

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. TBD
Patent No. 10,947,555

Case No. TBD
Patent No. 11,149,283

Case No. TBD
Patent No. 11,299,745

DECLARATION OF DR. ARON SILVERSTONE, Ph.D.

Inari Exhibit 1054 Inari v Corteva

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I, Aron Silverstone, Ph.D., hereby declare under penalty of perjury:

I. INTRODUCTION

1. 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. A true and correct copy of my curriculum vitae describing my background and experience is found at EX1055.

2. I understand that Patent Owner Corteva Agriscience LLC (“Corteva”) is the assignee of U.S. Patent No. 10,947,555 (the “’555 patent”), U.S. Patent No. 11,149,283 (the “’283 patent”), and U.S. Patent No. 11,299,745 (the “’745 patent”) (collectively, “the Corteva patents” or “the challenged patents”). On behalf of Petitioner Inari Agriculture, Inc.(“Inari”), I have been asked to provide expert opinions in this matter that I understand relate to whether the claims of the Corteva patents are anticipated and/or rendered obvious by prior-art references.

3. I am over the age of 18 and otherwise competent to make this declaration. 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.

4. I understand that this declaration is being submitted in support of Inari's petitions for inter partes review ("IPR") of the Corteva patents. Because there are a number of common issues across the three IPR petitions, I am providing a single declaration in support of all three petitions.

5. In this declaration, I provide my opinions regarding the challenged Corteva patents and claims, the prior art, the level of skill of the person of ordinary skill in the art ("POSA"), and how the POSA would understand the prior art. The bases and reasons for my opinions, including the references I rely upon for the opinions in this declaration, are stated herein.

6. I understand that each IPR petition will have its own set of exhibit numbers. Thus, I will refer to references by name. A chart summarizing the exhibit numbers and the short name I will use to refer to each reference is included at the end of this declaration.

7. In undertaking my analyses, I have considered the challenged Corteva patents and file histories and the materials cited herein and/or Appendix A. I have also relied upon my education, training, and experience.

8. As set forth in greater detail in this declaration, the POSA would have regarded the challenged claims of the Corteva patents as anticipated by the prior art and/or obvious based on the prior art, for at least the following reasons:

- a. The challenged claims of the Corteva patents are not entitled to a priority date any earlier than October 7, 2016, the date on which the application that led to the '555 patent was filed. That is because the preceding patent applications did not provide written description support for the claims of the '555, '283, and '745 patents
- b. As a result, the challenged claims of the Corteva patents are anticipated by Corteva's own patent publication, International Patent Publication No. WO 2005/107437 ("Corteva '437") published on November 17, 2005.
- c. Even if the challenged claims of the Corteva patents were entitled to a priority date of April 30, 2004, the challenged claims would have been invalid as obvious based on the prior art and the knowledge of the POSA regarding α KG dioxygenases, including 2,4-dichlorophenoxyacetic acid/ α KG dioxygenase ("TfdA") and (*R*)-2-(2,4-dichlorophenoxy)propanoic acid/ α KG dioxygenase ("RdpA"), and art describing transgenic crops expressing such enzymes.

II. BACKGROUND AND QUALIFICATIONS

9. 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.

10. 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.”

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

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

13. 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 lead 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, rice that produces beta-

carotene. This required expression and analysis of novel carotenoid biosynthetic enzymes in rice.

14. 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.

15. 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 US and Canada. I also supported the product development of new active ingredients and the expansion of the use of registered pesticides.

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

17. 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*. EX1055.

18. 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*. EX1055.

19. I provided expert testimony in *Inari Agriculture, Inc. v. Corteva Agriscience LLC*, PGR2023-00022.

III. THE CORTEVA PATENTS

20. I understand that the Corteva patents claim priority to U.S. Provisional Application No. 60/567,052 (the “’052 provisional”), filed April 30, 2004.

21. The first non-provisional patent application in this family, U.S. Patent Application No. 11/587,893 (the “’893 application”), was filed on May 2, 2005, as a national stage entry of International Patent Application No. PCT/US2005/014737 (the “’737 application”). The ’737 application was subsequently published as Corteva ’437 on November 17, 2005. The ’893 application issued as U.S. Patent No. 7,838,733.

22. I understand that the ’893 application was followed by two continuation applications with identical specifications: U.S. Patent Application No. 12/951,813, which issued as U.S. Patent No. 9,127,289, and U.S. Patent Application No. 14/820,893, which issued as U.S. Patent No. 10,174,337.

23. The continuation application which issued as the ’555 patent, U.S. Patent Application No. 15/288,406 (the “’406 application”), was filed on October 7, 2016. As discussed in more detail later in this declaration, the specification of the

'406 application was amended during the course of prosecution at the U.S. Patent & Trademark Office (“USPTO”) to add a description of an “AAD-1 motif.”

24. The continuation application which issued as the '283 patent, U.S. Patent Application No. 17/175,966, was filed on February 15, 2021.

25. The continuation application which issued as the '745 patent, U.S. Patent Application No. 17/403,476, was filed on August 16, 2021.

26. The claims of Corteva's '555, '283 and '745 patents are generally directed to transgenic plants or plant cells that have been transgenically modified to encode what the patents refer to as an “AAD-1” protein. The claims generally require the encoded AAD-1 protein to exhibit aryloxyalkanoate dioxygenase activity that enzymatically degrades a “phenoxy auxin” herbicide and an “(R)-aryloxyphenoxypropionate” herbicide.² The claims generally require the encoded AAD-1 protein to comprise an “amino acid sequence having at least 85% sequence

² The POSA would understand that the '555 patent uses the term “aryloxyalkanoate dioxygenase activity” to describe what can be more precisely referred to as “aryloxyalkanoate:αKG dioxygenase activity” or “aryloxyalkanoate/αKG dioxygenase activity” because in the relevant enzymatic reactions, one atom of dioxygen is incorporated into the substrate (*e.g.*, 2,4-D), and the other is incorporated into αKG.

identity with SEQ ID NO: 9.” And the claims generally require the encoded AAD-1 protein to comprise an “AAD-1 motif” having the form “HX₁₁₂D(X)₁₁₄₋₁₃₇T(X)₁₃₉₋₂₆₉H(X)₂₇₁₋₂₈₀R” (e.g., ’555 Pat. Claims 1, 34) or “HX₁₁₂D(X)₁₁₄₋₁₃₇T(X)₁₃₉₋₂₆₉H(X)₂₇₁₋₂₈₀R(X)₂₈₂₋₂₈₄R” (’555 Pat. Claim 2).

27. For example, claim 1 of the ’555 patent recites:

1. A transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises:

i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and

ii) an AAD-1 motif having the general formula of:

$HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$, wherein

X₁₁₂ represents a single amino acid at position 112,
relative to the sequence of SEQ ID NO: 9;

(X)₁₁₄₋₁₃₇ represents a sequence of 24 amino acids;

(X)₁₃₉₋₂₆₉ represents a sequence of 131 amino acids;

and

(X)₂₇₁₋₂₈₀ represents a sequence of 10 amino acids.

IV. PERSON OF ORDINARY SKILL IN THE ART

28. I understand that in patent law, the POSA is a hypothetical person to whom the challenged patents are directed. I have been informed that the factors for

determining the level of ordinary skill in the art may include the type of problems encountered in the art; prior-art solutions to those problems; the rapidity with which innovations are made; the sophistication of the technology; and the educational level of active workers in the field. I have considered these factors in my analysis.

29. The Corteva patents are directed to plant cells or plants that possess polynucleotides encoding an enzyme which has a particular amino acid “motif” and herbicide-degrading enzymatic activity. Thus, it is my opinion that across all potential priority dates, the POSA would have knowledge and experience regarding protein biochemistry, including expression and characterization, amino acid sequences, three-dimensional structure, and enzyme activity and substrate selectivity, as well as methods of evaluating those properties. The POSA would be able to apply these concepts to expression of enzymes in transgenic plant cells and plants and degradation of herbicides. The POSA generally would have an advanced degree in a relevant discipline and several years of advanced academic (e.g., postdoctoral or higher) and/or professional experience.

30. Under this definition, I am qualified to offer opinions regarding the claims of the Corteva patents. I have over 35 years of experience researching and practicing in the fields of plant physiology, biochemistry, molecular biology and genetics. This includes research on enzyme mechanisms, including extensive analyses of activity and structure-function relationships. I am familiar with the

transgenic expression of a variety of enzymes in heterologous cells in plants, and I am familiar with transgenic applications involving various enzymes.

V. LEGAL PRINCIPLES

31. I understand that the validity of a patent claim must be analyzed as of the “priority date” of that claim. I understand that in order for a patent claim to be entitled to a given priority date, the patent specification as filed on that date must adequately describe the claimed subject matter, such that the POSA would understand that the inventor was in possession of the claimed invention as of the priority date. I understand that if a patent claims a group or “genus” of subject matter (such as a group of enzymes), a sufficient written description requires the disclosure of either a representative number of species falling within the scope of the claimed genus, or structural features that the members of the genus have in common, so that a POSA can “visualize or recognize” the members of the genus.

32. I understand that a patent claim is “anticipated,” and thus invalid, if a single prior-art reference discloses every limitation of the claim, either expressly or inherently, as arranged in the claim. I understand that, in order to anticipate a claim, the prior-art reference must disclose to the POSA the invention later claimed. I have been informed that a reference can anticipate if it discloses a sufficiently limited

group of combinations such that the POSA could at once envisage the claimed combination.

33. I understand that a patent claim is “obvious,” and thus invalid, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to the hypothetical POSA in the art to which said subject matter pertains. I understand that factual determinations relevant to the obviousness inquiry include (a) the scope and content of the prior art, (b) the differences between the claimed invention and the prior art, (c) the level of ordinary skill in the art, and (d) secondary considerations (also referred to as “objective indicia”) of nonobviousness. I have been advised that, for an invention to be regarded as “obvious,” the POSA must have had a reason or been motivated to modify the prior art or to combine one or more prior-art references in a manner that would yield the claimed invention. I have also been informed that, for a claim to be obvious, the POSA must have a reasonable expectation of success with respect to the claimed invention. I understand that a reasonable expectation of success does not, however, require absolute certainty of success.

34. I understand that a patentee may cite certain secondary considerations of nonobviousness, such as unexpected properties, failure of others, and copying, to support the nonobviousness of a challenged patent claim. I further understand that

secondary considerations of nonobviousness are only relevant if there is a nexus between the merits of the claimed invention and the evidence of such secondary considerations. I further understand that, in order to show nexus, a patentee must show that the evidence of secondary considerations results both from what is claimed and what is novel in the claim. I also understand that, to support nonobviousness, any secondary considerations must be reasonably commensurate with the scope of the claim that is challenged as obvious. I am not aware of any secondary considerations of nonobviousness that would support the nonobviousness of the challenged claims. However, if Corteva contends that the challenged claims are supported by one or more secondary considerations of nonobviousness, I reserve the right to respond.

VI. SCIENTIFIC AND TECHNICAL BACKGROUND

35. I have been asked to provide a brief summary of what was known in the prior art about α KG dioxygenases including TfdA and RdpA. This information would have been known to the POSA and generally accepted as of April 30, 2004.

A. Transgenic Gene Expression

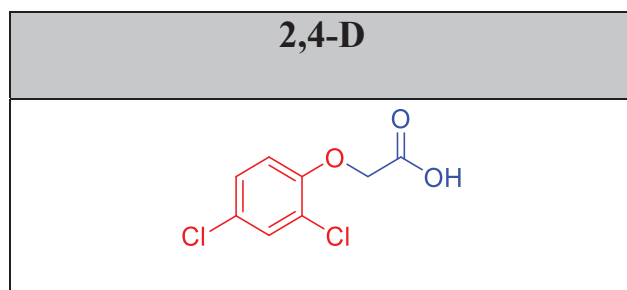
36. Proteins, including enzymes, are encoded by genes. Genes consist of a sequence of DNA nucleotides. Each nucleotide carries one of four nitrogenous bases: adenine (A), guanine (G), cytosine (C), or thymine (T). In order to express a gene and produce the protein it encodes, the cell first makes an RNA sequence

complementary to the DNA, a process called “transcription.” The cell then uses the RNA transcript as a template to synthesize a protein, in a process called “translation.”

37. Bacteria, plants, and animals all use DNA to encode proteins. Thus, standard recombinant DNA and molecular biology techniques can be used to transfer a gene sequence from one species to another. For example, biochemistry labs commonly isolate bacterial genes of interest and insert them into *Escherichia coli*, so that the encoded protein can more easily be produced, purified, and analyzed. Recombinant techniques also can be used to express bacterial genes of interest in plant or animal cells.

B. Phenoxy Herbicides

38. As of April 2004, phenoxy herbicides had been known and used for decades, as alternatives to glyphosate and other herbicides. *See, e.g.*, EX1039 (Rao 2000 (pp. 88-92)); EX1022 (Cutler 1999 (pp. 6-10 & Fig. 1.6)); EX1026 (Hee 1981 (pp. 1-321)). Phenoxy herbicides share certain structural features with phenoxyacetic acid, including a phenoxy group and a carboxylic acid, such as acetic or propionic acid. The figure below depicts the phenoxy herbicide 2,4-dichlorophenoxyacetic acid (“2,4-D”), with the substituted phenoxy group in red, and the carboxylic acid in blue:

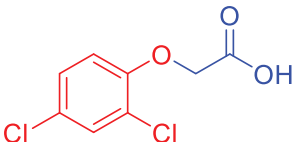
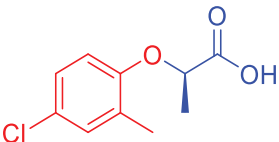
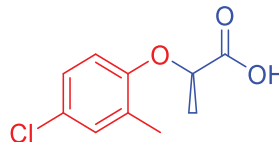


39. 2,4-D is a widely used herbicide that acts by mimicking indoleacetic acid, a naturally occurring plant growth hormone also known as an “auxin.” *See* EX1001 (’555 Pat.), 2:27-49; EX1040 (Saari 1998 (Abstract; p. 2)); EX1041 (Saari 1999 (p. 421)). 2,4-D was one of the first herbicides to be used with this mechanism of action. EX1040 (Saari 1998 (Abstract)). 2,4-D and other phenoxy herbicides that share this mechanism of action can be described as “phenoxy auxins.” Before 2004, numerous phenoxy auxin herbicides had been developed, and phenoxy auxins were commonly used in commercial agriculture. *See* EX1001 (’555 Pat.), 8:42-9:67, Tbl. 1; EX1039 (Rao 2000 (pp. 88-92)); EX1022 (Cutler 1999 (pp. 6-10 & Fig. 1.6)).

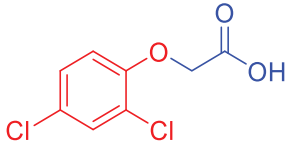
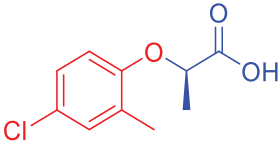
40. Some phenoxy auxins exist as enantiomers. Enantiomers are pairs of compounds that are mirror-images of one another, like a right hand and a left hand. Compounds that exhibit handedness and exist as enantiomers are called “chiral” compounds. The right-handed form of the compound is the “*R*” enantiomer, and the left-handed form is the “*S*” enantiomer.

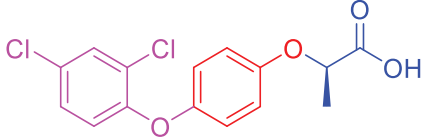
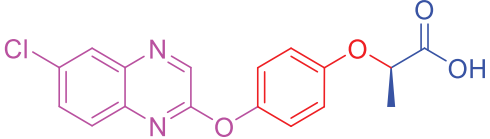
41. Phenoxy auxins such as mecoprop and dichlorprop exhibit chirality due to the addition of a methyl group to the carboxylic acid group, which creates a chiral

center. The (*R*)-enantiomers of these herbicides are herbicidally active, while the (*S*)-enantiomers are not. The figure below shows the structures of 2,4-D (not chiral), (*R*)-mecoprop (chiral, with the methyl group depicted in front of the plane of the page), and (*S*)-mecoprop (chiral, with the methyl group depicted behind the plane of the page):

2,4-D	(<i>R</i>)-Mecoprop	(<i>S</i>)-Mecoprop
		

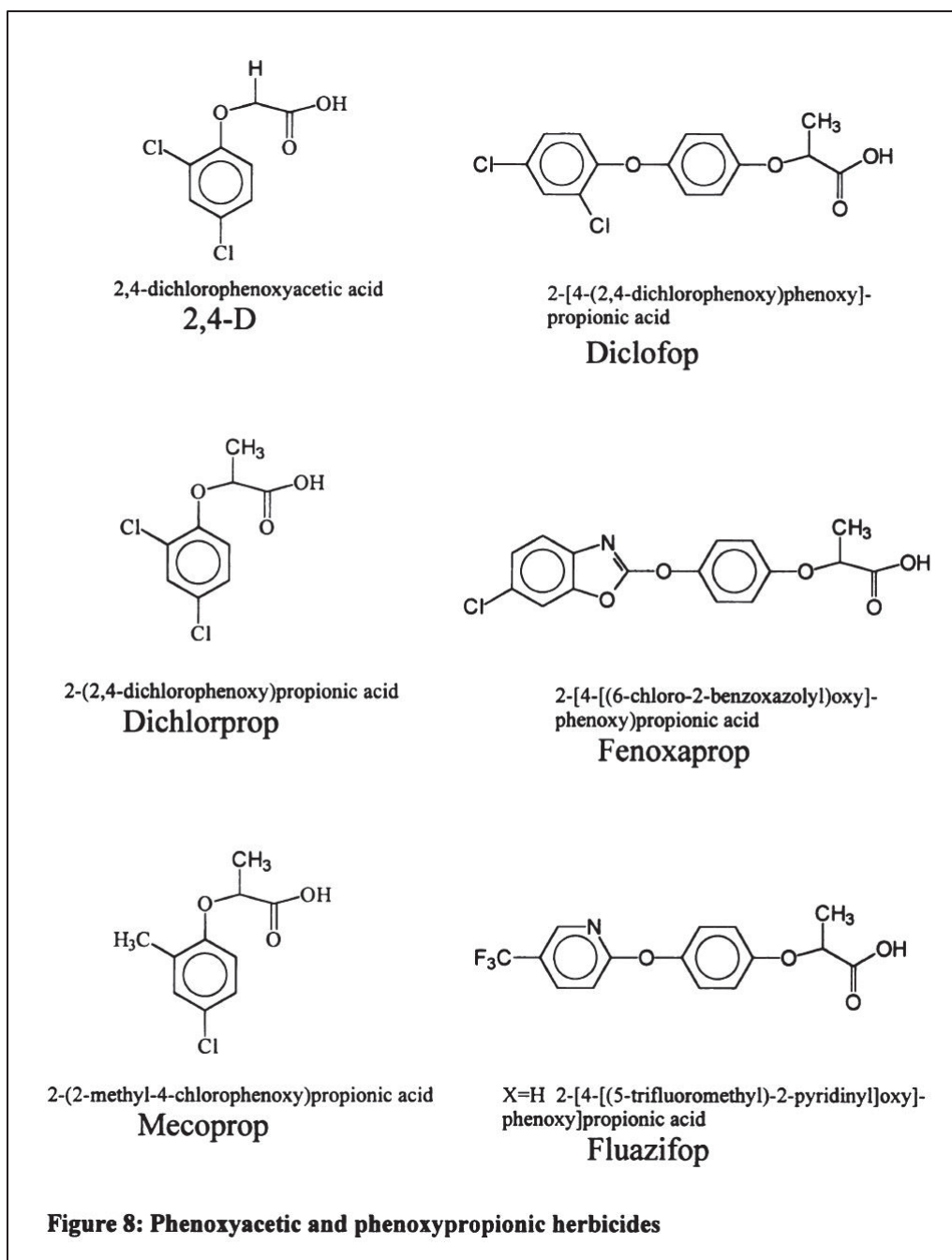
42. The aryloxyphenoxypropionates (sometimes referred to as “AOPPs” or “FOPs”) are another group of chiral phenoxy herbicides. As shown in the figure below, aryloxyphenoxypropionates such as diclofop and quizalofop share the substituted phenoxy group (red) and carboxylic acid (blue) group characteristic of phenoxy herbicides, with an additional aryloxy group (purple):

2,4-D	(<i>R</i>)-Mecoprop
	

(<i>R</i>)-Diclofop	(<i>R</i>)-Quizalofop
	

Similar to the chiral phenoxy auxins mecoprop and dichlorprop, the (*R*)-enantiomers of aryloxyphenoxypropionates are herbicidally active, while the (*S*)-enantiomers are not.

43. The aryloxyphenoxypropionates have a different herbicidal mechanism of action from phenoxy auxins. Rather than mimicking auxins, aryloxyphenoxypropionates inhibit the naturally occurring plant enzyme acetyl-coenzyme A carboxylase (“ACCase”). Nonetheless, the POSA would have recognized that achiral phenoxy auxins, chiral phenoxy auxins, and aryloxyphenoxypropionates are structurally related as illustrated in the following figure from Saari 1998:



EX1040 (Saari 1998 (p. 72)); *id.* (p. 71) (“2,4-Dichlorophenoxyacetic acid (2,4-D) and structurally related phenoxy herbicides (Figure 8) are widely used”); *id.* (pp. 8-10).

44. The '555 patent uses the term “aryloxyalkanoate” to refer collectively to a group of herbicides including the achiral phenoxy auxins, such as 2,4-D; the chiral phenoxy auxins, such as dichlorprop and mecoprop; and chiral aryloxyphenoxypropionates, such as diclofop. EX1001 ('555 Pat.), 3:49-56 (“Aryloxyalkanoate chemical substructures are a common entity of many commercialized herbicides including the phenoxy auxins (such as 2,4-D and dichlorprop)” and “aryloxyphenoxypropionates (AOPP) acetyl-coenzyme A carboxylase (ACCase) inhibitors (such as haloxyfop, quizalofop, and diclofop)”), claims 6-10.

C. α KG Dioxygenases

45. For more than half a century, scientists have known that certain soil bacteria can degrade phenoxy herbicides. In the 1950s, researchers identified bacteria that could degrade 2,4-D and another phenoxy herbicide, 2-methyl-4-Cl-phenoxyacetate (MCPA). This work led to the identification of the gene encoding the TfdA enzyme from the bacterium *Alcaligenes eutrophus* JMP134.³ Remarkably,

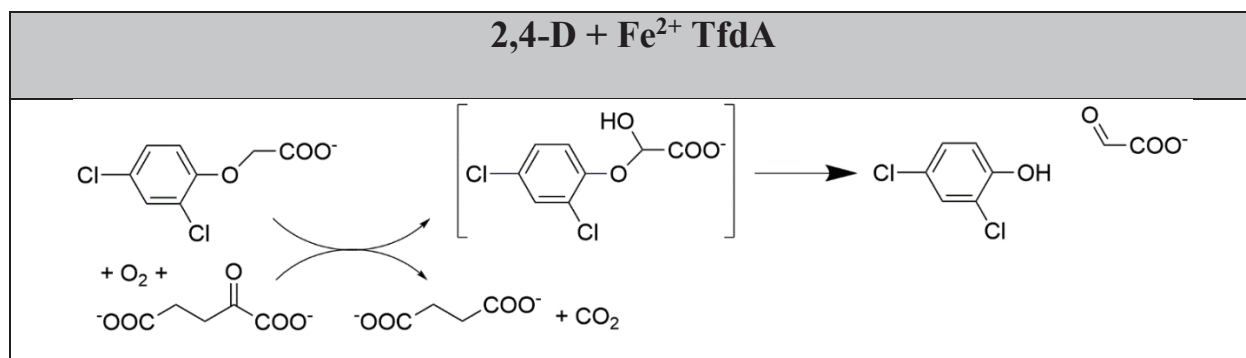
³ *A. eutrophus* JMP134 was later renamed *Ralstonia eutropha* JMP134, and then renamed *Cupriavidus necator* JMP134. The *tfdA* gene is encoded by the pJP4 plasmid in this strain. In this declaration, I will refer to the canonical JMP134 TfdA enzyme as “TfdA,” unless otherwise noted.

this bacterial strain is capable of using 2,4-D as its only source of carbon and energy. See EX1041 (Saari 1999 (p. 422)); EX1040 (Saari 1998 (pp. 7, 71)); EX1022 (Cutler 1999 (pp. 7-8)); EX1001 ('555 Pat.), 3:3-6.

46. TfdA was initially mischaracterized as a monooxygenase. In the early 1990s, researchers identified the mechanism by which TfdA degrades 2,4-D and established that TfdA belongs to the superfamily of α KG dioxygenases (Fukumori & Hausinger 1993). Based on these findings, the name 2,4-D/ α KG dioxygenase was proposed. EX1024 (Fukumori & Hausinger 1993 (pp. 2084-2085)).

47. The α KG dioxygenase superfamily is large and diverse. In addition to detoxifying enzymes like TfdA, it includes enzymes involved in plant biosynthetic pathways, antibiotic biosynthesis, and lipid metabolism. EX1025 (Hausinger 2004 (pp. 21, 29-38)); EX1040 (Saari 1998 (pp. 16-18)).

48. α KG dioxygenases catalyze a variety of oxidation reactions including the incorporation of an oxygen atom into substrates in the presence of α KG and ferrous ion (Fe^{2+}). EX1025 (Hausinger 2004 (pp. 21-57)); EX1040 (Saari 1998 (pp. 16-18)). As shown below, TfdA initiates the degradation of 2,4-D by cleaving it into phenol and a carboxylic acid. Molecular oxygen (O_2), the cosubstrate α KG, and Fe^{2+} are necessary for this reaction to take place. The products of the reaction are 2,4-dichlorophenol, succinate, glyoxylate, and CO_2 :



49. TfdA and related α KG dioxygenases, such as TauD, share certain features. The prior art had identified a consensus motif characteristic of TfdA and related α KG dioxygenases. A 2000 paper disclosed that Group II α KG dioxygenases, which include TfdA, shared the motif **HX(D/E)X₁₃₈₋₂₀₇HX₁₀₋₁₃R**. EX1027 (Hogan 2000 (p. 12401)). Furthermore, a 2002 paper stated that TfdA, TauD, and related α KG dioxygenases share the consensus motif **HX(D/E)X₂₃₋₂₆(T/S)X₁₁₄₋₁₈₃HX₁₀₋₁₃R**. EX1023 (Elkins 2002 (p. 5185)). The letters in the motif represent amino acids: “H” is His (histidine), “D/E” can be Asp (aspartate) or Glu (glutamate), “T/S” can be Thr (threonine) or Ser (serine), and “R” is Arg (arginine). “X” can be any amino acid, and the numeric subscripts refer to the number of amino acids. A 2004 review entitled “Fe(II)/ α -Ketoglutarate-Dependent Hydroxylases and Related Enzymes” discussed several α KG dioxygenases known to have this HX(D/E)X₂₃₋₂₆(T/S)X₁₁₄₋₁₈₃HX₁₀₋₁₃R motif, including TfdA, CarC or carbapenem synthase, shown in Scheme 11; TauD or taurine/ α KG dioxygenase, shown in Scheme 29; and AtsK or alkylsulfatase, shown in Scheme 31. EX1025 (Hausinger 2004 (pp. 22, 31, 39)).

50. The '555 patent reproduces the generic consensus motif published in Elkins 2002 while citing Hogan 2000. EX1001 ('555 Pat.), 18:2-7. The POSA would have readily understood that the generic motif in the patent uses the same notation as in the Elkins and Hogan publications. "X₂₃₋₂₆" for example indicates that from 23 to 26 unspecified amino acids may be present (not that those amino acids are located at positions 23-26). This is also evident from the fact that the segment X₁₀₋₁₃ appears after the segment X₁₁₄₋₁₈₃.

51. Site-directed mutagenesis was used to investigate the role played by various amino acids, including motif amino acids, in TfdA's catalytic activity (Hogan 2000). Researchers reported that His113, Asp115, and His262 act as metal ligands, interacting with the Fe²⁺ ion, and that His213 has another role. EX1027 (Hogan 2000 (p. 12408)).

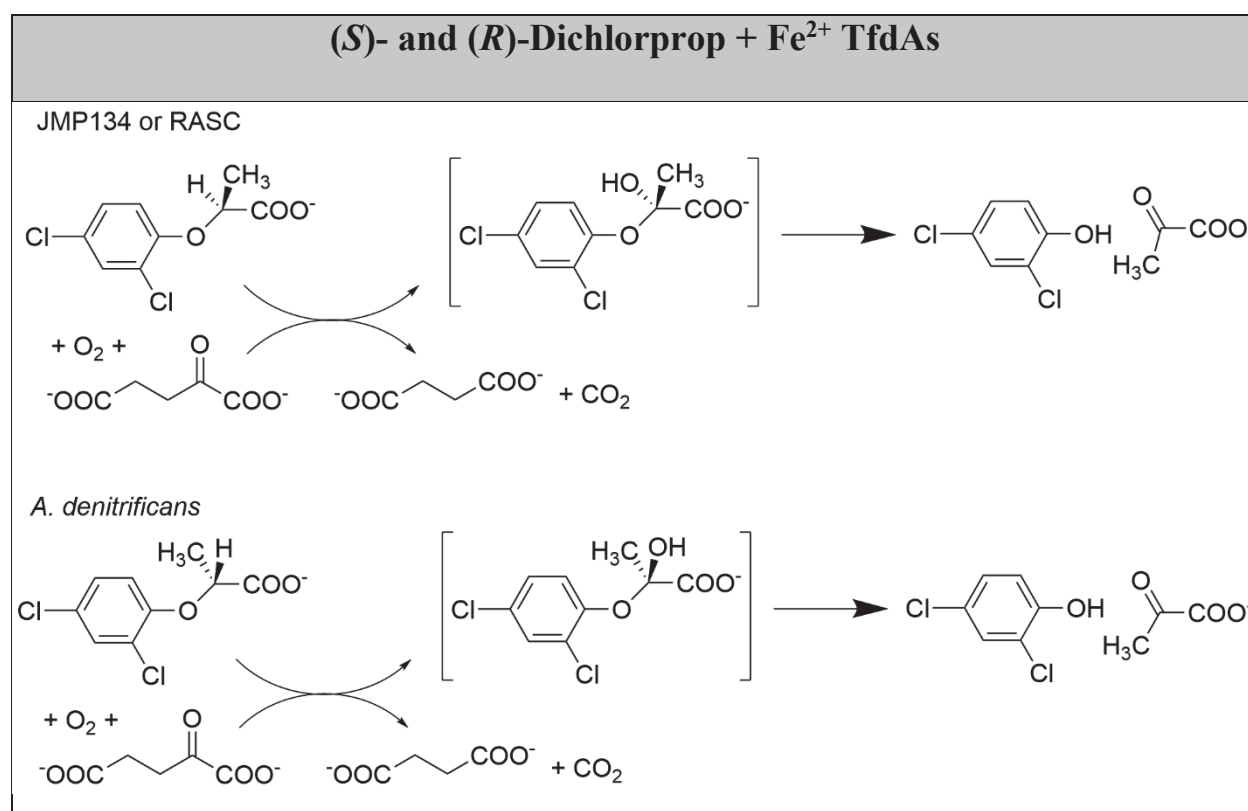
52. Researchers also conducted studies showing that TfdA can degrade a range of chemical substrates besides 2,4-D (Hotopp 2001). Researchers expanded the substrate range of TfdA and showed it could accommodate dual aromatic ring species: 1- or 2-naphthoxyacetic acid. EX1028 (Hotopp 2001 (Abstract, p. 158)). This result demonstrated the ability of enzymes in this family to accept large changes in substrate structure that are distant from the site of hydroxylation. EX1028 (Hotopp 2001 (p. 161)); *see also* EX1040 (Saari 1998 (pp. 5-6)) (explaining that TfdA "showed relatively broad specificity towards the aromatic substituent,

accepting various methyl- and chloro-substituted aryl rings including the herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), as well as the derivative in which a methyl group was added at the acetate side chain (*i.e.*, the herbicide dichlorprop; 2-(2,4-dichlorophenoxy)propionate)"); EX1028 (Hotopp 2001 (p. 158)).

53. In 2002, researchers reported a three-dimensional model of the TfdA protein structure docked with 2,4-D within a paper focused on the crystal structure of another α KG dioxygenase, TauD (EX1023, Elkins 2002). The TfdA model, based in part on mutagenesis studies, was deposited to the PDB (1gqx) and archived in 2002. The model shows the carboxyl group of 2,4-D pointing into the protein, with its methylene carbon appropriately positioned for hydroxylation, whereas the aromatic ring points out to solvent. Consistent with earlier substrate specificity studies, the model indicates that critical interactions exist between the enzyme's active site and the carboxyl end of the substrate, whereas the C4 end of the substrate phenoxy group lacks such interactions. EX1023 (pp. 5185-5192).

