the written description does little to resolve the meaning of the contested claims. The specification provides four examples: tobacco, tomato, potato and sugarbeet-all of which are dicots. While the defendant vigorously argued both at trial and in its briefs that the lack of monocot examples in the specification compels the conclusion that "the plant and seed claims must be construed to [cover only] dicot plants and seeds," such suggestion is misplaced. While the inclusion of a working monocot example may have had considerable impact in allowing the Court to conclude that the plant and seed claims covered monocots, the lack of such example does not necessarily mean that the contested claims are limited only to dicots. It is well settled that a specification need not recite "every conceivable and possible future embodiment of [the] invention." SRI Int'l v. Matsushita Elec. Corp. of America, 775 F.2d 1107, 1121 (Fed.Cir.1985). Reading limitations into the claims from the specification is improper. *See, e.g.,* Transmatic Inc. v. Gulton Indus., Inc., 53 F.3d 1270, 1277-78 (Fed.Cir.1995). While the Court does note that a significant portion of the plant kingdom, namely monocots, are not represented in the enumerated examples contained in the specification of the '236 patent, such omission is not necessarily determinative. The Court next turns to the prosecution history.

3. Prosecution History

The prosecution history reveals that numerous exchanges occurred between the patentees and the examiner on the subject of whether the plant and seed claims covered both monocots and dicots.

On April 27, 1989, the examiner rejected an initial set of consolidated claims directed at plant cells, plants and seeds because such claims were not enabled pursuant to 35 U.S.C. s. 112 The examiner indicated that

[T]he disclosure is enabling only for claims limited to specific source cells or tissue of dicotyledonous plants in which transformation and regeneration has been shown .... In point of fact, there is a large body of evidence that regeneration can only be accomplished from cells or tissue derived from specific sources, such as immature embryos of leaf protoplasts, and with certain species and genotypes. Further, evidence exists that only certain dicotyledonous plants can be regenerated after plant cell/tissue transformation in which the end product is a fertile transformed plant capable of sexually transmitting the desired trait. Although gene transfer has been demonstrated with monocotyledonous plant protoplasts, there was at the time of filing, no report of plant regeneration from transformed monocot cells. Actually, to date there is no evidence that fertile transgenic plants can be regenerated in most agronomic monocots, as in the case of maize or rice ....

See Plaintiffs' Exhibit 4, Tab 3, at 4-5 (internal cites omitted).

On August 17, 1990, after a series of exchanges with the examiner, the applicants separated the plant cell claims from the plant and seed claims. The revised plant and seed claims were now limited to those plants and seeds which are "susceptible of infection by *Agrobacterium*." *See* Plaintiffs' Trial Exhibit 4, Tab 12, at 2-4.

On November 19, 1990, the examiner rejected this new language for the plant and seed claims, indicating that it did not limit the claims to dicots. He repeated his assertion that the relevant scientific art did not

demonstrate that the infection of monocots by *Agrobacterium* led to transformation. The examiner suggested that the rejection under s. 112 would be obviated if the applicants limited "the claimed invention to plant cells and plant[s] which are capable of transformation by *Agrobacterium* and capable of regeneration." Plaintiffs' Trial Exhibit 4, Tab 13, at 3:15-19. On April 18, 1991, the applicants adopted the proposed language and the examiner subsequently withdrew his enablement rejection.

There can be little question from the exchanges between the examiner and the applicants that the issue of whether the plant and seed claims would cover both dicots and monocots arose on several occasions. The examiner's view was that, at the time the claims were being prosecuted, monocots were not susceptible to infection, transformation and regeneration "[E]vidence exists that only certain dicotyledonous plants can be regenerated after plant cell/tissue transformation in which the end product is a fertile, transformed plant capable of sexually transmitting the desired trait." He was concerned that the plant and seed claims, as originally proposed, were not enabled for monocots such as corn. After several exchanges, the examiner did not require the applicants to limit their plant and seed claims to dicots. Instead, the modification limits the claim to only those plants "susceptible to infection and transformation by *Agrobacterium* and capable of regeneration thereafter." The intent of these modifications, however, is to limit the coverage of the issued claims to dicots.

While the intrinsic evidence indicates that this limitation was specifically added to exclude monocots, "it is entirely appropriate, perhaps even preferable, for a court to consult trustworthy extrinsic evidence to ensure that the claim construction ... is not inconsistent with clearly expressed, plainly apposite and widely held understandings in the pertinent technical field." Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1308 (Fed.Cir.1999). In this case, the Court had the benefit of hearing extensive testimony at trial concerning the technical capabilities and limitations in the art of plant transformation at the relevant time.

C. Extrinsic Evidence

As discussed *supra,* a substantial portion of the testimony offered at trial was dedicated to establishing whether monocots could be transformed by *Agrobacterium*. As this Court has previously concluded, there is no evidence that a general methodology existed in 1987 by which a person skilled in the art could produce a transgenic monocot.

Further, the defendant offered evidence at trial that two of the plaintiffs' principal scientists. Dr. Leemans and Dr. Botterman, published articles indicating that monocots were not susceptible to *Agrobacterium* infection and transformation to insert a heterologous gene, such as the *bar* gene. For example, in 1987 Leemans co-authored a paper that stated " *Agrobacterium*-mediated transformation of [the] Graminae, including the important cereal crops, has not yet been achieved." Deblaere et al., *Vectors for Cloning in Plant Cells,* 153 Methods in Enzymology 277 (1987). Additionally, in 1990-three years after the '236 patent was filed-Leemans and a co-author wrote

Most [genetically] engineered plants have been generated by infection with *Agrobacterium tumefaciens,* a plant pathogen[ ] causing tumorous crown galls. *Agrobacterium tumefaciens* is widely used because it is a very efficient and versatile vector to stably introduce genes into plants. However, *Agrobacterium tumefaciens* seems unsuccessful in the transformation of most monocotyledonous plants, especially of cereals.

