

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INARI AGRICULTURE, INC.,
Petitioner,

v.

CORTEVA AGRISCIENCE LLC,
Patent Owner.

Case No. IPR2024-01014
Patent No. 8,901,378

DECLARATION OF DR. ARON SILVERSTONE, Ph.D.

Inari Exhibit 1007 Inari v. Corteva
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I, Aron Silverstone, Ph.D., hereby declare under penalty of perjury:

I. INTRODUCTION

1. My name is Aron Silverstone, and I have been retained by counsel for Petitioner Inari Agriculture, Inc. (“Inari” or “Petitioner”) as an expert witness to provide assistance regarding U.S. Patent No. 8,901,378 (the “’378 Patent”), which I understand has been designated as EX1001. Specifically, I have been asked to consider the patentability of claims 1-8 of the ’378 Patent (the “Challenged Claims”) in view of the prior art and the understanding of a person of ordinary skill in the art (“POSA”) at the time of the invention as it relates to the ’378 Patent. I have personal knowledge of the facts and opinions set forth in this declaration and believe them to be true. If called upon to do so, I would testify competently thereto.

2. I am being compensated for my time at my standard consulting rate. I am also being reimbursed for expenses that I incur during the course of this work. My compensation is not contingent upon the results of my study, the substance of my expert opinions, or the outcome of any proceeding involving the challenged claims. I have no financial interest in the outcome of this matter or on the pending litigation between Petitioner and Patent Owner.

3. My analysis here is based on my years of education, research and experience, as well as my investigation and study of relevant materials, including those cited herein.

4. I may rely upon these materials, my knowledge and experience, and/or additional materials to rebut arguments raised by the Patent Owner. Further, I may also consider additional documents and information in forming any necessary opinions, including documents that may not yet have been provided to me.

5. My analysis of the materials produced in this proceeding is ongoing and I will continue to review any new material as it is provided. This declaration represents only those opinions I have formed to date. I reserve the right to revise, supplement, and/or amend my expert opinions stated herein based on new information and on my continuing analysis of the materials already provided.

II. BACKGROUND AND QUALIFICATIONS

6. I am an expert in the fields of plant physiology, biochemistry, molecular biology and genetics. I have studied, taught, practiced, and researched this field for over 35 years. I have summarized in this section my educational background, work experience, and other relevant qualifications. I understand that a true and correct copy of my curriculum vitae describing my background and experience is being filed herewith as EX1008.

7. I earned my Bachelor of Arts degree in Biology from Harvard University in 1987. In 1994, I earned my Doctor of Philosophy degree in Plant Physiology from University of California, Davis, with my dissertation being on “The Physiology and Biochemistry of Tryptophan Malonylation in Higher Plants.”

8. During my dissertation research, I investigated the biosynthetic pathways of the plant hormones auxin and ethylene, and I identified novel amino acid metabolism reactions.

9. After obtaining my Doctor of Philosophy degree, I worked as a postdoctoral fellow in the Botany Department of Duke University where I conducted research on the biosynthesis and signal response pathway of the plant hormone gibberellin.

10. In June of 1999, I joined Syngenta Biotechnology, Inc. as a Staff Scientist I. In this position, I designed and built constructs to express a sweet protein in corn and analyzed transgenic plants. In February of 2001, I was promoted to a Staff Scientist II position. In this role, I discovered and validated seed-specific promoters. In June of 2003, I was promoted to Project Leader. I led teams that developed novel starch degrading enzymes and expressed them in transgenic corn. I also managed the development of a new transgenic product expressing a high temperature amylase in corn for the corn starch-to-ethanol industry. Another team I led generated the second generation of Golden Rice—

that is, rice that produces beta-carotene. This required expression and analysis of novel carotenoid biosynthetic enzymes in rice.

11. In April of 2007, I received a promotion to Senior Project Leader. While in this position, I developed technologies to enhance the ability to express heterologous proteins in plants.

12. In July of 2010, I received a promotion to Global Project Manager for Soybean Traits in Syngenta Seeds, LLC. While in this position, I led a multifunctional team to develop a novel herbicide-tolerant soybean. The work included lab-based assays, field studies, regulatory strategy, product safety studies, marketing, and IP. I also led a multifunctional team to develop a novel insect control transgenic trait stack in soybean. The activities included coordinating lab studies, field activities, IP, product safety studies and regulatory strategy, and marketing. In June 2014, I became a Product Biology Lead for Abiotic Stress Management, North America for Syngenta Crop Protection, LLC. My work in this position entailed overseeing the field trial program to test chemical products for performance in mitigating yield loss from abiotic stresses. It also included designing trials and testing methods to identify crop enhancement benefits from fungicides. In January 2019, I became a Senior Team Lead in Product Safety Operations. As Senior Team Lead, I led a team of specialists supporting 100+ Product Safety scientists for budgeting, outsourcing, document management,

knowledge management and lab management. In November 2020, I became a Technical Lead in Human Safety Residue Science. While in this position, I led a team of scientists overseeing residue studies for regulatory submissions in the United States and Canada. I also supported the product development of new active ingredients and the expansion of the use of registered pesticides.

13. In February 2023, I accepted a position as a Scientific Consultant at AgStone Research, LLC. My work in this position has entailed consulting on scientific strategy in the field of biotechnology for agriculture.

14. I have authored and co-authored over 17 journal publications, conference proceedings, technical papers, patents, book chapters, and delivered over 100 technical presentations in a broad array of subjects specific to my research programs as well as on the subject of plant biotechnology and crop improvement. I have also served as a guest lecturer on plant biotechnology at Duke University since 1997. A complete list of my publications and selected list of invited talks is also contained in my curriculum vitae (EX1008).

15. I have also received a number of awards and recognitions, including the Rising Sun Award at the 16th International Conference on Plant Growth Substances among others, which are listed in my curriculum vitae.

III. LEVEL OF ORDINARY SKILL IN THE ART

16. In rendering the opinions set forth in this declaration, I was asked to consider the patent claims and the prior art through the eyes of one of ordinary skill at the time of the claimed invention. I understand that the '378 Patent claims priority to a provisional application filed on May 2, 2003 (EX1005), although as discussed below it is my conclusion that the Challenged Claims are not entitled to the benefit of either that May 2, 2003 provisional application or the subsequent non-provisional application Patent Owner filed on April 30, 2004 (EX1006)—meaning that the Challenged Claims instead are unpatentable as anticipated and/or obvious based on a February 16, 2006 publication (Barbour, EX1009) given that the next application in the '378 Patent's priority chain was not filed until July 6, 2007. My analysis in this declaration is equally applicable throughout this timeframe from 2003-2007—including but not limited to the specific dates of May 2, 2003, April 30, 2004, February 16, 2006, and July 6, 2006 (i.e., one year before the July 6, 2007 filing date of the next application in the chain).

17. I understand that the factors considered in determining the ordinary level of skill in a field of art include the level of education and experience of persons working in the field; the types of problems encountered in the field; the teachings of the prior art, and the sophistication of the technology at the time of the claimed invention. I understand that one of ordinary skill is not a specific real

individual, but rather is a hypothetical individual having the qualities reflected by the factors above. I understand that one of ordinary skill would also have knowledge from the teachings of the prior art, including the art cited below.

18. Taking these factors into consideration, a POSA in the 2003-2007 timeframe would have had a Ph.D. in biochemistry, cell biology, genetics, molecular biology, or a related field, and 3-5 years of experience in the design or development of transgenic plants including genomics, proteomics, biochemistry, plant transformation and crop science, or the equivalent. Additional graduate education could substitute for professional experience, or significant experience in the field could substitute for formal education.

19. Before the 2003-2007 time frame, my level of skill in the art was at least that of one of ordinary skill. I am qualified to provide opinions concerning what one of ordinary skill would have known and understood at that time, and my analysis and conclusions herein are from the perspective of one of ordinary skill as of that date.

IV. MATERIALS CONSIDERED AND RELIED UPON

20. In reaching the conclusions described in this declaration, I have relied on the '378 Patent, the prosecution history of the '378 Patent, the prior art, and other documents and materials cited herein. For ease of reference, the full list of documents that I have considered is included in Appendix A.

21. These materials comprise patents, related documents, and printed publications. Each of these materials is a type of document that experts in my field would have reasonably relied upon when forming their opinions.

22. I have also relied on my education, training, research, knowledge, and personal and professional experience in the relevant technologies and systems that were already in use prior to the 2003-2007 timeframe.

V. LEGAL STANDARDS

23. I am not a lawyer and do not provide any legal opinions, but I have been advised that certain legal standards are to be applied by technical experts in forming opinions regarding meaning and patentability of patent claims. I have applied the legal standards described below, which were provided to me by counsel for Petitioner.

A. Claim Construction

24. I have been informed that patent claims are to be construed in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent. In particular, I have been informed that this means that patent claims are construed from the viewpoint of a person of ordinary skill at the time of the alleged invention. I have been informed that patent claims generally should be interpreted consistent with their plain and ordinary meaning as understood by a person of

ordinary skill in the relevant time period (i.e., at the time of the purported invention, or the so called “effective filing date” of the patent application), after reviewing the patent claim language, the specification and the prosecution history (i.e., the intrinsic record).

B. Anticipation

25. I have been informed that a patent claim may be unpatentable under 35 U.S.C. § 102 as “anticipated” by the prior art (and therefore not novel), when each and every claim limitation of the claim is disclosed, actually or inherently, in a single prior art reference. I understand that a claim limitation is disclosed for the purpose of anticipation if a POSA would have understood the reference to disclose the limitation based on inferences that a POSA would reasonably be expected to draw from the explicit teachings in the reference when read in light of the POSA’s knowledge and experience.

26. I have also been informed that in order to anticipate a claim, the prior art in question must be enabled. However, as discussed in further detail in Section X.A.2.c below, I also understand that the standard for assessing whether prior art is enabled under § 102 is not identical to the standard for assessing whether a patent specification enables the corresponding claims as required under 35 U.S.C. § 112.

C. Obviousness

27. I have been informed that a claim may be unpatentable under 35 U.S.C. § 103(a) if the subject matter described by the claim as a whole would have been obvious in view of a prior art reference or in view of a combination of references at the time the alleged invention was made. I have been informed that obviousness is determined from the perspective of a POSA and that the challenged claims of the patent should be read from the point of view of such a person at the time the alleged invention was made. I have been informed that a hypothetical person of ordinary skill is assumed to know and to have all relevant prior art in the field of endeavor covered by the patent in suit, and would thus have been familiar with each of the references cited herein, as well as the background knowledge in the art, and the full range of teachings they contain.

28. I have been informed that there are two criteria for determining whether prior art is analogous and thus can be considered prior art: (1) whether the art is from the same field of endeavor, regardless of the problem addressed, and (2) if the reference is not within the field of the patentee's endeavor, whether the reference still is reasonably pertinent to the particular problem with which the patentee is involved. I have also been informed that the field of endeavor of a patent is not limited to the specific point of novelty, the narrowest possible conception of the field, or the particular focus within a given field. I have also

been informed that a reference is reasonably pertinent if, even though it may be in a different field from that of the patentee's endeavor, it is one which, because of the matter with which it deals, logically would have commended itself to a patentee's attention in considering the problem.

29. I have also been informed that an analysis of whether an alleged invention would have been obvious should be considered in light of the scope and content of the prior art, the differences (if any) between the prior art and the alleged invention, and the level of ordinary skill in the pertinent art involved. I have been informed as well that a prior art reference should be viewed as a whole.