54. Researchers also investigated the stereoselectivity of TfdA and related enzymes and reported that certain bacteria expressing α KG dioxygenases could degrade chiral phenoxy herbicides such as mecoprop and dichlorprop. EX1041 (Saari 1999 (p. 422)); EX1040 (Saari 1998 (pp. 90-92, 127)); EX1036 (Nickel 1997 (p. 6678)). This degradation took place in a stereoselective or stereospecific manner, meaning that a given enzyme would preferentially break

down one of the two enantiomers of a chiral substrate. EX1041 (Saari 1999 (p. 422)); EX1040 (Saari 1998 (pp. 90-92, 127)); EX1036 (Nickel 1997 (p. 6678)). For example, purified TfdA or cell extracts from JMP134 could degrade (*S*)-dichlorprop, as could cell extracts from *Burkholderia cepacia* RASC, but extracts of the bacterium *Alcaligenes denitrificans* preferentially degraded the opposite enantiomer, (*R*)-dichlorprop:



EX1041 (Saari 1999 (pp. 426-27)). Amplification of *A. denitrificans* DNA yielded a TfdA-like sequence similar to the sequences of JMP134 TfdA and RASC TfdA, despite their opposite stereospecificities. *Id.*; EX1040 (Saari 1998 (Abstract, pp. 73-74, 86-94)).

55. At the same time, several labs were studying two bacterial strains that could degrade both of the (*S*)- and (*R*)-enantiomers of the phenoxy herbicides mecoprop and dichlorprop. *Sphingomonas herbicidovorans* MH and *Delftia acidovorans* MC1 were found to express two stereoselective relatives of TfdA, which were named SdpA and RdpA, respectively. EX1036 (Nickel 1997 (p. 6678)); EX1034 (Müller 2001 (p. 228)); EX1047 (Westendorf 2002 (p. 317)); EX1040 (Saari 1998 (p. 127)); EX1041 (Saari 1999 (p. 426-427)). Substrate specificity analyses of the RdpA and SdpA from *Delftia* showed that these enzymes use 2,4-D and several of the phenoxypropionates of appropriate stereochemistry as substrates. EX1048 (Westendorf 2003 (pp. 10-11, 15)). The *S. herbicidovorans* RdpA amino acid sequence corresponds to SEQ ID NO: 9 in the '555 patent. EX1001 ('555 Pat.), 6:56-58. The genes encoding RdpA from *Delftia* and *Rhodospirillum rubrum* P230 encode the same amino acid sequence as *Sphingomonas* RdpA. See EX1001 ('555 Pat.), 31:61-64; EX1042 (Schleinitz 2004 (p. 5362)). As of 2004, RdpA sequences had been deposited in public databases such as GenBank and NCBI and were publicly available from those databases. See EX1001 ('555 Pat.) pp. 1-2, 44:37-40; EX1013 (Accession No. AF516751, published Aug. 6, 2002) (Schleinitz); EX1014 (Accession No. AF516752, published Aug. 6, 2002); EX1016 (Accession No. Q8KSC8, published Oct. 1, 2002); EX1015 (Accession No. AJ628859, published March 3, 2004).

56. In the early 2000s, researchers created structural models and site-directed variants of *Sphingomonas* RdpA and SdpA to better understand the basis of their enantiospecificities. Researchers published this work in 2006 (Müller 2006) and showed that, as previously observed for TfdA in 2002, the carboxyl group of mecoprop points into the active site and the aromatic ring points to the exterior and allows for a larger species, presumably including an aryloxyphenoxypropionate. EX1035 (Müller 2006 (pp. 1359-60)).

57. A crystal structure of RdpA was not published until 2019. EX1019 (Chekan 2019).

D. Herbicide-Resistant Plants

58. The discovery of bacterial genes encoding herbicide-detoxifying enzymes led to interest in applications of those enzymes. By 1990, researchers had succeeded in modifying plants to express several bacterial enzymes. *E.g.*, EX1037 (Oxtoby 1990 (pp. 64-65)). 2,4-D was an attractive target for plant modification due to its widespread agricultural use. In 1987, the notion of transferring *tfdA* from JMP134 into plants for 2,4-D resistance was proposed. EX1038 (Perkins 1987 (pp. 17-18)). By the mid-1990s, TfdA had been successfully expressed in plants like cotton, tobacco, and tomato. EX1041 (Saari 1999 (p. 422)); EX1040 (Saari 1998 (p. 93)). Researchers reported that plants synthesizing TfdA showed increased resistance to 2,4-D, as well as other phenoxy herbicides, confirming the feasibility

of the approach suggested by Perkins 1987. EX1043 (Streber), 1:41-48, 2:52-62, 4:19-6:61, 7:58-12:67, 22:56-32:9, claim 6; EX1032 (Lyon 1989 (pp. 533-39)); EX1033 (Lyon 1993) (pp. 162-69)); EX1045 (Streber 1989 (pp. 811-15)); EX1018 (Bayley 1992 (pp. 645-49)).

VII. INVALIDITY ANALYSIS FOR THE '555 PATENT

59. As explained in detail below and summarized in the following chart, the claims of the '555 patent (and '283 and '745 patents) are invalid for anticipation and/or obviousness:

Petition Ground	Assumed Priority Date	References	Basis	Claims Challenged
IA	October 7, 2016	Corteva '437	Anticipation (§ 102)	'555 Pat., claims 1-34 '283 Pat., claims 1-29 '745 Pat., claims 1-29
IB	October 7, 2016	Corteva '437	Obviousness (§ 103)	'555 Pat., claims 1-34 '283 Pat., claims 1-29 '745 Pat., claims 1-29

IIA	April 30, 2004	Saari 1998 or Saari 1999 in combination with Schleinitz and Streber	Obviousness (§ 103)	'555 Pat., claims 1-10, 13-16, 34 '283 Pat., claims 1-6, 9-12, 29 '745 Pat., claims 1-6, 9-12, 29
IIB	April 30, 2004	Saari 1998 or Saari 1999 in combination with Schleinitz, Streber, and Jepson	Obviousness (§ 103)	'555 Pat., claims 11-12, 17-33 '283 Pat., claims 7-8, 13-28 '745 Pat., claims 7-8, 13-28

A. Invalidity Analysis as of October 7, 2016

1. The Challenged Claims Are Not Entitled to a Priority Date Earlier Than October 7, 2016.

60. The '555 patent specification as originally filed does not discuss any set (“genus”) of proteins that has an AAD-1 motif, at least 85% sequence identity to SEQ ID NO 9, and the claimed activity. The first mention of “an AAD-1 motif” or a genus of proteins having it was in the claims that the applicant submitted to the USPTO on October 7, 2016.

61. I understand that for a patent specification filed on a particular date to adequately describe a claimed genus, so that the claims are entitled to that particular

priority date, the specification must provide representative examples of the genus, or common features that would allow the POSA to recognize members of the genus.

62. As explained in more detail below, at a minimum, the original '555 patent specification and the earlier applications in the family sharing that specification did not satisfy those requirements. Based on the application as originally filed, the POSA would not have understood the inventors to have identified or described the claimed genus of AAD-1 proteins, to have disclosed representative examples of it, or to have provided sufficient information to recognize the members of that genus. Therefore, the earliest possible priority date for the challenged claims of the '555 patent is October 7, 2016. I have not been asked to offer an opinion regarding whether the application as it existed on October 7, 2016, itself satisfies these requirements, and I express no opinion on that issue.

a. The Original Specification Did Not Disclose the Claimed AAD-1 Motifs.

63. All of the claims of the '555 patent require an AAD-1 protein that has an “AAD-1 motif”. In claim 1, the motif is “**HX₁₁₂D(X)₁₁₄₋₁₃₇T(X)₁₃₉₋₂₆₉H(X)₂₇₁₋₂₈₀R**”. In claim 2, the motif is “**HX₁₁₂D(X)₁₁₄₋₁₃₇T(X)₁₃₉₋₂₆₉H(X)₂₇₁₋₂₈₀R(X)₂₈₂₋₂₈₄R**”.

64. The '555 patent specification as originally filed did not disclose either of these motifs. Instead, it disclosed the same generic consensus motif already known and published in the prior art: **HX(D/E)X₂₃₋₂₆(T/S)X₁₁₄₋₁₈₃HX₁₀₋₁₃R**. *See*

EX1023 (Elkins 2002 (p. 5185)). This generic consensus motif differs in several ways from the AAD-1 motifs in the issued claims.

65. First, the number of unspecified amino acids in the original generic consensus motif can vary, but in the AAD-1 motifs, the number of unspecified amino acids is fixed. In the original motif, “X₂₃₋₂₆,” “X₁₁₄₋₁₈₃” and “X₁₀₋₁₃” indicate that from 23-26 unspecified amino acids, from 114-183 unspecified amino acids, and from 10-13 unspecified amino acids are present, respectively. The first X in the consensus motif does not have a subscript because that portion of the motif does not vary in length. In contrast, the AAD-1 motif selects one length from each of those generic ranges: 24, 131, and 10 unspecified amino acids, respectively. In other words, each AAD-1 motif represents a subset (“subgenus”) within the original motif, having a fixed number of unspecified amino acids in each series.

66. Second, the numeric subscripts in the original generic consensus motif and the AAD-1 motifs convey different information. The POSA would have understood that the original motif was a typical consensus motif: it specifies a pattern of amino acids, but does not provide information about their positions. The applicant could have chosen to write the AAD-1 motif in the same manner, using the subscripts to indicate the number of unspecified amino acids present in each series. That version of the AAD-1 motif would have looked like this: **HXDX₂₄TX₁₃₁HX₁₀R**. See EX1008 (’406 Appl. & File History), COR-AAD1-

00000461-62 (Wright-I Decl. ¶ 12) (“One skilled in the art would recognize the much more limited group having the desired functional dual-MOA activity would be defined by the more refined motif $\text{HXDX}_{24}\text{TX}_{131}\text{HX}_{10}\text{R}$, which effectively excludes AAD-2.”). Instead, as explained in the issued claims of the ’555 patent, the applicant repurposed the subscripts to provide information about the *position* of each unspecified amino acid: $\text{HX}_{112}\text{D}(\text{X})_{114-137}\text{T}(\text{X})_{139-269}\text{H}(\text{X})_{271-280}\text{R}$.⁴ Thus, as

⁴ I understand that the parties have proposed competing constructions for certain claim terms in the co-pending district court litigation. *See* EX1056. I have not been asked to offer an opinion as to which of those constructions is correct, and I offer no opinion on those issues. However, the differences in the parties’ proposed constructions do not affect my opinions here. For example, the Petitioners’ proposed constructions require the amino acid residues in the motif to be at specific positions “in the encoded amino acid sequence, as in the sequence of SEQ ID NO: 9.” The Patent Owner’s broader proposed constructions permit the amino acid sequence of the AAD-1 protein to be “aligned with SEQ ID NO: 9.” Under either proposal, the challenged claims of the ’555, ’283, and ’745 patents encompass an enormous genera of proteins that is not supported by the ’406 applications’ predecessor applications, and are therefore entitled to a priority date of October 2016 at the earliest based on the opinions set forth in Sections VII.A.1, VIII.A.1, IX.A.1.

explained in the issued claims of the '555 patent, the first X, which did not have a subscript in the generic consensus motif, is identified as “X₁₁₂”, and “(X)₁₁₄₋₁₃₇” denotes 24 amino acids and positions 114-137.

67. Third, the AAD-1 motifs further restrict the second and third conserved amino acid residues, from (D/E) to **D** and from (T/S) to **T**, respectively.

68. Finally, the AAD-1 motif in claim 2 includes four additional amino acid residues (“(X)₂₈₂₋₂₈₄R”) at the C-terminal end of the motif: **HX₁₁₂D(X)₁₁₄₋₁₃₇T(X)₁₃₉₋₂₆₉H(X)₂₇₁₋₂₈₀R(X)₂₈₂₋₂₈₄R**. These additional amino acids are not part of the motif originally included in the specification. If they had been part of that motif, they could have been notated as “X₃R” consistent with the original position-neutral notation of that motif. While the consensus motif was included in the original

Likewise, under either set of proposed constructions, RdpA (AAD-1 v1) and AAD-1 v2 are within the scope of the challenged claims; thus, the challenged claims would have been anticipated and/or obvious based on the opinions set forth in Sections VII.A.2, VII.A.3, VII.B, VIII.A.2 VIII.A.3 VIII.B, IX.A.2, IX.A.3, and IX.B. Indeed, Corteva’s broader proposed constructions only enhance the case for anticipation by Corteva ’437, as it would mean that another species disclosed in the reference (AAD-1 v3) would fall within the claims, assuming an October 7, 2016 priority date.

specification, the AAD-1 motifs first appeared in connection with the '555 patent claims and an amendment to the original specification. *See, e.g.* EX1001 ('555 Pat.), 18:20-28 ("Mapping the α -ketoglutarate-dependent dioxygenase motif disclosed in the previous paragraph to the sequence of SEQ ID NO: 9 reveals the AAD-1 motif of HX₁₁₂D(X)₁₁₄₋₁₃₇T(X)₁₃₉₋₂₆₉H(X)₂₇₁₋₂₈₀R"). The specification amendment did not include the AAD-1 motif in claim 2 or otherwise address the "(X)₂₈₂₋₂₈₄R" portion of the claim 2 motif.

b. The Original Specification Does Not Disclose Any Genus of Proteins Having an AAD-1 Motif, with at Least 85% or 90% Sequence Identity to SEQ ID NO: 9, and Conferring the Required Phenoxy Herbicide Degrading Activity.

69. The original specification does not describe any subgenus of proteins having an AAD-1 motif and at least 85% sequence identity to SEQ ID NO: 9, and the information in it would not have suggested to the POSA that the inventors had known of such a subgenus.

70. The original application included only the original prior art consensus motif. It did not suggest narrowing the set of α KG dioxygenases with that motif down to a defined subset of α KG dioxygenases with a modified version of the motif. It does not identify any defined subgenus of proteins within the larger α KG superfamily, with or without an AAD-1 motif. It did not identify the particular aspects of the consensus motif that are changed in the AAD-1 motifs, such as the

lengths of the series of unspecified amino acids and the addition of the X₃R to the end of the AAD-1 motif in claim 2, or suggest that these aspects were particularly important. The original application described particular species within the α KG superfamily, including RdpA and two RdpA variants nearly identical to it, as discussed in more detail below. From the perspective of the POSA, describing an amino acid sequence is not equivalent to defining a genus that includes that sequence and numerous other sequences.

71. In addition to the AAD-1 motif, the claims require at least 85% identity to SEQ ID NO: 9 (*e.g.*, '555 patent, claim 1) and at least 90% identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9 (*e.g.*, '555 patent, claim 34). As with the AAD-1 motif, the original application did not describe subgenera of α KG dioxygenases meeting these requirements. The original application included SEQ ID NO: 9, but it did not describe any genus of proteins having any specified percentage sequence identity to SEQ ID NO: 9. In the specification, 85% is just one value in a generic list of “identity and/or similarity” values between 49% and 99% “as compared to a sequence exemplified or suggested herein,” and “any number listed above can be used to define the upper and lower limits.” EX1001 ('555 Pat.), 37:49-53. It does not identify 85% as a preferred value. The POSA would not have understood this generic list of options, which could yield more than 1,000 possible combinations of upper and lower limits, to specifically

describe a genus with a claimed cutoff of at least 85% amino acid sequence identity to SEQ ID NO: 9. The generic paragraph indicates that 90% is a preferred value, but again, it does not link that value to any particular sequence, including SEQ ID NO: 9 or the portion of SEQ ID NO: 9 corresponding to the AAD-1 motifs. The POSA would not have understood the specific examples of AAD-1 proteins in the specification, which are either identical or nearly identical to SEQ ID NO: 9, to define a genus of AAD-1 enzymes. To the extent those examples might suggest a genus of proteins with a defined percentage identity cutoff, they would at best suggest a genus having approximately 99% sequence identity to SEQ ID NO: 9, not the much larger genera covered by the claims.

72. Finally, all of the claims require that the AAD-1 protein is capable of degrading one or more phenoxy auxin herbicides and one or more (*R*)-aryloxyphenoxypropionate herbicides. The patent describes RdpA as possessing this activity, but it never describes a genus of amino acid sequences possessing such activity, or any characteristics that would enable the POSA to recognize the amino acid sequences of the claimed AAD-1 proteins.

73. As explained in the patent and taught in the prior art, RdpA is an α KG dioxygenase that can degrade substrates including phenoxy herbicides, and it is selective for (*R*)-enantiomers. The '555 patent describes testing with RdpA/AAD-1 v1 and confirms that it can degrade a range of phenoxy herbicides including 2,4-D,

(*R*)-phenoxy auxins, and (*R*)-aryloxyphenoxypropionates. EX1001 ('555 Pat.), 4:32-46, 8:11-17, 11:1-4, 17:62-66, 18:10-20, 50:58-67. The patent repeatedly emphasizes that (*R*)-enantioselective activity differentiates RdpA/AAD-1 from the other α KG dioxygenases, including TfdA and TfdA homologues. EX1001 ('555 Pat.), 4:32-36 ("The subject invention relates in part to the identification of an enzyme" that has "novel properties, . . . which distinguish the enzyme of the subject invention from previously known TfdA proteins" and "is capable of degrading both 2,4-D and AOPP herbicides, in an enantiospecific manner."), 17:62-66 (same); 4:39-42 ("No α -ketoglutarate-dependent dioxygenase enzyme has previously been reported to have the ability to degrade herbicides of different classes and modes of action."), 18:10-20 (same); 50:58-67 ("[T]his is the first reported observation for any members of this class of enzyme to be active on herbicides outside the phenoxy auxins."); 8:11-17 ("[U]nlike all TfdA homologues characterized to date, AAD-1 is able to degrade the *R*-enantiomers (herbicidally active isomers) of the chiral phenoxy auxins (e.g., dichlorprop and mecoprop)."), 51:1-53:13, Figs. 6A-6B, Tbls. 3-4.

74. Although the '555 specification emphasizes RdpA's activity, which includes (*R*)-enantioselective activity for chiral phenoxy auxins and aryloxyphenoxypropionates, the patent never identifies which of RdpA's 295 amino acids are important to that activity. The POSA would have understood from the

patent and the prior art that the residues specified in the AAD-1 motifs (H, D, T, H, R, and R), while relevant to α KG dioxygenase activity generally, are not determinative of RdpA's particular activity, because the same residues are present in other α KG dioxygenases that are distinguished by the patent as lacking the activity possessed by RdpA. EX1001 ('555 Pat.), 4:32-42, 8:11-17, 17:62-66, 18:10-20, 50:58-67. The '555 patent states that many TfdA homologues have "the characteristic residues associated with α -ketoglutarate dioxygenase Fe^{+2} dioxygenases," but it is "not obvious what the substrate specificities of these divergent dioxygenases are." EX1001 ('555 Pat.), 3:20-25. The '555 patent includes an example of one of those α KG dioxygenases, a *Bradyrhizobium japonicum* enzyme identified as AAD-2 (SEQ ID NO: 13). EX1001 ('555 Pat.), 111:15-28. The patent explains that "AAD-2 (v1) is specific for (*S*)-enantiomer substrates, in contrast to AAD-1 (v.1) which is specific for (*R*)-enantiomers." EX1001 ('555 Pat.), 112:59-61. Both AAD-1 v1 and AAD-2 possess the generic α KG motif. As indicated in the figure below, submitted by Dr. Wright, one of the named inventors, during prosecution, the motif residues H, D, T, H, R, and R are present in both AAD-1 v1 and AAD-2:

		1		80
AAD-1v1	{1}	MHAALSPLSQRFERIAVQPLTGVLGAEITGVDLREPLDDSTWNEILDAFHTYQVIYFPGQAITNEQHIAFSRRFG-----		
AAD-2	{1}	-----MTIAIRQLQTHFVGQVSGLDLRKPLTPGEAREVESAMDKYAVLVFHDQDITDEQQMAFALNFGQREDA		
		81		160
AAD-1v1	{76}	---FVDPVPLLKSIEGYPEVQMIRREANESGR-----VIGDDWSTFLDAPFAAVVMRAIDVPEHGGIGFLSMY		
AAD-2	{69}	RGCTVTKEKDYRLQSGLNDVSNLGGKDKPLAKDSRTHLFNLGNCLWSSFRPIPAKFSLLSARVVNPTGGREFADMR		
		161		240
AAD-1v1	{145}	TAWETLSPTMQATIEGLNVVHSATRVFGSLYQAQNRFRSNTSVKVMVDVAGDRETVDHPLVVTHPGSGRGGLYVNOVYCQR		
AAD-2	{149}	RAYDALDDETKAEIEDLVCEHSLMYSRSGSLGFTEYTDDE-----KOMFKPULORIVRTHPVIRFSLVLSSEHACK		
		241		317
AAD-1v1	{225}	IEGMTDAESKPLLQFLYEHATRFDFTCRVRWKKDQVLVWNLCTMEAVPDYAGKFIYLRRTTVGGVRPAR-----		
AAD-2	{219}	IASMSVPEGRLLLRDLNEHATQPEFVYVHKWKLHDLVMWDNRQTMFVRRYDQSQPDMMRRATVAGTEPTVQQQAAE		

EX1008 ('406 Appl. & File History), COR-AAD1-00000470 (Wright-I Decl. App'x II); EX1001 ('555 Pat.), SEQ ID NO: 13. TfdA is another α KG dioxygenase that does not degrade (*R*)-enantiomers, but has the same motif residues as RdpA. *See, e.g.*, EX1020 (Chekan 2019 Suppl. Info. (p. 16, Fig. 10)); *supra* ¶ 54.

75. Because RdpA and α KG dioxygenases that do not have the (*R*)-enantioselective activity shown by RdpA share the same motif residues, the POSA would have inferred that other residues important to RdpA's enantioselective activity are among the 289 amino acids left unspecified by the AAD-1 motifs. But the POSA could not have determined from the information in the patent specification which of those residues were important or why. The original application never identified any feature of RdpA as important or necessary to RdpA's enantioselective activity in degrading (*R*)-phenoxy auxins or (*R*)-aryloxyphenoxypropionates, much less defined a genus of proteins possessing those features and that particular activity. Thus, the POSA would not have understood the applicant to have described such a genus.

c. The Specification Does Not Disclose Representative Examples of the Claimed Genera of AAD-1 Proteins.

76. I understand that even if a claimed genus is not explicitly described in so many words, a specification can adequately describe a genus by providing representative examples of it. The original specification of the '555 patent does not satisfy that requirement. As explained in detail below, a massive number of proteins would have possessed the required motifs and met the sequence identity cutoffs. Based on the patent, the POSA had no way to know which of them would have exhibited the required activity. The specification discloses only three examples of proteins (AAD-1 v1, v2, and v3) with the required activity, and their amino acid sequences are nearly identical to one another. Three nearly identical amino acid sequences are not representative examples of the massive and diverse genera covered by the claims, even assuming all three are covered by the claims.

77. The number of amino acid sequences having an AAD-1 motif is enormous. While RdpA consists of 295 amino acids, the AAD-1 motif in claims 1 and 34 specifies only five of those amino acids. EX1001 ('555 Pat.), SEQ ID NO: 9. Even taking only the twenty naturally occurring amino acids into account, the hypothetical genus of proteins with 295 amino acids and an AAD-1 motif as in claims 1 and 34 encompasses 20^{295-5} proteins (this excludes insertions and deletions). The AAD-1 motif in claim 2 specifies only six amino acids. Thus, the genus of

proteins with 295 amino acids and the AAD-1 motif in claim 2 encompasses 20^{295-6} proteins.

78. For practical purposes, these sequence identity limitations do not meaningfully reduce the size of the claimed genus. Apart from the handful of residues required by the AAD-1 motif limitations (just five residues in claim 1, and just 6 residues in claim 2), the claims do not place any restrictions on which amino acids can be modified or how they are substituted. The genus of proteins with as little as 85% sequence identity to SEQ ID NO: 9 would include, for example, a 295 amino acid protein with up to 44 amino acid substitutions as compared to AAD-1/RdpA (SEQ ID NO: 9). Each of those substitutions could be any amino acid, at almost any position in the protein.

79. Similar to the calculation above, a rough lower estimate of the number of possible amino acid sequences having a length of 295 amino acids, the AAD-1 motif of claim 1, and any naturally occurring amino acid at 44 of the unspecified positions (resulting in just over 85% sequence identity to SEQ ID NO: 9) might be 20^{44} proteins. But the actual number of amino acid sequences in the claimed genus is much larger than that, because each change can be located at almost any position in the sequence, and there are many potential combinations of different changes at different positions in the sequence.

80. The additional limitation in claim 34 that requires “90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9” still permits as many as 17 amino acid substitutions at positions 111-281, each one of which could be located at any of the 166 unspecified residues in that region. Like claim 1, claim 34 allows the amino acid sequence as a whole to have as little as 85% sequence identity, so a rough lower estimate of the amino acid sequences satisfying claim 34’s sequence requirements would also be 20^{44} proteins. Put differently, the additional limitation in claim 34 does not reduce the number of permitted substitutions, it merely redistributes where those substitutions are permitted to be made.

81. Compared to these estimates, the number of AAD-1 proteins exemplified in the specification is disproportionately small. The patent provides three sequences that the applicant pointed to during prosecution: AAD-1 v1, v2, and v3. The amino acid sequence of AAD-1 v1, SEQ ID NO: 9, corresponds to the amino acid sequence of *S. herbicidovorans* RdpA. EX1001 (’555 Pat.), 6:56-58. The patent also discloses two “variants” of AAD-1 v1: AAD-1 v2, in which an alanine is substituted for the histidine at position 2, and a cysteine is substituted for arginine at position 212 (which the specification states is “inadvertent”), EX1001 (’555 Pat.), 6:38-43, and AAD-1 v3, in which an extra alanine is inserted at position 2, before the histidine, EX1001 (’555 Pat.), 6:38-43. The ’555 patent reports that

when tested *in vitro*, AAD-1 v1 selectively degrades (*R*)-enantiomers of various phenoxy herbicides (but not (*S*)-enantiomers). EX1001 ('555 Pat.), 22:11-25, 51:1-55:34, 111:9-115:57, Figs. 6A-6B, Tbls. 3-4, 8-9, 33.

82. The figure below, submitted by Dr. Wright during prosecution, depicts the amino acid sequences of AAD-1 v1, v2, and v3. Amino acid changes from the naturally occurring, or wild-type, AAD-1 v1 (wild-type *S. herbicidovorans* RdpA) are highlighted in green and the amino acids required by the claim 1 AAD-1 motif are in blue:

AAD-1v1	(1)	M-HAALSPLSQRFERIAVQPLTGVLGAEITGVDLREPLDDSTWNEILDAPHTYQVIYFPGQAITNEQHIAFSRRFGFVDP	80
AAD-1v2	(1)	M-HAALSPLSQRFERIAVQPLTGVLGAEITGVDLREPLDDSTWNEILDAPHTYQVIYFPGQAITNEQHIAFSRRFGFVDP	
AAD-1v3	(1)	M-HAALSPLSQRFERIAVQPLTGVLGAEITGVDLREPLDDSTWNEILDAPHTYQVIYFPGQAITNEQHIAFSRRFGFVDP	
AAD-1 motif		-----	
AAD-1v1	(80)	VPLLSIEGYPEVQMIRREANESGRVIGDDW ~~X~~ STFLDAPPAAVVMRAIDVPEHGCD ~~X~~ FLSMYTAWETLSPTMQATIE	160
AAD-1v2	(80)	VPLLSIEGYPEVQMIRREANESGRVIGDDW ~~X~~ STFLDAPPAAVVMRAIDVPEHGCD ~~X~~ FLSMYTAWETLSPTMQATIE	
AAD-1v3	(80)	VPLLSIEGYPEVQMIRREANESGRVIGDDW ~~X~~ STFLDAPPAAVVMRAIDVPEHGCD ~~X~~ FLSMYTAWETLSPTMQATIE	
AAD-1 motif		-----X ~~X~~ XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	
AAD-1v1	(160)	GLNVVHSATRVFGSLYQAQNRFRSNTSVKVMVDVAGDRET ~~VH~~ PLV ~~V~~ THPGSG ~~R~~ KGLYV ~~N~~ QVY ~~C~~ QRIEGMTDAESKPLLQF	240
AAD-1v2	(160)	GLNVVHSATRVFGSLYQAQNRFRSNTSVKVMVDVAGDRET ~~VH~~ PLV ~~V~~ THPGSG ~~R~~ KGLYV ~~N~~ QVY ~~C~~ QRIEGMTDAESKPLLQF	
AAD-1v3	(161)	GLNVVHSATRVFGSLYQAQNRFRSNTSVKVMVDVAGDRET ~~VH~~ PLV ~~V~~ THPGSG ~~R~~ KGLYV ~~N~~ QVY ~~C~~ QRIEGMTDAESKPLLQF	
AAD-1 motif		XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX ~~X~~ ₁₃₁	
AAD-1v1	(240)	LYEHATRFDFTCRV ~~R~~ WKKDQVLV ~~W~~ DNLC ~~T~~ M ~~R~~ AV ~~P~~ DYAG ~~K~~ F ~~V~~ L ~~T~~ RTTVGGV ~~R~~ PAR	296
AAD-1v2	(240)	LYEHATRFDFTCRV ~~R~~ WKKDQVLV ~~W~~ DNLC ~~T~~ M ~~R~~ AV ~~P~~ DYAG ~~K~~ F ~~V~~ L ~~T~~ RTTVGGV ~~R~~ PAR	
AAD-1v3	(241)	LYEHATRFDFTCRV ~~R~~ WKKDQVLV ~~W~~ DNLC ~~T~~ M ~~R~~ AV ~~P~~ DYAG ~~K~~ F ~~V~~ L ~~T~~ RTTVGGV ~~R~~ PAR	
AAD-1 motif		XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX ~~X~~ ₁₀ ----- ~~X~~ ₃ R	

EX1008 ('406 Appl. & File History), COR-AAD1-00000471 (Wright-I Decl. App'x II) (color added); *id.* ("AAD-1 is the wildtype enzyme. Changes from wildtype are highlighted in light green. Defined AAD-1 motif residues are highlighted in blue . . .

and the additional R285 residue in . . . gray”). As a result of the insertion at position 2, AAD-1 v3 is 296 amino acid residues in length.⁵

83. As this figure clearly shows, AAD-1 v2 and v3 are nearly identical to AAD-1 v1. In AAD-1 v2, for example, just 2 out of 295 amino acids have been substituted, representing a change of less than 1%. Both AAD-1 v2 and v3 are approximately 99% identical to AAD-1 v1. (And AAD-1 v1 is, by definition, 100% identical to itself.) The POSA would have understood that AAD-1 v1 itself and two amino acid sequences that are approximately 99% identical to it are simply not representative of proteins having as little as 85% sequence identity to AAD-1 v1 (SEQ ID NO: 9).

84. First, the POSA would have recognized that the effect of an amino acid substitution can vary greatly depending on charge, hydrophobicity, size, reactivity, and the surrounding environment—including whether the amino acid is positioned on the protein’s surface, in the protein’s interior, or near a catalytic or substrate-binding site, or if it is involved in intra-protein or protein-substrate interactions. But the specification of the ’555 patent does not provide any structural information that might have allowed the POSA to make inferences about the effect of a given change.

⁵ To the extent claim 1 encompasses such insertions, it would only increase the number of amino acid sequences covered by the claim.

85. Second, the POSA would have realized that changes at one or two amino acid positions would not be representative of the much greater degree of variation allowed by the claims. For example, a single substitution in a 295 amino acid protein, such as the substitution of cysteine for arginine 212 in AAD-1 v2, represents just one of 20 possible residues that could occur at each of the 289 (or 288) amino acid positions not already specified by the claimed AAD-1 motifs. A 295-amino acid protein could have more than 40 substitutions as compared to SEQ ID NO 9, yet still have at least 85% sequence identity to SEQ ID NO: 9, as required by claim 1. The POSA would recognize that changing two amino acid residues, as in v2, cannot begin to represent the degree of amino acid sequence variation allowed in the claimed genera of AAD-1 proteins.

86. The locations of the changes in the variants further support the conclusion that the three examples are not representative. Nothing in the patent would have suggested to the POSA that changes at these positions would be particularly informative. The only change located within the claimed AAD-1 motif is the replacement of arginine 212 with cysteine in v2. The specification explains that the substitution of cysteine at that position was inadvertent, as opposed to the deliberate changes that would typically be made in a structural or mutagenesis study. EX1001 ('555 Pat.), 6:38-44. Arginine 212 is not adjacent to the five catalytic site residues and the specification does not provide any structural information indicating

the residue's role in the RdpA protein or the effect of a substitution at that position. The other changes in the variants are clustered near the N-terminus of the sequence, even more distant in sequence from the catalytic residues, and for similar reasons, would not have been informative. The POSA would not have thought it possible to extrapolate from these examples to other proteins within the genus, including proteins with combinations of 20, 30, 40 or more changes at amino acid positions that the applicant never discussed or modified, and including amino acid positions adjacent to the active site.

d. The Specification Does Not Describe Any Common Features Shared by AAD-1 Proteins Such that the POSA Can Identify the Proteins Belonging to that Genus.