M. Peferoen and J. Leemans, *Engineering of Insect Resistant Plants with Bacillus turigiensis Crystal*

Protein Genes, Proceedings of the 6th International Symposium of Genetics of Industrial Microorganisms, at 844, Strasbourg, 1990.FN29

FN29. In its brief, the defendant cites numerous other articles co-authored by Leemans and/or Botterman that reach a similar conclusion. *See* Defendant's Initial Post-trial Brief at 10-11.

The defendant also presented evidence that Leemans' conclusions concerning the inability of *Agrobacterium tumefaciens* to transform monocots were shared by the scientific community. In 1987, Dr. Goodman published an article in Science saying that

"[a]lthough data have been cited that *Agrobacterium* can transfer T-DNA to monocotyledonous hosts, clear evidence of T-DNA integration exists only for asparagus and, even in that case, no transformed plants have been described. Because *A[grobacterium] tumefaciens* does not induce crown galls on monocotyledonous plants, such as rice, corn and wheat, other methods of gene transfer are being developed for these important crops." Goodman et al., *Gene Transfer in Crop Improvement,* 236 Science 52 (1987).

Thus, the extrinsic evidence confirms what the intrinsic evidence suggests, as of the filing date of the '236 patent no methodology existed by which monocots could be infected and transformed by *Agrobacterium* to produce plants capable of regeneration. A person skilled in the art would have been aware of this limitation, as apparently Leemans and Botterman both were, and would understand the wording of the plant and seed claims to mean that they did not cover monocots such as corn.

D. Scope of the Plant and Seed Claims and Application to the Accused Products

The intrinsic evidence indicates that the plant and seed claims do not extend to monocots, which conclusion is overwhelmingly confirmed by the extrinsic evidence presented at trial. Thus, the '236 patent does not vest the plaintiffs with the ability to exclude others from making, using, selling or offering for sale monocotylenous plants that contain the bar gene. It is undisputed that all of the accused products are monocots, and therefore do not literally infringe Claims 8-9, 12-15 (the plant and seed claims) of the '236 patent.FN30

FN30. For the sake of clarity, the Court emphasizes that its ruling today does not impact the validity of the plant and seed claims as they apply to dicots. Indeed, it is readily apparent from the evidence that the plant and seed claims are valid and enabled with respect to dicots.

[23] Further, the accused products do not infringe the plant and seed claims under the doctrine of equivalents. As discussed above, during the prosecution of the '236 patent, the examiner and the applicants engaged in discussions concerning the applicability of the plant and seed claims to monocots. Specifically, when the proposed claims were limited to cells that were "susceptible of infection by Agrobacterium," the examiner rejected the claims and stated:

[The claims] remain rejected under U.S.C. s. 112, first paragraph, as the disclosure is enabling only for claims limited to specific source cells or tissues of dicotyledonous plants in which transformation and regeneration have been shown.

Plants susceptible to infection are both de facto necessarily susceptible to transformation as the early work of DeCleene for example (newly cited) amply demonstrates that infection of monocots does not necessarily lead to transformation...

In view of the teachings set forth in the instant specification, limiting the claimed invention to plant cells and plants which are capable of transformation by Agrobacterium and capable of regeneration would serve to obviate this rejection. *See* Plaintiffs' Exhibit 4 at Tab 13, 2:4-10 and 2:20-24.

[24] [25] As discussed above, the applicants adopted a form of the examiner's language and the patent issued. Because the examiner's concerns and proposed changes were designed to exclude monocots from the coverage of the claims, the applicants forever surrendered coverage of monocots under the plant and seed claims. It is well settled that an applicant is estopped from reclaiming under the doctrine of equivalents what he has surrendered during prosecution. *See generally* Warner-Jenkinson Co. v. Hilton Davis Chemical Co., 520 U.S. 17, 117 S.Ct. 1040, 137 L.Ed.2d 146 (1997). "Prosecution history estoppel prevents a patentee from recapturing subject matter surrendered during the prosecution of the patent." Augustine Medical Inc. v. Gaymar Idus. Inc., 181 F.3d 1291, 1298 (Fed.Cir.1999). Because any reasonable competitor reviewing the prosecution history would conclude that the applicant surrendered coverage of monocots, PGS can not recapture such subject matter under the doctrine of equivalents. *See* Pharmacia & Upjohn Co. v. Mylan Pharmaceuticals Inc., 170 F.3d 1373, 1377 (Fed.Cir.1999); *see also* Desper Prods. Inc. v. QSound Labs Inc., 157 F.3d 1325, 1340 (Fed.Cir.1998).

IV. Conclusion

For the reasons stated above, the Court concludes that:

1. The defendant has sustained its burden of proving by clear and convincing evidence that Claims 1-5 and 10-11 (the cell claims) of United States Patent No. 5,561,236 are invalid due to lack of enablement under 35 U.S.C. s. 112; and

2. The evidence presented at trial indicates that the scope of Claims 8-9 and 12-15 (the plant and seed claims) of United States Patent No. 5,561,236 is limited to dicotyledonous plants and does not cover monocotyledonous plants, such as corn. The accused products do not infringe the '236 patent either literally or under the doctrine of equivalents.

Pursuant to these findings of fact and conclusions of law, judgment shall be entered for the defendant on all counts. The Parties shall bear their own costs and fees in this matter. The Clerk is directed to close this case.