30. I have also been informed that in considering whether an invention for a claimed combination would have been obvious, I may assess whether there are apparent reasons to combine known elements in the prior art in the manner claimed in view of interrelated teachings of multiple prior art references, the effects of demands known to the design community or present in the market place, and/or the background knowledge possessed by a person of ordinary skill. I have been informed that other principles may be relied on in evaluating whether an alleged invention would have been obvious, and that these principles include the following:

- A combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results;
- When a device or technology is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or in a different one, so that if a person of ordinary skill can implement a predictable variation, the variation is likely obvious;
- If a technique has been used to improve one device, and a person of ordinary skill would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill;
- An explicit or implicit teaching, suggestion, or motivation to combine two prior art references to form the claimed combination may demonstrate obviousness, but proof of obviousness does not depend on or require showing an explicit teaching, suggestion, or motivation to combine;
- Market demand, rather than scientific literature, can drive design trends and may show obviousness;

- In determining whether the subject matter of a patent claim would have been obvious, neither the particular motivation nor the avowed purpose of the named inventor controls;
- One of the ways in which a patent's subject can be proved obvious is by noting that there existed at the time of invention a known problem for which there was an obvious solution encompassed by the patent's claims;
- Any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed;
- "Common sense" teaches that familiar items may have obvious uses beyond their primary purposes, and in many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle;
- A person of ordinary skill is also a person of ordinary creativity, and is not an automaton;
- A patent claim can be proved obvious by showing that the claimed combination of elements was "obvious to try," particularly when there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions such that a person of

ordinary skill would have had good reason to pursue the known options within his or her technical grasp; and

- One should be cautious of using hindsight in evaluating whether an alleged invention would have been obvious.

31. I have further been informed that, in making a determination as to whether or not the alleged invention would have been obvious to a person of ordinary skill, the Board may consider certain objective factors if they are present, such as: commercial success of products practicing the alleged invention; long-felt but unsolved need; teaching away; unexpected results; copying; and praise by others in the field. These factors are generally referred to as “secondary considerations” or “objective indicia” of nonobviousness. I have been informed, however, that for such objective evidence to be relevant to the obviousness of a claim, there must be a causal relationship (called a “nexus”) between the claim and the evidence and that this nexus must be based on what is claimed and novel in the claim rather than something in the prior art. I also have been informed that even when they are present, secondary considerations may be unable to overcome primary evidence of obviousness (e.g., motivation to combine with predictable results) that is sufficiently strong.

32. I have been asked to consider the patentability of claims 1-8 (the “Challenged Claims”) of the ’378 Patent that are challenged in the Petition.

D. Priority (Effective Filing) Date

33. I have been informed that a patent application may obtain the benefit of an earlier patent application's filing date for purposes of determining what is "prior art" for purposes of the anticipation and obviousness analyses discussed above. I have also been informed that in order for a particular patent claim in a later-filed application to receive the benefit of an earlier patent application's filing date, the earlier application must disclose the claimed invention in the manner provided by 35 U.S.C. § 112(a), including the enablement requirement discussed below. I understand that priority is assessed on a claim-by-claim basis.

E. Enablement Requirement

34. I have been informed that the enablement requirement under 35 U.S.C. § 112(a) is based on the text of the statute requiring that:

(a) IN GENERAL.—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...

35. I have been informed that a specification does not comply with the enablement requirement under 35 U.S.C. § 112(a) with respect to a particular claimed invention if the specification does not teach a POSA how to make and use

the invention as broadly as it is claimed, without undue experimentation as of the relevant date. In the case of assessing whether a patent claim is entitled to the benefit of an earlier-filed application, I have been informed that the relevant timeframe to consider is the date of the earlier application (as discussed above in paragraph 33).

36. I have been informed that a finding of undue experimentation must consider multiple factors to determine if there is sufficient evidence to support such a determination. I have been informed that these factors, which are referred to as *Wands* factors, include (1) the nature of the invention, (2) the relative skill of those in the art, (3) the breadth of the claims, (4) the presence or absence of working samples, (5) the amount of direction or guidance presented, (6), the state of the prior art, (7) the predictability or unpredictability of the art, and (8) the quantity of experimentation necessary.

37. I have been informed that the specification need not teach what is well known in the art. *Hybritech v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986).

38. I have been informed that the determination of non-enablement must be based on the evidence as a whole.

VI. DESCRIPTION OF THE RELEVANT FIELD AND THE RELEVANT TIMEFRAME

39. I understand that the '378 Patent issued from U.S. Patent Application 12/914,271, filed on October 28, 2010. The '271 Application was filed as a division of application No. 12/333,044, which was filed on March 13, 2009, as a continuation of application No. 11/774,236, which was filed on July 6, 2007, as a division of application No. 10/837,105, which was filed on April 30, 2004, and claims priority to provisional application No. 60/467,772, filed on May 2, 2003.

40. I have been instructed by counsel to assume the relevant timeframe for my analysis in this declaration to be 2003-2007. Based on my review of this material, I believe that the relevant general fields for the purposes of the '378 Patent are, as identified above, biochemistry, cell biology, genetics, molecular biology, or a related field.

VII. OVERVIEW OF THE '378 PATENT

41. The '378 Patent relates to the transformation of a corn (maize) plant by incorporating foreign DNA genes into the corn plant's genome such that the corn plant produces proteins (based on the foreign genes) that provide the plant with certain properties corn plants would not otherwise possess—including resistance to certain insects as well as commonly-applied herbicides. In particular, the patent describes “transforming a corn cell” with “DNA construct PHI8999A (SEQ ID NO:25).” EX1001, 5:24-26. The result is a “transgenic” corn plant that

passes down the foreign genes (with the related desirable properties) to offspring when the plant is bred. EX1001, 10:26-30 (noting that “transformation” yields “genetically stable inheritance”); *see also id.*, 2:10-11 (“Progeny of such crosses maintain the transgene expression characteristics of the original transformant.”).

42. As the specification acknowledges, however, transformation via the microprojectile bombardment technique described in the application leads to the “*random integration* of the foreign DNA” into host organisms. EX1001, 7:31-33. Any given transformation—also known as a transgenic “event” (EX1001, 9:35-37)—yields “flanking regions” at either end of the foreign DNA “unique” for each event (EX1001, 7:31-35). Even if researchers started with identical plant cells and transformed each with identical sequences of foreign DNA, each event would have unique junction sequences uniquely characteristic of the particular event. *E.g.*, EX1066 (De Bolle et al., Analysis of the influence of promoter elements and a matrix attachment region on the inter-individual variation of transgene expression in populations of *Arabidopsis thaliana*, Plant Science 165 (2003) 169-179), 170 (“As the integration of foreign DNA in the plant genome occurs via illegitimate recombination, it can take place at virtually any site. As a consequence, sequences flanking the transgene are different in independently obtained transformants.”). I also note that Patent owner filed a subsequent patent application acknowledging

this same point—that is “multiple transgenic plant events...will not be identical” even if “using the same genetic construct.” EX1026, ¶3.

A. Described Embodiments

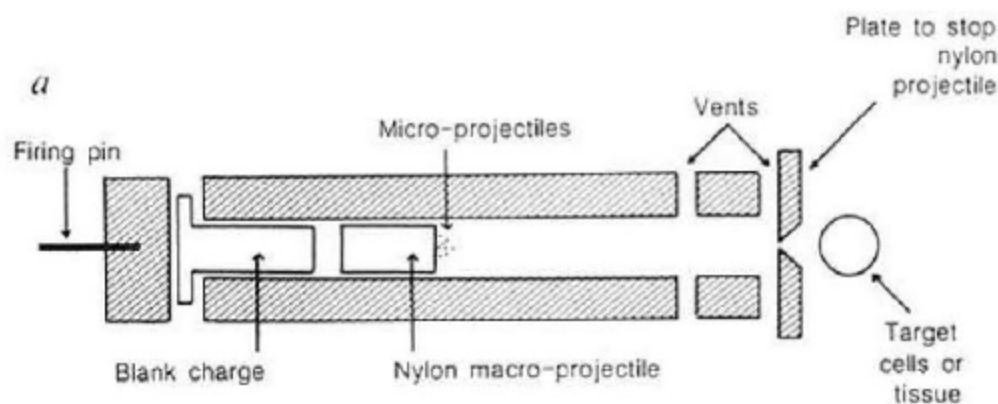
43. The '378 Patent itself concerns “maize event TC1507”—in other words, “plant TC1507.” EX1001, 1:26-28. TC1507 is the only ostensibly new plant variety that the '378 Patent discloses.

44. Example 1 describes generating event TC1507 using “microprojectile bombardment” to incorporate the DNA molecule designated PHI8999A as reflected in FIG. 1 and SEQ ID NO:25. EX1001, 17:50-18:48. This technique is also known as “biolistics.” As Patent Owner’s expert in another proceeding has stated, “biolistics” is “shooting small DNA-coated metal particles...into plant tissue with sufficient force to break through the cell wall and membrane and release the foreign DNA” researchers seek to integrate into the plant genome. *See* EX1027 (Declaration of Paul Christou, Ph.D, *Inari Agriculture v. Corteva Agriscience*, PGR2023-00022, Exhibit 2012), ¶48.

45. In this case, the PHI8999A insert included two different “transgene expression cassettes” for delivering two different genes the inventors sought to incorporate into corn. EX1001, 2:44-3:6. The first cassette incorporated a gene encoding for “Cry1F”—a protein that was known to have insecticidal properties and be effective against various corn pests. EX1001, 2:53-63. The second cassette

incorporated a gene encoding for phosphinothricin acetyltransferase (“PAT”)—an enzyme known to catalyze the elimination of phosphinothricin (also known as glufosinate)—a widely used herbicide. EX1001, 2:63-3:6. In other words, the inventors sought to create a transgenic corn line that resisted insects while tolerating herbicides.

46. After coating “microscopic tungsten particles...with purified PHI8999A DNA (SEQ ID NO:25), the inventors used a “particle gun” to shoot the particles with the genes encoding for these two proteins into “immature embryos” that had been cultured for several days. *Id.*, 18:13-22. The ’378 Patent incorporates by reference an article by Klein, et al. (EX1057) that describes this “gene gun” transformation technology.” EX1001, 10:33-34; *see also id.* 18:13-16. The article illustrates an example of a gene gun and describes using such a device for the “bombardment” of plant cells with the tungsten microprojectiles. Klein, et al., “High-velocity microprojectiles for delivering nucleic acids into living cells,” *Nature* 327 (May 1987). EX1057, 71:



Id.

47. After the embryos were bombarded with microprojectiles delivered using a “Biolistics® PDS-1000He particle gun,” the inventors transferred them to separate cultures, each of which contained glufosinate as a “selection agent.” EX1001, 25:27. To the extent particular embryos survived despite the presence of this herbicide, it suggested that they had been successfully transformed by the incorporation of the above-discussed PAT gene included in the PHI8999A insert coated on the microprojectiles.

48. While the “majority of explants died on the selective medium,” some survived and yielded “healthy, glufosinate-resistant callus tissue.” EX1001, 18:29-31. Those embryos were each “assigned unique identification codes representing putative transformation events” and continued to be screened in fresh selection media (i.e., incorporating glufosinate”). EX1001, 18:31-32. Given the nature of the biolistics process, a POSA would have understood that “TC1507” was merely one such identification code (out of many). Indeed, given the nature of the biolistics process, researchers often needed to create even “thousands of events with a given construct to identify a single event that possesses all desired qualities.” EX1026, ¶3. While EX1026 reflects an application filed by the Patent Owner in 2008, the statement was true as of the earlier 2003-2007 timeframe as well.