87. I understand that another way a patent specification can adequately describe a claimed genus is by describing the features shared by the members of the genus, so the POSA can visualize or recognize the members of the genus. The '555 patent does not satisfy that requirement. The applicant never identified or described the particular amino acid residues within RdpA that are important to the claimed activity, which includes (*R*)-enantioselective activity for chiral phenoxy auxins and aryloxyphenoxypropionates, and without that information, the POSA could not have identified which of the proteins having an AAD-1 motif and at least 85% sequence identity to RdpA would have possessed the required activity.

88. As discussed above, neither the generic consensus motif in the original specification, nor the AAD-1 motifs first proposed by the applicant during prosecution of the '555 patent, defined a genus of enzymes having the activity required by the claims. The original consensus motif identified conserved residues known to be important to the catalytic activity of TfdA and related proteins in general. The applicant narrowed down that generic motif to the options that matched the sequence positions and spacing of AAD-1/RdpA, then claimed any protein including that “AAD-1 motif,” at least 85% sequence identity to AAD-1/RdpA, and the claimed activity. However, the original application provided no basis to believe that the genus of proteins having an AAD-1 motif would correspond to the genus of proteins with the claimed activity. Neither the patent specification nor the prior art disclosed the type of structural information that might have been used to identify the residues that are important to RdpA’s activity. The first structural analysis of RdpA was a 2006 paper that described the results of homology modeling, substrate docking, and site-directed mutagenesis. EX1035 (Müller 2006). Crystal structures of RdpA and the RdpA-substrate complex were not published until more than ten years after that. EX1019 (Chekan 2019); EX1052 (Larue 2019).

89. During prosecution, the applicant argued that the original application sufficiently described a genus of AAD-1 proteins with the claimed activity because “those skilled in the art are well familiar with the structure of α -ketoglutarate-

dependent dioxygenases.” EX1008 (’406 Appl. & File History), COR-AAD1-00000565 (Response (Jan. 10, 2020) (pp. 16-17). As support, the applicant cited two papers (Hotopp 2002, Müller 2006), arguing that “earlier published articles (e.g., Hotopp et al, Biochemistry 2002, 41, 9787-9794; see abstract) reference a published TfdA structural model and describe the identity of substrate-binding residues in tfdA,” and that “the AAD-1 proteins of the present invention bind to the same phenoxy auxin herbicide substrates as the tfdA protein and presumably retain similar structural domains as the homologous tfdA proteins.” *Id.* These arguments do not accurately characterize the prior art and publications describing work on TfdA and TfdA-like proteins. The prior art clearly taught that RdpA/AAD-1 and TfdA were *not* active on “the same phenoxy auxin herbicide substrates,” because it reported that TfdA was (*S*)-enantioselective while RdpA/AAD-1 was (*R*)-enantioselective. *See supra* ¶¶ 54-55. While the POSA would have expected to see similarities between RdpA/AAD-1 and other α KG dioxygenases, including the defined residues in the consensus motif, the POSA would have understood that there must be important differences between the structure of an (*R*)-enantioselective α KG dioxygenase like RdpA/AAD-1 and the previously modeled (*S*)-enantioselective TfdA protein. The prior art did not identify those differences (nor does the ’555 patent). *See, e.g.*, EX1035 (Müller 2006 (p. 1358)) (“In contrast to these conserved residues, essentially nothing is known about

the phenoxypropanoic acid-binding sites of [RdpA and SdpA], especially with regard to the structural basis of enantiospecificity.”). The POSA’s structural knowledge of α KG dioxygenases generally would not have allowed the POSA to identify α KG dioxygenases with the claimed activity, which includes (*R*)-enantioselective activity against chiral phenoxy auxin herbicides and aryloxyphenoxypropionate herbicides.

90. As noted above, the original specification discloses at most three examples that have the claimed activity, which includes (*R*)-enantioselectivity against chiral phenoxy auxins and (*R*)-aryloxyphenoxypropionates, as compared to the enormous number of proteins that have an “AAD-1 motif” and at least 85% percentage identity to SEQ ID NO: 9. As such, if the POSA had wanted to try to determine in April 2004 which residues correspond to the claimed activity, it would have been, at best, a massive research project involving an intensive experimental process of trial and error. The POSA would recognize that changing a single amino acid in a protein sequence can alter the protein’s structure and function. Understanding how changing one amino acid will affect a protein’s structure and function is frequently unpredictable, especially where, as here, there was no crystal structure for RdpA. The POSA would further recognize that adding more changes to a protein’s amino acid sequence increases the likelihood of unpredictable changes to structure and function. The ’555 patent’s predecessors do not provide the POSA

with any indication of what the results of that research project might be. The specification contemplates, for example, the possibility of substitutions. But at the same time, it acknowledges that even so-called “conservative” substitutions can affect whether a protein has a given activity. EX1001 (’555 Pat.), 38:6-31. Likewise, the specification states that proteins having a given activity can be identified via a variety of methods, EX1001 (’555 Pat.), 31:28-53, but it does not indicate that the inventors performed those methods, and instead leaves it to the POSA to try to identify which proteins actually have the claimed activity and which do not.

91. The 85% sequence identity limitation does not fix the problems with the claims. The POSA would not have assumed that any minimum sequence identity cutoff would adequately define a genus of proteins with the claimed (*R*)-enantioselective activity, because such a cutoff does not account for the different roles played by different amino acids in the protein. Given that only AAD-1 itself and two variant sequences were exemplified and tested in the patent, all of which have approximately 99-100% sequence identity, the sequence identity cutoffs in the claims would appear particularly arbitrary to the POSA. As discussed above, these cutoffs allow a wide range of sequence variation. For example, a 295-amino acid protein with more than 40 amino acid changes as compared to SEQ ID NO: 9 would satisfy the at least 85% sequence identity requirement in claim 1. The POSA would

expect that the impact of such change(s) would vary depending on the location of the change(s) as well as the selected residue(s)' charge, hydrophobicity, size, reactivity, and surrounding protein environment. While the POSA would have deduced that certain amino acids in RdpA must be important to its claimed activity, including its (*R*)-enantioselectivity, the patent does not identify which amino acids are important, how many there are, or where they are. Thus, the POSA would not have been in a position to predict the effects of a substitution at any given position, much less the cumulative impact of multiple changes at multiple positions in the protein. The POSA could not have known, and would not have been able to predict, based on the limited information in the patent, whether any given amino acid sequence possessing the required motif and percent identity would have had the claimed activity. That uncertainty is particularly true given the recognition in the prior art that a few changes to the amino acid sequence of an enzyme could correspond to opposite stereoselectivities. *See* EX1041 (Saari 1999 (p. 427)) (“recent crystallographic characterization of two tropinone reductases demonstrate the presence of almost identical overall protein folding, but the closely related enzymes exhibit opposite substrate stereoselectivities due to differences in a few charged residues at the active site.”); *id.* (pp. 426-47 & Fig. 5)); EX1023 (Elkins 2002 (p. 5185, 5190 & Fig. 5)), EX1035 (Müller 2006 (pp. 1358-66)); *see also* EX1040 (Saari 1998 (p. 21)) (“The lack of close sequence relationship between

TfdA and other members of the α -KG-dependent dioxygenase family is not very surprising as these enzymes as a group do not display much overall sequence identity, even amongst dioxygenases acting on related substrates.”).

e. The Prosecution History of the '555 Patent Confirms that the Original Specification Did Not Describe the AAD-1 Motifs or the Claimed Genera of AAD-1 Proteins.

92. During the prosecution of the '555 patent, the applicant offered various arguments that the claims were supported by the original specification. Because the original specification did not include the claimed AAD-1 motifs, and the two AAD-1 variants provided were approximately 99% identical to RdpA, the POSA would not have understood it to have described the claimed AAD-1 motifs and genera of AAD-1 proteins. As explained below, the information discussed during prosecution further confirms that the application as originally filed did not describe the genera of proteins in the '555 patent claims.

93. During prosecution of the '406 application, the applicant stated that “support for the new claims is found throughout the specification, including for example in paragraphs [0050], [0078], [0079], [0082], [0085], [0089], [0093], [0099], [00107] and the original claims.” EX1008 ('406 Appl. & File History), COR-AAD1-00000010 (Prelim. Amend. (Oct. 7, 2016) (p. 8)). I disagree with that statement. The cited portions of the original application do not describe an AAD-1 motif or a genus of proteins having such a motif. These citations would not have

allowed the POSA to conclude that the inventors had identified such a motif or such a genus when they filed the original specification years earlier.

94. After an initial rejection of the claims by the examiner, the applicant amended the specification and claims to add the AAD-1 motif as it appears in claim 1 of the '555 patent. EX1001 ('555 Pat.), 18:20-28, claim 1. The amendment to the specification stated: "Mapping the α -ketoglutarate-dependent dioxygenase motif disclosed in the previous paragraph to the sequence of SEQ ID NO: 9 reveals the AAD-1 motif of HX₁₁₂D(X)₁₁₄₋₁₃₇T(X)₁₃₉₋₂₆₉H(X)₂₇₁₋₂₈₀R." *Id.*; EX1008 ('406 Appl. & File History), COR-AAD1-00000480, COR-AAD1-00000486-487 (Response (Apr. 12, 2019) (pp. 2, 8-9)). In the accompanying submission, the applicant argued that "the original specification highlights the key amino acid residues of aryloxyalkanoate dioxygenase by providing the structure of a motif comprising the active site of the enzyme." EX1008 ('406 Appl. & File History), COR-AAD1-00000488-89 (Response (April 12, 2019) (pp. 10-11)). The applicant further argued that the generic motif "could be used to identify an AAD-1 motif as a means of identifying important residues of the AAD-1 active site" and "provides a roadmap to identify the corresponding positions" in AAD-1 v1, v2, and v3, *id.*, and that this "allow[s] one to generate an 'AAD-1 motif' . . . that is specific to the claimed genus of AAD-1 proteins," *id.* The applicant further argued that the claims "have been narrowly tailored to be directed to AAD-1 proteins that enzymatically degrade a

phenoxy auxin herbicide and an (*R*) aryloxyphenoxypropionate herbicide by requiring the claimed peptides to comprise the functional element of the AAD-1 motif.” *Id.*

95. These arguments incorrectly conflate the “active site” residues that are identified by the generic consensus α KG motif with the residues responsible for the stereoselective activity that, according to the ’555 patent, distinguishes RdpA from other α KG dioxygenases, in particular its (*R*)-enantioselective activity against chiral phenoxy auxins and aryloxyphenoxypropionate herbicides. “Mapping” the generic consensus α KG motif onto RdpA only confirms what the prior art already taught, that RdpA shares the canonical active site residues characteristic of α KG dioxygenases. While the five or six active site residues required by the consensus motif and AAD-1 motifs are important to the function of α KG dioxygenases, these residues are shared by α KG dioxygenases with varied substrates and enantioselectivities, most of which were not known as of April 2004 to have (*R*)-enantioselectivity. Thus, it is not correct that the claims are “narrowly tailored to be directed to AAD-1 proteins that enzymatically degrade a phenoxy auxin herbicide and an (*R*) aryloxyphenoxypropionate herbicide by requiring the claimed peptides to comprise the functional element of the AAD-1 motif.” EX1008 (’406 Appl. & File History), COR-AAD1-00000488-89 (Response (Apr. 12, 2019) (pp. 10-11)). Requiring the claimed AAD-1 proteins to have the active site residues characteristic

of α KG dioxygenases does not “narrowly tailor” the claimed genus to the set of proteins possessing the claimed activity, including the relevant (*R*)-enantioselective activity. *Id.* Nothing in the specification identifies the residues that correspond to the claimed activity, much less other information that could support a claim to the recited “AAD-1” motifs and 85% sequence identity.

96. In addition, the original consensus motif does not include any residues corresponding to the “(X)₂₈₂₋₂₈₄R” in the claim 2 motif, and the applicant did not attempt to amend the specification to include the claim 2 motif. Dr. Wright argued that the original application nonetheless described that motif because “at the time of the invention, the analogous arginine in TfdA had been concluded to be involved in 2,4-D carboxylate binding,” citing a 2002 paper (EX1029 (Hotopp 2002)). EX1008 (’406 Appl. & File History), COR-AAD1-00000462 (Wright-I Decl. ¶ 13). I disagree that the original application disclosed the claim 2 AAD-1 motif or a genus of proteins with that motif. The original application did not cite or discuss the 2002 paper or this additional arginine residue, and the original consensus motif in the application could not reasonably be interpreted by the POSA as describing additional residues that it did not include, and that the application did not otherwise identify as important. The additional arginine is in the sequences of the three proteins cited by the applicant in the file history—*i.e.*, AAD-1 v1, v2, and v3—along with more than 280 other residues not specified

in the generic consensus motif, but those amino acids were not described as part of a generic “motif” describing a broad genus of sequences. Because the additional arginine is present in enzymes that the applicant distinguished as lacking (*R*)-enantioselective activity, including AAD-2, the POSA would not have understood from the ’406 application that the additional arginine is important to confer that type of activity.

97. In his first declaration, Dr. Wright submitted test results for nine additional “AAD-1 variants,” three of which had the claim 2 motif and “~94-95%” sequence identity to SEQ ID NO. 9, and six of which included a modification disrupting the claim 2 motif. EX1008 (’406 Appl. & File History), COR-AAD1-00000462-63, COR-AAD1-00000472-74 (Wright-I Decl. ¶¶ 14-15, App’x III). The declaration describes these results as confirming that the additional arginine included in the claim 2 motif is essential to the activity of AAD-1. It is not possible to tell from the limited testing in the declaration what role this arginine plays in the activity of RdpA, although as explained above, it seems unlikely to be responsible for RdpA’s (*R*)-enantioselective activity. That said, the testing does show that the claim 1 motif is not sufficient to describe AAD-1 proteins possessing the claimed activity, because the claim 1 motif does not require this essential arginine, and the original application does not otherwise indicate that it is necessary.

98. The applicant next argued that the POSA would have recognized the AAD-1 motifs as important based on a comparison of the amino acid sequences of AAD-1 v1 (SEQ ID NO: 9) and AAD-2 (SEQ ID NO: 13). EX1008 ('406 Appl. & File History), COR-AAD1-00000462 (Wright-I Decl. ¶ 13). The '555 patent explains that AAD-2 selectively degrades (*S*)-enantiomers, but not (*R*)-enantiomers. EX1001 ('555 Pat.), 112:55-61. Dr. Wright observed that one aspect of the consensus motif, the “large undefined residue spacer between the defined T/S and H,” differs between AAD-1 and AAD-2: AAD-1 v1, v2, and v3 have 131 unspecified amino acids in this location, while AAD-2 has 121. EX1008 ('406 Appl. & File History), COR-AAD1-00000461-62, COR-AAD1-00000470-71 (Wright-I Decl. ¶ 12, App'x II) (comparing AAD-1 v1 to AAD-2). Dr. Wright argued that “[o]ne skilled in the art would recognize the much more limited group having the desired functional dual-MOA activity would be defined by the more refined motif HXDX₂₄TX₁₃₁HX₁₀R, which effectively excludes AAD-2.” EX1008 ('406 Appl. & File History), COR-AAD1-00000461-462 (Wright-I Decl. ¶ 12).

99. This rationale is flawed, and it is not reflected in the original application. The specification never identifies the “large undefined residue spacer between the defined T/S and H” as important to the “desired functional dual-MOA activity.” Dr. Wright’s hypothesis that a length of exactly 131 unspecified amino acids correlates to that activity was never proposed, tested, or supported in the

original application. If the specification had disclosed that the inventors had excised ten amino acids from the RdpA sequence and observed a resulting change in its enantiospecificity, that might have been a supportive result. But that is not the case, and nothing suggests to the POSA that the inventors thought of doing so in 2004.

100. The application's discussion of AAD-2 does not justify a different conclusion. The original application did not identify any aspects of the AAD-2 sequence as particularly important to AAD-2's (S)-enantioselective activity and it does not include any comparisons of the AAD-1 and AAD-2 sequences. If it had, the comparison would only highlight that AAD-1 and AAD-2 have numerous differences aside from the "large undefined residue spacer between the defined T/S and H." The applicant characterized AAD-2 as having just 27% sequence identity to AAD-1. EX1008 ('406 Appl. & File History), COR-AAD1-00000488 (Response (Apr. 12, 2019) (p. 10)). This is illustrated in a modified version of the comparison from Dr. Wright's declaration shown above, reproduced below, with highlighting in orange at the positions where AAD-1 v1 and AAD-2 differ:

		1		80
AAD-1v1	(1)	MHAALSPLSQRFERTIAVQPLTGVLGAEITGVDLREPLDDSTWNEILDAFHTYQVIYFPGQAITNEQHIAPSRRFG-----		
AAD-2	(1)	-----MTIAIRQLQTHFVGQVSGLDLRKPLTPGEAREVESAMDKYAVLVFHDQDITDEQQMAFALNFGQREDA		
		81		160
AAD-1v1	(76)	---FVDPVPLLKSIIEGYPEVQIRREANESGR-----VIGDDWITSTFLDAPPAAVVMRAIDVPEHGGDGFLSMY		
AAD-2	(69)	RGGITVTKEDYRLQSGLNVDVSNLGKDGKPLAKDSRTHLFLNGLNCLMSSSFRPIPAKFSLLSARVVNPTGGNIEFADMR		
		161		240
AAD-1v1	(145)	TAWETLSPTMQATIEGLNVVHSATRVFGSLYQAQNRFSNTSVKVMVDVDAGDRETVHPLVVTHPGSGRKLQLYVNOVYCQR		
AAD-2	(149)	AAYDALDDETKAEIEDLVCEHSLMYSRGLGFTTEYTDDEE-----KMPKPEVLQRLVETHPVHRRSLYLS-SHAGK		
		241		317
AAD-1v1	(225)	IEGMTDAESKPLLQFLYEHATRFDFTCRVRWKKDQVLVWDNLCTMIRAVPDYAGKFIYLTRTTVGGVRPAR-----		
AAD-2	(219)	IASMSVPEGRLLLRDLNEHATQPEFVYVHKWKLHDLVMWDNRQTMIRVRRYDQSQPIDMRRATVAGTEPTVQQQAAE		

EX1008 ('406 Appl. & File History), COR-AAD1-00000470 (Wright-I Decl. App'x II). As the illustration shows, fewer than 85 of the 317 positions shown are identical, and in addition to the difference of ten amino acids emphasized by Dr. Wright, there are other regions that also differ in length (highlighted in yellow). Given the hundreds of differences between AAD-1 and AAD-2, none of which are discussed in the patent, the POSA would not have assumed that the enzymes' opposite enantioselectivities were attributable to any particular distinction. Without more information, the POSA could not have drawn any conclusion about which differences correspond to the claimed activity.

101. Indeed, the fact that the α KG dioxygenase motif encompasses AAD-2, *e.g.*, EX1001 ('555 Pat.), SEQ ID NO: 13; EX1008 ('406 Appl. & File History), COR-AAD1-00000470-471 (Wright-I Decl. App'x II), means that one would not “map” the α KG dioxygenase motif onto RdpA and expect to obtain a group of proteins that have (*R*)-enantioselective activity required by the claims of the '555 patent.

102. Dr. Wright's first declaration suggests that the POSA would have focused on the length of this undefined amino acid series, ignoring the other differences between AAD-1 and AAD-2, because that length is one of the variables in the generic α KG consensus motif. But this rationale is flawed. The POSA would not have looked to the generic α KG consensus motif, which describes characteristics

that are commonly shared by α KG dioxygenases, for guidance on the characteristics that distinguish RdpA's activity from that of other α KG dioxygenases. The '555 patent repeatedly emphasizes that RdpA's activity, including its (*R*)-enantiospecific activity, is not shared by other α KG dioxygenases. For example, because most α KG dioxygenases do not have (*R*)-stereospecific activity, the α KG dioxygenase consensus motif would not be expected to capture the characteristics important to that stereospecificity. The POSA would have understood this, and would not have expected the variables in that consensus motif, or a derivative of it, to define and describe a genus of AAD-1 proteins limited to those with the claimed activity.

103. After the claims were rejected again, the applicant submitted a declaration from Dr. Nair, EX1008 ('406 Appl. & File History), COR-AAD1-00000590-608 (Nair Decl.), and argued that "both witness declarations emphasize the importance of the AAD-1 motif as the structure that provides the dual MOA activity that is common to members of the genus, and assert that [the POSA] would recognize the AAD-1 motif as disclosed in the originally-filed specification." EX1008 ('406 Appl. & File History), COR-AAD1-00000565 (Response (Jan. 10, 2020) (p. 16)). This assertion again confuses the active site residues specified by the α KG dioxygenase consensus motif with the (unidentified) residues responsible for RdpA's activity, including its (*R*)-stereospecific activity. Nothing in the original

application identified the structural features important to the so-called “dual MOA” activity required by the claims.

104. The accompanying declaration from Dr. Nair described the findings of a 2019 crystal structure paper co-authored with Dr. Wright. EX1008 ('406 Appl. & File History), COR-AAD1-00000594-595 (Nair Decl. ¶ 11) (citing EX1019 (Chekan 2019)). Dr. Nair argued that comparisons of the sequence of AAD-1 with “(S)-specific enantiomer dioxygenases (including AAD-2, TfdA, and another homologue, AAD-12) confirmed a divergence in the length and identity of residues which mapped to the substrate capping loop as identified by comparison of substrate-bound crystal structures,” and that “crystallography data further validates the importance of the spacing between the critical active site amino acids as defined in the AAD-1 motif of the claimed invention.” EX1008 ('406 Appl. & File History), COR-AAD1-00000594-595 (Nair Decl. ¶ 11).

105. One basic problem with these arguments is that the POSA would not have had the benefit of substrate-bound crystal structures or crystallography data until that information was published in 2019. That information was not known when the original application was filed in 2004. Without structural information, there was insufficient information available to distinguish the amino acid sequences of “AAD-1 proteins” with the claimed activity from those of the other α KG dioxygenases. As Drs. Nair and Wright explained in their 2019 paper, “[t]o date, no crystal structure

has been reported for any member of the AAD family, and there is, therefore, an insufficient knowledge base to distinguish bona fide AADs from other enzymes of the Fe(II)/ α KG dioxygenase class.” EX1019 (Chekan 2019 (p. 13300)).

106. An additional problem is that the 2019 paper indicates that multiple features are relevant to the (*R*)-enantioselective activity that distinguishes RdpA/AAD-1 from other α KG enzymes, including features not identified as important in the original application, and features that are not required by the generic α KG consensus motif (or the more limited AAD-1 motifs). EX1019 (Chekan 2019 (pp. 13301-13303, Figs. 3-4)); EX1020 (Chekan 2019 Suppl. (Fig. 10)). For example, in connection with AAD-1’s activity on a range of substrates, the paper points to a number of residues—specifically, Arg104, Asp108, and Asp109 in RdpA/AAD-1, as well as “residues Asn90 through Cys112” in AAD-2, all of which are located outside the claimed “AAD-1 motif”—involved in a “solvent exposed tunnel [that] was not evident in earlier modeling studies.” EX1019 (Chekan 2019 (p. 13302)). In connection with AAD-1’s enantioselectivity, the paper states that “the differences between AAD-1 and AAD-2 are the result of an ~20-residue insertion” in AAD-2 consisting “of residues Asn90 through Cys112 in AAD-2” in the “ β 2/ β 3 loop,” which “likely results in the change in substrate stereospecificity.” EX1019 (Chekan 2019 (p. 13303)). None of the residues identified in these statements is discussed in the original application or specified by the consensus

motif. Arg104, Asp108, Asp109, and the ~20 residues in AAD-2 are located outside the consensus motif. EX1020 (Chekan 2019 Suppl. Info. (Fig. 10)). Thus, the 2019 paper is consistent with what the POSA would have understood in 2004: the consensus motif does not describe the residues important to the distinctive (*R*)-enantioselective activity of RdpA. Thus, the original application is inadequate to describe a genus of AAD-1 proteins having that activity as distinguished from other α KG dioxygenases.

107. Dr. Nair's declaration fails to mention most of the differences discussed in the 2019 paper, instead focusing on a "divergence in the length and identity of residues which mapped to the substrate capping loop." EX1008 ('406 Appl. & File History), COR-AAD1-00000594-595 (Nair Decl. ¶ 11). Dr. Nair's declaration indicates that this substrate capping loop falls within the series of undefined amino acids that is shorter in AAD-2 than AAD-1, EX1008 ('406 Appl. & File History), COR-AAD1-00000594-595 (Nair Decl. ¶ 11); EX1020 (Chekan 2019 Suppl. Info. (Fig. 10)), and the 2019 paper states that "[c]hanges in both the length and identity of residues in this loop may result in differences in enantioselectivity among AADs." EX1019 (Chekan 2019 (p. 13303)). In my opinion the evidence in the 2019 paper falls short of establishing that this substrate capping loop is important to RdpA's (*R*)-enantiospecific activity. But regardless, the declaration and the 2019 paper acknowledge that it is not just the loop's length that is important, but also the

“identity of residues in this loop.” Both the original generic consensus motif and the AAD-1 motifs are silent with respect to the “identity of residues” in the substrate capping loop that might be required for RdpA’s activity.

108. Dr. Nair’s declaration also asserts that “even without crystallography information” the POSA “would have compared and recognized the importance of the sequence differences between AAD-1 variants [(*R*)-specific dioxygenase] having dual herbicide MOA Fe/ α KG dioxygenase activity and (*S*)-specific dioxygenases”. EX1008 (’406 Appl. & File History), COR-AAD1-00000594-595 (Nair Decl. ¶ 11) (brackets in original). The declaration includes a comparison of the sequences of AAD-1, AAD-2, TfdA, and AAD-12 from the 2019 paper. EX1008 (’406 Appl. & File History), COR-AAD1-00000594-595 (Nair Decl. ¶ 11); EX1020 (Chekan 2019 Suppl. (Fig. 10)). The sequences of TfdA and AAD-12 are not in the ’555 patent, and Dr. Nair does not explain why the POSA would have compared these particular sequences. Regardless, the POSA would not have concluded from such a comparison that selecting a fixed length from the options in the α KG consensus motif would describe a genus of α KG dioxygenases with either (*R*)- or (*S*)-enantioselectivity. As explained above, the POSA would not have understood the variables in the α KG consensus motif, or any motif derived from it, to be responsible for giving RdpA its distinctive (*R*)-enantioselective activity. But if the POSA had considered that possibility that a length of exactly 131 undefined amino

acids was required for that activity, as the Nair and Wright declarations suggest, the POSA would have rejected that hypothesis as inconsistent with the prior art, including prior art discussing work done in my lab.

109. In 1999, researchers reported that different strains of bacteria had opposite enantioselective activity on phenoxy herbicides (Saari 1999). It was reported that JMP134 and *Burkholderia cepacia* RASC degraded (*S*)-dichlorprop, while for *Alcaligenes denitrificans* “activity exhibited stereospecificity opposite to that of the JMP134 and RASC strains.” EX1041 (Saari 1999 (Abstract)). Researchers amplified a TfdA-like gene from *A. denitrificans* and compared its amino acid sequence to those of JMP134 and RASC:

	150	160	170	180	190	200
JMP134	RAAYDALPRDLQSELEGLRAEHYALNSRFLGDTDYSEAQRNAMPPVNWPLVRTHAGSGRK : ::: : : : : :					
<i>A. denitrificans</i>	RAAYDDLPEDFKKELQGLRAEHYALNSRFILGDTDYESQQRNAMPVSWPLVRTHAGSGRK : : : : : : : :					
RASC	RAAYDDLPEDFKKELQGLRAEHYALHSRIFLGDETESESQQRNAMPVSWPLIRTHAGSGRK 170 180 190 200 210 220					
	210	220	230	240	250	
JMP134	FLFIGAHASHVEGLPVAEGRMLLAELLEHATQREFVYRHRWNVGDLVM : : : : :					
<i>A. denitrificans</i>	FLFIGAHAGHIEGRPVAEGRMLLAELLEHATQPKFVYRHSWKVGDLVM : : : : : : : :					
RASC	FLFIGAHASHIEGRPVAEGRMLLAELLEHATQPKFVYRHSWKVGDLVM 230 240 250 260 270					

Fig. 5. Comparison of an *A. denitrificans* TfdA-like sequence with the enzymes from RASC and JMP134. The deduced sequence encoded by the PCR amplification product arising from *A. denitrificans* DNA was compared to the indicated portions of the RASC and JMP134 TfdA sequences. Identical amino acids are indicated by a solid vertical bar and similar amino acids by a dashed bar.

EX1041 (Saari 1999 (Fig. 5)). The sequences in Fig. 5 include the region identified by Drs. Nair and Wright, where the sequences of AAD-1 and AAD-2 differ in length. But despite the different enantioselectivities of the three enzymes represented in Fig.

5, the three sequences do not have different lengths. Researchers prepared a figure comparing the 109 amino acid sequence from *A. denitrificans* (“Ad”) in Figure 5 with the corresponding sequences from RdpA/AAD-1 (SEQ ID NO: 9) and AAD-2 (SEQ ID NO: 13). This comparison shows that although RdpA/AAD-1 and the TfdA-like enzyme from *A. denitrificans* both have (*R*)-enantioselective activity, their sequences are not the same length. This region of the *A. denitrificans* enzyme instead resembles AAD-2:

AAD-1	YTAWETLSPTMQATIEGLNVVHSATRVFGSLYQAQNRFRSNTSVKVM DV	DAGDRET V HPL	60
Ad	RAAYDDLPEDFKKELQGLRAEHYALNSR FILGDT---	DYSESQ-----RNAMPPVSWPL	51
AAD-2	RAAYDALDDETKAEIEDLVCEHSLMYSRGLGFT---	EYTD EE-----KQMF KPVLQRL	51
	:*:: *	: :::.* *	* : ::: . *
AAD-1	VVTHPGSGRKGLYVNQVYCQRIEGMTDAESKPLLQFLYEHATRFDFTCRVRWKKDQVLVW		120
Ad	VRTHAGSGRKFLFIGA-HAGHIEGRPVAEGRMLIAELLEHATQRKFVYRHSWKVGD LVM-		109
AAD-2	VRTHPVHRRKSLYLSS-HAGKIASMSVPEGRLLLLRDLNEHATQPEFVYVHKWKLHDLVMH		110
	* ** ** *: : . : . : *	* . : * : * **** : . * . ** : : :	
AAD-1	DNLCTMH		127
Ad	-----		109
AAD-2	-----		110

Although Drs. Nair and Wright did not mention the findings reported in Saari 1999 in their declarations, the POSA would have been aware of them. These findings provide yet another reason that the POSA would not have believed that the length of the 131-amino acid region in RdpA was determinative of its enantioselectivity.⁶

⁶ In 2004, after *A. denitrificans* was reclassified as *Achromobacter xylosoxidans* subsp. *denitrificans*, another group published the complete sequence of the *A. denitrificans* enzyme reported in Saari 1999. EX1046 (Vedler 2004); see EX1012

110. After the examiner again rejected the claims, the applicant submitted a second declaration from Dr. Wright describing additional *in vitro* testing for variant enzymes identified as “Var1” through “Var8.” The declaration stated that these variants had as little as 82% sequence identity to SEQ ID NO: 9, but the amino acid sequences of the variants were not provided, and the declaration did not describe how or where they were modified, other than to state that the AAD-1 motif was “retained in the variants tested” and that [a]mino acid changes were made throughout the protein sequence.” EX1008 (’406 Appl. & File History), COR-AAD1-00000660 (Wright-II Decl. ¶ 18). No rationale was provided for the particular modifications and sequences selected for testing. Without more information, the test results provided do not support a general conclusion that the genus of amino acid sequences possessing an AAD-1 motif and the required sequence identity to SEQ ID NO: 9 possess the required activity. Moreover, even had Dr. Wright submitted the identity of the amino acid sequences for Var1-Var8, such a small number of variants would not have supported a conclusion that the claimed genus exhibits the claimed activity.

(Accession No. AAS49436.1, submitted Feb. 04, 2004). The full-length sequence supports the same conclusions as the 109-amino acid sequence reported in Saari 1999.

2. Corteva '437 Anticipates the Challenged Claims.

111. Corteva '437 is the publication of the international patent application to which the '555 patent claims priority. Although, as I explain above in Section VII.A.1, Corteva '437 does not support the '555 patent's claims to an "AAD-1 protein" with an "AAD-1 motif" and at least 85% sequence identity with SEQ ID NO: 9, Corteva '437 discloses individual proteins (*e.g.*, AAD-1 v1 (RdpA) and v2) that fall within the scope of those claims. Thus, Corteva '437 anticipates each of the challenged claims.

a. Claim 1

112. Claim 1 recites:

1. A transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises:
 - i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and
 - ii) an AAD-1 motif having the general formula of:

$HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$, wherein

X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9;

$(X)_{114-137}$ represents a sequence of 24 amino acids;

(X)₁₃₉₋₂₆₉ represents a sequence of 131 amino acids;

and

(X)₂₇₁₋₂₈₀ represents a sequence of 10 amino acids.