49. For “each unique event,” the inventors grew plants and tested leaf samples to verify the presence of the transgene, confirm expression of the Cry1F protein, and test the plants against European corn borer insects. EX1001, 18:35-39. Plants passing these screens “were crossed with inbred lines to obtain seed from the initial transformed plants,” and multiple “lines were evaluated in the field.” EX1001, 18:39-41. The inventors ultimately selected “[t]he TC1507 event from a population of independent transgenic events” based on its “superior combination of characteristics, including insect resistance” as well as “agronomic performance” (EX1001, 18:42-28)—in other words, how well and efficiently the TC1507 corn plants grew under real-world agricultural conditions.

B. Person of Ordinary Skill in the Art

50. As discussed above in Section III, in my opinion, a POSA as of 2004 (or for that matter throughout the 2003-2007 timeframe) would have had a Ph.D. in biochemistry, cell biology, genetics, molecular biology, or a related field, and 3-5 years of experience in the design or development of transgenic plants including genomics, proteomics, biochemistry, plant transformation and crop science, or the equivalent. Additional graduate education could substitute for professional experience, or significant experience in the field could substitute for formal education.

C. Prosecution History

51. I have reviewed and considered the prosecution history of the '378 Patent, which I understand has been designated as EX1002.

D. Related EP Prosecution Histories

52. I have also reviewed and considered prosecution histories of what I understand to be two European patent applications related to the '378 Patent. I understand that these prosecution histories have been designated EX1003 (in the case of European Patent Application No. 04 751 097.9) and EX1004 (in the case of European Patent Application No. 15 168 051.9).

VIII. CLAIM INTERPRETATION

53. I understand that claim terms are to be construed using the standard used in civil actions under 35 U.S.C. § 282(b), in accordance with the ordinary and customary meaning as understood by a POSA. 37 C.F.R. § 42.100(b).

A. The Challenged Claims Require the Particular Flanking Sequences Uniquely Characterizing the TC1507 Event

1. Independent Claim 1

54. Independent claim 1 is the only independent claim in the '378 Patent. As described further in the sections below, the other claims depend from claim 1 and require “the corn plant of claim 1” (in the case of claims 2 and 8) or “the DNA construct of claim 1” (in the case of claims 3-7, which concern methods of producing an insect resistant corn plant).

55. Claim 1 requires:

A corn plant comprising a DNA construct, said DNA construct comprising a first and a second expression cassette, wherein said first expression cassette in operable linkage comprises:

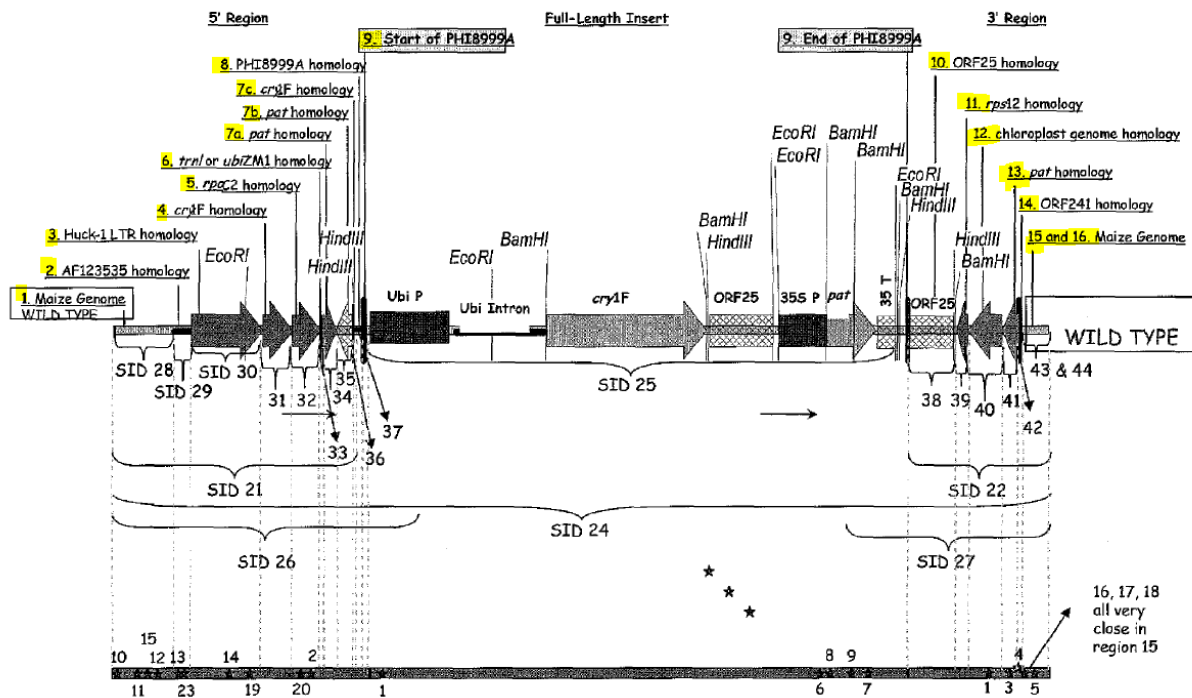
- (a) a maize ubiquitin promoter;
- (b) a 5' untranslated exon of a maize ubiquitin gene;
- (c) a maize ubiquitin intron;
- (d) a Cry1F encoding DNA molecule; and
- (e) a 3' ORF25 transcriptional terminator;

and said second expression cassette comprising in operable linkage

- (i) a CaMV 35S promoter;
 - (ii) a pat encoding DNA molecule; and
 - (iii) a 3' transcriptional terminator from (CaMV) 35S comprising the nucleic acid sequence of positions 5843 to 6032 of SEQ ID NO: 25;
- and wherein the first and second expression cassettes are flanked by SEQ ID NO: 26 at the 5' end and SEQ ID NO: 27 at the 3' end.

56. A POSA reviewing claim 1 in view of the '378 Patent's specification and file history (as discussed in Section V.A above) would understand that claim 1 requires a corn plant incorporating foreign DNA—including genes coding for the Cry1F and PAT proteins—at a particular location within the corn genome defined based on SEQ ID NO:26 at the 5' end and SEQ ID NO:27 at the 3' end. EX1001, 85:24-42. Flanking sequences 26 and 27 incorporate various “junctions” that were formed during the TC1507 event and which do not occur in natural corn DNA, as reflected in the table below and the accompanying annotated version of Figure 1:

SEQ ID NO	Location	
45	junction between regions 3 and 4	<i>Included in SEQ ID NO:26</i>
46	junction between regions 4 and 5	
47	junction between regions 5 and 6	
48	junction between regions 6 and 7a	
49	junction between regions 7a and 7b	
50	junction between regions 7b and 7c	
51	junction between regions 7c and 8	
52	junction between regions 8 and 9	<i>Included in SEQ ID NO: 27</i>
53	junction between regions 9 and 10	
54	junction between regions 10 and 11	
55	junction between regions 11 and 12	
56	junction between regions 12 and 13	
57	junction between regions 13 and 14	



57. As the '378 Patent acknowledges, these flanking regions—including junction sequences created during the integration event—are “unique” for any

given transformation event given the “random” integration of the DNA. EX1001, 4:59-61 (describing “junction sequences” as “unique” for any given transgenic event); *id.*, 7:31-35 (“Transformation procedures leading to random integration of the foreign DNA will result in transformants containing different flanking regions characteristic and unique for each transformant.”).

58. During prosecution of a related European application, Patent Owner stressed that “part of what distinguishes one event from another is the flanking sequence at either end of the insert.” EX1003, 294. These flanking sequences contain “partly inserted construct sequence and partly original plant sequence.” EX1003, 294. These sequences meet at the “junction” and form junction sequences, which span “the junction between heterologous DNA inserted into the genome and the DNA from the corn cell flanking the insertion site.” EX1001, 5:4-12.

59. Given that these “junction sequences” are “unique” for any given transgenic event (EX1001, 4:59-61), they are different for even “two different events with the same transgene” (EX1003, 294). Two different events would each result in the transgene “in two different genomic locations, and possibly in different orientations,” as well as “different losses, duplications, rearrangements etc. of nucleotide[s].” EX1003, 294; *see also id.*, 329 (“Each event is defined by its unique ‘junction’ sequences.”).

60. In sum, a POSA would understand that claim 1 requires the particular junction sequences that are unique to the TC1507 Event and reflected in SEQ ID NOS. 26 and 27. In other words, a transgenic corn plant incorporating the first expression cassette (with the Cry1F gene) and the second expression cassette (with the PAT gene) elsewhere in the corn genome would not be covered by claim 1.

2. Dependent Claims 2 and 8

61. A POSA would understand that the regions and related junctions unique to the TC1507 Event are also required to practice Challenged Claims 2 and 8, which recite “[t]he corn plant of claim 1” and then specify additional requirements. Claim 2 requires that the corn plant be a “seed” (EX1001, 85:42-43) while claim 8 recites that the “DNA construct comprises the polynucleotide of SEQ ID NO:24” (EX1001, 86:41-42). As reflected in Figure 1, SEQ ID NO:24 indeed includes SEQ ID NO: 26 at the 5' end and SEQ ID NO:27 at the 3' end while also including SEQ ID NO:25, which is in between SEQ ID NO: 26 and SEQ ID NO:27 while overlapping both.

3. Dependent Claims 3-7

62. Claims 3-7 directly or indirectly depend from claim 1. Claim 3 depends directly on claim 1, as it requires “the DNA construct of claim 1.” Claims 4-7 depend from claim 1 via claim 3; they refer to the “method of claim 3.” Claims 3-7 concern breeding methods requiring a transgenic corn plant with the

same regions and related junctions as that specified by claim 1 and uniquely characteristic of the TC1507 event.

63. Claim 3 requires a method of “breeding with an insect resistant corn plant comprising in its genome DNA *the DNA construct of claim 1.*” EX1001, 86:26-27. A POSA would understand that the “DNA construct” includes the flanking regions recited by claim 1—in other words, “SEQ ID NO:26 at the 5' end and SEQ ID NO:27 at the 3' end”—and unique to TC1507 as explained above concerning claim 1.

64. Dependent claim 8 confirms that understanding. In particular, a POSA would note that claim 8 depends from claim 1 and requires that “the *DNA construct* comprises the polynucleotide of SEQ ID NO:24.” EX1001, 86:41-42. SEQ ID NO: 24 includes SEQ ID NO:26 at the 5' end and SEQ ID NO:27 at the 3' end. EX1001, Figure 1. If the “DNA construct” excluded these flanking regions unique to the TC1507 Event, the construct would not encompass SEQ ID NO:24 even though claim 8 specifically requires that the construct encompass SEQ ID NO:24. In other words, if the “DNA construct of claim 1” did not cover the flanking regions unique to TC1507, claim 8 would be inconsistent with claim 1.

B. The Challenged Claims Encompass the TC1507 Event

65. In addition to understanding that the Challenged Claims require the particular flanking sequences uniquely characterizing the TC1507 event and

distinguishing it from other transgenic events, a POSA would understand that Challenged Claims 1-2 and 8 encompass TC1507 corn plants themselves while Challenged Claims 3-7 cover methods of breeding such plants.

66. The '378 Patent discloses that the “invention...relates to the TC1507 corn plant” (EX1001, 5:61), and TC1507 indeed is the only event described. Moreover, the title of the patent is “Corn Event TC1507 and Methods for Detection Thereof.” Similarly, in the “Field of the Invention” section, the '378 Patent explains that the “invention more specifically relates to an insect resistant corn plant TC1507.” EX1001, 1:19-20. The first sentence of the “Background of the Invention” section likewise describes the “invention” as “relat[ing] to the insect resistant corn (*Zea mays*) plant TC1507.” EX1001, 1:26-27. In addition, all of the sequences disclosed in the '378 Patent concern the TC1507 event.

67. Consistent with these disclosures, TC1507 is the only allegedly new corn plant (or for that matter any other plant) described anywhere in the '378 Patent. In other words, TC1507 is the only embodiment of a corn plant described in the '378 Patent.

68. In the context of this evidence, a POSA would understand that Challenged Claim 1's requirement that the “first and second expression cassettes” be “*flanked by* SEQ ID NO:26 at the 5' end and SEQ ID NO: 27 at the 3' end” encompasses configurations in which SEQ ID NO:26 overlaps with the first

expression cassette and SEQ ID NO: 27 overlaps with the second expression cassette.

69. As Figure 1 illustrates, the 3' end of SEQ ID NO: 26 includes a portion of the ubiquitin promoter, which the '378 Patent (including Challenged Claim 1 itself) confirms is part of the first expression cassette. EX1001, 2:53-56, 17:58-61, 85:27-29 (“wherein said first expression cassette in operable linkage comprises (a) a maize ubiquitin promoter”). Consistent with these disclosures, the patent describes SEQ ID NO:26 as a “novel transgene/flanking insertion region.” EX1001, 3:62-64.

70. Figure 1 likewise illustrates that SEQ ID NO: 27 includes a portion of the DNA sequence encoding for the PAT protein and a 3' transcriptional terminator from (CaMV) 35S comprising the nucleic acid sequence of positions 5843 to 6032 of SEQ ID NO:25, which the '378 Patent (including Challenged Claim 1 itself) confirms is part of the second expression cassette. EX1001, 2:63-3:6, 18:2-12, 85:32-38. Consistent with these disclosures, the patent describes SEQ ID NO:27 as a “novel transgene/flanking insertion region.” EX1001, 4:3-4.

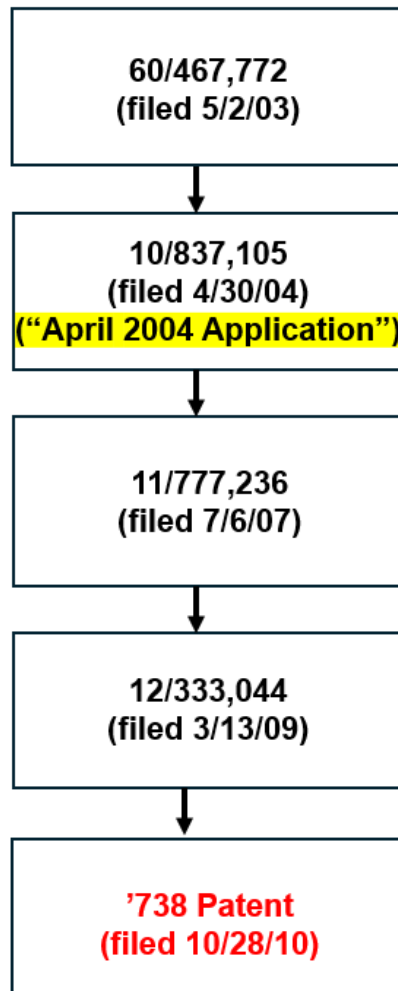
71. Given these disclosures, a POSA would understand that the “ordinary meaning of “flanked by” encompasses scenarios in which an expression cassette is “flanked by” a given DNA sequence even if the DNA sequence overlaps with the expression cassette.

72. If “flanked by” were instead construed to have a narrower meaning and prohibit overlap, the Challenged Claims would exclude TC1507 even though it is the only embodiment described in the ’378 Patent as noted above. I understand that construing patent claims to exclude a preferred embodiment described in the patent’s specification is disfavored and requires highly persuasive evidentiary support. There is no such support in the ’378 Patent for excluding TC1507.

73. Construing “flanked by” to prohibit overlap would also contradict dependent claim 8, which depends from claim 1 and recites “SEQ ID NO: 24,” which comprises SEQ ID NO: 26 and SEQ ID NO: 27 overlapping with the first and second expression cassettes.

IX. EFFECTIVE FILING DATE OF THE CHALLENGED CLAIMS

74. I understand that the ’378 Patent claims priority through a series of earlier applications dating back to an April 30, 2004 utility application (“April 2004 Application”) and further to a May 2, 2003 provisional application:



75. Pursuant to the legal standards described in Section V above, I was asked to determine whether the April 2004 Application enables the Challenged Claims under section 112(a) such that the Challenged Claims could potentially be entitled to an effective filing date of April 30, 2004. I understand that if the April 2004 Application does not enable the Challenged Claims, the earliest potential effective filing date for the Challenged Claims would be July 6, 2007—the filing date of the subsequent application in the patent family as noted above.

76. As detailed below, the April 2004 Application fails to enable a POSA to practice any of the Challenged Claims without undue experimentation. Accordingly, I understand that the Challenged Claims are therefore not entitled to an effective filing date earlier than July 6, 2007.

77. I understand that in order for the Challenged Claims to be entitled to an effective filing date of July 6, 2007, the application filed on that date would need to allow a POSA to practice the Challenged Claims without undue experimentation. I was not asked to assess that issue. Even if the Challenged Claims were entitled to the July 6, 2007, they would be unpatentable for the reasons discussed in Section X below. All the materials discussed in Section X—for example Barbour (EX1009)—were published more than one year before July 6, 2007.

A. The April 2004 Application Does Not Enable the Challenged Claims Under § 112

78. The April 2004 Application (EX1006) does not enable the Challenged Claims as required by § 112(a) because the disclosure does not permit a POSA to produce the claimed corn plant (claims 1-2 and 8) or practice the claimed method of producing a corn plant (claims 3-7) without undue experimentation. As I discussed above in Section VIII.A, the Challenged Claims require inserting exogenous DNA at a *specific location* within the corn genome. However, given the nature of the microprojectile bombardment technique used to generate the

TC1507 event (as discussed in Section VII.A above), that location reflected *random* chance. E.g., EX1066, 169-170 (noting the “high inter-transformant variability”: “As the integration of foreign DNA in the plant genome occurs via illegitimate recombination, it can take place at virtually any site. As a consequence, sequences flanking the transgene are different in independently obtained transformants.”). The specification of the ’378 Patent admits that such transformation events lead to the “*random integration* of the foreign DNA” into host organisms. EX1001, 7:31-33. As one commentator noted, such “random insertion of transgenes” amounts to “throwing a grenade into the genome.” EX1014 (Kloppenburg, *First the Seed*) 311.

79. Even as of today, it would be extraordinarily difficult to reproduce such random insertion of foreign transgenes into plants using gene editing technologies such as CRISPR-Cas9—a platform that did not exist in the 2003-2007 timeframe. Indeed, as an expert previously acknowledged on Patent Owner’s behalf, controlling where within the plant genome a transgene is inserted constitutes one of the “holy grails of plant biotechnology.” EX1017, Transcript of the March 5, 2024 Deposition of Paul Christou, Ph.D., in PGR2023-00022, 46:4-12.

80. In the 2003-2007 timeframe itself (which was that which I was asked to consider), it would have been essentially impossible to independently reproduce

TC1507—or for that matter any other particular transformation event obtained by microprojectile bombardment. Instead, a POSA would have needed access to TC1507 germplasm itself—that is, genetic material tracing its lineage back to the actual transformation event described in Example 1 of the '378 Patent as discussed in Section VII.A above. While not necessary to my conclusion, I note that during prosecution of a related European patent application, Patent Owner acknowledged that the claimed TC1507 “event in the absence of any physical sample would be almost impossible.” EX1003, 520.

81. Similarly, I note that Patent Owner filed numerous other patent applications on transgenic plants referencing seeds or other biological material deposited with recognized depositories. *E.g.*, EX1018, 4:42-54; EX1019, 5:61-6:12; EX1021, 5:8-26; EX1022, 6:34-7:6; EX1024, 19:12-35; EX1025, 10:39-55.

82. By contrast, the April 2004 Application (EX1006) fails to identify *any* deposit of biological material—much less a TC1507 plant including the exogenous foreign DNA at the specific location required by the claims and arising randomly from the microparticle bombardment described in the application (EX1006, 24:8-25:18).

83. Given this lack of a deposit, the April 2004 Application failed to enable a POSA to practice the Challenged Claims without undue experimentation. While it would have been possible for a POSA to generate a different

transformation event incorporating a “Cry1F encoding DNA molecule” and “a pat encoding DNA molecule” (as recited in claim 1) into the corn genome, the above-discussed randomness of the process would have essentially guaranteed that the genes were incorporated elsewhere (as compared to TC1507), with different unique flanking sequences. E.g., EX1066, 170 (“[S]equences flanking the transgene are different in independently obtained transformants.”). But as discussed in Section VIII.A above, the Challenged Claims require the particular flanking sequences uniquely characteristic of TC1507. In other words, a transgenic corn plant incorporating the first expression cassette (with the Cry1F gene) and the second expression cassette (with the PAT gene) elsewhere in the corn genome would **not** be covered by the Challenged Claims. Given the specificity of this requirement, it would have been essentially impossible for a POSA to practice the Challenged Claims without access to actual TC1507 germplasm deriving from the actual transgenic event described in the April 2004 Application.

84. I say “essentially impossible” to account for the underlying randomness of the process—just like one would say it is “essentially impossible” (as opposed to “literally impossible”) for monkeys randomly pressing typewriter keys to independently reproduce the complete works of William Shakespeare. In reality, of course, that chance is so small as to essentially be zero.

85. Likewise, even if a researcher used the exact same “microprojectile bombardment” technique as described in the April 2004 Application (EX1006, 24:29-25:7) with the exact same PHI8999A plasmid as described in the April 2004 Application (EX1006, SEQ ID NO:25) and targeted the exact same “[i]mmature embryos isolated from maize ears” as described in the April 2004 Application (EX1006, 24:31-25:1), the chance of recreating TC1507—including TC1507’s “unique” flanking regions and junctions (EX1006, 9:27-32)—would be essentially zero.

B. The *Wands* Factors Confirm the April 2004 Application Does Not Enable the Challenged Claims Under § 112

86. As noted in Section V above, I understand that the Board may consider the *Wands* factors in determining whether undue experimentation would have been required to practice a claimed invention. *See* above, ¶36. The *Wands* factors confirm that undue experimentation would have been required to practice the Challenged Claims based on the April 2004 Application as of its April 30, 2004 filing date given the lack of a deposit, as I explain below.

1. Breadth of the Claims

87. The Challenged Claims are simultaneously broad and specific. They are broad in the sense that they cover any corn plant including the required DNA incorporated into a particular location in the plant genome. At the same time, however, they are specific because the required location—defined by the recitation

of the flanking sequences in SEQ ID NO:26 at the 5' end and SEQ ID NO:27 at the 3' end—is a unique amalgamation comprising both natural corn DNA together with exogenous DNA incorporated during the transformation event.