113. Corteva '437 anticipates this claim.

i. “A transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein”

114. Corteva '437 discloses and claims a transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein. EX1021 (Corteva '437), [00018]-[00020], [00095]-[00105], [00149]-[00151], claims 1-4. In particular, Corteva '437 discloses that transgenic plant cells may be modified to express recombinant polynucleotides that encode the exemplary AAD-1 proteins that both Corteva '437 and the '555 patent refer to as AAD-1 v1 and v2 (SEQ ID NO: 9 and 10). EX1021 (Corteva '437), [0050]-[0051], SEQ ID NOS: 9-10; EX1001 ('555 Pat.), 6:56-60, SEQ ID NOS: 9-10. Corteva '437 states: “The transgenic expression of the subject *AAD-1* genes is exemplified in, for example, *Arabidopsis*, corn (maize), tobacco, cotton, rice, soybean, and canola,” and “can be applied to any other desired types of plants.” EX1021 (Corteva '437), [00104].

115. Claim 1 of the '555 patent and claim 1 of Corteva '437 are as follows:

'555 Patent, Claim 1	Corteva '437, Claim 1
1. A transgenic plant cell comprising a recombinant polynucleotide that	1. A transgenic plant cell comprising a polynucleotide that encodes an AAD-1

encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R,$ wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(X)_{114-137}$ represents a sequence of 24 amino acids; $(X)_{139-269}$ represents a sequence of 131 amino acids; and $(X)_{271-280}$ represents a sequence of 10 amino acids.	protein comprising the amino acid sequence of SEQ ID NO:9 or a variant of SEQ ID NO:9 wherein said variant has aryloxyalkanoate dioxygenase activity, at least one amino acid deletion or conserved substitution, and at least 95% sequence identity with SEQ ID NO:9.
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EX1001 ('555 Pat.), claim 1; EX1021 (Corteva '437), claim 1.

116. Notably, both claim 1 of the '555 patent and claim 1 of Corteva '437 encompass AAD-1 v1 (SEQ ID NO: 9). Claim 1 of the '555 patent encompasses AAD-1 v1 (SEQ ID NO: 9) because, by definition, AAD-1 v1 has more than 85% sequence identity to itself and has the claimed AAD-1 motif. *See infra* Section VII.A.2.a.iii. Claim 1 of Corteva '437 expressly encompasses “an AAD-1 protein comprising the amino acid sequence of SEQ ID NO:9.” Claims 2-43 and 57-60 of Corteva '437 refer, directly or indirectly, back to claim 1. As I explain in the sections below in further detail, Corteva '437's dependent claims disclose elements that overlap with the challenged claims 4-33 (*i.e.*, various dependent claims of the '555 patent). The POSA would understand that because claim 1 of Corteva '437 encompasses at least AAD-1 v1, Corteva '437's dependent claims would apply to that protein. Moreover, the POSA would understand that because AAD-1 v1 (SEQ ID NO: 9) and v2 (SEQ ID NO: 10) were exemplary AAD-1 proteins described in the examples, *e.g.*, EX1021 (Corteva '437), [00230]-[0264] & Tbls. 15-16, Corteva '437's dependent claims would also be applicable to those proteins for purposes of what Corteva '437 teaches. As a result, Corteva '437 anticipates the dependent claims of the '555 patent as well.

- ii. **“that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically**

degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide”

117. Corteva '437 discloses and claims transgenic plant cells expressing AAD-1 proteins, such as AAD-1 v1 (SEQ ID NO: 9) and AAD-1 v2 (SEQ ID NO: 10), that enzymatically degrade phenoxy auxin and (*R*)-aryloxyphenoxypropionate herbicides. EX1021 (Corteva '437), Abstract, [0020], [0074]-[0076], [0092]-[0099], [00179]-[0211], [00260]-[00264] & Tbls. 6-8, 16, claims 1-4. Both Corteva '437 and the '555 patent describe degradation of phenoxy auxins and (*R*)-aryloxyphenoxypropionate herbicides as “aryloxyalkanoate dioxygenase activity.” EX1021 (Corteva '437), claim 1, [0020], [0086]-[0087], [0097]; EX1001 ('555 Pat.), claim 1. They attribute the ability to exhibit this activity as benefits of AAD-1 and certain variants. EX1021 (Corteva '437), [0074]-[0077]; EX1001 ('555 Pat.), 7:35-12:15.

118. For example, Corteva '437 discloses that one “benefit” of the “AAD-1” protein is that it “is able to degrade the R-enantiomers (herbicidally active isomers) of the chiral phenoxy auxins (*e.g.*, dichlorprop and mecoprop) in addition to achiral phenoxy auxins (*e.g.*, 2,4-D, MCPA, 4-chlorophenoxyacetic acid).” EX1021 (Corteva '437), [0074], Tbl. 1. It also discloses that an “additional benefit of the *AAD-1* gene” is its ability to “degrade a host of commercial and non-commercial graminicidal compounds of the general class aryloxyphenoxypropionates (AOPPs),” which “may allow the use of any of a

number of AOPP compounds in transgenic crops containing *AAD-1*,” including “corn, rice, wheat, barley, rye, oats, sorghum, warm and cool-season turf species, grass pasture species, and many others.” EX1021 (Corteva ’437), [0076]. Tbl. 2.

119. Corteva ’437 also includes experimental examples demonstrating that AAD-1 v1 and v2 have the claimed aryloxyalkanoate dioxygenase activity. For example, Corteva ’437 discloses that transgenic *Arabidopsis* plants expressing AAD-1 v2 (SEQ ID NO:10) are tolerant to phenoxy auxin herbicides (including 2,4-D). EX1021 (Corteva ’437), [00260]-[0264] & Tbl. 16. It also discloses that AAD-1 v1 degrades (*i.e.*, “cleaved”) both phenoxy auxin herbicides (including 2,4-D, MCPA, (*R*)-dichlorprop, and (*R*)-mecoprop) and (*R*)-aryloxyphenoxyalkanoate herbicides (including (*R*)-cyhalofop, (*R*)-diclofop, (*R*)-haloxyfop, and (*R*)-quizalofop), EX1021, [00107]-[00109], [00185]-[0215] & Tbls. 3-4, 6-9, Figs. 5-6B. Corteva ’437 discloses that the same principles “can be applied to any other desired types of plants.” EX1021 (Corteva ’437), [00104].

120. In addition, as exemplified by Corteva ’437’s disclosures, the POSA would have understood that the recited aryloxyalkanoate dioxygenase activity is a necessary and natural result of the disclosed AAD-1 v1 and v2 enzymes. As I explain above, AAD-1 v1 and v2 catalyze degradation of phenoxy auxin herbicides (including 2,4-D) and (*R*)-aryloxyphenoxypropionate herbicides by hydroxylation of carbon-2 in the modified alkanoic acids, resulting in elimination of the substituted

phenols from the carboxylic acid portions of their chemical structures. The POSA would have understood that the recited aryloxyalkanoate dioxygenase activity resulted from the chemical properties of AAD-1 v1 and v2.

- iii. “further wherein said AAD-1 protein comprises:
i) an amino acid sequence having at least 85%
sequence identity with SEQ ID NO: 9; and ii)
[the claim 1 AAD-1 motif]”**

121. Corteva '437 discloses and claims AAD-1 proteins that satisfy this limitation. For example, as explained above, Corteva '437 discloses the “AAD-1” proteins AAD-1 v1 and v2, which it discloses to have the amino acid sequences set forth in SEQ ID NO: 9 and 10, respectively. EX1001 ('555 Pat.), SEQ ID NO: 9-10; EX1021 (Corteva '437), SEQ ID NO: 9-10. Comparison of these amino acid sequences demonstrates that AAD-1 v1 and AAD-1 v2 have at least 85% sequence identity with SEQ ID NO: 9. By definition, SEQ ID NO: 9 is 100% identical to itself. Corteva '437 discloses that SEQ ID NO:10 is identical to SEQ ID NO: 9 except that an alanine is substituted for the histidine at position 2, and a cysteine is substituted for the arginine at position 212. EX1021 (Corteva '437), [0045]-[0046], [0050]-[0051], [00230]-[00233], SEQ ID NO:10; *see also* EX1001 ('555 Pat.), 6:38-43, SEQ ID NO: 9-10; EX1008 ('406 Appl. & File History), COR-AAD1-00000470-471 (Wright-I Decl. App'x II). The SEQ ID NO: 10 sequence thus has approximately 99% sequence identity to SEQ ID NO: 9.

122. Corteva '437 also discloses proteins having the AAD-1 motif recited in this claim. During prosecution of the '555 patent, the applicant represented to the USPTO that AAD-1 v1 and v2 (SEQ ID NO: 9-10) have the claimed AAD-1 motif, which requires a histidine (H) at position 111, aspartic acid (D) at position 113, threonine (T) at position 138, histidine (H) at position 270, and arginine (R) at position 281. EX1008 ('406 Appl. & File History), COR-AAD1-00000487-489 (Response (Apr. 12, 2019) (pp. 9-11)) ("This disclosed AAD-1 motif is embodied in the disclosed AAD-1 sequences of SEQ ID Nos: 9, 10 . . . "); EX1008 ('406 Appl. & File History), COR-AAD1-00000679 (Response (Sept. 9, 2020) (p. 11)). Corteva '437 discloses that SEQ ID NOS:9 and 10 have the required amino acids at those positions. EX1021 (Corteva '437), [0051], [0052], SEQ ID NO: 9-10.

b. Claim 2

123. Claim 2 refers back to claim 1 and recites: "The plant cell of claim 1 wherein said AAD-1 motif has the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R(X)_{282-284}R$, wherein $(X)_{282-284}$ represents a sequence of 3 amino acids."

124. Corteva '437 anticipates this claim.

125. Corteva '437 discloses the limitations of claim 1, as discussed above. In addition, as shown below, the AAD-1 motifs recited in claims 1 and 2 are identical except that the claim 2 motif contains the additional segment $(X)_{282-284}R$.

<u>Claim 1 “AAD-1” Motif</u>	<u>Claim 2 “AAD-1” Motif</u>
$HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$	$HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R(X)_{282-284}R$

126. Corteva '437 discloses that AAD-1 v1 and v2 (SEQ ID NO: 9 and 10) have a sequence of 3 unspecified amino acid residues (X) at positions 282-284 and an arginine (R) at position 285. EX1021 (Corteva '437), [0051]-[0052], SEQ ID NOS:9-10. Thus, Corteva '437 discloses and claims proteins that satisfy the requirements of this claim.

c. Claim 3

127. Claim 3 refers back to claim 1 and recites: “The plant cell of claim 1 wherein the AAD-1 protein comprises an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 9.”

128. Corteva '437 anticipates this claim.

129. Corteva '437 discloses the limitations of claim 1, as discussed above. In addition, as explained above, AAD-1 v1 (SEQ ID NO: 9) is 100% identical to SEQ ID NO: 9. AAD-1 v2 (SEQ ID NO:10) has approximately 99% sequence identity to SEQ ID NO: 9. *See supra* ¶ 121.

d. Claims 4-5

130. Claims 4 and 5 refer back to claim 1.

131. Claim 4 recites: “The plant cell of claim 1 wherein said plant cell is dicotyledonous and selected from the group consisting of a cotton cell, a tobacco cell, a canola cell, a soybean cell, and an *Arabidopsis* cell.”

132. Claim 5 recites: “The plant cell of claim 1 wherein said plant cell is a monocotyledonous cell selected from the group consisting of a rice cell and a maize cell.”

133. Corteva ’437 anticipates these claims.

134. Corteva ’437 discloses the limitations of claim 1, as discussed above. In addition, Corteva ’437 discloses and claims transgenic plant cells within the scope of claim 1, wherein the plant cell is dicotyledonous, for example, an *Arabidopsis* cell, EX1021 (Corteva ’437), [0104], [0242]-[0263], claim 3; or monocotyledonous, specifically, a rice cell or a maize cell, EX1021 (Corteva ’437), [0104], claim 4.

e. Claim 6

135. Claim 6 refers back to claim 1 and recites: “A transgenic plant comprising a plurality of the plant cells of claim 1, wherein expression of said polynucleotide renders said plant tolerant to an aryloxyalkanoate herbicide.”

136. Corteva ’437 anticipates this claim.

137. Corteva ’437 discloses the limitations of claim 1, as discussed above. In addition, Corteva ’437 discloses and claims that certain AAD-1 proteins, such as AAD-1 v1 and v2, degrade various aryloxyalkanoate herbicides. EX1021 (Corteva

'437), [0074]-[0078], Tbl. 1, claim 5-10; *supra* ¶¶ 117-120. Corteva '437 further discloses and claims that the expression of these AAD-1 proteins, including AAD-1 v1 and v2, renders at least some plants expressing those herbicides tolerant to aryloxyalkanoate herbicides (achiral phenoxy auxins as well as the herbicidally active (*R*)-enantiomers of chiral phenoxy auxins and (*R*)-aryloxyphenoxypropionate compounds). EX1021 (Corteva '437), [0074]-[0078], [00110] ("Plants producing proteins of the subject invention will preferably produce "an effective amount" of the protein so that when the plant is treated with a herbicide, the level of protein expression is sufficient to render the plant completely or partially resistant or tolerant to the herbicide"), [00110] ("Transformed plants and plant cells of the subject invention are preferably rendered resistant or tolerant to an herbicide, as discussed herein, meaning that the transformed plant and plant cells can grow in the presence of effective amounts of one or more herbicides as discussed herein."), Tbl. 1, claims 5-10; *supra* ¶¶ 117-120.

138. I further address Corteva '437's disclosures regarding this claim below, in connection with claims 7-10, which refer back to claim 6.

f. Claims 7-10

139. Claims 7-10 refer back to claim 6.

140. Claim 7 recites: "The plant of claim 6 wherein said aryloxyalkanoate herbicide is a phenoxy auxin herbicide."

141. Claim 8 recites: “The plant of claim 6 wherein said aryloxyalkanoate herbicide is selected from the group consisting of 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop.”

142. Claim 9 recites: “The plant of claim 6 wherein said aryloxyalkanoate herbicide is an (R)-aryloxyphenoxypropionate.”

143. Claim 10 recites: “The plant of claim 6 wherein said aryloxyalkanoate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofop.”

144. Corteva ’437 anticipates these claims.

145. Corteva ’437 discloses the limitations of claim 6, as discussed above. In addition, with respect to claims 7-8, Corteva ’437 discloses and claims that one “benefit” of the invention is that expression of an AAD-1 protein renders plants tolerant to phenoxy auxin herbicides, including 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop. EX1021 (Corteva ’437), [0074]-[0075], Tbl. 1, claim 5 (“A transgenic plant comprising a plurality of cells according to claim 1, wherein expression of said polynucleotide renders said cells tolerant to an aryloxyalkanoate herbicide.”), claim 6 (“The plant of claim 5 wherein said herbicide is a phenoxy auxinic herbicide.”), claim 7 (“The plant of claim 5 wherein said

herbicide is selected from the group consisting of 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop.”).

146. With respect to claims 9-10, Corteva '437 discloses and claims the “additional benefit” that expression of an AAD-1 protein renders at least some plants tolerant to aryloxyalkanoate herbicides, including (*R*)-fluazifop, (*R*)-haloxyfop, (*R*)-diclofop, (*R*)-quizalofop, (*R*)-fenoxaprop, (*R*)-metamifop, (*R*)-cyhalofop, and (*R*)-clodinofop. EX1021 (Corteva '437), [0076]-[0078], [00109] (“Effect of purified AAD-1 (v1) on various AOPP graminicides and analogs,” including (*R*)-quizalofop, (*R*)-fenoxaprop, and (*R*)-cyhalofop), [00206] (based on data for (*R*)-haloxyfop, “AAD-1 (v1) has R specificity on AOPPs”), [00214], Tbls. 2, 4, 9, claim 5 (“A transgenic plant comprising a plurality of cells according to claim 1, wherein expression of said polynucleotide renders said cells tolerant to an aryloxyalkanoate herbicide.”), claim 8 (“The plant of claim 5 wherein said herbicide is an aryloxyphenoxypropionate.”), claim 9 (“The plant of claim 5 wherein said herbicide is selected from the group consisting of fluazifop, haloxyfop, diclofop, quizalofop, fenoxaprop, metamifop, cyhalofop, and clodinofop.”). Moreover, Corteva '437 discloses that the (*R*)-enantiomers of chiral phenoxy auxins and aryloxyphenoxypropionates are herbicidally active (as opposed to the (*S*)-enantiomers), and the POSA would understand Corteva '437's disclosure in view of that concept. *See* EX1021 (Corteva '437), [0074]-[0075], [0077], Tbls. 1-2.

147. As noted above, Corteva '437 discloses examples purporting to show that expression of AAD-1 v1 and v2 (SEQ ID NO: 9 and 10) renders at least some plants in which they are expressed tolerant to various phenoxy auxin and aryloxyphenoxypropionate herbicides. For example, Corteva '437 discloses that transgenic *Arabidopsis* plants expressing AAD-1 v2 (SEQ ID NO:10) are tolerant to phenoxy auxin herbicides (including 2,4-D). EX1021 (Corteva '437), [00260]-[0264] & Tbl. 16. It also discloses that AAD-1 v1 degrades (*i.e.*, “cleaved”) both phenoxy auxin herbicides (including 2,4-D, MCPA, (*R*)-dichlorprop, and (*R*)-mecoprop) and (*R*)-aryloxyphenoxyalkanoate herbicides (including (*R*)-cyhalofop, (*R*)-diclofop, (*R*)-haloxyfop, and (*R*)-quizalofop). EX1021 (Corteva '437), [00109], [00185]-[0215] & Tbls. 3-4, 6-8, 9, Figs. 5-6B. Corteva '437 discloses that the same principles “can be applied to any other desired types of plants.” EX1021 (Corteva '437), [00104].

g. Claims 11-12

148. Claims 11-12 refer, directly or indirectly, back to claim 6.

149. Claim 11 recites: “The plant of claim 6 wherein said plant further comprises a second herbicide resistance gene.”

150. Claim 12 recites: “The plant of claim 11 wherein said second herbicide resistance gene renders said plant resistant to an herbicide selected from the group consisting of glyphosate, glufosinate, acetolactate synthase (ALS) inhibitors,

inhibitors of 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD), dicamba, and inhibitors of protoporphyrinogen oxidase (PPO).”

151. Corteva ’437 anticipates these claims.

152. Corteva ’437 discloses the limitations of claim 6, as discussed above. In addition, Corteva ’437 discloses and claims plants within the scope of claim 6, which further comprise a second herbicide resistance gene that renders the plant resistant to an herbicide selected from the group consisting of glyphosate, glufosinate, an ALS inhibitor, an HPPD inhibitor, and a PPO inhibitor, as recited in claims 11-12. *See, e.g.*, EX1021 (Corteva ’437), [0078]-[0080], claim 11 (“The plant of claim 5 wherein said plant further comprises a second herbicide resistance gene.”), claim 12 (“The plant of claim 11 wherein said second herbicide resistance gene renders said plant resistant to a herbicide selected from the group consisting of glyphosate, glufosinate, ALS inhibitors, inhibitors of 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD), and inhibitors of protoporphyrinogen oxidase (PPO).”). Corteva ’437 refers to combinations of multiple herbicide resistance genes as “stacks,” as in, for example, a “glyphosate resistance gene/AAD-1 stack.” EX1021 (Corteva ’437), [0078]-[0080].

h. Claim 13

153. Claim 13 refers back to claim 6 and recites: “A method of controlling at least one weed in a field, wherein said field contains at least one plant of claim 6,

wherein said method comprises applying to at least a portion of said field a first herbicide selected from the group consisting of a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide.”

154. Corteva ’437 anticipates this claim.

155. Corteva ’437 discloses the limitations of claim 6, as discussed above. In addition, Corteva ’437 discloses and claims methods of controlling weeds in fields that contain plants within the scope of claim 6, comprising a phenoxy auxin or (R)-aryloxyphenoxypropionate herbicide. EX1021 (Corteva ’437), [0078], claim 13 (“A method of controlling at least one weed in a field, wherein said field contains at least one plant of claim 5, wherein said method comprises applying to at least a portion of said field a first herbicide selected from the group consisting of a phenoxy auxin herbicide and an aryloxyphenoxypropionate herbicide.”), claims 14-39. Corteva ’437 states: “Combinations of these different chemistry classes and herbicides with different modes of action and spectra in the same field (either sequentially or in tank mix combination) shall provide control of most potential weeds.” See EX1021 (Corteva ’437), [0078].

i. Claims 14-16

156. Claims 14-16 refer back to claim 13.

157. Claim 14 recites: “The method of claim 13 wherein said phenoxy auxin herbicide is an R-enantiomer of a chiral phenoxy auxin.”

158. Claim 15 recites: “The method of claim 13 wherein said phenoxy auxin herbicide is an achiral phenoxy auxin selected from the group consisting of 2,4-D and MCPA.”

159. Claim 16 recites: “The method of claim 13 wherein said (R)-aryloxyphenoxypropionate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofof.”

160. Corteva ’437 anticipates these claims.

161. Corteva ’437 discloses the limitations of claim 13, as discussed above. In addition, Corteva ’437 discloses and claims methods within the scope of claim 13 wherein the phenoxy auxin is an (R)-enantiomer of a chiral phenoxy auxin, such as (R)-dichlorprop or (R)-mecoprop. EX1021 (Corteva ’437), [0074]-[0076] & Tbl. 1, claim 15 (“The method of claim 13 wherein said herbicide is an R-enantiomer of a chiral phenoxy auxin.”); claim 16 (“The method of claim 14 wherein said herbicide is selected from the group consisting of R-dichlorprop and R-mecoprop.”). It also discloses and claims methods within the scope of claim 13, wherein the achiral phenoxy auxin is 2,4-D and MCPA. EX1021 (Corteva ’437), [00074]-[0076] & Tbl. 1, claim 17 (“The method of claim 16 wherein said herbicide is selected from the group consisting of 2,4-D and MCPA.”). It also discloses and claims methods within the scope of claim 13, wherein the (R)-aryloxyphenoxypropionate herbicide is

selected from the group recited in claim 17. EX1021 (Corteva '437), [00077]-[00078], [00109] (“Effect of purified AAD-1 (v1) on various AOPP graminicides and analogs,” including (*R*)-quizalofop, (*R*)-fenoxaprop, and (*R*)-cyhalofop), [00206] (based on data for (*R*)-haloxyfop, “AAD-1 (v1) has R specificity on AOPPs”), [00214], Tbls. 2, 4, 9, claim 36 (“The method of claim 35 wherein said first herbicide is selected from the group consisting of quizalofop, haloxyfop, and cyhalofop.”). Moreover, Corteva '437 discloses that the (*R*)-enantiomers of chiral phenoxy auxins and aryloxyphenoxypropionates are herbicidally active (as opposed to the (*S*)-enantiomers), and the POSA would understand Corteva '437's disclosure in view of that concept. *See* EX1021 (Corteva '437), [00074]-[00075], [00077], Tbls. 1-2.

j. Claims 17-20

162. Claims 17-20 refer, directly or indirectly, back to claim 13.

163. Claim 17 recites: “The method of claim 13 wherein said method comprises applying a second herbicide.”

164. Claim 18 recites: “The method of claim 17 wherein said first herbicide and said second herbicide are applied sequentially.”

165. Claim 19 recites: “The method of claim 17 wherein said first herbicide and said second herbicide are applied concurrently.”

166. Claim 20 recites: “The method of claim 17 wherein said first herbicide is a phenoxy auxin and said second herbicide is an (*R*)-aryloxyphenoxypropionate.”

167. Corteva '437 anticipates these claims.

168. Corteva '437 discloses the limitations of claim 13, as discussed above. In addition, Corteva '437 discloses and claims methods within the scope of claim 13 (and claim 17), wherein a first and second herbicide are applied “sequentially or tank mixed” (*i.e.*, concurrently). EX1021 (Corteva '437), [0078], claim 22 (“The method of claim 13 wherein said method comprises applying a second herbicide.”), claim 23 (“The method of claim 22 wherein said first herbicide and said second herbicide are applied sequentially.”), claim 24 (“The method of claim 22 wherein said first herbicide and said second herbicide are applied concurrently.”). It also discloses and claims methods within the scope of claim 13 (and claims 17 and 22), comprising applying both a phenoxy auxin and an (R)-aryloxyphenoxypropionate (*i.e.*, “AOPP”) herbicide. EX1021 (Corteva '437), [0078], claim 25 (“The method of claim 22 wherein said first herbicide is a phenoxy auxin and second herbicide is an aryloxyphenoxypropionate.”). Moreover, Corteva '437 discloses that the (*R*)-enantiomers of chiral phenoxy auxins and aryloxyphenoxypropionates are herbicidally active (as opposed to the (*S*)-enantiomers), and the POSA would understand Corteva '437's disclosure in view of that concept. *See* EX1021 (Corteva '437), [0074]-[0075], [0077], Tbls. 1-2.

k. Claims 21-23

169. Claims 21 and 23 refer back to claim 17.

170. Claim 21 recites: “The method of claim 17 wherein said second herbicide is selected from the group consisting of glyphosate, glufosinate, dicamba, acetolactate synthase (ALS) inhibitors, protoporphyrinogen oxidase (PPO) inhibitors, and 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD) inhibitors.”

171. Claim 22 recites: “The method of claim 17, wherein said first herbicide is 2,4-D and said second herbicide is glyphosate or glufosinate.”

172. Claim 23 recites: “The method of claim 17, wherein said first herbicide is an (R)-aryloxyphenoxypropionate and said second herbicide is glyphosate or glufosinate.”

173. Corteva ’437 anticipates these claims.

174. Corteva ’437 discloses the limitations of claim 17, as discussed above. In addition, Corteva ’437 discloses and claims methods within the scope of claim 17 comprising applying combinations of herbicides within the scope of each of claims 21-23. EX1021 (Corteva ’437), [0079]-[0083], claim 30 (“The method of claim 28 wherein said second herbicide is selected from the group consisting of glyphosate, glufosinate, dicamba, acetolactate synthase inhibitors, protoporphyrinogen oxidase inhibitors, and hydroxyphenyl-pyruvate-dioxygenase inhibitors.”), claim 34 (“The method of claim 33 wherein said phenoxy auxin is 2,4-D and said second herbicide is glyphosate.”), claim 35 (“The method of claim 28 wherein said first herbicide is an aryloxyphenoxypropionate and said second herbicide is glyphosate.”). Moreover,

Corteva '437 discloses that the (*R*)-enantiomers of chiral phenoxy auxins and aryloxyphenoxypropionates are herbicidally active (as opposed to the (*S*)-enantiomers), and the POSA would understand Corteva '437's disclosure in view of that concept. *See* EX1021 (Corteva '437), [0074]-[0075], [0077], Tbls. 1-2. Corteva '437 also discloses transforming plants used in these methods with multiple resistance traits to impart resistance to each of the herbicides applied. EX1021 (Corteva '437), [0079]-[0083], [0098].

I. Claim 24

175. Claim 24 refers back to claim 17.

176. Claim 24 recites: "The method of claim 17 wherein said plant further comprises a second herbicide resistance gene that renders said plant resistant to said second herbicide."

177. Corteva '437 anticipates this claim for the reasons addressed above in connection with claims 17 and 21-23 (which are incorporated here by reference).

178. Corteva '437 discloses the limitations of claim 17, as discussed above. In addition, Corteva '437 discloses and claims methods within the scope of claim 17, wherein the plants comprise an AAD-1 gene, such as the genes encoding AAD-1 v1 and v2, and another herbicide resistance gene. EX1021 (Corteva '437), [0079]-[0083], [0098], claim 28 ("The method of claim 22 wherein said plant further

comprises a second herbicide resistance gene that renders said plant resistant to said second herbicide.”).

m. Claims 25-26

179. Claims 25-26 refer, directly or indirectly, back to claim 24.

180. Claim 25 recites: “The method of claim 24 wherein said second herbicide resistance gene is selected from the group consisting of a modified acetolactate synthase (ALS) gene, a glyphosate resistance gene, a glufosinate resistance gene, and a dicamba-degrading enzyme gene.”

181. Claim 26 recites: “The method of claim 25 wherein: (a) said modified ALS gene is selected from the group consisting of SurA, SurB, Csr1, Csr1-1, and Csr1-2; (b) said glyphosate resistance gene is selected from the group consisting of modified EPSPS (5-enolpyruvylshikimate-3-phosphate synthase), GOX, and GAT; and, (c) said glufosinate resistance gene is selected from the group consisting of phosphinothricin-N-acetyltransferase (PAT) and bar.”

182. Corteva ’437 anticipates these claims.

183. Corteva ’437 discloses the limitations of claim 24, as discussed above. In addition, Corteva ’437 discloses and claims methods within the scope of claim 24, wherein the second herbicide resistance gene is selected from the groups and subgroups recited in claims 25-26. EX1021 (Corteva ’437), [0082]-[0083], [0098], claim 29 (“The method of claim 28 wherein said second gene is selected from the

group consisting of a modified AHAS (acetohydroxyacid synthase), SurA, SurB, CsrI, CsrI-1, CsrI-2, a modified EPSPS (5-enolpyruvylshikimate-3-phosphate synthase), GOX, GAT, PAT (phosphinothricin-N-acetyltransferase), bar, and a dicamba-degrading enzyme.”).

n. Claims 27-29

184. Claims 27-29 refer, directly or indirectly, back to claim 17.

185. Claim 27 recites: “The method of claim 17 wherein said method further comprises applying a third herbicide.”

186. Claim 28 recites: “The method of claim 27, wherein said third herbicide is selected from the group consisting of glyphosate, glufosinate, HPPD-inhibitors, PPO-inhibitors, ALS inhibitors, and dicamba.”

187. Claim 29 recites: “The method of claim 28 wherein said first, second and third herbicides are 2,4-D, quizalofop, and glyphosate.”

188. Corteva ’437 anticipates these claims.

189. Corteva ’437 discloses the limitations of claim 17, as discussed above. In addition, Corteva ’437 discloses and claims methods within the scope of claim 17, comprising applying three herbicides, including a method in which the three herbicides are 2,4-D, quizalofop, and glyphosate. EX1021 (Corteva ’437), [0078]-[0083], [0098], claim 38 (“The method of claim 28 wherein said method further

comprises applying a third herbicide.”), claim 39 (“The method of claim 38 wherein said herbicides are 2,4-D; quizalofop; and glufosinate.”).

o. Claim 30

190. Claim 30 refers back to claim 1.

191. Claim 30 recites: “A seed comprising a plurality of the plant cells of claim 1.”

192. Corteva ’437 anticipates this claim.

193. Corteva ’437 discloses the limitations of claim 1, as discussed above. In addition, Corteva ’437 discloses and claims seeds produced by or used to generate the plants containing the plant cells of claim 1. EX1021 (Corteva ’437), [00151] (“Seeds produced by and/or used to generate plants of the subject invention are also included within the scope of the subject invention.”), claim 57 (“A seed comprising a plant cell of claim 1.”). Corteva ’437’s examples also involve seeds containing plant cells transformed with, for example, the gene encoding AAD-1 v2. *E.g.*, EX1021 (Corteva ’437), [00253] (“Freshly harvested T1 seed (transformed with native [*AAD-1* (v2)] . . . gene) was allowed to dry for 7 days at room temperature.”).

p. Claim 31

194. Claim 31 refers back to claim 30.

195. Claim 31 recites: “A method of controlling weeds in a field, wherein said method comprises applying an aryloxyalkanoate herbicide to said field and

planting a seed of claim 30 in said field within 14 days of applying said aryloxyalkanoate herbicide.”

196. Corteva ’437 anticipates this claim.

197. Corteva ’437 discloses the limitations of claim 30, as discussed above. In addition, Corteva ’437 discloses seeds within the scope of claim 30. Claim 40 of Corteva ’437 further discloses and claims a “method of controlling weeds in a field, wherein said method comprises applying a first herbicide to said field and planting a seed in said field within 14 days of applying said first herbicide,” “wherein said first herbicide is selected from the group consisting of a phenoxy auxin and an aryloxyphenoxypropionate.” EX1021 (Corteva ’437), claim 40. (As noted above, the ’555 patent and Corteva ’437 refer to herbicides including phenoxy auxins and aryloxyphenoxypropionates collectively as “aryloxyalkanoates.” EX1001 (’555 Pat.), 3:49-62; EX1021 (Corteva ’437), [0015].)

q. Claims 32-33

198. Claims 32 and 33 refer, directly or indirectly, back to claim 30.

199. Claim 32 recites: “A plant grown from the seed of claim 30.”

200. Claim 33 recites: “A part, progeny, or asexual propagate of the plant of claim 32, wherein said part, progeny, or sexual propagate comprises said polynucleotide.”

201. Corteva ’437 anticipates this claim.

202. Corteva '437 discloses the limitations of claim 30, as discussed above. In addition, Corteva '437 discloses and claims that seeds transformed to express certain AAD-1 proteins, such as AAD-1 v1 or v2 (SEQ ID NO: 9 or 10), can be used to generate additional plants comprising those proteins. *See, e.g.*, EX1021 (Corteva '437), [00151] (“Seeds produced by and/or used to generate plants of the subject invention are also included within the scope of the subject invention.”), claim 58 (“A plant grown from the seed of claim 57.”). Corteva '437 also discloses and claims that such plants can be used to generate additional parts, progeny, and propagates. *See, e.g.*, EX1021 (Corteva '437), [00151] (“Seeds produced by and/or used to generate plants of the subject invention are also included within the scope of the subject invention. Other plant tissues and parts are also included in the subject invention.”), claim 59 (“A part, progeny, or asexual propagate of the plant of claim 5.”).

r. Claim 34

203. As shown below, claim 34 is similar to claim 1, but requires (1) the transgenic plant cell to be an “(R)-aryloxyphenoxypropionate herbicide tolerant transgenic plant cell,” and (2) the “AAD-1 motif” to have “90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9.”

<u>Claim 1</u>	<u>Claim 34</u>
1. A transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$, wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(X)_{114-137}$ represents a sequence of 24 amino acids; $(X)_{139-269}$ represents a sequence of 131 amino acids; and	1. A <u>(R)-aryloxyphenoxypropionate herbicide tolerant</u> transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$, wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(X)_{114-137}$ represents a sequence of 24 amino acids;

(X) ₂₇₁₋₂₈₀ represents a sequence of 10 amino acids.	(X) ₁₃₉₋₂₆₉ represents a sequence of 131 amino acids; and (X) ₂₇₁₋₂₈₀ represents a sequence of 10 amino acids, <u>wherein said motif has 90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9.</u>
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204. Corteva '437 anticipates this claim.

205. As discussed above in connection with claims 6 and 9-10, Corteva '437 discloses that at least some transgenic plant cells comprising an AAD-1 protein, such as AAD-1 v1 or v2, renders those plant cells tolerant to (R)-aryloxyphenoxypropionate herbicides. *See, e.g.*, EX1021 (Corteva '437), [0076]-[0078], [00109] (“Effect of purified AAD-1 (v1) on various AOPP graminicides and analogs,” including (R)-quizalopfop, (R)-fenoxaprop, and (R)-cyhalofop)), [00206] (based on data for (R)-haloxyfop, “AAD-1 (v1) has R specificity on AOPPs”), [00214], Tbls. 2, 4, 9, claim 5 (“A transgenic plant comprising a plurality of cells according to claim 1, wherein expression of said polynucleotide renders said cells tolerant to an aryloxyalkanoate herbicide.”), claim 8 (“The plant of claim 5 wherein said herbicide is an aryloxyphenoxypropionate.”), claim 9 (“The plant of claim 5

wherein said herbicide is selected from the group consisting of fluazifop, haloxyfop, diclofop, quizalofop, fenoxaprop, metamifop, cyhalofop, and clodinofof.”); *supra* ¶¶ 135-138, 142-147. Moreover, Corteva ’437 discloses that the (*R*)-enantiomers of chiral phenoxy auxins and aryloxyphenoxypropionates are herbicidally active (as opposed to the (*S*)-enantiomers), and the POSA would understand Corteva ’437’s disclosure in view of that concept. *See* EX1021 (Corteva ’437), [0074]-[0075], [0077], Tbls. 1-2.

206. Additionally, AAD-1 v1 has the amino acid sequence listed in SEQ ID NO: 9 and is therefore 100% identical to it at all amino acid positions, including positions 111 to 281. Except at position 212, AAD-1 v2, which has the amino acid sequence listed in SEQ ID NO: 10, is also identical to SEQ ID NO: 9 at those positions; it thus also has much greater than 85% sequence identity at those positions. EX1001 (’555 Pat.) SEQ ID NOS:9-10; *supra* ¶ 121.

207. I address the remaining limitations of this claim in connection with claim 1, which also contains those limitations (the discussions of which are incorporated here by reference). *See supra* ¶¶ 112-122.

3. Corteva ’437 Renders Obvious the Challenged Claims.

208. I understand that if a claim is anticipated based on a given reference, it also would have been obvious based on that reference. As I explain above, Corteva

'437 anticipates each of the challenged claims of the '555 patent. It therefore also renders obvious those claims.

B. Invalidity Analysis as of April 30, 2004

209. As explained in Section VII.A.1, the challenged claims of the Corteva patents are not entitled to a priority date earlier than October 7, 2016. Even if the challenged claims were entitled to the earliest possible priority date of April 30, 2004, however, the challenged claims would have been obvious based on the prior art and the knowledge of the POSA.

1. The POSA Would Have Been Motivated To Express RdpA in Transgenic Plants To Confer Resistance to Phenoxy Herbicides, with a Reasonable Expectation of Success.

210. The challenged Corteva patents describe and claim the transgenic expression of a known bacterial enzyme, RdpA/AAD-1, and other “AAD-1 proteins,” to confer herbicide resistance in plants. By 2004, it had been known for decades that certain bacteria expressed enzymes that enabled them to degrade herbicides. Multiple genes encoding bacterial enzymes had been transformed into plants to provide resistance to particular herbicides. *See* EX1037 (Otoxby 1990 (pp. 61-65)), EX1030 (Jepson), [0012], [0024], [0026]-[0027], Ex. 1-2. For example, researchers had successfully transformed various plants with recombinant constructs encoding TfdA in order to confer resistance to phenoxy auxins. EX1040 (Saari 1998 (p. 93)); EX1041 (Saari 1999 (p. 422)); EX1043 (Streber), 1:41-48, 2:52-62, 4:19-6:62, 7:58-12:67, 22:56-32:9, claim 6; EX1045 (Streber 1989 (pp. 811-15)); EX1032 (Lyon 1989 (pp. 533-39)); EX1033 (Lyon 1993) (pp. 162-69)); EX1037 (Otoxby

1990 (p. 65)); EX1039 (Rao 2000 (p. 303)); *supra* Section VI.D. Based on all of this information, the POSA would have recognized that plant cells and plants could be transformed to encode RdpA, and would have been motivated to do so to take advantage of the enzyme's herbicide-degrading properties.

211. The herbicides in commercial use prior to 2004 included a number of chiral phenoxy herbicides. EX1039 (Rao 2000 (pp. 69, 88-92)); EX1022 (Cutler 1999 (pp. 6-10 & Fig. 1.6)). While 2,4-D and certain other early phenoxy herbicides were achiral, the literature reflected a trend towards chiral phenoxy herbicides, such as the chiral phenoxy auxins and aryloxyphenoxypropionates. EX1022 (Cutler 1999 (pp. 9-10 & Fig. 1.6)). It was well-known that the herbicidally active forms of the chiral phenoxy herbicides are the (*R*)-enantiomers, not the (*S*)-enantiomers. Thus, the POSA would have been motivated to express an enzyme capable of degrading these (*R*)-phenoxy herbicides. That motivation was acknowledged in a paper (EX1041 (Saari 1999)), published in 1999, on the stereospecificity of three TfdA-like enzymes, which explained that “the genes encoding an enzyme specific for the R isomer could be used to develop genetically engineered crops that are resistant to the herbicide of interest.” EX1041 (Saari 1999 (p. 422)). EX1041 is a true and correct copy of the paper.

212. Dr. Saari included similar observations in her doctoral thesis. EX1040 (Saari 1998 (p. 93)). I understand that Dr. Saari's doctoral thesis was

provided to the MSU library for cataloguing in 1998. As such, prior to April 2004, the POSA would have been able to find and retrieve Saari 1998 by searching the MSU library catalog for publications regarding alpha-ketoglutarate dioxygenases. Additionally, to the best of my knowledge, prior to April 2004, the POSA would have been able to find and retrieve Saari 1998 via ProQuest or its predecessor, UMI. ProQuest is a database service that provides access to dissertations and other publications, including dissertations written by MSU graduate students. *See* EX1062 (MSU Library Website) (“ProQuest Dissertations and Theses Comprehensive collection of fulltext dissertations and theses since 1997 and strong retrospective full text coverage for earlier periods. Includes MSU dissertations and theses.”). ProQuest enables users to search the publications that it indexes by keyword and subject matter. EX1040 is a true and correct copy of Saari 1998 that I obtained through ProQuest (which I accessed through the MSU library), page 4 of which bears the UMI copyright date of 1998. This is consistent with my understanding that, shortly after Dr. Saari defended her thesis, the thesis was submitted to UMI to become part of its database collection.

213. The POSA would have understood that most of the α KG dioxygenases that had been reported in the literature to degrade phenoxy herbicides did not have the appropriate enantioselectivity to provide resistance to chiral phenoxy herbicides. JMP134 TfdA and RASC TfdA selectively degraded (*S*)-phenoxy auxins, not (*R*)-

phenoxy auxins. EX1041 (Saari 1999 (pp. 422-27)); EX1040 (Saari 1998 (ch. 3, pp. 70-95)). As recognized in each of Saari 1998 and Saari 1999 (which I will refer to as the “Saari References”), the POSA would have been motivated to select an α KG dioxygenase reported to have the opposite enantioselectivity. See EX1040 (Saari 1998 (p. 93)) (“A potential application for *A. denitrificans* or the *tfdA*-like gene it contains would be protection of crops from mecoprop and dichlorprop. . . . [T]he gene from *A. denitrificans* could be used since its gene product degrades the R-enantiomer.”); EX1041, (Saari 1999 (pp. 422, 427)).

214. As of April 2004, the best-known enzyme reported to have (*R*)-enantioselective activity on chiral phenoxy herbicides was RdpA. EX1041 (Saari 1999 (p. 427)); EX1040 (Saari 1998 (pp. 92, 127)). As summarized in Section VI.C, genes encoding RdpA had been identified in *Sphingomonas*, *Delftia*, and *Rhodoferrax*, and RdpA sequences had been deposited in and were available from public databases. The prior art reported, and the POSA would have understood, that RdpA possessed activity on chiral phenoxy herbicides including (*R*)-mecoprop and (*R*)-dichlorprop, as well as a lesser degree of activity on the achiral phenoxy herbicide 2,4-D. EX1036 (Nickel 1997 (pp. 6677-78 & Tbl. 2)), EX1040 (Saari 1998 (pp. 90-92, 127)); EX1041 (Saari 1999 (p. 427)); EX1047 (Westendorf 2003 (pp. 11, 14-15 & Tbl. 3)); EX1035 (Müller 2006 (pp. 1358-66)). The POSA would have been motivated to transform plants with a gene encoding an α KG

dioxygenase—specifically, RdpA—because it was reported to degrade (*R*)-phenoxy herbicides in order to confer resistance to such herbicides. *See* EX1041 (Saari 1999 (p. 427)); EX1040 (Saari 1998 (p. 93)); EX1034 (Müller 2001 (pp. 228, 1034)). In other words, the POSA would have been motivated to choose RdpA because the prior art reported that RdpA had (*R*)-enantioselective dioxygenase activity on phenoxy herbicide substrates, not because RdpA had a particular amino acid sequence. While the POSA would have appreciated that RdpA’s amino acid sequence shares certain characteristics with other α KG dioxygenases like TfdA, including the consensus, prior art α KG dioxygenase motif, **HX(D/E)X₂₃₋₂₆(T/S)X₁₁₄₋₁₈₃HX₁₀₋₁₃R**, the POSA also would have realized that those α KG dioxygenases did not degrade (*R*)-phenoxy herbicides (with the exception of RdpA and the (*R*)-enantioselective TfdA-like *A. denitrificans* enzyme that we reported in Saari 1999).

215. During the prosecution of the ’555 patent application, the applicant argued that the POSA would not have been motivated to select RdpA over other α KG dioxygenases with amino acid sequences having higher sequence identity to TfdA.⁷ *E.g.*, EX1008 (’406 Appl. & File History), COR-AAD1-00000492

⁷ The ’555 patent specification refers to the canonical TfdA enzyme expressed in the JMP134 strain. *See* EX1001 (’555 Pat.), 3:11-12 (citing EX1045 (Streber 1989); EX1032 (Lyon 1989); EX1033 (Lyon 1993); U.S. Patent No. 5,608,147). Although

(Response (April 12, 2019) (p. 14)). I disagree. As I explain in the prior paragraph, that logic is flawed. The POSA would have selected RdpA because it was reported to have (*R*)-enantioselective dioxygenase activity, not because it had a particular amino acid sequence. The POSA would have appreciated that, given the limited structural information available regarding α KG dioxygenase enzymes, it would be inefficient and unproductive to select candidate proteins based on percentage sequence identity to TfdA rather than their reported activity. As discussed in Section VII.A.1.d-VII.A.1.e, the prior art did not provide sufficient information about RdpA for the POSA to have identified the residues in RdpA's amino acid sequence that correlated with its (*R*)-enantioselectivity. Even supposing for purposes of argument that the applicant were correct that the POSA would have expected only enzymes with relatively high sequence identity to TfdA to have activity like that of TfdA, *see* EX1001 ('555 Pat.), 44:27-29 ("Traditionally only sequences with high homology would be expected to retain similar properties to the input sequence."); EX1008 ('406 Appl. & File History), COR-AAD1-00000492 (Response (April 12, 2019) (p. 14)), the POSA would have recognized that TfdA did not have the appropriate enantioselectivity for degrading (*R*)-phenoxy herbicides. EX1040 (Saari 1998 (p.

the applicant's references to "TfdA" are not always clear, I understand the applicant to be referring to the same TfdA enzyme referenced in the specification.

93)) (“For protection against the chiral phenoxypropionate herbicides, the pJP4-derived gene product would be ineffective (because it would not degrade the herbicidal *R*-enantiomer), but the gene from *A. denitrificans* could be used since its gene product degrades the *R*-enantiomer.”). The POSA would have considered RdpA’s empirically demonstrated (*R*)-enantioselective activity to be more important than RdpA’s calculated percentage identity to any other amino acid sequence.

216. The POSA would have had a reasonable expectation of success in transforming plant cells with a sequence encoding the RdpA amino acid sequence in order to transgenically express RdpA. The prior art described, and the POSA would have known, methods of constructing a recombinant nucleotide sequence encoding a protein such as RdpA and confirming that the encoded protein was expressed. EX1043 (Streber), 3:10-6:61, 11:40-21:28, 25:9-43, 27:39-29:4; EX1044 (Streber 1987 (pp. 2950-51)); EX1045 (Streber 1989 (p. 811-12)); EX1032 (Lyon 1989 (pp. 534-35); EX1033 (Lyon 1993 (pp. 163-64)); EX1030 (Jepson) [0001]-[0004], [0024], Ex. 1-8. The prior art taught assays that could be used to evaluate RdpA’s α KG dioxygenase activity on different substrates. EX1024 (Fukumori & Hausinger 1993 (pp. 2083-85)); EX1036 (Nickel 1997 (pp. 6675-78)); EX1041 (Saari 1999 (pp. 423-27)); EX1040 (Saari 1998 (pp. 74-94)); EX1043 (Streber), 23:20-34, 25:9-43, 27:4-36, 30:19-31:67; EX1044 (Streber 1987 (p. 2951)); EX1045 (Streber 1989 (p. 811)); EX1032 (Lyon 1989 (pp. 535)); EX1033 (Lyon 1993 (p. 164)); EX1030

(Jepson) [0001]-[0004], [0024], Ex. 1-8. The prior art also described methods for transforming a recombinant genetic construct encoding a desired protein into a heterologous cell type such as a plant cell. EX1043 (Streber), 7:11-9:23, 21:30-31:67; EX1044 (Streber 1987 (p. 2951)); EX1045 (Streber 1989 (pp. 813-14); EX1032 (Lyon 1989 (pp. 535-36); EX1033 (Lyon 1993 (p. 164)). These methods were known and had been used in the 1990s and 2000s to successfully generate transgenically modified plants expressing various bacterial proteins and herbicide resistance traits, including TfdA. EX1041 (Saari 1999 (p. 422)); EX1040 (Saari 1998 (p. 93)); EX1043 (Streber); EX1044 (Streber 1987); EX1045 (Streber 1989); EX1032 (Lyon 1989); EX1033 (Lyon 1993); EX1030 (Jepson) [0012], [0024], [0026]-[0027], Examples 1-8, claims 4, 13, 15; EX1018 (Bayley 1992); EX1037 (Otoxby 1990 (p. 65)); *see also id.* (“Progress in this area during the past five years has been rapid - due, partly, to the development of efficient plant transformation and regeneration systems for certain species. Transgenic plants have now been reported in more than 30 species. Genetically engineered soybean, cotton, rice, oil-seed rape, corn, sugar beet and alfalfa crops are expected to enter the market by the year 2000.”).

217. I am aware that at various times during the prosecution of applications in the '555 patent family, the applicant argued that it would not have been obvious to transform plants using the gene encoding RdpA because the specification

describes a different enzyme, AAD-2, as having lower activity on certain substrates *in vitro* than *in vivo*. See EX1008 ('406 Appl. & File History), COR-AAD1-00000575 (Response (Jan. 10, 2020) (p. 26)); EX1006 ('813 Appl. & File History), 283-84 (Response (Oct. 27, 2014) (pp. 8-9)) ("If AAD-2 were used as the point of reference, one would predict no activity in plants for bacterial genes.") (emphasis in original). I do not agree with these arguments. The cited results were not part of the prior art, and were not available to the POSA in April 2004. The POSA would have had no motivation to express AAD-2 in plants in the first place, because its activity had not been characterized in the prior art as of April 2004. Even had the limited results in the specification been reported in the literature, the POSA would have considered the prior art examples of successful heterologous expression of bacterial proteins, including TfdA, to be more persuasive. As discussed in Section VII.C.1.e, the applicant emphasized to the USPTO that AAD-2 does not possess the claimed (*R*)-phenoxy herbicide degrading activity that is possessed by RdpA and AAD-2 is not in the claimed genus of AAD-1 proteins. Thus, there is no apparent reason why the POSA would have considered the limited AAD-2 data in the patent more pertinent than the prior art references cited above that confirmed the successful expression of TfdA in various plants.

218. I understand that the applicant further argued that although the prior art taught that RdpA was active on 2,4-D, the POSA would not have been motivated to

select RdpA because it had “low activity” on 2,4-D. EX1008 (’406 Appl. & File History), COR-AAD1-00000686 (Response (Sept. 9, 2020) (p. 18)). It is unclear what exactly the applicant meant by this statement. RdpA was known to have activity on 2,4-D. The fact that RdpA was reported to have lower activity on 2,4-D than on the chiral phenoxy herbicides (*R*)-mecoprop or (*R*)-dichlorprop would not have deterred the POSA because other α KG dioxygenase enzymes reported to have higher activity on 2,4-D, like TfdA, had the wrong enantioselectivity to degrade (*R*)-phenoxy herbicides. *See* EX1040 (Saari 1998 (p. 93)).

2. The POSA Would Have Been Motivated To Express RdpA in at Least Some Transgenic Plants in Order To Confer Resistance to (*R*)-Aryloxyphenoxypropionates, with a Reasonable Expectation of Success.

219. As explained above, the prior art reporting RdpA’s activity on (*R*)-phenoxy auxins would have provided sufficient motivation for the POSA to express RdpA in plants for the purpose of degrading phenoxy auxin herbicides. In addition, that prior art would have motivated the POSA to express RdpA in at least some plants in order to confer resistance to (*R*)-aryloxyphenoxypropionates. While the prior art I discuss above did not report testing of RdpA on (*R*)-aryloxyphenoxypropionate substrates, the POSA would have understood that the degradation of an (*R*)-aryloxyphenoxypropionate, like the degradation of (*R*)-mecoprop and (*R*)-dichlorprop, would involve an α KG dioxygenase catalyzing the hydroxylation of the C2 carbon atom to release the phenol and pyruvate. As the

applicant acknowledged during prosecution, these herbicides have “similar phenoxyalkanoate substructures.” *See* EX1008 (’406 Appl. & File History), COR-AAD1-00000493 (Response (April 12, 2019) (p. 15)) (“The implications are that this enzyme is promiscuous enough to utilize chemicals with similar phenoxyalkanoate substructures even though they have completely different modes of action as herbicides.”). In addition, the POSA would have reasonably expected that RdpA, which was known to have (*R*)-enantioselectivity for degrading (*R*)-mecoprop and (*R*)-dichlorprop, would likewise have (*R*)-enantioselectivity for degrading (*R*)-aryloxyphenoxypropionates.

220. The applicant later argued that despite the similar phenoxyalkanoate substructures they previously emphasized, “phenoxy auxin class herbicides and the AOPP class of herbicides are structurally quite distinct,” apparently referring to the additional aryl groups on the AOPP herbicides. EX1008 (’406 Appl. & File History), COR-AAD1-00000686 (Response (Sept. 9, 2020) (p. 18)). While (*R*)-aryloxyphenoxypropionates include additional aryl groups, these are located on the opposite side of the molecule from the chiral center, where the hydroxylation and elimination reactions take place. Based on prior structural and functional studies of α KG dioxygenases, the POSA would have expected that RdpA would have less interaction with the second aryl group of the herbicide, and that the second aryl group would not be critical to substrate specificity.

221. The '555 patent specification asserts, and the applicant argued, that RdpA's ability to degrade both phenoxy auxins and aryloxyphenoxypropionates as a "dual MOA" would have been "surprising" because phenoxy auxins and aryloxyphenoxypropionates have different herbicidal mechanisms of action. EX1001 ('555 Pat.), 4:32-36, 17:62-18:28, 19:52-63, 112:42-115:57; EX1008 ('406 Appl. & File History), COR-AAD1-00000493 (Response (April 12, 2019) (p. 15)) ("AAD-1 has surprising advantages that are not contemplated by Kohler, i.e. it acts on two completely different categories of herbicides."); EX1008 ('406 Appl. & File History), COR-AAD1-00000686 (Response (Sept. 9, 2020) (p. 18)) (similar). I disagree with these characterizations of RdpA's activity. In my opinion, it would not have been surprising or unexpected to the POSA that RdpA can degrade (*R*)-aryloxyphenoxypropionates as well as (*R*)-phenoxy auxins. As shown in Sections VI.B-VI.C, and discussed in the paragraph above, the chiral portion of an (*R*)-phenoxy auxin that is cleaved during oxidation has a chemical structure that is similar in structure to the chiral portion of an (*R*)-aryloxyphenoxypropionate. Whether a given substrate is cleaved by a particular α KG dioxygenase is primarily a function of the substrate's chemical structure, not the substrate's mechanism of action (whether herbicidal or otherwise). Because RdpA had already been shown to selectively degrade (*R*)-phenoxy auxins, the POSA would have reasonably expected RdpA to degrade (*R*)-aryloxyphenoxypropionates, regardless of whether (*R*)-

aryloxyphenoxypropionates act through the same herbicidal mechanism of action as (*R*)-phenoxy auxins.

222. For the reasons stated above, the POSA would have been motivated to transgenically modify plants to express RdpA in order to confer resistance to phenoxy herbicides, as suggested in each of the Saari References. The POSA would have had a reasonable expectation of success in expressing RdpA in plants, as the prior art described for TfdA. As I explain in more detail below, all of the '555 patent claims would have been obvious based on the combination of the information in each of the Saari References with what was known about RdpA's sequence and activity, and the transformation of genes encoding α KG enzymes including TfdA into plants.

3. Saari 1999 or Saari 1998 in Combination with Schleinitz and Streber Render Obvious Claims 1-10, 13-16, and 34.

223. In light of the above, even as of April 2004, the POSA would have regarded the challenged claims of the '555 patent to have been obvious based on the prior art. For example, as I explain below in further detail, challenged claims 1-10, 13-16, and 34 would have been obvious based on the disclosures in either of the Saari references in combination with Schleinitz and Streber regarding RdpA's (*R*)-stereoselectivity and amino acid sequence and the transformation of genes encoding α KG enzymes into plants.

a. Claim 1

224. Claim 1 recites:

1. A transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises:

- i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and
- ii) an AAD-1 motif having the general formula of:

$HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$, wherein

X_{112} represents a single amino acid at position 112,
relative to the sequence of SEQ ID NO: 9;

$(X)_{114-137}$ represents a sequence of 24 amino acids;

$(X)_{139-269}$ represents a sequence of 131 amino acids;

and

$(X)_{271-280}$ represents a sequence of 10 amino acids.

225. The POSA would have regarded claim 1 to have been obvious based on either of the Saari References in combination with Schleinitz and Streber.

- i. “A transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein”**

226. The POSA would have been motivated to transform a plant cell to express a recombinant polynucleotide that encodes RdpA (*i.e.*, AAD-1 v1, SEQ ID

NO: 9). Each of the Saari References suggests that genes encoding RdpA could be used to transform plant cells to increase their resistance to phenoxy herbicides. See EX1041 (Saari 1999 (p. 422)) (“[T]he genes encoding an enzyme specific for the *R* isomer could be used to develop genetically engineered crops that are resistant to the herbicide of interest.”), *id.* (p. 427) (“[A] gene encoding an *R* isomer selective enzyme, such as that in *A. denitrificans*, may be useful for development of herbicide-resistant transgenic plants.”); EX1040 (Saari 1998 (p. 93)) (“A potential application for *A. denitrificans* or the *tfdA*-like gene it contains would be protection of crops from mecoprop and dichlorprop. . . . [T]he gene from *A. denitrificans* could be used since its gene product degrades the *R*-enantiomer.”).

227. In addition, each of the Saari References identified empirical studies involving RdpA, *i.e.*, the (*R*)-stereospecific α KG dioxygenase enzyme expressed by *S. herbicidovorans*, which demonstrated that RdpA selectively degraded (*R*)-phenoxy herbicides, including (*R*)-dichlorprop and (*R*)-mecoprop. EX1041 (Saari 1999 (p. 427)) (“The present work extends the conclusions derived from studies with a strain of *Sphingomonas herbicidovorans* that is capable of degrading both enantiomers of mecoprop [32]. In that strain, two α -KG-dependent dioxygenases appear to be present, each specific for a separate enantiomer of the substrate [33]. Based on our findings, it is probable that the two *S. herbicidovorans* enzymes are closely related in sequence.”); EX1040 (Saari 1998) (p. 92)) (“Related to these

findings, a recent publication (Nickel et al. 1997) reported that α -KG-dependent dioxygenases acting on phenoxypropionates can have opposite stereochemistry; *Sphingomonas herbicidovorans* has two α -KG-dependent dioxygenases for degradation of (S)- and (R)-dichlorprop, as shown by different activities in cell extracts corresponding to differential expression of two different size proteins when grown on one or the other enantiomer. The sequence relationship between the two *S. herbicidovorans* proteins is unknown, but my results comparing the *R. eutropha* JMP134 and *A. denitrificans* systems suggests that the *S. herbicidovorans* enzymes of opposite stereochemistry may be derived from the same ancestral sequence.”), *id.* (p. 127) (“Opposite stereopreferences have also been observed in a dichlorprop-degrading isolate *Sphingomonas herbicidovorans* which has α -KG dependent dioxygenases, one of which degrades (R)-dichlorprop and the other which degrades (S)-dichlorprop (Nickel et al. 1997).”). Based on these disclosures, the POSA would have viewed the gene encoding RdpA as a promising candidate for transformation into plant cells.

228. The POSA would have also reasonably expected to succeed in transforming plant cells to express RdpA. Each of the Saari Reference’s disclosures regarding RdpA would have led the POSA to Schleinitz. As of April 2004, nucleotide and amino acid sequences encoding RdpA had been deposited in public

databases such as GenBank and NCBI and were publicly available from those databases. *See* EX1001 ('555 Pat.), cols. 1-2, 44:37-40; EX1013 (Schleinitz).

229. As demonstrated by Schleinitz, for example, those databases contained the amino acid sequence for RdpA, which the '555 patent lists as SEQ ID NO: 9.

On Jun 26, 2003 this sequence version replaced gi:22087565.

Key	Location/Qualifiers
source	1..888 /db_xref="taxon:103036"

gene	<1..>888 /gene="rdpA"
CDS	1..888 /codon_start=1 /db_xref="GOA:Q8KSC9" /db_xref="TrEMBL:Q8KSC9" /note="FeII and alpha-ketoglutarate-dependent dioxygenase; similar to TauD and TfdA" /transl_table=11 /gene="rdpA" /product="R-2,4-dichlorophenoxypropionate dioxygenase" /protein_id="AAM90964.2" /translation="MHAALSPLSQRFERIAVQPLTGVLGAEITGVDLREPLDDSTWNEI LDAFHTYQVIYFPGQAITNEQHIAFSRRFGPVDVPLLSIEGYPEVQMIRREANESGR VIGDDWHTDSTFLDAPPAAVVMRAIDVPEHGGDTGFLSMYTAWETLSPTMQATIEGLNV VHSATRVFGSLYQAQNRFRSNTSVKVMVDVDAGDRETVHPLVVTHPGSGRKGLYVNQVYC QRIEGMTDAESKFLLOFLYEHATRFDFTCRVRWKKDQVLVWDNLCTMHRVAVPDYAGKFR YLTRTTVGGVRPAR"

EX1013 (Schleinitz) (p. 2) (highlighting added). Indeed, the '555 patent admits that this information was available as of April 2004. *See* EX1001 ('555 Pat.), cols. 1-2, 44:37-40 (citing, *e.g.*, EX1014 (Accession No. AF516752, published Aug. 6, 2002); EX1016 (Accession No. Q8KSC8, published Oct. 1, 2002); EX1015 (Accession No. AJ628859, published March 3, 2004)).

230. The POSA also would have known of methods for transforming genes encoding bacterially expressed α KG dioxygenase enzymes, such as the gene encoding TfdA, into plants. Each of the Saari References disclosed that researchers had transformed cotton cells using *tfdA*, which resulted in increased resistance to 2,4-D and other phenoxy herbicides. EX1040, (Saari 1998 (p. 93)) (“Cotton shows enhanced tolerance of 2,4-D in the presence of the pJP4-derived *tfdA* transformed either into the plant (Lyon et al. 1993) or into root-associated microbes (Feng and Kennedy 1997).”); EX1041 (Saari 1999 (p. 422)) (“Genetic engineering has already been used for crop protection from (achiral) phenoxyacetate herbicides: cotton has shown enhanced tolerance towards 2,4-D when *tfdA* was transformed directly into the plant [15] or into root-associated microbes [16].”).

231. These disclosures would have led the POSA to Streber, which disclosed methods used to transform plants to express TfdA. EX1043 (Streber), 7:58-9:24, 11:30-32:9. For example, Streber describes “known” methods for isolating a naturally occurring bacterial plasmid that contains a gene encoding an α KG dioxygenase enzyme, determining the nucleotide sequence of that gene, creating a recombinant bacterial/plant gene, and transforming that gene into plants, such as through the use of bacterial vectors. EX1043 (Streber), 3:10-13 (“The plasmids of this invention can be produced by digesting DNA from wild-type bacteria exhibiting genes for metabolizing 2,4-D or compounds similar to 2,4-D . . . ”), 7:58-9:24,

11:30-32:9. The '555 patent admits that such methods were well known: EX1001 ('555 Pat.), 31:24-27, 32:23-33:9, 35:45-37:27, 38:42-55; 39:37-42 (“A wide variety of methods are available for introducing a gene encoding a desired protein into the target host under conditions that allow for stable maintenance and expression of the gene. These methods are well known to those skilled in the art and are described, for example, in U.S. Pat. No. 5,135,867.”).

ii. “that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide”

232. RdpA (AAD-1 v1) exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide. *See supra* ¶¶ 120, 227. Moreover, each of the Saari References disclosed that RdpA was an (R)-selective α KG enzyme, which degrades the phenoxy auxins (R)-dichlorprop and (R)-mecoprop. EX1041 (Saari 1999 (p. 427)); EX1040 (Saari 1998 (pp. 92, 127)). Based on each of those disclosures, the POSA would have expected that RdpA would enzymatically degrade phenoxy auxin and (R)-aryloxyphenoxypropionate herbicides, which the POSA would have understood to degrade via the same hydroxylation and elimination reactions. *See supra* ¶¶ 210-215, 219-222.

233. Thus, plant cells transformed to express RdpA satisfy this limitation.

- iii. “further wherein said AAD-1 protein comprises:
i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) [the claim 1 AAD-1 motif]”

234. RdpA (AAD-1 v1) corresponds to the amino acid sequence listed in SEQ ID NO: 9; it therefore comprises an amino acid sequence having 100% sequence identity with SEQ ID NO: 9. *See supra* ¶ 121. RdpA also has the AAD-1 motif recited in this claim. *See supra* ¶ 122.

235. Thus, plant cells transformed to express RdpA satisfy this limitation.

b. Claim 2

236. Claim 2 refers back to claim 1 and recites: “The plant cell of claim 1 wherein said AAD-1 motif has the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R(X)_{282-284}R$, wherein $(X)_{282-284}$ represents a sequence of 3 amino acids.”