88. Without ready access to the TC1507 plant itself, a POSA would not have been able to practice the Challenged Claims without undue experimentation as of April 30, 2004 based on the April 2004 Application.

2. Nature of the Invention

89. The Challenged Claims concern a transgenic corn plant and related methods of use comprising (1) a gene encoding a bacterial endotoxin conferring resistance to lepidopteran insects (i.e., Cry1F); and (2) a gene encoding a bacterial enzyme that eliminates herbicidal activity of glufosinate herbicides (i.e., PAT). EX1001, 85:24-41.

90. The claims require the specific integration of the DNA construct comprising these genes into the plant genome at a position defined by the flanking sequences recited in the claims and reflecting one random transformation event (i.e., TC1507) following physical bombardment of corn embryos with metal microprojectiles coated with a DNA insert incorporating the desired genes.

91. Such introduction of exogenous DNA stimulates the plant cell's "wound response" (EX1012, 186; EX1015, 250), with the associated "DNA repair mechanisms" (EX1013, 308) triggering a "panoply of enzymes" acting on the

exogenous DNA itself—often causing “degradation” of the DNA during the integration process (EX1015, 250; EX1016, 284). As a result, the incorporated DNA is often “truncated and otherwise rearranged.” EX1016, 284.

92. The TC1507 event underlying the Challenged Claims is itself a case in point. As Table 1 reflects and Patent Owner admitted during prosecution of a related European application, the TC1507 event was “not a straightforward insertion of the PHI8999A insert neatly into the wild-type genome.” EX1003, 329. Instead, there are “broken-up, complex, repeated/fragmented sequences[s]” at either end of PHI8999A,” including “regions 4, 5, 6, 7 and 8 at the 5' end and regions 10, 11, 12, 13, and 14 at the 3' end.” EX1003, 329. Regions 4, 5, 6, 7, and 8 are included in SEQ ID NO:26 at the 5' end of the DNA construct recited in Challenged Claim 1, while Regions 10, 11, 12, 13, and 14 are included in SEQ ID NO:27 at the 3' end. These regions and related junctions—combining corn DNA with foreign DNA—were created by “random” chance during the TC1507 event and are thus uniquely characteristic of that event. EX1001, 7:31-35. But those unique junctions and related flanking sequences are required to practice the Challenged Claims, as discussed in Section VIII.A above.

3. Level of Skill in the Art

93. While a POSA as of 2004 would have been highly educated (as noted in Section VII.B above) and able to transform plants with foreign genes (e.g.,

genes isolated from bacteria), inserting such genes into vectors, and using the vectors to incorporate the genes into plants, the level of skill in the art was not high in relevant respect—that is, concerning the Challenged Claims’ requirement of junction sequences specific to the TC1507 event (as discussed above in Section VIII). The relevant transformation technologies—for example, the “biolistics” technique of bombarding plant cells with microprojectiles as described in the ’378 Patent—did not allow a POSA to control where within the genome the exogenous DNA was incorporated.

94. Even today, an expert witness for Patent Owner describes the quest for such control as one of the “holy grails of plant biotechnology.” EX1017, 46:4-12. Nor did the level of skill in the art permit control as to whether and how the exogenous DNA was truncated or otherwise rearranged. As a result, a POSA could not reproduce a given transformation event and independently create plant cells with the exact junction sequences as the original event.

95. I also note that Patent Owner acknowledged this in connection with a related European patent application—explaining that “physical access to TC1507 germplasm” was required “to reproduce” the TC1507 event, as “[r]eproducing the event of the invention in the absence of any physical sample would be almost impossible.” EX1003, 520. Patent Owner acknowledged that even the “same plant” were “transformed many times with the same transgene,” each

transformation “would represent many different events because the transgene would incorporate in different place and orientations, and also because more or less flanking sequence from the transformation construct might be lost, duplicated, rearranged etc. during each transformation.” EX1003, 294 (emphasis original). Accordingly, as Patent Owner explained, the “junction sequences” would be different each time. EX1003, 294. Relevant literature confirms the same. E.g., EX1066, 170 (“[S]equences flanking the transgene are different in independently obtained transformants.”).

96. In a subsequent patent application, Patent Owner likewise explained that “multiple transgenic plant events created using the same genetic construct will not be identical,” as “plant genomes are very large, and in different events the transgene will have inserted at different locations within the genome.” EX1026, ¶3.

97. Similarly, in a different patent to a different transgenic event, Patent Owner explained that it provided a deposit of the transgenic plant seed in question because transgenic “‘events’ are random events and generally cannot be duplicated.” EX1018, 4:41-47. By contrast, the 2004 Application does not make any reference to a deposit of TC1507.

4. State of the Prior Art

98. As of April 30, 2004 (i.e., when Patent Owner filed its first utility application), microprojectile bombardment—the method used to generate the TC1507 event—constituted the state of the art for transformation of monocot plants such as corn. Modern gene editing technologies such as CRISPR-Cas9 were unknown.

99. The literature as of 2004 reflected significant limitations and lack of understanding concerning transgenic plants in general and microprojectile bombardment in particular. A POSA had a “relatively poor understanding of the mechanisms that control transgene expression, especially in monocots” such as corn. EX1016, Mehlo, *et al.*, “Structural Analysis of Transgene Rearrangements and Effects on Expression in Transgenic Maize Plants Generated by Particle Bombardment,” *Maydica* 45:277-287, 277 (2000) (2000 article noting that “little [was] known of the precise causes and mechanisms of transgene rearrangement,” and the “mechanism of DNA integration in transgenic plants” was “also poorly understood”); EX1033, Twyman, et al., “Foreign DNA: Integration and Expression in Transgenic Plants,” in *Genetic Engineering: Principles and Methods*, Vol. 24, 107 (2002) (“rather little is known about the actual mechanism of DNA integration, and there is currently no convenient way to control it”). The scientific literature also included “wide misconceptions” concerning transformation

technologies and transgene expression. EX1012, Kohli, et al., “The Quest to Understand the Basis and Mechanisms that Control Expression on Introduced Transgenes in Crop Plants,” *Plant Signaling & Behavior*, 185-195, 186 (2006).

100. While alternative methods of transformation (i.e., aside from microprojectile bombardment) were known as of April 30, 2004, such methods suffered from similar challenges. Aside from microprojectile bombardment, the most extensively used method at the time was *Agrobacterium*-mediated gene transfer. EX1064, K Veluthambi et al, The Current Status of Plant Transformation Technologies, *Current Science*, 84:368-380 (2003). However, *Agrobacterium*-based techniques were originally developed for dicots and proved more challenging to adapt for monocots such as corn. *Id.* They were also less versatile than microprojectile bombardment. EX1013, Altpeter et al., Particle bombardment and the genetic enhancement of crops: myths and realities, 15 *Molecular Breeding* 305–27 (2005). Moreover, while *Agrobacterium*-based techniques were sometimes perceived to be “cleaner” and more controllable than particle bombardment, closer studies indicated otherwise. E.g., *id.* (article co-authored by Dr. Paul Cristou, who later acknowledged that controlling where within the plant genome a transgene is inserted constitutes one of the “holy grails of plant biotechnology,” EX1017, 46:4-12).

101. Even more recent reports illustrate how *Agrobacterium*-based techniques lead to unpredictable insertions and rearrangements—consistent with the above-discussed limitations in the state of the art, which was even less developed in the 2003-2007 timeframe. *E.g.*, EX1065 (Gelvin, Stanton B. Integration of *Agrobacterium* T-DNA into the Plant Genome, 2017, ANNUAL REVIEW OF GENETICS, 51:195-217 (“T-DNA/plant DNA junctions are generally not clean, i.e., they are not comprised of precisely cleaved T-DNA borders precisely integrating into a plant sequence. Often deletions, insertions, and rearrangements occur at the junctions.”); EX1067 (F. Jupe et al. The complex architecture and epigenomic impact of plant T-DNA insertions. PLoS Genet. 2019 Jan 18;15(1) (analyzing “four randomly selected T-DNA lines revealed between one and seven insertions/rearrangements, and the length of individual insertions from 27 to 236 kilobases”); EX1068 (N. Kleinboelting et al, The Structural Features of Thousands of T-DNA Insertion Sites Are Consistent with a Double-Strand Break Repair-Based Insertion Mechanism, Molecular Plant, 8:1651-1664 (2015)) (noting “filler” DNA sequences regularly occurring on both the “left border” and “right border” of the T-DNA); EX1069 (An evaluation of new and established methods to determine T-DNA copy number and homozygosity in transgenic plants, Głowacka Plant, Cell & Environment, 39:908-917 (2016)) (“Comparison of segregation analyses and ddPCR of T1 progeny from 26 T0

plants showed that at least 19% of the lines carried multiple T-DNA insertions per locus, which can lead to unstable transgene expression....Insertions, deletions and complex rearrangements of both T-DNA and the host genome are in fact very common.”); EX1070 (B. Edwards et al. High-throughput detection of T-DNA insertion sites for multiple transgenes in complex genomes. BMC Genomics 23, 685 (2022)) (“Insertions, deletions and complex rearrangements of both T-DNA and the host genome are in fact very common....This prevalence of aberrant insertion has almost become the ‘rule’ of T-DNA insertion, rather than the exception.”).

5. Level of Predictability in the Art

102. The level of predictability in relevant respect is low; transformation of plant cells via a biolistic event is a random and unpredictable process.

“[P]roducing useful transgenic plants” was “often a matter of ‘pot luck.’”

EX1033, 108. Integration of the foreign DNA into the plant genome depends on plant “proteins involved in DNA replication, repair and recombination,” and it was “highly unpredictable” even after 2004 as to how “such proteins interact with” the foreign DNA researchers desired to integrate. EX1012, 185.

103. In particular, “the exact way in which these proteins interact with exogenous DNA and the plant’s own genome is unpredictable, leading to wide variation in locus structure.” EX1015, 255.

104. Indeed, “[b]oth the position of integration and the structure of the transgenic locus vary considerably among independent transformants, and both these factors have a profound effect on transgene expression.” EX1033, 107. Even “transgenic plants containing the same transgene(s) often exhibit unpredictable and to some extent unstable expression patterns.” EX1012, 185; *see also id.*, 187 (“[E]ven subtle changes in the integrated transgene construct can cause unpredictable expression patterns associated with altered DNA cytosine methylation patterns in the transgene and the flanking endogenous sequences.”)

105. Summarizing the situation even as of December 2008, Patent Owner acknowledged in a separate patent application that “the skilled artisan may need to create tens to thousands of events with a given construct to identify a single event that possesses all desired qualities.” EX1026, ¶3. If anything, the level of skill and predictability in the art was even lower in the earlier 2003-2007 timeframe.

106. Patent Owner itself noted the unpredictability of the art:

TC1507 was a biolistic event, in other words the PHI8999 construct was shot into the tissue at high velocity by microprojectile bombardment. The sequence of the introduced plasmid was known, but nothing was known about, for example, the orientation of the resultant insert, whether or not and if so to what extent, it had been fragmented and/or truncated, or its location in the plant genome.

EX1003, 294 (emphasis original).