237. The POSA would have regarded this claim to have been obvious based on either of the Saari References in combination with Schleinitz and Streber.

238. The limitations of claim 1 are addressed above. In addition, as shown below, the AAD-1 motifs recited in claims 1 and 2 are identical except that the claim 2 motif contains the additional segment $(X)_{282-284}R$.

<u>Claim 1 “AAD-1” Motif</u>	<u>Claim 2 “AAD-1” Motif</u>
$HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$	$HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R(X)_{282-284}R$

239. RdpA (AAD-1 v1) corresponds to the amino acid sequence listed in SEQ ID NO: 9, which satisfies the AAD-1 motif recited in this claim. *See supra* ¶ 121.

240. Thus, plant cells transformed to express RdpA satisfy this limitation.

241. As explained above in connection with claim 1, which this claim refers back to, the POSA would have been motivated to transform and reasonably expected to succeed in transforming plant cells to express RdpA based on the prior art's disclosures and the POSA's knowledge. *See supra* ¶¶ 226-231.

c. Claim 3

242. Claim 3 refers back to claim 1 and recites: "The plant cell of claim 1 wherein the AAD-1 protein comprises an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 9."

243. The POSA would have regarded this claim to have been obvious based on either of the Saari References in combination with Schleinitz and Streber.

244. The limitations of claim 1 are addressed above. In addition, RdpA (AAD-1 v1) corresponds to the amino acid sequence listed in SEQ ID NO: 9; it therefore comprises an amino acid sequence having 100% identity to SEQ ID NO: 9. *See supra* ¶ 121.

245. As explained above in connection with claim 1, which this claim refers back to, the POSA would have been motivated to transform and reasonably expected

to succeed in transforming plant cells to express RdpA based on the prior art's disclosures and the POSA's knowledge. *See supra* ¶¶ 226-231.

d. Claims 4-5

246. Claims 4-5 refers back to claim 1.

247. Claim 4 recites: "The plant cell of claim 1 wherein said plant cell is dicotyledonous and selected from the group consisting of a cotton cell, a tobacco cell, a canola cell, a soybean cell, and an *Arabidopsis* cell."

248. Claim 5 recites: "The plant cell of claim 1 wherein said plant cell is a monocotyledonous cell selected from the group consisting of a rice cell and a maize cell."

249. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz and Streber.

250. The limitations of claim 1 are addressed above. In addition, the POSA would have understood that the plants listed in claims 4-5 were commonly grown as agricultural crops and/or used in research (as in the case of *Arabidopsis*). The POSA would have also understood that although researchers had developed plants listed in these claims that were resistant to glyphosate, overuse of glyphosate had led to the development of glyphosate-resistant weeds. *See, e.g.*, EX1001 ('555 Pat.), 1:21-29, 1:63-2:19. As a result, the POSA would have desired to use alternative herbicides, including phenoxy herbicides, in combination with these plants and would have been

motivated to transform such plant cells to express RdpA, which each of the Saari References disclosed to degrade those herbicides. Consistent with the POSA's understanding, each of the Saari References and Streber identify plants listed in claim 4 as candidates for transformation. EX1040 (Saari 1998 (p. 92)) (cotton); EX1041 (Saari 1999 (p. 422)) (cotton); EX1043 (Streber) 9:13-23, 30:36-31:35 (tobacco).

251. As explained above in connection with claim 1, to which these claims refer back, the POSA would have been motivated to transform and reasonably expected to succeed in transforming such plant cells to express RdpA based on the prior art's disclosures and the POSA's knowledge. *See supra* ¶¶ 226-231.

e. Claims 6-10

252. Claims 6-10 refer, directly or indirectly, back to claim 1.

253. Claim 6 recites: "A transgenic plant comprising a plurality of the plant cells of claim 1, wherein expression of said polynucleotide renders said plant tolerant to an aryloxyalkanoate herbicide."

254. Claim 7 recites: "The plant of claim 6 wherein said aryloxyalkanoate herbicide is a phenoxy auxin herbicide."

255. Claim 8 recites: "The plant of claim 6 wherein said aryloxyalkanoate herbicide is selected from the group consisting of 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop."

256. Claim 9 recites: “The plant of claim 6 wherein said aryloxyalkanoate herbicide is an (R)-aryloxyphenoxypropionate.”

257. Claim 10 recites: “The plant of claim 6 wherein said aryloxyalkanoate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofop.”

258. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz and Streber.

259. The limitations of claim 1 are addressed above. In addition, as explained above in connection with claim 1, each of the Saari References would have motivated the POSA to transform plants to express RdpA, to render them tolerant to phenoxy herbicides (*i.e.*, “aryloxyalkanoate herbicides”). EX1041 (Saari 1999 (pp. 422, 427)); EX1040 (Saari 1998 (p. 93)); *supra* ¶¶ 226-231. Each of the Saari References reported that RdpA was an (R)-selective α KG enzyme which degrades (R)-dichlorprop and (R)-mecoprop. EX1041 (Saari 1999 (p. 427)); EX1040 (Saari 1998 (pp. 91, 127)); *supra* ¶¶ 210-215, 219-222, 226-227, 232.

260. Each of the Saari References further suggested that RdpA was capable of degrading phenoxy herbicides listed in each of claims 6-10, including 2,4-D, (R)-dichlorprop, (R)-mecoprop, (R)-fluazifop, (R)-diclofop, (R)-fenoxaprop. EX1040 (Saari 1998 (pp. 71-72 & Scheme 13, Fig. 72)); EX1041 (Saari 1999 (p. 427)).

Based on the Saari References' disclosures regarding RdpA's reported activity, EX1041 (Saari 1999 (p. 427)); EX1040 (Saari 1998 (pp. 91, 127)), the POSA would have reasonably expected RdpA to degrade herbicides listed in each of claims 6-10. *See supra* ¶¶ 210-215, 219-222, 226-227, 232.

261. The '555 patent likewise admits that RdpA (AAD-1 v1) degrades each of the herbicides listed in claims 6-10. EX1001 ('555 Pat.), Fig. 4, Tbls. 3-4.

262. As explained above in connection with claim 1, to which these claims refer back, directly or indirectly, the POSA would have been motivated and reasonably expected to succeed in transforming plant cells to express RdpA based on the prior art's disclosures and the POSA's knowledge. *See supra* ¶¶ 226-231. The POSA would have reasonably expected that at least some plants transformed to express RdpA would be tolerant to the herbicides listed in these claims. *See supra* ¶¶ 210-215, 219-222, 226-227, 232.

f. Claims 13-16

263. Claims 13-16 refer, directly or indirectly, back to claim 6.

264. Claim 13 recites: "A method of controlling at least one weed in a field, wherein said field contains at least one plant of claim 6, wherein said method comprises applying to at least a portion of said field a first herbicide selected from the group consisting of a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide."

265. Claim 14 recites: “The method of claim 13 wherein said phenoxy auxin herbicide is an R-enantiomer of a chiral phenoxy auxin.”

266. Claim 15 recites: “The method of claim 13 wherein said phenoxy auxin herbicide is an achiral phenoxy auxin selected from the group consisting of 2,4-D and MCPA.

267. Claim 16 recites: “The method of claim 13 wherein said (R)-aryloxyphenoxypropionate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofop.”

268. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz and Streber.

269. As explained above in connection with claims 1 and 6-10, the POSA would have reasonably expected at least some plants transformed with the gene encoding RdpA to be tolerant to the herbicides listed in each of these claims based on RdpA’s reported activity. *See supra* ¶¶ 210-215, 219-222, 226-227, 232, 252-262. The POSA would further have understood that 2,4-D, MCPA, (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, and (R)-fenoxaprop were herbicides used for weed control. *See also* EX1039 (Rao 2000 (pp. 69, 88-92, Tbl. 5.1)). The POSA would therefore have been motivated to apply the herbicides listed in these claims to plants transformed to express RdpA.

270. Thus, the POSA would have been motivated to practice the methods recited in these claims and would have reasonably expected to succeed in doing so.

g. Claim 34

271. As shown below, claim 34 is similar to claim 1, but requires (1) the transgenic plant cell to be an “(R)-aryloxyphenoxypropionate herbicide tolerant transgenic plant cell,” and (2) the “AAD-1 motif” to have “90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9.”

<u>Claim 1</u>	<u>Claim 34</u>
1. A transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R, \text{ wherein}$	34. A <u><i>(R)-aryloxyphenoxypropionate herbicide tolerant</i></u> transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of:

X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(X)_{114-137}$ represents a sequence of 24 amino acids; $(X)_{139-269}$ represents a sequence of 131 amino acids; and $(X)_{271-280}$ represents a sequence of 10 amino acids.	$HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$, wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(X)_{114-137}$ represents a sequence of 24 amino acids; $(X)_{139-269}$ represents a sequence of 131 amino acids; and $(X)_{271-280}$ represents a sequence of 10 amino acids, <u><i>wherein said motif has 90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9.</i></u>
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272. The POSA would have regarded this claim to have been obvious based on either of the Saari References in combination with Schleinitz and Streber.

273. As discussed above in connection with claims 1, 6 and 9-10, each of the Saari References would have motivated the POSA to transform at least some plant cells to express RdpA, to confer tolerance to (R)-aryloxyphenoxypropionate

herbicides. *See* EX1041 (Saari 1999 (pp. 422, 427)); EX1040 (Saari 1998 (pp. 91, 93, 127)); *supra* ¶¶ 210-215, 219-222, 226-227, 232, 252-262.

274. Additionally, RdpA (*i.e.*, AAD-1 v1) has the amino acid sequence listed in SEQ ID NO: 9 and is therefore 100% identical to SEQ ID NO: 9 at positions 111 to 281.

275. I address the remaining limitations of this claim in connection with claim 1, which also contains those limitations (the discussions of which are incorporated here by reference). *See supra* ¶¶ 224-235.

276. As explained above in connection with claim 1, the POSA would have been motivated to transform and reasonably expected to succeed in transforming plant cells to express RdpA based on the prior art's disclosures and the POSA's knowledge. *See supra* ¶¶ 210-222.

4. Saari 1999 or Saari 1998 in Combination with Schleinitz, Streber, and Jepson Render Obvious Claims 11-12 and 17-33.

277. The POSA would have regarded the remaining challenged claims of the '555 patent to have been obvious based on the references discussed in the prior section and Jepson.

a. Claims 11-12

278. Claims 11-12 refer, directly or indirectly, back to claim 6.

279. Claim 11 recites: "The plant of claim 6 wherein said plant further comprises a second herbicide resistance gene."

280. Claim 12 recites: “The plant of claim 11 wherein said second herbicide resistance gene renders said plant resistant to an herbicide selected from the group consisting of glyphosate, glufosinate, acetolactate synthase (ALS) inhibitors, inhibitors of 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD), dicamba, and inhibitors of protoporphyrinogen oxidase (PPO).”

281. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson.

282. The limitations of claim 1 are addressed above. In addition, the POSA would have understood that applying multiple herbicides to fields containing crop plants would prevent or delay the evolution of herbicide-resistance weeds. *See also* EX1039 (Rao 2000 (pp. 308-09)). The POSA would have been motivated to transform plants to express multiple herbicide resistance genes, which rendered the plants resistant to those multiple herbicides, to facilitate the application of those herbicides. Jepson disclosed polynucleotides combining the gene encoding TfdA and another herbicide resistance gene. EX1030 (Jepson), [0012], [0026]-[0027], [0054], [00135]-[00180], claim 4. Jepson discloses that “Preferred combinations,” includes *ESPS*, *GOX*, *GAT*, and *PAT*, which the ’555 patent identifies as glyphosate or glufosinate resistance genes. EX1030 (Jepson), [0026] (“Preferred combinations of herbicide resistance conferring genes are . . . the tfdA gene obtainable from

Alcaligenes eutrophus and an EPSPS and/or GOX and/or PAT and/or PDS gene.”); EX1001 (’555 Pat.), 17:17-41, claim 26.

283. As explained above in connection with claim 1, to which claim 6 refers back indirectly, the POSA would have been motivated to transform and would have reasonably expected to succeed in transforming plants to express RdpA based on the prior art’s disclosures and the POSA’s knowledge. *See supra* ¶¶ 226-231.

b. Claims 17-19

284. Claims 17-19 refer, directly or indirectly, back to claim 13.

285. Claim 17 recites: “The method of claim 13 wherein said method comprises applying a second herbicide.”

286. Claim 18 recites: “The method of claim 17 wherein said first herbicide and said second herbicide are applied sequentially.”

287. Claim 19 recites: “The method of claim 17 wherein said first herbicide and said second herbicide are applied concurrently.”

288. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson.

289. The limitations of claim 13 are addressed above. In addition, as explained above in connection with claims 11-12, the POSA would have been motivated to apply multiple herbicides to prevent or delay the evolution of herbicide-

resistant weeds. *See supra* ¶¶ 278-283. The POSA would have recognized that such herbicides should be applied concurrently or sequentially depending on the circumstances under which those herbicides were known to be effective. *See* EX1030 (Jepson), [0005]-[0011], [0026], claims 3, 12; *see also* EX1039 (Rao 2000 (pp. 69, 88-92)). For example, the POSA would have recognized that herbicides should be applied concurrently in the case of two or more pre- or post-emergence herbicides; or sequentially, in the case of a pre- and post-emergence herbicide. *See* EX1030 (Jepson), [0005]-[0011], [0026], claims 3, 12; *see also* EX1039 (Rao 2000 (pp. 88-92)).

290. Thus, the POSA would have been motivated to practice the methods recited in these claims and would have reasonably expected to succeed in doing so.

c. Claim 20

291. Claim 20 refers back to claim 17 and recites: “The method of claim 17 wherein said first herbicide is a phenoxy auxin and said second herbicide is an (R)-aryloxyphenoxypropionate.”

292. The POSA would have regarded this claim to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson.

293. As explained above in connection with claims 1 and 6-10, the POSA would have reasonably expected at least some plants transformed with the gene

encoding RdpA to be tolerant to phenoxy auxin and (*R*)-aryloxyphenoxypropionate herbicides based on RdpA's reported activity. *See supra* ¶¶ 210-215, 219-222, 226-227, 232, 252-262. The POSA would have been motivated to apply a phenoxy auxin and an (*R*)-aryloxyphenoxypropionate herbicide.

294. Thus, the POSA would have been motivated to practice the methods recited in these claims and would have reasonably expected to succeed in doing so.

d. Claims 21-23

295. Claims 21 and 23 refer back to claim 17.

296. Claim 21 recites: "The method of claim 17 wherein said second herbicide is selected from the group consisting of glyphosate, glufosinate, dicamba, acetolactate synthase (ALS) inhibitors, protoporphyrinogen oxidase (PPO) inhibitors, and 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD) inhibitors."

297. Claim 22 recites: "The method of claim 17, wherein said first herbicide is 2,4-D and said second herbicide is glyphosate or glufosinate." Claim 23 recites: "The method of claim 17, wherein said first herbicide is an (*R*)-aryloxyphenoxypropionate and said second herbicide is glyphosate or glufosinate."

298. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson.

299. The limitations of claim 17 are addressed above. In addition, the POSA also would have understood that 2,4-D, glyphosate, and glufosinate, for example, were commonly used herbicides. *See also* EX1039 (Rao 2000 (pp. 89, 111)). Moreover, as explained above in connection with claims 11-12, Jepson discloses polynucleotides for combining the gene encoding TfdA and another herbicide resistance gene. EX1030 (Jepson), [0012], [0026]-[0027], [0054], [00135]-[00180], claims 4. Jepson discloses that “Preferred combinations” of resistance genes include the gene encoding TfdA, which confers resistance to 2,4-D, and the glyphosate and glufosinate resistance genes modified *ESPS*, *GOX*, *GAT*, and *PAT*. EX1030 (Jepson), [0026].

300. Thus, the POSA would have been motivated to practice the methods recited in these claims and would have reasonably expected to succeed in doing so.

e. Claim 24

301. Claim 24 refers back to claim 17. Claim 24 recites: “The method of claim 17 wherein said plant further comprises a second herbicide resistance gene that renders said plant resistant to said second herbicide.”

302. The POSA would have regarded this claim to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson for the reasons discussed in connection with claims 21-23. In addition, as discussed in connection with claims 11-12, the POSA would have been motivated to transform

plants to express multiple herbicide resistance genes, which render the plants resistant to those multiple herbicides, to facilitate the application of those herbicides.

f. Claims 25-26

303. Claims 25-26 refer, directly or indirectly, back to claim 24.

304. Claim 25 recites: “The method of claim 24 wherein said second herbicide resistance gene is selected from the group consisting of a modified acetolactate synthase (ALS) gene, a glyphosate resistance gene, a glufosinate resistance gene, and a dicamba-degrading enzyme gene.”

305. Claim 26 recites: “The method of claim 25 wherein: (a) said modified ALS gene is selected from the group consisting of SurA, SurB, Csr1, Csr1-1, and Csr1-2; (b) said glyphosate resistance gene is selected from the group consisting of modified EPSPS (5-enolpyruvylshikimate-3-phosphate synthase), GOX, and GAT; and, (c) said glufosinate resistance gene is selected from the group consisting of phosphinothricin-N-acetyltransferase (PAT) and bar.”

306. The POSA would have regarded these claims to have been obvious for the reasons discussed in connection with claims 21-23. For example, Jepson discloses recombinant polynucleotides for combining a gene encoding TfdA with a second resistance gene, which in “Preferred combinations,” includes modified EPSPS, GOX, GAT, and PAT. EX1030 (Jepson), [0026].

g. Claims 27-29

307. Claims 27-29 refer, directly or indirectly, back to claim 17.

308. Claim 27 recites: “The method of claim 17 wherein said method further comprises applying a third herbicide.”

309. Claim 28 recites: “The method of claim 27, wherein said third herbicide is selected from the group consisting of glyphosate, glufosinate, HPPD-inhibitors, PPO-inhibitors, ALS inhibitors, and dicamba.”

310. Claim 29 recites: “The method of claim 28 wherein said first, second and third herbicides are 2,4-D, quizalofop, and glyphosate.”

311. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson.

312. The limitations of claim 17 are addressed above. In addition, as explained above in connection with claims 1 and 6-10, the POSA would have been motivated to transform plants with the gene encoding RdpA and would have reasonably expected that at least some plants transformed with the gene encoding RdpA to degrade phenoxy auxin and (*R*)-aryloxyphenoxypropionate herbicides based on RdpA’s reported activity. *See supra* ¶¶ 210-215, 219-222, 226-227, 232, 252-262.

313. The POSA would have also been motivated to combine plants transformed with the gene encoding RdpA with 2,4-D, quizalofop, and glyphosate specifically. The POSA would have understood that 2,4-D, quizalofop, and glyphosate were all commercially used herbicides. *See also* EX1039 (Rao 2000 (pp. 89, 91-92)). Moreover, as explained in connection with claims 11-12, Jepson discloses polynucleotides for combining a gene encoding TfdA and another herbicide resistance gene. EX1030 (Jepson), [0012], [0026]-[0027], [0054], [00135]-[00180], claims 4. “Preferred combinations” of resistance genes include a gene encoding TfdA, which confers resistance to 2,4-D, and the glyphosate resistance genes modified *ESPS*, *GOX*, and *GAT*. EX1030 (Jepson), [0026]. The POSA would have recognized that transforming plants with the gene encoding RdpA would permit the use of quizalofop across multiple plant species.

314. Thus, the POSA would have been motivated to practice the methods recited in these claims and would have reasonably expected to succeed in doing so.

h. Claim 30

315. Claim 30 refers back to claim 1 and recites: “A seed comprising a plurality of the plant cells of claim 1.”

316. The POSA would have regarded this claim to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson.

317. The limitations of claim 1 are addressed above. In addition, Jepson discloses seeds containing transgenic plant cells comprising a resistance gene. EX1030 (Jepson), [00122]-[00123], [00131]-[00132], [00144], [00168]-[00169], [00180]-[00183], [00187]-[00188], claims 13, 15.

318. As explained above in connection with claim 1, to which this claim refers back, the POSA would have reasonably expected to succeed in transforming such plant cells to express RdpA based on the prior art's disclosures and the POSA's knowledge. *See supra* ¶¶ 226-231.

i. Claim 31

319. Claim 31 refers back to claim 30 and recites: "A method of controlling weeds in a field, wherein said method comprises applying an aryloxyalkanoate herbicide to said field and planting a seed of claim 30 in said field within 14 days of applying said aryloxyalkanoate herbicide."

320. The POSA would have regarded this claim to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson.

321. The limitations of claim 30 are addressed above. In addition, as explained above in connection with claims 1 and 6-10, the POSA would have been motivated to transform plants with the gene encoding RdpA and would have reasonably expected plants transformed with the gene encoding RdpA to be tolerant

to an aryloxyalkanoate (*i.e.*, phenoxy) herbicide based on RdpA's reported activity. *See supra* ¶¶ 210-215, 219-222, 226-227, 232, 252-262. The POSA would therefore have been motivated to apply the herbicides listed in these claims to plants transformed to express RdpA.

322. The POSA would have understood that phenoxy herbicides were routinely applied less than 14 days before planting a crop plant. For example, the POSA would have understood that pre-planting applications had been used extensively in the production of maize and soybean. *See, e.g.*, EX1051 (Krausz (p. 906)). The POSA would have understood that such pre-planting applications were advantageous because, among other things, “[r]ainfall probabilities are usually greater earlier in the growing season” and pre-planting applications “conserve soil moisture under low moisture conditions.” EX1051 (Krausz (p. 906)). The POSA would have been aware of studies reporting that applying 2,4-D as little as 14, 7, or 0 days before planting had no significant effect on crop yield and would not have considered pre-planting to be detrimental. EX1051 (Krausz (p. 909-10 & Tbls. 5-6)).

323. Thus, the POSA would have been motivated to practice the methods recited in this claim and would have reasonably expected to succeed in doing so.

j. Claims 32-33

324. Claims 32 and 33 refer, directly or indirectly, back to claim 30.

325. Claim 32 refers back to claim 31 and recites: “A plant grown from the seed of claim 30.”

326. Claim 33 recites: “A part, progeny, or asexual propagate of the plant of claim 32, wherein said part, progeny, or sexual propagate comprises said polynucleotide.”

327. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson.

328. The limitations of claim 30 are addressed above. In addition, for example, Jepson discloses transgenic plants grown from seeds containing the recombinant polynucleotide that contains the herbicide resistance gene. EX1030 (Jepson), [0168]-[0170], [0172]-[0179].

329. As explained above in connection with claim 1, to which claim 30 refers back indirectly, the POSA would have reasonably expected to succeed in transforming such plant cells to express RdpA based on the prior art’s disclosures and the POSA’s knowledge. *See supra* ¶¶ 226-231.

VIII. INVALIDITY ANALYSIS FOR THE '283 PATENT

A. Invalidity Analysis as of October 7, 2016

330. The challenged claims of the '555 and '283 patents are similar, except that the challenged claims of the '283 patent (1) require the transgenic plant cell or plant to be a maize plant cell or maize plant, (2) parenthetically assign sequence identity numbers to the claimed AAD-1 motifs, (3) specify that the phenoxy auxin herbicide and the (R)-aryloxyphenoxypropionate herbicide are “aryloxyalkanoate herbicides,” and (4) require that the “AAD-1 protein when expressed in a maize plant cell renders said maize plant cell tolerant to a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, as compared to an untransformed maize plant cell.”

331. The following comparison between claim 1 of the '555 patent and claim 1 of the '283 patent illustrates these differences, *emphasized* below:

<u>'555 Patent, Claim 1</u>	<u>'283 Patent, Claim 1</u>
1. A transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate	1. A transgenic <u><i>maize</i></u> plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide

herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R,$ wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(X)_{114-137}$ represents a sequence of 24 amino acids; $(X)_{139-269}$ represents a sequence of 131 amino acids; and $(X)_{271-280}$ represents a sequence of 10 amino acids.	<u><i>which are aryloxyalkanoate herbicides,</i></u> further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$ <u><i>(SEQ ID NO: 34),</i></u> wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(X)_{114-137}$ represents a sequence of 24 amino acids; $(X)_{139-269}$ represents a sequence of 131 amino acids; and $(X)_{271-280}$ represents a sequence of 10 amino acids, <u><i>wherein said AAD-1 protein when expressed in a maize plant cell renders said maize plant cell tolerant to a phenoxy auxin</i></u>
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	<u>herbicide and an (R)-</u> <u>aryloxyphenoxypropionate</u> <u>herbicide, as compared to an</u> <u>untransformed maize plant cell.</u>
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332. As shown in the sections below, the limitations recited in the dependent claims of the '283 patent overlap with the limitations recited in the dependent claims of the '555 patent.

1. The Challenged Claims Are Not Entitled to a Priority Date Earlier Than October 7, 2016.

333. I understand that in order for a patent to be entitled to priority based on an earlier application or chain of applications, each previous application in the chain must be entitled to a priority to an earlier application, and each application in the priority chain must adequately describe the subject matter such that the POSA would understand that the inventor was in possession of the claimed invention as of the priority date.

334. As I explain in Section VII.A.1, which is incorporated here by reference, the '555 patent is not entitled to a priority date earlier than October 7, 2016, because the original specification of the '406 application did not adequately describe a genus of AAD-1 proteins having an AAD-1 motif, with at least 85% or 90% sequence identity to SEQ ID NO: 9, and conferring the required herbicide degrading activity. The '283 patent likewise is not entitled to a priority date earlier

than October 7, 2016, because the claims of the '283 patent recite the same limitations, which the original application does not support.

335. The prosecution history of the '283 patent provides additional confirmation that the inventors did not have possession of the invention on an earlier date. During prosecution of the application that led to the '283 patent, the applicant amended the specification to add the AAD-1 motif as it appears in claim 1 of the '555 patent. EX1002 ('283 Pat.) 18:61-19:5, Claim 1. (The applicant also parenthetically assigned sequence identity numbers to the prior-art α KG motif and the claim 1 AAD-1 motif.) As before, the amendment stated: "Mapping the α -ketoglutarate-dependent dioxygenase motif disclosed in the previous paragraph to the sequence of SEQ ID NO: 9 reveals the AAD-1 motif of HX₁₁₂D(X)₁₁₄₋₁₃₇T(X)₁₃₉₋₂₆₉H(X)₂₇₁₋₂₈₀R." *Id.*; EX1010 ('966 Appl. & File History) COR-AAD1-00006142 (Response (Apr. 26, 2021) p. 3).

336. As I explain in Section VII.A.1.e, which is incorporated here by reference, the applicant's "mapping" argument is flawed because the specification did not support the applicant's rationales for selecting that motif, as demonstrated, for example, by the applicant's reliance on information outside of the prior art and the original application. For example, the original specification demonstrates that proteins satisfying the prior-art α KG motif do not necessarily have the claimed activity, as evidenced by AAD-2, which satisfies the prior-art α KG motif but is not

(*R*)-enantioselective. The applicant's assertion that the POSA could ascertain which proteins have the claimed activity by "mapping" the prior-art α KG motif onto RdpA is therefore incorrect.

2. Corteva '437 Anticipates the Challenged Claims.

337. As I explain in Section VII.A.2, which is incorporated here by reference, Corteva '437 is the publication of the international patent application to which the '283 patent claims priority. Corteva '437 discloses transgenic maize plant cells and plants expressing proteins (*e.g.*, AAD-1 v1 and v2) that fall within the scope of the challenged claims. Thus, Corteva '437 anticipates each of the challenged claims of the '283 patent.

a. Claim 1

338. Claim 1 of the '283 patent is similar to claim 1 of the '555 patent, but (1) requires the transgenic plant cell or plant to be a maize plant cell or maize plant, (2) parenthetically assigns a sequence identity number to the claimed AAD-1 motif, (3) specifies that the phenoxy auxin herbicide and the (*R*)-aryloxyphenoxypropionate herbicide are "aryloxyalkanoate herbicides," and (4) requires that the "AAD-1 protein when expressed in a maize plant cell renders said maize plant cell tolerant to a phenoxy auxin herbicide and an (*R*)-aryloxyphenoxypropionate herbicide, as compared to an untransformed maize plant cell."

339. Corteva '437 anticipates this claim.

340. First, Corteva '437 discloses that AAD-1 proteins, such as AAD-1 v1 and v2, can be expressed in maize plant cells. Corteva '437 states: “The transgenic expression of the subject AAD-1 genes is exemplified in, for example, *Arabidopsis*, corn (maize), tobacco, cotton, rice, soybean, and canola,” and “can be applied to any other desired types of plants.” EX1021 (Corteva '437), [00104]. Claim 4 of Corteva '437 recites: “The cell of claim 2 wherein said plant cell is a monocotyledonous cell selected from the group consisting of a rice cell and a maize cell.”

341. Second, the addition of a sequence identity number to the AAD-1 motif assigns an identifier to the motif; it does not affect whether Corteva '437 disclosure of AAD-1 proteins, such as AAD-1 v1 and v2, satisfies this limitation.

342. Third, the statement that the phenoxy auxin herbicide and (R)-aryloxyphenoxypropionate herbicide are “aryloxyalkanoate herbicides” reflects only that phenoxy auxin herbicides and aryloxyphenoxypropionate herbicides belong to the broader class of phenoxy (*i.e.*, “aryloxyalkanoate”) herbicides; it does not affect whether Corteva '437's disclosure anticipates this claim.

343. Fourth, Corteva '437 discloses that the expression of AAD-1 proteins in a maize plant cell renders the maize plant cell tolerant to a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, as compared to an untransformed maize plant cell. Corteva '437 discloses that its inventions fulfill a

need for plant cells and plants to have tolerance to the claimed herbicides. *See, e.g.*, EX1021 (Corteva '437), Abstract (“This highly novel discovery is the basis of significant herbicide tolerant crop trait opportunities . . .”), [0074]-[0078] (“A single gene (*AAD-1*) has now been identified which, when genetically engineered for expression in plants, has the properties to allow the use of phenoxy auxin herbicides in plants where inherent tolerance never existed or was not sufficiently high to allow use of these herbicides.”), [00110] (“Plants producing proteins of the subject invention will preferably produce ‘an effective amount’ of the protein so that when the plant is treated with a herbicide, the level of protein expression is sufficient to render the plant completely or partially resistant or tolerant to the herbicide”), [00110] (“Transformed plants and plant cells of the subject invention are preferably rendered resistant or tolerant to an herbicide, as discussed herein, meaning that the transformed plant and plant cells can grow in the presence of effective amounts of one or more herbicides as discussed herein.”), Tbls. 1-2, claim 5 (“A transgenic plant comprising a plurality of cells according to claim 1, wherein expression of said polynucleotide renders said cells tolerant to an aryloxyalkanoate herbicide.”). It also discloses examples comparing the effects of herbicides on transformed and untransformed plants. EX1021 (Corteva '437), [00260]-[00264] & Tbls. 6-8, 16. The POSA would therefore understand Corteva '437 to disclose that maize plant cells transformed with a gene encoding an AAD-1 protein would be rendered

tolerant to phenoxy auxin and (*R*)-aryloxyphenoxypropionate herbicides relative to an untransformed plant cell.

344. I address the remaining limitations of this claim in connection with claim 1 of the '555 patent (the discussions of which are incorporated here by reference). *See supra* Section VII.A.2.a. Relatedly, claims 2-43 and 57-60 of Corteva '437 refer, directly or indirectly, back to claim 1. As I explain in the sections below in further detail, Corteva '437's dependent claims disclose elements that overlap with the challenged claims 3-28 (*i.e.*, various dependent claims of the '283 patent). The POSA would understand that because claim 1 of Corteva '437 encompasses at least AAD-1 v1, Corteva '437's dependent claims would apply to that protein. Moreover, the POSA would understand that because AAD-1 v1 (SEQ ID NO: 9) and v2 (SEQ ID NO: 10) were exemplary AAD-1 proteins described in the examples, *e.g.*, EX1021 (Corteva '437), [00230]-[0264] & Tbls. 15-16, Corteva '437's dependent claims would also be applicable to those proteins for purposes of what Corteva '437 teaches. As a result, Corteva '437 anticipates the dependent claims of the '283 patent as well.

b. Claim 2

345. Claim 2 refers back to claim 1 and recites: "The plant cell of claim 1 wherein said AAD-1 motif has the general formula of: $\text{HX}_{112}\text{D}(\text{X})_{114-137}\text{T}(\text{X})_{139-}$

${}_{269}\text{H}(\text{X})_{271-280}\text{R}(\text{X})_{282-284}\text{R}$ (SEQ ID NO: 35), wherein $(\text{X})_{282-284}$ represents a sequence of 3 amino acids.”

346. Claim 2 of the '283 patent and claim 2 of the '555 patent recite similar additional limitations. Claim 2 of the '283 patent parenthetically assigns a sequence identity number to the AAD-1 motif (which does not affect whether Corteva '437 disclosure of AAD-1 proteins, such as AAD-1 v1 and v2, satisfies this limitation), and the claims have slightly different formatting.

<u>'555 Patent, Claim 2</u>	<u>'283 Patent, Claim 2</u>
2. The plant cell of claim 1 wherein said AAD-1 motif has the general formula of: $\text{HX}_{112}\text{D}(\text{X})_{114-137}\text{T}(\text{X})_{139-269}\text{H}(\text{X})_{271-280}\text{R}(\text{X})_{282-284}\text{R}$, wherein $(\text{X})_{282-284}$ represents a sequence of 3 amino acids.	2. The plant cell of claim 1 wherein said AAD-1 motif has the general formula of: $\text{HX}_{112}\text{D}(\text{X})_{114-137}\text{T}(\text{X})_{139-269}\text{H}(\text{X})_{271-280}\text{R}(\text{X})_{282-284}\text{R}$ <u>(SEQ ID NO: 35)</u>, wherein $(\text{X})_{282-284}$ represents a sequence of 3 amino acids.

347. Corteva '437 anticipates this claim for the reasons discussed in connection with claim 1 of the '283 patent and claim 2 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.b, VIII.A.2.a.

c. Claim 3

348. Claim 3 refers back to claim 1 and recites: “A transgenic maize plant comprising a plurality of the maize plant cell of claim 1, wherein expression of said polynucleotide renders said plant tolerant to said aryloxyalkanoate herbicide.”

349. Claim 3 of the '283 patent and claim 6 of the '555 patent recite similar additional limitations. Claim 3 of the '283 patent requires the plant cell to be a maize plant cell, a limitation that is required by claim 1 of the '283 patent. Claim 3 of the '283 patent also uses the term “said,” rather than the term “an,” to refer to the term “aryloxyalkanoate herbicide,” a term that is used in claim 1 of the '283 patent.

<u>'555 Patent, Claim 6</u>	<u>'283 Patent, Claim 3</u>
6. A transgenic plant comprising a plurality of the plant cells of claim 1, wherein expression of said polynucleotide renders said plant tolerant to <i>an</i> aryloxyalkanoate herbicide.	3. A transgenic <i><u>maize</u></i> plant comprising a plurality of the <i><u>maize</u></i> plant cell of claim 1, wherein expression of said polynucleotide renders said plant tolerant to <i>said</i> aryloxyalkanoate herbicide.

350. Corteva '437 anticipates this claim for the reasons discussed in connection with claim 1 of the '283 patent and claim 6 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.e, VIII.A.2.a.

d. Claims 4-6

351. Claims 4-6 refer back to claim 3.

352. Claim 4 recites: “The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop.”

353. Claim 5 recites: “The plant of claim 3 wherein said aryloxyalkanoate herbicide is an (R)-aryloxyphenoxypropionate.”

354. Claim 6 recites: “The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofof.”

355. Claims 4-6 of the '283 patent and claims 8-10 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 8-10</u>	<u>'283 Patent, Claims 4-6</u>
8. The plant of claim 6 wherein said aryloxyalkanoate herbicide is selected from the group consisting of 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop.	4. The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop.
9. The plant of claim 6 wherein said aryloxyalkanoate herbicide is an (R)-aryloxyphenoxypropionate.	5. The plant of claim 3 wherein said aryloxyalkanoate herbicide is an (R)-aryloxyphenoxypropionate.
10. The plant of claim 6 wherein said aryloxyalkanoate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofof.	6. The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofof.

356. Corteva '437 anticipates these for the reasons discussed in connection with claim 3 of the '283 patent and claims 7-10 of the '555 patent (which are incorporated here by reference). *See supra* sections VII.A.2.f, VIII.A.2.c.

e. Claims 7-8

357. Claims 7 and 8 refer, directly or indirectly, back to claim 3.

358. Claim 7 recites: “The plant of claim 3 wherein said plant further comprises a second herbicide resistance gene.”

359. Claim 8 recites: “The plant of claim 7 wherein said second herbicide resistance gene renders said plant resistant to an herbicide selected from the group consisting of glyphosate, glufosinate, acetolactate synthase (ALS) inhibitors, inhibitors of 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD), dicamba, and inhibitors of protoporphyrinogen oxidase (PPO).”

360. Claims 7-8 of the '283 patent and claims 11-12 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 11-12</u>	<u>'283 Patent, Claims 7-8</u>
11. The plant of claim 6 wherein said plant further comprises a second herbicide resistance gene.	7. The plant of claim 3 wherein said plant further comprises a second herbicide resistance gene.
12. The plant of claim 11 wherein said second herbicide resistance gene renders said plant resistant to an	8. The plant of claim 7 wherein said second herbicide resistance gene renders said plant resistant to an

herbicide selected from the group consisting of glyphosate, glufosinate, acetolactate synthase (ALS) inhibitors, inhibitors of 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD), dicamba, and inhibitors of protoporphyrinogen oxidase (PPO).	herbicide selected from the group consisting of glyphosate, glufosinate, acetolactate synthase (ALS) inhibitors, inhibitors of 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD), dicamba, and inhibitors of protoporphyrinogen oxidase (PPO).
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361. Corteva '437 anticipates these claims for the reasons discussed in connection with claim 3 of the '283 patent and claims 11-12 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.g, VIII.A.2.c.

f. Claim 9

362. Claim 9 refers back to claim 3 and recites: “A method of controlling at least one weed in a field, wherein said field contains at least one plant of claim 3, wherein said method comprises applying to at least a portion of said field a first herbicide selected from the group consisting of a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide.”

363. Claim 9 of the '283 patent and claim 13 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claim 13</u>	<u>'283 Patent, Claim 9</u>
13. A method of controlling at least one weed in a field, wherein said field	9. A method of controlling at least one weed in a field, wherein said field

contains at least one plant of claim 6, wherein said method comprises applying to at least a portion of said field a first herbicide selected from the group consisting of a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide.	contains at least one plant of claim 3, wherein said method comprises applying to at least a portion of said field a first herbicide selected from the group consisting of a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide.
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364. Corteva '437 anticipates this claim for the reasons discussed in connection with claim 3 of the '283 patent and claim 13 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.h, VIII.A.2.c.

g. Claims 10-12

365. Claims 10-12 refer back to claim 9.

366. Claim 10 recites: “The method of claim 9 wherein said phenoxy auxin herbicide is an R-enantiomer of a chiral phenoxy auxin.”

367. Claim 11 recites: “The method of claim 9 wherein said phenoxy auxin herbicide is an achiral phenoxy auxin selected from the group consisting of 2,4-D and MCPA.”

368. Claim 12 recites: “The method of claim 9 wherein said (R)-aryloxyphenoxypropionate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofof.”

369. Claims 10-12 of the '283 patent and claims 14-16 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 14-16</u>	<u>'283 Patent, Claims 10-12</u>
14. The method of claim 13 wherein said phenoxy auxin herbicide is an R-enantiomer of a chiral phenoxy auxin.	10. The method of claim 9 wherein said phenoxy auxin herbicide is an R-enantiomer of a chiral phenoxy auxin.
15. The method of claim 13 wherein said phenoxy auxin herbicide is an achiral phenoxy auxin selected from the group consisting of 2,4-D and MCPA.	11. The method of claim 9 wherein said phenoxy auxin herbicide is an achiral phenoxy auxin selected from the group consisting of 2,4-D and MCPA.
16. The method of claim 13 wherein said (R)-aryloxyphenoxypropionate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofop.	12. The method of claim 9 wherein said (R)-aryloxyphenoxypropionate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofop.

370. Corteva '437 anticipates these claims for the reasons discussed in connection with claim 9 of the '283 patent and claims 14-16 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.i, VIII.A.2.f.

h. Claims 13-16

371. Claims 13-16 refer, directly or indirectly, back to claim 9.

372. Claim 13 recites: “The method of claim 9 wherein said method comprises applying a second herbicide.”

373. Claim 14 recites: “The method of claim 13 wherein said first herbicide and said second herbicide are applied sequentially.”

374. Claim 15 recites: “The method of claim 13 wherein said first herbicide and said second herbicide are applied concurrently.”

375. Claim 16 recites: “The method of claim 13 wherein said first herbicide is a phenoxy auxin and said second herbicide is an (R)-aryloxyphenoxypropionate.”

376. Claims 13-16 of the '283 patent and claims 17-20 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 17-20</u>	<u>'283 Patent, Claims 13-16</u>
17. The method of claim 13 wherein said method comprises applying a second herbicide.	13. The method of claim 9 wherein said method comprises applying a second herbicide.
18. The method of claim 17 wherein said first herbicide and said second herbicide are applied sequentially.	14. The method of claim 13 wherein said first herbicide and said second herbicide are applied sequentially.
19. The method of claim 17 wherein said first herbicide and said second herbicide are applied concurrently.	15. The method of claim 13 wherein said first herbicide and said second herbicide are applied concurrently.
20. The method of claim 17 wherein said first herbicide is a phenoxy auxin	16. The method of claim 13 wherein said first herbicide is a phenoxy auxin

and said second herbicide is an (R)-aryloxyphenoxypropionate.	and said second herbicide is an (R)-aryloxyphenoxypropionate.
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377. Corteva '437 anticipates these claims for the reasons discussed in connection with claim 9 of the '283 patent and claims 17-20 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.j, VIII.A.2.f.

i. Claims 17-19

378. Claims 17-19 refer back to claim 13.

379. Claim 17 recites: “The method of claim 13 wherein said second herbicide is selected from the group consisting of glyphosate, glufosinate, dicamba, acetolactate synthase (ALS) inhibitors, protoporphyrinogen oxidase (PPO) inhibitors, and 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD) inhibitors.”

380. Claim 18 recites: “The method of claim 13, wherein said first herbicide is 2,4-D and said second herbicide is glyphosate or glufosinate.”

381. Claim 19 recites: “The method of claim 13, wherein said first herbicide is an (R)-aryloxyphenoxypropionate and said second herbicide is glyphosate or glufosinate.”

382. Claims 17-19 of the '283 patent and claims 21-23 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 21-23</u>	<u>'283 Patent, Claims 17-19</u>
21. The method of claim 17 wherein said second herbicide is selected from the group consisting of glyphosate, glufosinate, dicamba, acetolactate synthase (ALS) inhibitors, protoporphyrinogen oxidase (PPO) inhibitors, and 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD) inhibitors.	17. The method of claim 13 wherein said second herbicide is selected from the group consisting of glyphosate, glufosinate, dicamba, acetolactate synthase (ALS) inhibitors, protoporphyrinogen oxidase (PPO) inhibitors, and 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD) inhibitors.
22. The method of claim 17, wherein said first herbicide is 2,4-D and said second herbicide is glyphosate or glufosinate.	18. The method of claim 13, wherein said first herbicide is 2,4-D and said second herbicide is glyphosate or glufosinate.
23. The method of claim 17, wherein said first herbicide is an (R)-aryloxyphenoxypropionate and said second herbicide is glyphosate or glufosinate.	19. The method of claim 13, wherein said first herbicide is an (R)-aryloxyphenoxypropionate and said second herbicide is glyphosate or glufosinate.

383. Corteva '437 anticipates these claims for the reasons discussed in connection with claim 13 of the '283 patent and claims 21-23 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.k, VIII.A.2.h.

j. Claims 20-21

384. Claims 20-21 refer, directly or indirectly, back to claim 13.

385. Claim 20 recites: “The method of claim 13 wherein said plant further comprises a second herbicide resistance gene that renders said plant resistant to said second herbicide.”

386. Claim 21 recites: “The method of claim 20 wherein said second gene is selected from the group consisting of a modified acetolactate synthase (ALS) gene, a glyphosate resistance gene, a glufosinate resistance gene, and a dicamba-degrading enzyme gene.

387. Claims 20-21 of the '283 patent and claims 24-25 of the '555 patent recite similar additional limitations. Claim 25 of the '555 patent states that the second gene is a “second herbicide resistance gene,” a limitation that is required by claim 20 of the '283 patent and claim 24 of the '555 patent.

<u>'555 Patent, Claims 24-25</u>	<u>'283 Patent, Claims 20-21</u>
24. The method of claim 17 wherein said plant further comprises a second herbicide resistance gene that renders said plant resistant to said second herbicide.	20. The method of claim 13 wherein said plant further comprises a second herbicide resistance gene that renders said plant resistant to said second herbicide.
25. The method of claim 24 wherein said second <i><u>herbicide resistance</u></i> gene is selected from the group consisting of a	21. The method of claim 20 wherein said second gene is selected from the group consisting of a modified

modified acetolactate synthase (ALS) gene, a glyphosate resistance gene, a glufosinate resistance gene, and a dicamba-degrading enzyme gene.	acetolactate synthase (ALS) gene, a glyphosate resistance gene, a glufosinate resistance gene, and a dicamba-degrading enzyme gene.
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388. Corteva '437 anticipates these claims for the reasons discussed in connection with claim 13 of the '283 patent and claims 24-25 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.1-VII.A.2.m, VIII.A.2.h.

k. Claims 22-24

389. Claims 22-24 refer, directly or indirectly, back to claim 13.

390. Claim 22 recites: “The method of claim 13 wherein said method further comprises applying a third herbicide.”

391. Claim 23 recites: “The method of claim 22, wherein said third herbicide is selected from the group consisting of glyphosate, glufosinate, HPPD-inhibitors, PPO-inhibitors, ALS inhibitors, and dicamba.”

392. Claim 24 recites: “The method of claim 23 wherein said first, second and third herbicides are 2,4-D, quizalofop, and glyphosate.”

393. Claims 22-24 of the '283 patent and claims 27-29 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 27-29</u>	<u>'283 Patent, Claims 22-24</u>
27. The method of claim 17 wherein said method further comprises applying a third herbicide.	22. The method of claim 13 wherein said method further comprises applying a third herbicide.
28. The method of claim 27, wherein said third herbicide is selected from the group consisting of glyphosate, glufosinate, HPPD-inhibitors, PPO-inhibitors, ALS inhibitors, and dicamba.	23. The method of claim 22, wherein said third herbicide is selected from the group consisting of glyphosate, glufosinate, HPPD-inhibitors, PPO-inhibitors, ALS inhibitors, and dicamba.
29. The method of claim 28 wherein said first, second and third herbicides are 2,4-D, quizalofop, and glyphosate.	24. The method of claim 23 wherein said first, second and third herbicides are 2,4-D, quizalofop, and glyphosate.

394. Corteva '437 anticipates these claims for the reasons discussed in connection with claim 13 of the '283 patent and claims 27-29 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.n, VIII.A.2.h.

I. Claim 25

395. Claim 25 refers back to claim 1 and recites: “A seed comprising the plant cell of claim 1.”

396. Claim 25 of the '283 patent and claim 30 of the '555 patent recite similar additional limitations. Claim 25 of the '283 patent requires a plant cell; claim 30 of the '555 patent requires a plurality of plant cells.

<u>'555 Patent, Claim 30</u>	<u>'283 Patent, Claim 25</u>
30. A seed comprising <u>a plurality of</u> the plant cells of claim 1.	25. A seed comprising the plant cell of claim 1.

397. Claim 25 is anticipated, irrespective of this difference in language. If a seed contains a “plurality of the plant cells” (*i.e.*, multiple plant cells) it also includes at least a “plant cell.” Thus, Corteva ’437 anticipates this claim for the reasons discussed in connection with claim 1 of the ’283 patent and claim 30 of the ’555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.o, VIII.A.2.a.

398. Additionally, Corteva ’437 discloses a seed comprising a plant cell transformed to express the gene that encodes an AAD-1 protein, such as AAD-1 v1 or v2. EX1021 (Corteva ’437), [00151] (“Seeds produced by and/or used to generate plants of the subject invention are also included within the scope of the subject invention.”), [00253] (“Freshly harvested T₁ seed (transformed with native [*AAD-1* (v2)] . . . gene) was allowed to dry for 7 days at room temperature.”), claim 57 (“A seed comprising a plant cell of claim 1.”).

m. Claim 26

399. Claim 26 refers back to claim 25 and recites: “A method of controlling weeds in a field, wherein said method comprises applying an aryloxyalkanoate

herbicide to said field and planting a seed of claim 25 in said field within 14 days of applying said aryloxyalkanoate herbicide.”

400. Claim 26 of the '283 patent and claim 31 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claim 31</u>	<u>'283 Patent, Claim 26</u>
31. A method of controlling weeds in a field, wherein said method comprises applying an aryloxyalkanoate herbicide to said field and planting a seed of claim 30 in said field within 14 days of applying said aryloxyalkanoate herbicide.	26. A method of controlling weeds in a field, wherein said method comprises applying an aryloxyalkanoate herbicide to said field and planting a seed of claim 25 in said field within 14 days of applying said aryloxyalkanoate herbicide.

401. Corteva '437 anticipates this claim for the reasons discussed in connection with claim 25 of the '283 patent and claim 31 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.p, VIII.A.2.l.

n. Claims 27-28

402. Claims 27-28 refer, directly or indirectly, back to claim 25.

403. Claim 27 recites: “A plant grown from the seed of claim 25 comprising said polynucleotide.”

404. Claim 28 recites: “A part, progeny, or asexual propagate of the plant of claim 27, wherein said part, progeny, or sexual propagate comprises said polynucleotide.”

405. Claims 27-28 of the '283 patent and claims 32-33 of the '555 patent recite similar additional limitations. Claim 27 of the '283 patent states that the seed comprises “said polynucleotide,” a limitation that is required by claim 1 of the '283 patent, from which claim 25 depends.

<u>'555 Patent, Claim 32-33</u>	<u>'283 Patent, Claims 27-28</u>
32. A plant grown from the seed of claim 30.	27. A plant grown from the seed of claim 25 <u>comprising said polynucleotide.</u>
33. A part, progeny, or asexual propagate of the plant of claim 32, wherein said part, progeny, or sexual propagate comprises said polynucleotide.	28. A part, progeny, or asexual propagate of the plant of claim 27, wherein said part, progeny, or sexual propagate comprises said polynucleotide.

406. Corteva '437 anticipates these claims for the reasons discussed in connection with claim 25 of the '283 patent and claims 32-33 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.q, VIII.A.2.1.

o. Claim 29

407. Claim 29 is similar to claim 1, but requires (1) the transgenic maize plant cell to be an “(R)-aryloxyphenoxypropionate herbicide tolerant maize transgenic plant cell” and (2) the “AAD-1 motif” to have “90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9.”

408. Claim 29 of the '283 patent is also similar to claim 34 of the '555 patent.

The only differences are also present in claim 1 of the '283 patent.

<u>'555 Patent, Claim 34</u>	<u>'283 Patent, Claim 29</u>
34. An (R)-aryloxyphenoxypropionate herbicide tolerant transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$, wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9;	29. An (R)-aryloxyphenoxypropionate herbicide tolerant transgenic <u>maize</u> plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$ <u>(SEQ ID NO: 34)</u>, wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9;

(X)₁₁₄₋₁₃₇ represents a sequence of 24 amino acids; (X)₁₃₉₋₂₆₉ represents a sequence of 131 amino acids; and (X)₂₇₁₋₂₈₀ represents a sequence of 10 amino acids, wherein said motif has 90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9.	(X)₁₁₄₋₁₃₇ represents a sequence of 24 amino acids; (X)₁₃₉₋₂₆₉ represents a sequence of 131 amino acids; and (X)₂₇₁₋₂₈₀ represents a sequence of 10 amino acids, wherein said motif has 90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9, and <u>wherein said AAD-1 protein when expressed in a maize plant cell renders said maize plant cell tolerant to a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, as compared to an untransformed maize plant cell.</u>
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409. Corteva '437 anticipates this claim for the reasons discussed in connection with claim 1 of the '283 patent and claim 34 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.r, VIII.A.2.a.

3. Corteva '437 Renders Obvious the Challenged Claims.

410. I understand that if a claim is anticipated based on a given reference, it also would have been obvious based on that reference. As I explain above, Corteva '437 anticipates each of the challenged claims of the '283 patent. It therefore also renders obvious those claims.

B. Invalidity Analysis as of April 30, 2004

411. As explained in Section VII.A.1, which is incorporated here by reference, the challenged claims of the Corteva patents are not entitled to a priority date earlier than October 7, 2016. Even if the challenged claims were entitled to the earliest possible priority date of April 30, 2004, however, the challenged claims of the '283 patent would have been obvious based on the prior art and the knowledge of the POSA.

1. Saari 1999 or Saari 1998 in Combination with Schleinitz and Streber Renders Obvious Claims 1-6, 9-12, and 29.

412. As I explain above in Sections VII.B.1-VII.B.2, which is incorporated here by reference, even as of April 2004, the POSA would have regarded it as obvious based on either of the Saari References in combination with Schleinitz or Streber to express RdpA in transgenic plant cells and plants. In light of the above, even as of April 2004, the POSA would have regarded the challenged claims of the '283 patent to have been obvious based on the prior art. For example, as I explain below in further detail, challenged claims 1-6, 9-12, and 29 would have been obvious

based on the disclosures in either of the Saari References, Schleinitz, and Streber regarding RdpA's (*R*)-stereoselectivity and amino acid sequence and the transformation of genes encoding α KG enzymes into maize.

a. Claim 1

413. Claim 1 of the '283 patent is similar to claim 1 of the '555 patent, but (1) requires the transgenic plant cell or plant to be a maize plant cell or maize plant, (2) parenthetically assigns a sequence identity number to the claimed AAD-1 motif, (3) specifies that the phenoxy auxin herbicide and the (*R*)-aryloxyphenoxypropionate herbicide are "aryloxyalkanoate herbicides," and (4) requires that the "AAD-1 protein when expressed in a maize plant cell renders said maize plant cell tolerant to a phenoxy auxin herbicide and an (*R*)-aryloxyphenoxypropionate herbicide, as compared to an untransformed maize plant cell."

<u>'555 Patent, Claim 1</u>	<u>'283 Patent, Claim 1</u>
1. A transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (<i>R</i>)-aryloxyphenoxypropionate	1. A transgenic <u>maize</u> plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (<i>R</i>)-aryloxyphenoxypropionate herbicide

herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R,$ wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(X)_{114-137}$ represents a sequence of 24 amino acids; $(X)_{139-269}$ represents a sequence of 131 amino acids; and $(X)_{271-280}$ represents a sequence of 10 amino acids.	<u><i>which are aryloxyalkanoate herbicides</i></u>, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$ <u><i>(SEQ ID NO: 34)</i></u>, wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(X)_{114-137}$ represents a sequence of 24 amino acids; $(X)_{139-269}$ represents a sequence of 131 amino acids; and $(X)_{271-280}$ represents a sequence of 10 amino acids, <u><i>wherein said AAD-1 protein when expressed in a maize plant cell renders said maize plant cell tolerant to a phenoxy auxin herbicide and an</i></u>
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	<u><i>(R)-aryloxyphenoxypropionate</i></u> <u><i>herbicide, as compared to an</i></u> <u><i>untransformed maize plant cell.</i></u>
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414. The POSA would have regarded this claim to have been obvious based on either of the Saari References in combination with Schleinitz and Streber.

415. The POSA would have understood maize was commonly grown as an agricultural crop. The POSA would have also understood that although researchers had developed maize that was resistant to glyphosate, overuse of glyphosate had led to the development of glyphosate-resistant weeds. *See, e.g.*, EX1002 ('283 Pat.), 1:36-41, 2:8-31. As a result, the POSA would have desired to use alternative herbicides, including phenoxy herbicides, in combination with maize and would have been motivated to transform maize plant cells to express RdpA, which each of the Saari References disclosed to degrade those herbicides.

416. As I explain above in Sections VII.B.1-VII.B.2, VIII.A.2.a, which are incorporated here by reference, the POSA would have reasonably expected that maize plants transformed to express RdpA would be tolerant to phenoxy herbicides, and Corteva '437 (whose disclosures the '283 patent repeats) states that RdpA, when expressed in a maize plant cell, renders the maize plant tolerant to phenoxy auxin and (R)-aryloxyphenoxypropionate herbicides, as compared to an untransformed maize plant cell.

417. Additionally, as I explain above in Section VIII.A.2.a, which is incorporated here by reference, the parenthetical assignment of a sequence identity number to the claimed motif and the statement that the phenoxy auxin herbicide and the (R)-aryloxyphenoxypropionate herbicide are “aryloxyalkanoate herbicides” do not affect the scope of this claim.

418. I address the remaining limitations of this claim in connection with claim 1 of the '555 patent (the discussions of which are incorporated here by reference). *See supra* Section VII.B.3.a.

b. Claim 2

419. Claim 2 refers back to claim 1 and recites: “The plant cell of claim 1 wherein said AAD-1 motif has the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R(X)_{282-284}R$ (SEQ ID NO: 35), wherein $(X)_{282-284}$ represents a sequence of 3 amino acids.”

420. Claim 2 of the '283 patent and claim 2 of the '555 patent recite similar additional limitations. Claim 2 of the '283 patent parenthetically assigns a sequence identity number to the AAD-1 motif (which does not affect whether Corteva '437 disclosure of AAD-1 proteins, such as AAD-1 v1 and v2, satisfies this limitation), and the claims have slightly different formatting.

<u>'555 Patent, Claim 2</u>	<u>'283 Patent, Claim 2</u>
2. The plant cell of claim 1 wherein said AAD-1 motif has the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R(X)_{282-284}R$, wherein $(X)_{282-284}$ represents a sequence of 3 amino acids.	2. The plant cell of claim 1 wherein said AAD-1 motif has the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R(X)_{282-284}R$ <u>(SEQ ID NO: 35)</u>, wherein $(X)_{282-284}$ represents a sequence of 3 amino acids.

421. The POSA would have regarded this claim to have been obvious based on either of the Saari References in combination with Schleinitz and Streber for the reasons discussed in connection with claim 1 of the '283 patent and claim 2 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.3.b, VIII.B.1.a.

c. Claim 3

422. Claim 3 refers back to claim 1 and recites: “A transgenic maize plant comprising a plurality of the maize plant cell of claim 1, wherein expression of said polynucleotide renders said plant tolerant to said aryloxyalkanoate herbicide.”

423. Claim 3 of the '283 patent and claim 6 of the '555 patent recite similar additional limitations. Claim 3 of the '283 patent requires the plant cell to be a maize plant cell, a limitation that is required by claim 1 of the '283 patent. Claim 3 of the '283 patent also uses the term “said,” rather than the term “an,” to refer to the term “aryloxyalkanoate herbicide,” a term that is used in claim 1 of the '283 patent.

<u>'555 Patent, Claim 6</u>	<u>'283 Patent, Claim 3</u>
6. A transgenic plant comprising a plurality of the plant cells of claim 1, wherein expression of said polynucleotide renders said plant tolerant to <i>an</i> aryloxyalkanoate herbicide.	3. A transgenic <u>maize</u> plant comprising a plurality of the <u>maize</u> plant cell of claim 1, wherein expression of said polynucleotide renders said plant tolerant to <i>said</i> aryloxyalkanoate herbicide.

424. The POSA would have regarded this claim to have been obvious based on either of the Saari References in combination with Schleinitz and Streber for the reasons discussed in connection with claim 1 of the '283 patent and claim 6 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.3.e, VIII.B.1.a.

d. Claims 4-6

425. Claims 4-6 refer back to claim 3.

426. Claim 4 recites: “The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop.”

427. Claim 5 recites: “The plant of claim 3 wherein said aryloxyalkanoate herbicide is an (R)-aryloxyphenoxypropionate.”

428. Claim 6 recites: “The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-

diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofof.”

429. Claims 4-6 of the '283 patent and claims 8-10 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 8-10</u>	<u>'283 Patent, Claims 4-6</u>
8. The plant of claim 6 wherein said aryloxyalkanoate herbicide is selected from the group consisting of 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop.	4. The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop.
9. The plant of claim 6 wherein said aryloxyalkanoate herbicide is an (R)-aryloxyphenoxypropionate.	5. The plant of claim 3 wherein said aryloxyalkanoate herbicide is an (R)-aryloxyphenoxypropionate.
10. The plant of claim 6 wherein said aryloxyalkanoate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofof.	6. The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofof.

430. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz and Streber for the reasons discussed in connection with claim 3 of the '283 patent and claims

7-10 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.3.e, VIII.B.1.c.

e. Claim 9

431. Claim 9 refers back to claim 3 and recites: “A method of controlling at least one weed in a field, wherein said field contains at least one plant of claim 3, wherein said method comprises applying to at least a portion of said field a first herbicide selected from the group consisting of a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide.”

432. Claim 9 of the '283 patent and claim 13 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claim 13</u>	<u>'283 Patent, Claim 9</u>
13. A method of controlling at least one weed in a field, wherein said field contains at least one plant of claim 6, wherein said method comprises applying to at least a portion of said field a first herbicide selected from the group consisting of a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide.	9. A method of controlling at least one weed in a field, wherein said field contains at least one plant of claim 3, wherein said method comprises applying to at least a portion of said field a first herbicide selected from the group consisting of a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide.

433. The POSA would have regarded this claim to have been obvious based on either of the Saari References in combination with Schleinitz and Streber for the

reasons discussed in connection with claim 3 of the '283 patent and claim 13 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.3.f, VIII.B.1.c.

f. Claims 10-12

434. Claims 10-12 refer back to claim 9.

435. Claim 10 recites: “The method of claim 9 wherein said phenoxy auxin herbicide is an R-enantiomer of a chiral phenoxy auxin.”

436. Claim 11 recites: “The method of claim 9 wherein said phenoxy auxin herbicide is an achiral phenoxy auxin selected from the group consisting of 2,4-D and MCPA.”

437. Claim 12 recites: “The method of claim 9 wherein said (R)-aryloxyphenoxypropionate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofof.”

438. Claims 10-12 of the '283 patent and claims 14-16 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 14-16</u>	<u>'283 Patent, Claims 10-12</u>
14. The method of claim 13 wherein said phenoxy auxin herbicide is an R-enantiomer of a chiral phenoxy auxin.	10. The method of claim 9 wherein said phenoxy auxin herbicide is an R-enantiomer of a chiral phenoxy auxin.

15. The method of claim 13 wherein said phenoxy auxin herbicide is an achiral phenoxy auxin selected from the group consisting of 2,4-D and MCPA.	11. The method of claim 9 wherein said phenoxy auxin herbicide is an achiral phenoxy auxin selected from the group consisting of 2,4-D and MCPA.
16. The method of claim 13 wherein said (R)-aryloxyphenoxypropionate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofop.	12. The method of claim 9 wherein said (R)-aryloxyphenoxypropionate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofop.

439. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz and Streber for the reasons discussed in connection with claim 9 of the '283 patent and claims 14-16 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.3.f, VIII.B.1.e.

g. Claim 29

440. Claim 29 is similar to claim 1, but requires (1) the transgenic maize plant cell to be an “(R)-aryloxyphenoxypropionate herbicide tolerant maize transgenic plant cell” and (2) the “AAD-1 motif” to have “90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9.”

<u>'555 Patent, Claim 34</u>	<u>'283 Patent, Claim 29</u>
34. An (R)-aryloxyphenoxypropionate herbicide tolerant transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$, wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(X)_{114-137}$ represents a sequence of 24 amino acids;	29. An (R)-aryloxyphenoxypropionate herbicide tolerant transgenic <u>maize</u> plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$ <u>(SEQ ID NO: 34)</u>, wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(X)_{114-137}$ represents a sequence of 24 amino acids;

(X)₁₃₉₋₂₆₉ represents a sequence of 131 amino acids; and (X)₂₇₁₋₂₈₀ represents a sequence of 10 amino acids, wherein said motif has 90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9.	(X)₁₃₉₋₂₆₉ represents a sequence of 131 amino acids; and (X)₂₇₁₋₂₈₀ represents a sequence of 10 amino acids, wherein said motif has 90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9, and <u>wherein said AAD-1 protein when expressed in a maize plant cell renders said maize plant cell tolerant to a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, as compared to an untransformed maize plant cell.</u>
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441. The POSA would have regarded this claim to have been obvious based on either of the Saari References in combination with Schleinitz and Streber for the reasons discussed in connection with claim 1 of the '283 patent and claim 34 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.3.g, VIII.B.1.a.

2. Saari 1999 or Saari 1998 in Combination with Schleinitz, Streber, and Jepson Renders Obvious Claims 7-8 and 13-28.

442. The POSA would have regarded the remaining challenged claims of the '283 patent to have been obvious based on the references discussed in the prior section and Jepson.

b. Claims 7-8

443. Claims 7 and 8 refer, directly or indirectly, back to claim 3.

444. Claim 7 recites: “The plant of claim 3 wherein said plant further comprises a second herbicide resistance gene.”

445. Claim 8 recites: “The plant of claim 7 wherein said second herbicide resistance gene renders said plant resistant to an herbicide selected from the group consisting of glyphosate, glufosinate, acetolactate synthase (ALS) inhibitors, inhibitors of 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD), dicamba, and inhibitors of protoporphyrinogen oxidase (PPO).”