6. Amount of Direction Provided by the Inventor

107. While Example 1 in the April 2004 Application (EX1006, 24:8-28:18) describes *how* the TC1507 event was generated—that is, by coating metal particles with the transgene insert PHI8999A (SEQ ID NO:25) and bombarding immature corn embryos with these microprojectiles—it does not even attempt to disclose how others could independently reproduce TC1507. On the contrary, the application acknowledges that transformation led to “random integration of the foreign DNA,” with corresponding “flanking regions characteristic and *unique* for each transformant.” EX1006, 9:27-29.

108. The remaining examples in the application concern TC1507 and describe the extensive sequencing and verification efforts required to characterize the genetic sequence of those flanking regions. EX1006, 28:22-43:3.

7. Existence of Working Examples

109. As previously explained, the April 2004 Application discloses only a single working example—the TC1507 event itself. Moreover, as Figure 1 reflects, the TC1507 event “was not a straightforward insertion of the PHI8999A insert (SEQ ID NO: 25) neatly into the wild-type genome.” EX1003, 329. Instead, Figure 1 confirms that this single example includes many “broken-up, complex, repeated/fragmented sequence[s]” at either “end” of PHI8999A” (EX1003, 329)—

consistent with the above-discussed state of the art concerning plant transformation.

110. As the Patent Owner has acknowledged, identifying a transgenic plant with the desired qualities from a single DNA construct requires extensive experimentation. It requires the novel transgene(s) to be intact expressing at a level necessary to deliver the trait in the tissues where it is required. The transgene(s) must perform in multiple germplasm backgrounds and under a wide range of environmental conditions. Also, it cannot disrupt any native genes, which could have a deleterious impact on yield. The so-called position effect describes how the expression of a transgene is influenced by a combination of its location in the genome and nearby DNA regulatory sequences which can include the flanking sequence. In TC1507, the Patent Owner identified 9 novel discrete segments of DNA in the 5' flanking sequence and 5 novel segments in the 3' flanking sequence that were part of the original gene construct. This flanking DNA comes from both native and foreign DNA due to DNA repair mechanisms. There is a large degree of random chance on the DNA sequences that are inserted in the flanking sequence. The chance that this unique set of sequences would be recreated during a transformation experiment with tens of thousands or even hundreds of thousands of new transformants is so vanishingly small as to be zero.

8. Quantity of Experimentation Needed to Make or Use the Invention

111. Given the April 2004 Application's failure to identify a deposit of TC1507, it would have been essentially impossible at the time even with extensive experimentation for a POSA to make or use the inventions of the Challenged Claims.

112. As Patent Owner explained during prosecution of a related European Patent, reproducing the event and thereby recreating TC1507's junction sequences—required in all of the Challenged Claims (as discussed above in Section VIII.A)—would have required “physical access to TC1507 germplasm, or other suitable genetic material.” EX1003, 520. Those junction sequences are “unique” to any event (EX1006, 9:27-31) and “could not routinely be obtained again by transformation” (EX1003, 520). Instead, as Patent Owner stressed to the EPO, “[r]eproducing the event of the invention in the absence of any physical sample would be almost impossible.” EX1003, 520.

113. Moreover, given the unpredictability of the available methods for inserting transgenes into corn genome (as discussed above in Section IX.B.5), the April 2004 Application would at most be an invitation for one skilled in the art to pursue a research project attempting to identify TC1507 after transforming a plant cell with the transgenes. Patent Owner acknowledged in a separate patent application that “the skilled artisan may need to create tens to thousands of events

with a given construct to identify a single event that possesses all desired qualities.” EX1026, ¶3. *See also* EX1066, 169 (“This high inter-transformant variability is generally undesirable because it necessitates the screening of large numbers of transformants in order to identify individuals with an acceptable expression level and an expected phenotype. The time and effort spent on screening individual transformants represents a major bottleneck for high-throughput testing of transgene constructs.”)

X. BARBOUR (EX1009) ANTICIPATES OR RENDERS OBVIOUS ALL CHALLENGED CLAIMS

114. Barbour (EX1009)—a patent publication corresponding to Patent Owner’s April 2004 Application—discloses the claimed TC1507 event and anticipates or renders obvious all Challenged Claims as discussed below.

115. I understand that Barbour constitutes prior art to all of the Challenged Claims of the ’378 Patent because it was published on February 16, 2006, which is more than one year before July 6, 2007—the earliest conceivable effective filing date of the Challenged Claims given that the April 2004 Application does not enable the Challenged Claims as required by § 112 (as explained in Section IX above).

116. I understand that in order for the Challenged Claims to be entitled to an effective filing date even of July 6, 2007, the application filed on that date would need to practice the Challenged Claims without undue experimentation. I

was not asked to assess that issue. Instead, as explained here, Barbour anticipates or renders obvious all Challenged Claims even if one assumed the July 6, 2007 date applied. Thus, for purposes of this analysis, I have focused exclusively on Barbour as well as background information a POSA would have known as of July 6, 2006 (i.e., one year before July 6, 2007).

A. Barbour Anticipates Claims 1-2 and 8

117. Barbour discloses the same TC1507 event underlying the Challenged Claims. In particular, Barbour discloses the unique flanking sequences that distinguish TC1507 from other transgenic events. EX1009, ¶28 (“Linear map showing the transgenic insert PH18999A, as well as the sequences flanking the transgenic insert”).

1. Barbour Discloses the Purported Inventions as Claimed

a. Independent Claim 1: Corn Plant Comprising DNA Construct

118. As shown in the table below, Challenged Claim is identical to Barbour’s Claim 20 aside from the preamble (in which Challenged Claim 1 recites “[a] corn plant comprising a DNA construct,” whereas Barbour’s Claim 20 recites “[a] DNA construct”) and the concluding language following “a 3’ transcriptional terminator from (CaMV) 35S.”

Challenged Claim 1 (EX1001, 85:24-41)	Barbour Claim 20 (EX1009, 45-46)
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<i>A corn plant comprising</i> <i>a DNA construct, said</i> DNA construct comprising a first and a second expression cassette, wherein said first expression cassette in operable linkage comprises: (a) a maize ubiquitin promoter; (b) a 5' untranslated exon of a maize ubiquitin gene; (c) a maize ubiquitin intron; (d) a Cry1F encoding DNA molecule; and (e) a 3' ORF25 transcriptional terminator; and said second expression cassette comprising in operable linkage (i) a CaMV 35S promoter; (ii) a pat encoding DNA molecule; and (iii) a 3' transcriptional terminator from (CaMV) 35S <i>comprising the nucleic acid sequence of positions 5843 to 6032 of SEQ ID NO: 25;</i> <i>and wherein the first and second expression cassettes are flanked by</i>	A DNA construct comprising: a first and second expression cassette, wherein said first expression cassette in operable linkage comprises: (f) a maize ubiquitin promoter; (g) a 5' untranslated exon of a maize ubiquitin gene; (h) a maize ubiquitin intron; (i) a Cry1F encoding DNA molecule; and (j) a 3' ORF25 transcriptional terminator; and said second expression cassette comprising in operable linkage (i) a CaMV 35S promoter; (ii) a pat encoding DNA molecule; and (iii) a 3' transcriptional terminator from (CaMV) 35S
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<i>SEQ ID NO: 26 at the 5' end and</i> <i>SEQ ID NO: 27 at the 3' end.</i>	
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119. Barbour’s claim 21 descends from claim 20 and discloses “[a] plant comprising the DNA construct of claim 20,” while claim 22 descends from claim 21 and specifies that “said plant is a corn plant.” Barbour’s claim 22 is therefore identical to Challenged Claim 1 with the exception of Challenged Claim 1’s recitation that:

- (1) the (CaMV) 35S transcriptional terminator comprises “the nucleic acid sequence of positions 5843 to 6032 of SEQ ID NO: 25; and
- (2) “the first and second expression cassettes are flanked by SEQ ID NO: 26 at the 5' end and SEQ ID NO: 27 at the 3' end.”

However, a POSA would understand that these recitations simply characterize aspects of the TC1507 Event, which both Barbour and the ’378 Patent disclose in identical terms.

120. Barbour discloses the same “SEQ ID NO: 25,” “SEQ ID NO: 26,” and “SEQ ID NO: 27” as the corresponding sequences disclosed in the ’378 Patent while also characterizing these sequences in the same way:

- Barbour and the ’378 Patent both disclose that SEQ ID NO: 25 “represents the DNA molecule used to transform maize line TC1507,”

and in particular that “[t]his sequence represents insert PHI8999A.”

EX1001, columns 59-60; EX1009, 32

- Barbour and the '378 Patent both disclose that SEQ ID NO: 26 and NO:27 constitute the “transgene/flanking insertion region” (EX1001, 3:65-68, EX1009, ¶12) with
 - SEQ ID NO: 26 the “5' flanking maize DNA sequence” (EX1001, 4:13-15; EX1009, ¶15); and
 - SEQ ID NO: 27 the “3' flanking maize DNA sequence” (EX1001, 4:23-25; EX1009, ¶16)

121. In sum, the additional language in Challenged Claim 1 recites explicitly what a POSA would understand was already present in Barbour's claim 22.

122. In particular, Barbour separately discloses SEQ ID NO: 24 as “the transgenic insert in maize line TC1507 as well as the sequence flanking the insertion sites.” EX1009, 26; *see also* Table 1 (“Sequence summary for event TC1507 insert,” delineating each region within SEQ ID NO: 24). A POSA would recognize that SEQ ID NO: 24 reflects the combination of sequences 25, 26, and 27—with 26 at the 5' end, 25 in the middle, and 27 at the 3' end. The '378 Patent includes the same disclosure of SEQ ID NO: 24.

123. The '378 Patent also includes Challenged Claim 8, which depends from Claim 1 and recites that “[t]he DNA construct comprises the polynucleotide of SEQ ID NO: 24.” Barbour anticipates Challenged Claim 8 as detailed in Section X.A.1.b.ii below. I understand that if a narrower dependent claim is anticipated by a prior art reference, the broader independent claim is also necessarily anticipated by that same reference provided that it is prior art to both claims. Here, Barbour is prior art to both claims 1 and 8 given that they are not enabled by the April 2004 Application. Thus, Barbour’s anticipation of the dependent claim further confirms that Barbour also anticipates the independent claim from which Challenged Claim 8 depends.

b. Dependent Plant Product Claims 2 and 8

124. Barbour anticipates Challenged Claims 2 and 8, which recite the “corn plant of claim 1” while specifying additional requirements Barbour also discloses.

i. Claim 2: Corn Plant is a Seed

125. Challenged Claim 2—requiring that “the corn plant is a seed”—is anticipated by the disclosures in Barbour discussed above (in connection with claim 1) and related teaching that “plant” includes “seeds.” EX1009, ¶50; *see also id.*, ¶26 (disclosing “[t]he corn plant and seed TC1507” as “an aspect of the invention:); *id.*, ¶50 (“[T]he term ‘plant’ includes reference to whole plants [and] seeds....”).

ii. Claim 8: SEQ ID NO: 24

126. Challenged Claim 8—requiring that “the DNA construct comprises the polynucleotide of SEQ ID NO:24”—is anticipated by Barbour’s above-discussed disclosure together with Barbour’s teaching of “SEQ ID NO 24” and related explanation that this sequence—identical to the SEQ ID NO:24 disclosed in the ’378 Patent—“represents the transgenic insert in maize line TC1507 as well as the sequence flanking the insertion sites.” EX1009, pages 26-31.

127. Specifically, a POSA would understand that SEQ ID NO:24 reflects the TC1507 event in its entirety and constitutes a particular species that Barbour discloses for use in connection with Barbour’s claim 22, which anticipates Challenged Claim 1 as explained above in Section X.A.1.a. Claim 8 specifically requires SEQ ID NO:24, whereas Challenged Claim 1 is broader in the sense that it allows for variations in the sequence in the middle of the DNA construct (e.g., different forms of the cry1F gene—other than that specified by SEQ ID NO:24) so long as those variations are downstream of sequence 26 at the 5' end and upstream of sequence 27 at the 3' end. But even claim 1 requires the flanking sequences at each end unique to the TC1507 event, as discussed in Section VIII above.

2. Barbour Enables Claims 1-2 and 8 For Purposes of the Anticipation Analysis

128. As noted in Section V.A above, I have been informed that an anticipatory prior art reference must be enabled. In particular, I have further been

informed that the relevant question is whether a POSA could take the description of the invention in the prior art reference and combine it with his own knowledge of the particular art and from this combination be put in possession of the invention on which a patent is sought. In the context of plants in particular, I have been informed that the sale of a reproducible plant variety may enable an otherwise non-enabled printed publication disclosing that plant—that is, so long as the plant is commercially available.

129. Accordingly, Barbour is enabled for purposes of anticipating Challenged Claims 1-2 and 8 because Patent Owner had commercialized TC1507 corn more than a year before July 6, 2007, and further because a POSA could screen commercially available corn to identify germplasm expressing the TC1507 event, thereby possessing the invention as claimed. As explained below, Barbour itself discloses such screening methods and related kits. Such kits were also commercially available well before July 6, 2007.

a. TC1507 Germplasm Was Publicly Available Given Patent Owner’s Commercialization

130. Barbour is enabling prior art because a POSA could have taken Barbour’s “description of the invention” as of Barbour’s February 16, 2006 publication date and “combine[d] it with [their] own knowledge of the particular art” as of that date “and from this combination be put in possession of the invention” of the Challenged Claims.

131. By Barbour's publication date, the TC1507 event had been commercialized under Patent Owner's "Herculex" trademark and widely planted in the United States over the course of three growing seasons (i.e., 2003, 2004, and 2005).

132. Multiple reports and articles taught that "Herculex 1" reflected the TC1507 Event. *E.g.*, EX1011, 1128 (USDA report: "corn event TC1507 (Herculex™)"; EX1032; EX1034, 104; EX1035, 936; EX1036, 1347; EX1037.

133. Reports abounded in the agricultural trade press that TC1507/Herculex I was available starting in the 2003 growing season and continuing on to the 2004 and 2005 growing seasons. *E.g.*, EX1047 (November 2002 article noting that "[c]orn growers now have the option of purchasing" Patent Owner's "Herculex I"); EX1048 (February 2003 noting that Patent Owner's "Herculex I...seed type is slated to be available in farm fields in 2003"); EX1049, 8 (identifying "TC1507" among the "seed products available for the 2004 planting season"); EX1050 (Summer 2005 article noting "wider availability of Herculex I insect-resistant corn hybrids").

134. I understand that in European patent office proceedings, Patent Owner cited contractual provisions purportedly barring farmers from using TC1507 seed for "research purposes" or "transmitting the seed onwards to third parties" for such purposes. EX1003, 543 (emphasis original). However, I have been informed that

such alleged restrictions would not apply to bulk corn harvested (and then sold into commerce, making it commercially available) from the TC1507 seed that farmers planted. Such corn kernels would continue to express the TC1507 event. *See* EX1003, 294 (noting that “[a]ny given event can be transmitted by breeding from the original transformant plant, thereby to create descendent plants with the same event.”).

b. A POSA Could Have Detected the Presence of TC1507 in Commercially Available Corn Without Undue Experimentation

135. As disclosed in Barbour and confirmed by the availability of commercial test kits, a POSA could have identified TC1507 in bulk corn commercially sold following harvest prior to July 6, 2006—confirming that a POSA had possession of the invention as disclosed in Barbour.

i. Barbour Discloses Methods and Related Kits For Detecting TC1507 in Food or Feed Products

136. Aside from disclosing the “corn plant TC1507” itself as detailed above in Section X.A, Barbour discloses “assays for detecting the presence of corn plant TC1507 DNA in a sample” and in particular “detection of the transgene/flanking insertion region” underlying the Challenged Claims. EX1009, ¶¶2-3. Given Barbour’s teaching of such “methods for identifying [the] novel corn plant designated TC1507” using “primers or probes which specifically recognize the 5' and/or 3' flanking sequence of TC1507” (EX1009, ¶9), a POSA could have

readily performed such assays on commercially available corn and thereby identified kernels (i.e., corn seed) from TC1507 corn plants.

137. In particular, Barbour discloses a “DNA detection kit for identifying maize event TC1507 in biological samples,” with the kit including a probe that preferably includes a sequence that “corresponds to a specific region comprising part of the 5' or 3' flanking region of event TC1507.” EX1009, ¶24; *see also id.*, ¶58 (describing use of a “‘specific probe’ for identifying event TC1507 in biological samples”); *id.*, ¶60 (disclosing “kit” for “identification of the event TC1507 in biological samples,” such as “plant material, or material comprising or derived from plant material, such as but not limited to food or feed products”).

138. Barbour also discloses detailed procedures for developing such kits and performing such assays using polymerase chain reaction (PCR) or “or other conventional nucleic acid amplification methods.” EX1009, ¶56; *see also id.*, ¶¶75-76, ¶¶106-108.

139. Moreover, although Barbour’s “positive tissue DNA extract control” (EX1009, ¶107) was one way to identify the TC1507 sequence in an extract, a POSA would have understood that it was also possible to screen for TC1507 using a negative control. Such a negative control would have been available to a POSA—given Barbour’s disclosure of SEQ ID NO:24, a POSA could have identified corn samples that unquestionably were not TC1507. Further, a POSA

could have run PCR products from the test sample and the negative control along with size ladders to see if a correct size fragment is produced from the test sample, which should be absent or of a wrong size in the negative control. Alternatively, a POSA could have used PCR to amplify the fragments using Barbour's primers and sequence the fragments. For example, if a POSA followed steps similar to those Barbour taught in Examples 2-9 (PCR amplifying, screening for positive clones, and sequencing the fragments), the POSA would obtain sequences that could be compared to SEQ ID NO: 24 to determine if they reflect the TC1507 event. Such techniques (i.e., PCR and sequencing methods) were routine and widely available in the 2003-2007 timeframe, such that it was well within the skill of a POSA to determine whether a sample contained a specific DNA fragment so long as the POSA knew the sequence of the DNA fragment (which here is disclosed in Barbour) and/or knew the sequences of primers that were effective for amplifying the DNA fragment (which here are also disclosed in Barbour). Indeed, commercial sequencing services were available at the time for performing such work.

140. Accordingly, given Barbour's disclosures (including the primer sequences), a POSA could have screened commercially available corn from the 2003, 2004, or 2005 growing seasons (i.e., more than one year before July 6, 2007) and thereby gained possession of TC1507 as claimed. Barbour specifically discloses that the "methods and kits encompassed by the present invention "could

be used “to identify event TC1507 in plants, plant material or in products such as, but not limited to, food or feed products (fresh or processed) comprising, or derived from plant material.” EX1009, ¶25. By 2006, TC1507 was widely found in “food or feed products” commercially sold without restriction. *See* Section X.A.2.a above.

ii. TC1507 Detection Kits Were Commercially Available

141. I also note that test kits for detecting TC1507 corn were commercially available over a year before July 6, 2007. *E.g.*, EX1045 (August 2003 SEC filing noting availability of test “able to detect, in only 10 minutes, one Cry1F Herculex™ I corn kernel in 600 non-Cry1F Herculex™ corn kernels”); EX1044, 14-15 (August 2003 SEC filing noting USDA approval of kit for “detection of Cry1F Herculex™”); EX1051 (October 2003 article noting availability of “QuickStix” test to detect Herculex); EX1052 (November 2003 article noting availability of test kits for detection of Herculex); EX1053 (December 2003 article noting availability of “detection kit” to determine “presence...of Herculex in the corn seeds”). This further confirms my conclusion that a POSA would have had “possession of the invention” of the Challenged Claims by February 2006 in view of Barbour and a POSA’s own knowledge.

142. In particular, a POSA as of February 2006 would have been aware that TC1507 event-specific kits were available to determine whether commercially

available corn contained TC1507 germplasm. The exact form of that commercially available corn is immaterial. As defined in the '378 Patent, “plant” (as in the “corn plant” of Challenged Claim 1) encompasses even individual “plant cells.” EX1001, 10:8-10.

143. By way of example, a POSA seeking access to TC1507 (as disclosed in Barbour) could have obtained commercially available bulk corn following the 2003, 2004, or 2005 growing seasons and then planted the kernels in test rows using glufosinate as a selection agent—much like Barbour itself discloses in connection with the identification of the TC1507 event itself. EX1009, ¶85. To the extent that corn plants grew from the kernels despite the presence of the herbicide, it would have indicated the presence of the PAT gene incorporated into TC1507 along with several other transgenic corn products commercially available at the time. A POSA could have then harvested ears from the corn plants and used commercially available test methods to determine whether the corn harvested from particular ears reflected the TC1507 event or some other transgenic event.

c. Enablement for Priority Purposes Versus Enablement for Anticipation Purposes

144. I understand that Barbour (EX1009) is the patent publication corresponding to the April 2004 Application, which I discussed in Section IX above when explaining why the April 2004 Application fails to enable the Challenged Claims because it does not refer to any deposit of TC1507. As

explained immediately above, Barbour combined with a POSA's own knowledge (including the commercial availability of TC1507 as well as methods of screening for TC1507) would have put a POSA in possession of claims 1-2 and 8 of the '378 Patent by February 2006—meaning that Barbour is enabled for anticipation purposes.

145. I have been informed that the standard for whether a prior printed publication such as Barbour is enabled for anticipation purposes differs from the standard for whether a patent specification is enabled under § 112(a) or whether claims are entitled to an earlier effective filing date based on a previously filed application (which requires that the previously filed application enable the claims under § 112(a).

146. I have been informed that for purposes of anticipation, the question is whether a POSA could obtain the necessary information *if they wanted to*. As discussed above, a POSA could have used Barbour's disclosures and/or commercially available TC1507 detection kits to screen bulk corn as of Barbour's February 2006 publication date and thereby obtain possession of TC1507 (as reflected in claims 1-2 and 8) if the POSA wanted to.

147. I have also been informed that for purposes of § 112(a), the question is whether the necessary materials for practicing the claimed invention were *readily available* to the public. For the reasons explained in Section IX, TC1507

was not readily available to the public as of April 30, 2004 when the 2004 Application was filed. I understand that patent applicants can make biological materials readily available by depositing them in an established repository and committing to make those materials publicly available if the corresponding patent application is granted and becomes an issued U.S. patent. Such deposits ensure the availability of the material in question regardless whether or not the patent owner continues to sell it. However, as discussed in Section IX above, the 2004 Application does not refer to any deposit—in contrast to other instances in which Patent Owner has deposited transgenic plant germplasm. *E.g.*, EX1018, 4:42-54; EX1019, 5:61-6:12; EX1021, 5:8-26; EX1022, 6:34-7:6; EX1024, 19:12-35; EX1025, 10:39-55.

B. Ground 2: Barbour Anticipates or Renders Obvious Claims 3-4 and 7

148. Barbour also anticipates or at minimum renders obvious Challenged Claims 3-4 and 7, which depend from Challenged Claim 1 and recite methods of “producing an insect resistant corn plant” per claim 3’s preamble. EX1001, 86:24-25.

1. Barbour Discloses or Renders Obvious the Purported Inventions as Claimed

a. Claim 3: Breeding Method

149. Claim 3 requires “a method of producing an insect resistant corn plant comprising:

- (a) breeding with an insect resistant corn plant comprising in its genome DNA the DNA construct of claim 1 and
- (b) selecting a progeny of (a) by analyzing the genome of the progeny for the presence of the DNA construct of claim 1.”

EX1001, 86:26-30.

150. Barbour’s paragraph 22 discloses such “methods of producing an insect resistant corn plant that comprise the steps of: (a) sexually crossing a first parental corn line comprising the expression cassettes of the present invention, which confers resistance to insects, and a second parental corn line that lacks insect resistance, thereby producing a plurality of progeny plants; and (b) selecting a progeny plant that is insect resistant.” EX1009, ¶22. Similarly, Barbour’s paragraph 49 discloses that “[a]n insect resistant TC1507 corn plant can be bred by first sexually crossing a first parental corn plant consisting of a corn plant grown from the transgenic TC1507 corn plant and progeny thereof derived from transformation with the expression cassettes of the present invention that confers insect resistance, and a second parental corn plant that lacks insect resistance, thereby producing a plurality of first progeny plants.”

151. Barbour likewise discloses that “one aspect of the invention” includes incorporating a “DNA construct” with the “two transgene expression cassettes” of

PH18999A. EX1009, ¶8. Barbour further discloses that these expression cassettes are associated with Event TC1507. EX1009, ¶¶84-87.

152. A POSA would therefore understand that Barbour's paragraphs 22 and 49 disclose methods of breeding involving an insect resistant corn plant comprising the DNA construct of claim 1 as detailed above in Section X.A.1.a. As detailed therein, the "DNA construct" of Barbour's claim 20 is the same as that in Challenged Claim 1.

153. Barbour also discloses selecting particular plants resulting from the initial breeding process by analyzing their DNA as required by claim 3's element (b). Barbour's claim 54 concerns a method of "producing an insect resistant corn plant comprising breeding with a plant of claim 51 or 52, and selecting progeny by analyzing for at least one nucleotide sequence selected from the group consisting of SEQID NO: 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56 and 57." As explained above in Section VIII.A, sequence IDS 45-57 are unique to the TC1507 event, with sequences 45-52 reflecting junction sequences included in SEQ ID NO:26 and sequences 53-57 reflecting junction sequences included in SEQ ID NO:27. Moreover, a POSA would understand that Barbour's claim 54 is applicable for use with the method disclosed in paragraph 22 and also the closely related method disclosed in paragraph 49.

154. At minimum, it would have been obvious to practice the method disclosed in Barbour’s paragraph 22 (and also that in paragraph 49) by incorporating the technique disclosed in Barbour’s claim 54—that is, screening the progeny for the presence of the DNA construct unique to the TC1507 event and claimed by claim 1. Such screening techniques were standard in the transgenic plant field as of Barbour’s February 2006 publication date, and a POSA would have had reason to use such screens as an efficient and reliable means to analyze the results of the TC1507 breeding process. A POSA would have had a reasonable expectation of success when using such screens with Barbour’s paragraph 22 and/or 49 given that they were standard techniques in the 2003-2007 timeframe.

b. Claim 4: Using Second Plant

155. Claim 4 depends from claim 3 and specifies that the breeding be “with a second plant” (EX1001, 86:31-33)—distinguishing the method from self pollination (i.e., in which pollen from a given corn plant’s tassel fertilizes silks within an ear of that same corn plant). Barbour’s paragraph 22 discloses or at minimum renders obvious the method of claim 3 (as discussed immediately above) and further discloses that the “second parental corn line...lacks insect resistance,” thus distinguishing it from the “first parental corn line comprising the expression cassettes of the present invention, which confers resistance to insects.” EX1009 ¶22; *see also id.*, ¶23 (noting that the disclosed insect resistant corn plant can be

“crossed with compatible corn varieties” rather than “self pollinated”). Barbour’s paragraph 49 likewise discloses or at minimum renders obvious the method of claim 3 (as discussed immediately above) and further discloses that the “second parental corn line...lacks insect resistance.”

156. Barbour therefore discloses the requirement distinguishing claim 4 from claim 3 and therefore anticipates claim 4 or at minimum renders it obvious for the same reasons Barbour anticipates and at minimum renders obvious claim 3.

c. Claim 7: Yielding Insect Resistant Corn Plant

157. Claim 7 depends from claim 3 and requires that the “progeny comprises the insect resistance of the insect resistant corn plant of (a).” EX1001, 86:38-39. Barbour’s paragraph 22 discloses or at minimum renders obvious the method of claim 3 (as discussed above) and further discloses that the method yields “an insect resistant corn plant.” EX1009, ¶22. Barbour’s paragraph 49 likewise discloses or at minimum renders obvious the method of claim 3 (as discussed above) and further discloses that the method involves “selecting a first progeny plant that is resistant to insects. EX1009, ¶49.

158. Barbour therefore discloses the requirement distinguishing claim 7 from claim 3 and therefore anticipates claim 7 or at minimum renders it obvious for the same reasons Barbour anticipates and at minimum renders obvious claim 3.

2. Barbour Enables Claims 3-4 and 7 Under § 102

159. Barbour enables Challenged Claims 3-4 and 7 under § 102 for the same reasons Barbour enables Challenged Claims 1-2 and 8 under §102. As explained above in Section X.A.2, a POSA could have obtained TC1507 germplasm from commercially available bulk corn as of Barbour's February 2006 publication date given that Patent Owner had previously commercialized TC1507. A POSA could likewise have used that TC1507 germplasm to breed additional insect resistant corn plants as recited in claims 3-4 and 7.

C. Ground 3: Barbour in View of a POSA's Knowledge Renders Obvious Claims 5-6

160. Barbour in view of a POSA's knowledge renders obvious claims 5-6, which depend from claim 3 and specify which corn plant in the claimed breeding process serves as the "pollen parent." A POSA would have known that any given corn plant has separate male and female flowers, with the male flowers located on the tassel and the female flowers located on the ear, which contains numerous ovules and associated silks. EX1049, 1; EX1058, 1:29-31; EX1059, 737; EX1060, 131. Each ovule represents a potential corn kernel, which develops if the ovule receives pollen from a tassel.

161. A POSA likewise would have known that when breeding a transgenic corn plant with another corn plant (as covered by method claim 3), the transgenic corn plant can serve as "either the female or male parent." EX1061, 1409; *see also*

EX1062, 207-208; EX1063, 24:7-14. A POSA indeed would have known how to control pollination by mechanical means. EX1049, 1 (discussing treatment of the “plant that is to be used as a female”).

162. Given the competitive nature of the corn market (in which seed companies continually update their product offerings and offer farmers new varieties each growing season), there was a commercial need to continue developing new corn lines by cross-breeding existing lines with desirable properties. E.g., EX1049. This need was particularly pronounced with transgenic lines such as TC1507 given that transgenes are typically inserted initially into “agronomically inferior germplasm...selected specifically for its ability to provide a relatively high rate of successful transformation events.” EX1049, 3. In other words, when generating an initial transgenic event, a POSA would seek to integrate the foreign DNA into a corn variety that had an established track record of success with previous transformations—even though the variety does not necessarily perform well in the field. A POSA would take this approach given the ability to breed the resultant transformed plant with a different plant having more desirable agronomic properties. This approach is effective given that “transgenes are genetically dominant,” such that “only one line of a hybrid needs to contain the transgene for it to be expressed in the hybrid.” EX1049, 4.

163. To summarize, there was market pressure to solve a problem (i.e., the need to develop new transgenic corn lines from an existing one) and two identified, predictable solutions (i.e., using the transgenic line as either the male or the female). A POSA therefore had good reason to pursue both known options, which were within the POSA's technical grasp. A POSA would also have had a reasonable expectation of success given Barbour's own confirmation that the transgenic TC1507 line included both "pollen" and "ovules." EX1009, ¶26.

164. Claim 5 depends from claim 3 and specifies that the "insect resistant corn plant" used in the crossing is the "pollen parent" (EX1001, 86:34-35)—in other words, the "male" parent, which produces pollen to fertilize ovules in the female flower. Claim 5 merely recites one of the two identified, predictable solutions discussed above (i.e. for breeding transgenic plants into elite germplasm to have more desirable agronomic properties than the original transgenic event) and therefore is obvious over Barbour in view of ordinary skill and common sense. It would not have been inventive for a POSA to use the original transgenic (insect resistant) corn plant as the male in the crossing.

165. Claim 6 depends from claim 3 and requires that the "second plant" be the "pollen parent"—meaning that the "insect resistant corn plant" is the "female" parent into which the pollen is deposited. Claim 6 merely recites the other of the

two identified, predictable solutions discussed above and therefore is obvious over Barbour in view of ordinary skill and common sense.

166. Barbour enables Challenged Claims 5-6 for prior art purposes (i.e., under § 102) for the same reasons Barbour enables Challenged Claim 3 under § 102. *See* Section X.B.2 above.

XI. CONCLUSION

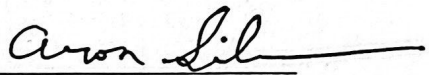
167. In summary, I have concluded that claims 1-8 of the '378 Patent lack novelty and are obvious in view of the prior art, and therefore claims 1-8 are unpatentable under 35 U.S.C. §§ 102 and 103.

168. I currently hold the opinions expressed in this declaration. But my analysis may continue, and I reserve the right to supplement my expert opinions in the future to respond to any arguments that Patent Owner or its expert(s) may raise and to take into account new information as it becomes available to me.

169. In signing this declaration, I recognize that the declaration will be filed as evidence in a contested case before the Patent Trial and Appeal Board of the United States Patent and Trademark Office. I also recognize that I may be subject to cross-examination in the case and that cross-examination will take place within the United States. If cross-examination is required of me, I will appear for cross-examination within the United States during the time allotted for cross-examination.

170. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Dated: June 13, 2024

By: 
Dr. Aron Silverstone

APPENDIX A – MATERIALS CONSIDERED

Exhibit	Description
1001	U.S. Patent No. 8,901,378
1002	Prosecution History of U.S. Patent No. 8,901,378
1003	Prosecution History of European Patent Application No. 04 751 097.9
1004	Prosecution History of European Patent Application No. 15 168 051.9
1005	Provisional Application No. 60/467,772
1006	Non-Provisional Application No. 10/837,105 (“April 2004 Application”)
1009	U.S. Patent Publication No. 20060037095 (“Barbour”)
1010	https://www.corteva.com/who-we-are/our-history.html
1011	U.S. Department of Agriculture Budget Summary and Annual Performance Plan 2006
1012	A. Kohli et al., <i>The Quest to Understand the Basis and Mechanisms that Control Expression of Introduced Transgenes in Crop Plants</i> , Plant Signaling & Behavior 1:4, 185-195 (2006)
1013	F Altpeter et al, <i>Particle bombardment and the genetic enhancement of crops: myths and realities</i> , Molecular Breeding 15:305–327 (2005)
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