446. Claims 7-8 of the '283 patent and claims 11-12 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 11-12</u>	<u>'283 Patent, Claims 7-8</u>
11. The plant of claim 6 wherein said plant further comprises a second herbicide resistance gene.	7. The plant of claim 3 wherein said plant further comprises a second herbicide resistance gene.
12. The plant of claim 11 wherein said second herbicide resistance gene	8. The plant of claim 7 wherein said second herbicide resistance gene

renders said plant resistant to an herbicide selected from the group consisting of glyphosate, glufosinate, acetolactate synthase (ALS) inhibitors, inhibitors of 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD), dicamba, and inhibitors of protoporphyrinogen oxidase (PPO).	renders said plant resistant to an herbicide selected from the group consisting of glyphosate, glufosinate, acetolactate synthase (ALS) inhibitors, inhibitors of 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD), dicamba, and inhibitors of protoporphyrinogen oxidase (PPO).
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447. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson for the reasons discussed in connection with claim 3 of the '283 patent and claims 11-12 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.a, VIII.B.1.c.

c. Claims 13-16

448. Claims 13-16 refer, directly or indirectly, back to claim 9.

449. Claim 13 recites: “The method of claim 9 wherein said method comprises applying a second herbicide.”

450. Claim 14 recites: “The method of claim 13 wherein said first herbicide and said second herbicide are applied sequentially.”

451. Claim 15 recites: “The method of claim 13 wherein said first herbicide and said second herbicide are applied concurrently.”

452. Claim 16 recites: “The method of claim 13 wherein said first herbicide is a phenoxy auxin and said second herbicide is an (R)-aryloxyphenoxypropionate.”

453. Claims 13-16 of the '283 patent and claims 17-20 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 17-20</u>	<u>'283 Patent, Claims 13-16</u>
17. The method of claim 13 wherein said method comprises applying a second herbicide.	13. The method of claim 9 wherein said method comprises applying a second herbicide.
18. The method of claim 17 wherein said first herbicide and said second herbicide are applied sequentially.	14. The method of claim 13 wherein said first herbicide and said second herbicide are applied sequentially.
19. The method of claim 17 wherein said first herbicide and said second herbicide are applied concurrently.	15. The method of claim 13 wherein said first herbicide and said second herbicide are applied concurrently.
20. The method of claim 17 wherein said first herbicide is a phenoxy auxin and said second herbicide is an (R)-aryloxyphenoxypropionate.	16. The method of claim 13 wherein said first herbicide is a phenoxy auxin and said second herbicide is an (R)-aryloxyphenoxypropionate.

454. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson for the reasons discussed in connection with claim 9 of the '283 patent and claims 17-20 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.b-VII.B.4.c, VIII.B.1.e.

d. Claims 17-19

455. Claims 17-19 refer back to claim 13.

456. Claim 17 recites: “The method of claim 13 wherein said second herbicide is selected from the group consisting of glyphosate, glufosinate, dicamba, acetolactate synthase (ALS) inhibitors, protoporphyrinogen oxidase (PPO) inhibitors, and 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD) inhibitors.”

457. Claim 18 recites: “The method of claim 13, wherein said first herbicide is 2,4-D and said second herbicide is glyphosate or glufosinate.”

458. Claim 19 recites: “The method of claim 13, wherein said first herbicide is an (R)-aryloxyphenoxypropionate and said second herbicide is glyphosate or glufosinate.”

459. Claims 17-19 of the '283 patent and claims 21-23 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 21-23</u>	<u>'283 Patent, Claims 17-19</u>
21. The method of claim 17 wherein said second herbicide is selected from the group consisting of glyphosate, glufosinate, dicamba, acetolactate synthase (ALS) inhibitors, protoporphyrinogen oxidase (PPO) inhibitors, and 4-hydroxyphenyl-	17. The method of claim 13 wherein said second herbicide is selected from the group consisting of glyphosate, glufosinate, dicamba, acetolactate synthase (ALS) inhibitors, protoporphyrinogen oxidase (PPO) inhibitors, and 4-hydroxyphenyl-

pyruvate-dioxygenase (HPPD) inhibitors.	pyruvate-dioxygenase (HPPD) inhibitors.
22. The method of claim 17, wherein said first herbicide is 2,4-D and said second herbicide is glyphosate or glufosinate.	18. The method of claim 13, wherein said first herbicide is 2,4-D and said second herbicide is glyphosate or glufosinate.
23. The method of claim 17, wherein said first herbicide is an (R)-aryloxyphenoxypropionate and said second herbicide is glyphosate or glufosinate.	19. The method of claim 13, wherein said first herbicide is an (R)-aryloxyphenoxypropionate and said second herbicide is glyphosate or glufosinate.

460. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson for the reasons discussed in connection with claim 13 of the '283 patent and claims 21-23 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.d, VIII.B.2.c.

e. Claims 20-21

461. Claims 20-21 refer, directly or indirectly, back to claim 13.

462. Claim 20 recites: “The method of claim 13 wherein said plant further comprises a second herbicide resistance gene that renders said plant resistant to said second herbicide.”

463. Claim 21 recites: “The method of claim 20 wherein said second gene is selected from the group consisting of a modified acetolactate synthase (ALS) gene, a glyphosate resistance gene, a glufosinate resistance gene, and a dicamba-degrading enzyme gene.

464. Claims 20-21 of the '283 patent and claims 24-25 of the '555 patent recite similar additional limitations. Claim 25 of the '555 patent states that the second gene is a “second herbicide resistance gene,” a limitation that is required by claim 20 of the '283 patent and claim 24 of the '555 patent.

<u>'555 Patent, Claims 24-25</u>	<u>'283 Patent, Claims 20-21</u>
24. The method of claim 17 wherein said plant further comprises a second herbicide resistance gene that renders said plant resistant to said second herbicide.	20. The method of claim 13 wherein said plant further comprises a second herbicide resistance gene that renders said plant resistant to said second herbicide.
25. The method of claim 24 wherein said second <i><u>herbicide resistance</u></i> gene is selected from the group consisting of a modified acetolactate synthase (ALS) gene, a glyphosate resistance gene, a glufosinate resistance gene, and a dicamba-degrading enzyme gene.	21. The method of claim 20 wherein said second gene is selected from the group consisting of a modified acetolactate synthase (ALS) gene, a glyphosate resistance gene, a glufosinate resistance gene, and a dicamba-degrading enzyme gene.

465. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and

Jepson for the reasons discussed in connection with claim 13 of the '283 patent and claims 24-25 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.e-VII.B.4.f, VIII.B.2.c.

f. Claims 22-24

466. Claims 22-24 refer, directly or indirectly, back to claim 13.

467. Claim 22 recites: “The method of claim 13 wherein said method further comprises applying a third herbicide.”

468. Claim 23 recites: “The method of claim 22, wherein said third herbicide is selected from the group consisting of glyphosate, glufosinate, HPPD-inhibitors, PPO-inhibitors, ALS inhibitors, and dicamba.”

469. Claim 24 recites: “The method of claim 23 wherein said first, second and third herbicides are 2,4-D, quizalofop, and glyphosate.”

470. Claims 22-24 of the '283 patent and claims 27-29 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 27-29</u>	<u>'283 Patent, Claims 22-24</u>
27. The method of claim 17 wherein said method further comprises applying a third herbicide.	22. The method of claim 13 wherein said method further comprises applying a third herbicide.
28. The method of claim 27, wherein said third herbicide is selected from the group consisting of glyphosate, glufosinate, HPPD-inhibitors, PPO-	23. The method of claim 22, wherein said third herbicide is selected from the group consisting of glyphosate, glufosinate, HPPD-inhibitors, PPO-

inhibitors, ALS inhibitors, and dicamba.	inhibitors, ALS inhibitors, and dicamba.
29. The method of claim 28 wherein said first, second and third herbicides are 2,4-D, quizalofop, and glyphosate.	24. The method of claim 23 wherein said first, second and third herbicides are 2,4-D, quizalofop, and glyphosate.

471. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson for the reasons discussed in connection with claim 13 of the '283 patent and claims 27-29 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.g, VIII.B.2.c.

g. Claim 25

472. Claim 25 refers back to claim 1 and recites: “A seed comprising the plant cell of claim 1.”

473. Claim 25 of the '283 patent and claim 30 of the '555 patent recite similar additional limitations. Claim 25 of the '283 patent requires a plant cell; claim 30 of the '555 patent requires a plurality of plant cells.

<u>'555 Patent, Claim 30</u>	<u>'283 Patent, Claim 25</u>
30. A seed comprising a plurality of the plant cells of claim 1.	25. A seed comprising the plant cell of claim 1.

474. Claim 25 is obvious, irrespective of this difference in language. If a seed contains a “plurality of the plant cells” (*i.e.*, multiple plant cells) it also includes at least a “plant cell.”

475. Thus, the POSA would regard this claim to have been obvious based on Schleinitz, Streber, and Jepson for the reasons discussed in connection with claim 1 of the '283 patent and claim 30 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.h, VIII.B.1.a.

476. Additionally, Jepson discloses seeds containing a transgenic plant cell comprising a resistance gene. EX1030 (Jepson), [00122]-[00123], [00131]-[00132], [00144], [00168]-[00169], [00180]-[00183], [00187]-[00188], claims 13, 15 (Jepson).

h. Claim 26

477. Claim 26 refers back to claim 25 and recites: “A method of controlling weeds in a field, wherein said method comprises applying an aryloxyalkanoate herbicide to said field and planting a seed of claim 25 in said field within 14 days of applying said aryloxyalkanoate herbicide.”

478. Claim 26 of the '283 patent and claim 31 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claim 31</u>	<u>'283 Patent, Claim 26</u>
31. A method of controlling weeds in a field, wherein said method comprises applying an aryloxyalkanoate herbicide to said field and planting a seed of claim 30 in said field within 14 days of applying said aryloxyalkanoate herbicide.	26. A method of controlling weeds in a field, wherein said method comprises applying an aryloxyalkanoate herbicide to said field and planting a seed of claim 25 in said field within 14 days of applying said aryloxyalkanoate herbicide.

479. The POSA would have regarded this claim to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson for the reasons discussed in connection with claim 25 of the '283 patent and claim 31 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.i, VIII.B.2.g.

i. Claims 27-28

480. Claims 27-28 refer, directly or indirectly, back to claim 25.

481. Claim 27 recites: “A plant grown from the seed of claim 25 comprising said polynucleotide.”

482. Claim 28 recites: “A part, progeny, or asexual propagate of the plant of claim 27, wherein said part, progeny, or sexual propagate comprises said polynucleotide.”

483. Claims 27-28 of the '283 patent and claims 32-33 of the '555 patent recite similar additional limitations. Claim 27 of the '283 patent states that the seed

comprises “said polynucleotide,” a limitation that is required by claim 1 of the ’283 patent, from which claim 25 depends.

<u>’555 Patent, Claim 32-33</u>	<u>’283 Patent, Claims 27-28</u>
32. A plant grown from the seed of claim 30 .	27. A plant grown from the seed of claim 25 <u><i>comprising said polynucleotide</i></u> .
33. A part, progeny, or asexual propagate of the plant of claim 32 , wherein said part, progeny, or sexual propagate comprises said polynucleotide.	28. A part, progeny, or asexual propagate of the plant of claim 27 , wherein said part, progeny, or sexual propagate comprises said polynucleotide.

484. The POSA would have regarded these claims to have been obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson for the reasons discussed in connection with claim 25 of the ’283 patent and claims 32-33 of the ’555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.j, VIII.B.2.g.

IX. INVALIDITY ANALYSIS FOR THE ’745 PATENT

A. Invalidity Analysis as of October 7, 2016

485. The challenged claims of the ’555 and ’745 patents are similar, except that the challenged claims of the ’745 patent (1) require the transgenic plant cell or plant to be a soybean plant cell or soybean plant, (2) parenthetically assign sequence identity numbers to the claimed AAD-1 motifs, (3) specify that the phenoxy auxin

herbicide and the (R)-aryloxyphenoxypropionate herbicide are “aryloxyalkanoate herbicides,” and (4) require that the “AAD-1 protein when expressed in a soybean plant cell renders said soybean plant cell tolerant to a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, as compared to an untransformed soybean plant cell.” The challenged claims of the ’745 and ’283 patents are likewise similar, except that that the ’745 patent claims are directed to soybeans, whereas the ’283 patent claims are directed to maize.

486. The following comparison between claim 1 of the ’745 patent and claim 1 of the ’555 patent illustrates these differences, ***emphasized*** below:

<u>’745 Patent, Claim 1</u>	<u>’555 Patent, Claim 1</u>
1. A transgenic <u>soybean</u> plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, <u>which are aryloxyalkanoate herbicides</u> , further wherein said AAD-1 protein comprises:	1. A transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and

i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$ <u>(SEQ ID NO: 34)</u>, wherein X₁₁₂ represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; (X)₁₁₄₋₁₃₇ represents a sequence of 24 amino acids; (X)₁₃₉₋₂₆₉ represents a sequence of 131 amino acids; and (X)₂₇₁₋₂₈₀ represents a sequence of 10 amino acids, <u>wherein said AAD-1 protein when expressed in a soybean plant cell renders said soybean plant cell tolerant to a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, as compared to an</u>	ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$ wherein X₁₁₂ represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; (X)₁₁₄₋₁₃₇ represents a sequence of 24 amino acids; (X)₁₃₉₋₂₆₉ represents a sequence of 131 amino acids; and (X)₂₇₁₋₂₈₀ represents a sequence of 10 amino acids.
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<u><i>untransformed soybean plant</i></u> <u><i>cell.</i></u>	
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487. The limitations recited in the dependent claims of the '745 patent overlap with the limitations recited in the dependent claims of the '555 patent.

1. The Challenged Claims Are Not Entitled to a Priority Date Earlier Than October 7, 2016.

488. I understand that in order for a patent to be entitled to priority based on an earlier application or chain of applications, each previous application in the chain must be entitled to a priority to an earlier application, each application in the priority chain must adequately describe the subject matter such that a POSA would understand that the inventor was in possession of the claimed invention as of the priority date.

489. As I explain in Section VII.A.1, which is incorporated here by reference, the '555 patent is not entitled to a priority date earlier than October 7, 2016, because the original specification of the '406 application did not adequately describe a genus of AAD-1 proteins having an AAD-1 motif, with at least 85% or 90% sequence identity to SEQ ID NO: 9, and conferring the required herbicide degrading activity. The '745 patent likewise is not entitled to a priority date earlier than October 7, 2016, because the claims of the '745 patent recite the same limitations, which the original application does not support.

490. The prosecution history of the '745 patent provides additional confirmation that the inventors did not have possession of the invention on an earlier date. During prosecution of the application that led to the '745 patent, the applicant amended the specification to add the AAD-1 motif as it appears in claim 1 of the '555 patent. EX1030 ('745 Pat.), 18:62-19:5, claim 1. (The applicant also parenthetically assigned sequence identity numbers to the prior-art α KG motif and the claim 1 AAD-1 motif.) As before, the amendment stated: "Mapping the α -ketoglutarate-dependent dioxygenase motif disclosed in the previous paragraph to the sequence of SEQ ID NO: 9 reveals the AAD-1 motif of HX₁₁₂D(X)₁₁₄₋₁₃₇T(X)₁₃₉₋₂₆₉H(X)₂₇₁₋₂₈₀R." *Id.*; EX1011 ('476 Appl. & File History) COR-AAD1-00005423, COR-AAD1-00005432 (Response (Jan. 14, 2022) pp. 2, 11). The applicant also amended the paragraph discussing amino acid identity/similarity to add the claim 1 motif. EX1003 ('745 Pat.), 37:43-52, claim 1.

491. As I explain in Section VII.A.1.e, which is incorporated here by reference, the applicant's "mapping" argument is flawed because the specification did not support the applicant's rationales for selecting that motif, as demonstrated, for example, by the applicant's reliance on information outside of the prior art and the original application. For example, the original specification demonstrates that proteins satisfying the prior-art α KG motif do not necessarily have the claimed activity, as evidenced by AAD-2, which satisfies the prior-art α KG motif but is not

(*R*)-enantioselective. The applicant's assertion that the POSA could ascertain which proteins have the claimed activity by "mapping" the prior-art α KG motif onto RdpA is therefore incorrect.

492. With respect to the 85% sequence identity limitation, the applicant emphasized that the original specification states: "Any number listed above can be used to define the upper and lower limits." EX1011 ('476 Appl. & File History), COR-AAD1-00005430 (Response (Jan. 14, 2022) (p. 9)). However, as I explain in Section VII.A.1.b, which is incorporated here by reference, the POSA would not have understood the inventors to have had possession of the claimed genera of proteins just because the original specification contains a laundry list of percentages, ranging from 49% to 99%. Rather, as I explain, nothing in the original specification suggests that the inventors contemplated a genus of proteins with as little as 85% amino acid sequence to SEQ ID NO. 9, and indeed, the original specification does not identify 85% as a preferred value.

2. The Challenged Claims Should be Deemed Anticipated Based on Corteva '437.

493. As I explain in Section VII.A.2, which is incorporated here by reference, Corteva '437 is the publication of the international patent application to which the '283 patent claims priority. Corteva '437 discloses transgenic soybean plant cells and plants expressing proteins that the '745 patent identifies as AAD-1

proteins (e.g., AAD-1 v1 and v2). As discussed below, the Challenged Claims should be deemed anticipated by Corteva '437.

b. Claim 1

494. Claim 1 of the '745 patent is similar to claim 1 of the '283 patent, but requires (1) the transgenic plant cell to be a transgenic soybean plant cell and (2) the transgenic plant cell to be compared to an untransformed soybean plant cell.

<u>'283 Patent, Claim 1</u>	<u>'745 Patent, Claim 1</u>
1. A transgenic <u>maize</u> plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide which are aryloxyalkanoate herbicides, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of:	1. A transgenic <u>soybean</u> plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, which are aryloxyalkanoate herbicides, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of:

HX₁₁₂D(X)₁₁₄₋₁₃₇T(X)₁₃₉₋₂₆₉H(X)₂₇₁₋₂₈₀R (SEQ ID NO: 34), wherein X₁₁₂ represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; (X)₁₁₄₋₁₃₇ represents a sequence of 24 amino acids; (X)₁₃₉₋₂₆₉ represents a sequence of 131 amino acids; and (X)₂₇₁₋₂₈₀ represents a sequence of 10 amino acids, wherein said AAD-1 protein when expressed in a <u>maize</u> plant cell renders said <u>maize</u> plant cell tolerant to a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, as compared to an untransformed <u>maize</u> plant cell.	HX₁₁₂D(X)₁₁₄₋₁₃₇T(X)₁₃₉₋₂₆₉H(X)₂₇₁₋₂₈₀R (SEQ ID NO: 34), wherein X₁₁₂ represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; (X)₁₁₄₋₁₃₇ represents a sequence of 24 amino acids; (X)₁₃₉₋₂₆₉ represents a sequence of 131 amino acids; and (X)₂₇₁₋₂₈₀ represents a sequence of 10 amino acids, wherein said AAD-1 protein when expressed in a <u>soybean</u> plant cell renders said <u>soybean</u> plant cell tolerant to a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, as compared to an untransformed <u>soybean</u> plant cell.
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495. The claim should be deemed anticipated based on Corteva '437.

496. Corteva '437 and the '745 patent both state that soybeans are a “preferred crop for transformation” and that “soybeans transformed with AAD-1

containing constructs had demonstrated high levels of resistance” to “AOPP herbicides” (*i.e.*, (R)-aryloxyphenoxypropionate herbicides). Compare, *e.g.*, EX1021 (Corteva ’437) [0099] (“*Arabidopsis*, corn, tobacco, cotton, soybean, canola, and rice have been transformed with AAD-1-containing constructs and have demonstrated high levels of resistance to both the phenoxy auxin and AOPP herbicides.”), [00104] (“The transgenic expression of the subject AAD-1 genes is exemplified in, for example, *Arabidopsis*, corn (maize), tobacco, cotton, rice, soybean, and canola. However, the subject invention can be applied to any other desired types of plants. Soybeans are a preferred crop for transformation according to the subject invention.”), [00149] (“Preferred plants (and plant cells) are corn, *Arabidopsis*, tobacco, soybeans, cotton, canola, rice, wheat, turf and pasture grasses, and the like.”), with EX1003 (’745 Pat.), 21:4-7, 21:47-22:1, 38:64-67 (all same).

497. Corteva ’437 and ’745 state that dicots, which include soybeans, “are generally considered naturally tolerant to AOPP herbicides.” EX1021 (Corteva ’437), [00264], EX1003 (’745 Pat.), 69:21-22. Nevertheless, the ’745 patent claims recite an “AAD-1 protein when expressed in a soybean plant cell renders said soybean plant cell tolerant to . . . an (R)-aryloxyphenoxypropionate herbicide, as compared to an untransformed soybean plant cell.” I have been informed that given that the ’745 patent only discloses AAD-1 and two variants, the fact that Corteva sought and obtained such claims constitutes an admission by Corteva that, from

Corteva's perspective, AAD-1 v1 and v2 when expressed in a soybean cell must satisfy that limitation. I have also been informed that given the overlapping disclosures of the '745 patent and Corteva '437, it further constitutes an admission by Corteva that, from Corteva's perspective, Corteva '437 discloses that AAD-1 v1 and v2 must satisfy this limitation. Therefore, and given that Corteva '437 discloses the other limitations of '745 patent claim 1, the claim should be deemed anticipated by Corteva '437.

498. I address the remaining limitations of this claim in connection with claim 1 of the '555 patent and claim 1 of the '283 patent (the discussions of which are incorporated here by reference). *See supra* Sections VII.A.2.a, VIII.A.2.a. Relatedly, claims 2-43 and 57-60 of Corteva '437 refer, directly or indirectly, back to claim 1. As I explain in the sections below in further detail, Corteva '437's dependent claims disclose elements that overlap with the challenged claims 3-28 (*i.e.*, various dependent claims of the '745 patent). The POSA would understand that because claim 1 of Corteva '437 encompasses at least AAD-1 v1, Corteva '437's dependent claims would apply to that protein. Moreover, the POSA would understand that because AAD-1 v1 (SEQ ID NO: 9) and v2 (SEQ ID NO: 10) were exemplary AAD-1 proteins described in the examples, *e.g.*, EX1021 (Corteva '437), [00230]-[0264] & Tbls. 15-16, Corteva '437's dependent claims would also be applicable to those proteins for purposes of what Corteva '437 teaches. As a result,

Corteva '437 should be deemed to anticipate the dependent claims of the '745 patent as well.

c. Claim 2

499. Claim 2 refers back to claim 1 and recites: “The plant cell of claim 1 wherein said AAD-1 motif has the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R(X)_{282-284}R$ (SEQ ID NO: 35), wherein $(X)_{282-284}$ represents a sequence of 3 amino acids.”

500. Claim 2 of the '745 patent and claim 2 of the '555 patent recite similar additional limitations. Claim 2 of the '745 patent parenthetically assigns a sequence identity number to the AAD-1 motif (which does not affect whether Corteva '437 disclosure of AAD-1 proteins, such as AAD-1 v1 and v2, satisfies this limitation), and the claims have slightly different formatting.

<u>'555 Patent, Claim 2</u>	<u>'745 Patent, Claim 2</u>
2. The plant cell of claim 1 wherein said AAD-1 motif has the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R(X)_{282-284}R$, wherein $(X)_{282-284}$ represents a sequence of 3 amino acids.	2. The plant cell of claim 1 wherein said AAD-1 motif has the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R(X)_{282-284}R$ <u>(SEQ ID NO: 35)</u>, wherein $(X)_{282-284}$ represents a sequence of 3 amino acids.

501. The claim should be deemed anticipated based on Corteva '437 for the reasons discussed in connection with claim 1 of the '745 patent and claim 2 of the

'555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.b, IX.A.2.b.

d. Claim 3

502. Claim 3 refers back to claim 1 and recites: “A transgenic soybean plant comprising a plurality of the soybean plant cell of claim 1, wherein expression of said polynucleotide renders said plant tolerant to said aryloxyalkanoate herbicide.”

503. Claim 3 of the '745 patent and claim 6 of the '555 patent recite similar additional limitations. Claim 3 of the '745 patent requires the plant cell to be a soybean plant cell, a limitation that is required by claim 1 of the '745 patent. Claim 3 of the '745 patent also uses the term “said,” rather than the term “an,” to refer to the term “aryloxyalkanoate herbicide,” a term that is used in claim 1 of the '745 patent.

<u>'555 Patent, Claim 6</u>	<u>'745 Patent, Claim 3</u>
6. A transgenic plant comprising a plurality of the plant cells of claim 1, wherein expression of said polynucleotide renders said plant tolerant to <i>an</i> aryloxyalkanoate herbicide.	3. A transgenic <u>soybean</u> plant comprising a plurality of the <u>soybean</u> plant cell of claim 1, wherein expression of said polynucleotide renders said plant tolerant to <i>said</i> aryloxyalkanoate herbicide.

504. The claim should be deemed anticipated based on Corteva '437 for the reasons discussed in connection with claim 1 of the '745 patent and claim 6 of the

'555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.e, IX.A.2.b.

e. Claims 4-6

505. Claims 4-6 refer back to claim 3.

506. Claim 4 recites: “The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop.”

507. Claim 5 recites: “The plant of claim 3 wherein said aryloxyalkanoate herbicide is an (R)-aryloxyphenoxypionate.”

508. Claim 6 recites: “The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofop.”

509. Claims 4-6 of the '745 patent and claims 8-10 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 8-10</u>	<u>'745 Patent, Claims 4-6</u>
8. The plant of claim 6 wherein said aryloxyalkanoate herbicide is selected from the group consisting of 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop.	4. The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop.

9. The plant of claim 6 wherein said aryloxyalkanoate herbicide is an (R)-aryloxyphenoxypropionate.	5. The plant of claim 3 wherein said aryloxyalkanoate herbicide is an (R)-aryloxyphenoxypropionate.
10. The plant of claim 6 wherein said aryloxyalkanoate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofop.	6. The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofop.

510. The claim should be deemed anticipated based on Corteva '437 for the reasons discussed in connection with claim 3 of the '745 patent and claims 7-10 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.f, IX.A.2.d.

f. Claims 7-8

511. Claims 7 and 8 refer, directly or indirectly, back to claim 3.

512. Claim 7 recites: “The plant of claim 3 wherein said plant further comprises a second herbicide resistance gene.”

513. Claim 8 recites: “The plant of claim 7 wherein said second herbicide resistance gene renders said plant resistant to an herbicide selected from the group consisting of glyphosate, glufosinate, acetolactate synthase (ALS) inhibitors,

inhibitors of 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD), dicamba, and inhibitors of protoporphyrinogen oxidase (PPO).”

514. Claims 7-8 of the ’745 patent and claims 11-12 of the ’555 patent recite the same additional limitations.

<u>’555 Patent, Claims 11-12</u>	<u>’745 Patent, Claims 7-8</u>
11. The plant of claim 6 wherein said plant further comprises a second herbicide resistance gene.	7. The plant of claim 3 wherein said plant further comprises a second herbicide resistance gene.
12. The plant of claim 11 wherein said second herbicide resistance gene renders said plant resistant to an herbicide selected from the group consisting of glyphosate, glufosinate, acetolactate synthase (ALS) inhibitors, inhibitors of 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD), dicamba, and inhibitors of protoporphyrinogen oxidase (PPO).	8. The plant of claim 7 wherein said second herbicide resistance gene renders said plant resistant to an herbicide selected from the group consisting of glyphosate, glufosinate, acetolactate synthase (ALS) inhibitors, inhibitors of 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD), dicamba, and inhibitors of protoporphyrinogen oxidase (PPO).

515. The claim should be deemed anticipated based on Corteva ’437 for the reasons discussed in connection with claim 3 of the ’745 patent and claims 11-12 of the ’555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.g, IX.A.2.d.

g. Claim 9

516. Claim 9 refers back to claim 3 and recites: “A method of controlling at least one weed in a field, wherein said field contains at least one plant of claim 3, wherein said method comprises applying to at least a portion of said field a first herbicide selected from the group consisting of a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide.”

517. Claim 9 of the '745 patent and claim 13 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claim 13</u>	<u>'745 Patent, Claim 9</u>
13. A method of controlling at least one weed in a field, wherein said field contains at least one plant of claim 6, wherein said method comprises applying to at least a portion of said field a first herbicide selected from the group consisting of a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide.	9. A method of controlling at least one weed in a field, wherein said field contains at least one plant of claim 3, wherein said method comprises applying to at least a portion of said field a first herbicide selected from the group consisting of a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide.

518. The claim should be deemed anticipated based on Corteva '437 for the reasons discussed in connection with claim 3 of the '745 patent and claim 13 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.h, IX.A.2.d.

h. Claims 10-12

519. Claims 10-12 refer back to claim 9.

520. Claim 10 recites: “The method of claim 9 wherein said phenoxy auxin herbicide is an R-enantiomer of a chiral phenoxy auxin.”

521. Claim 11 recites: “The method of claim 9 wherein said phenoxy auxin herbicide is an achiral phenoxy auxin selected from the group consisting of 2,4-D and MCPA.”

522. Claim 12 recites: “The method of claim 9 wherein said (R)-aryloxyphenoxypropionate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofop.”

523. Claims 10-12 of the '745 patent and claims 14-16 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 14-16</u>	<u>'745 Patent, Claims 10-12</u>
14. The method of claim 13 wherein said phenoxy auxin herbicide is an R-enantiomer of a chiral phenoxy auxin.	10. The method of claim 9 wherein said phenoxy auxin herbicide is an R-enantiomer of a chiral phenoxy auxin.
15. The method of claim 13 wherein said phenoxy auxin herbicide is an achiral phenoxy auxin selected from the group consisting of 2,4-D and MCPA.	11. The method of claim 9 wherein said phenoxy auxin herbicide is an achiral phenoxy auxin selected from the group consisting of 2,4-D and MCPA.

16. The method of claim 13 wherein said (R)-aryloxyphenoxypropionate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofof.	12. The method of claim 9 wherein said (R)-aryloxyphenoxypropionate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofof.
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524. These claims should be deemed anticipated based on Corteva '437 for the reasons discussed in connection with claim 9 of the '745 patent and claims 14-16 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.i, IX.A.2.g.

i. Claims 13-16

525. Claims 13-16 refer, directly or indirectly, back to claim 9.

526. Claim 13 recites: “The method of claim 9 wherein said method comprises applying a second herbicide.”

527. Claim 14 recites: “The method of claim 13 wherein said first herbicide and said second herbicide are applied sequentially.”

528. Claim 15 recites: “The method of claim 13 wherein said first herbicide and said second herbicide are applied concurrently.”

529. Claim 16 recites: “The method of claim 13 wherein said first herbicide is a phenoxy auxin and said second herbicide is an (R)-aryloxyphenoxypropionate.”

530. Claims 13-16 of the '745 patent and claims 17-20 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 17-20</u>	<u>'745 Patent, Claims 13-16</u>
17. The method of claim 13 wherein said method comprises applying a second herbicide.	13. The method of claim 9 wherein said method comprises applying a second herbicide.
18. The method of claim 17 wherein said first herbicide and said second herbicide are applied sequentially.	14. The method of claim 13 wherein said first herbicide and said second herbicide are applied sequentially.
19. The method of claim 17 wherein said first herbicide and said second herbicide are applied concurrently.	15. The method of claim 13 wherein said first herbicide and said second herbicide are applied concurrently.
20. The method of claim 17 wherein said first herbicide is a phenoxy auxin and said second herbicide is an (R)-aryloxyphenoxypropionate.	16. The method of claim 13 wherein said first herbicide is a phenoxy auxin and said second herbicide is an (R)-aryloxyphenoxypropionate.

531. These claims should be deemed anticipated based on Corteva '437 for the reasons discussed in connection with claim 9 of the '745 patent and claims 17-20 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.j, IX.A.2.g.

j. Claims 17-19

532. Claims 17-19 refer back to claim 13.

533. Claim 17 recites: “The method of claim 13 wherein said second herbicide is selected from the group consisting of glyphosate, glufosinate, dicamba, acetolactate synthase (ALS) inhibitors, protoporphyrinogen oxidase (PPO) inhibitors, and 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD) inhibitors.”

534. Claim 18 recites: “The method of claim 13, wherein said first herbicide is 2,4-D and said second herbicide is glyphosate or glufosinate.”

535. Claim 19 recites: “The method of claim 13, wherein said first herbicide is an (R)-aryloxyphenoxypropionate and said second herbicide is glyphosate or glufosinate.”

536. Claims 17-19 of the '745 patent and claims 21-23 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 21-23</u>	<u>'745 Patent, Claims 17-19</u>
21. The method of claim 17 wherein said second herbicide is selected from the group consisting of glyphosate, glufosinate, dicamba, acetolactate synthase (ALS) inhibitors, protoporphyrinogen oxidase (PPO) inhibitors, and 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD) inhibitors.	17. The method of claim 13 wherein said second herbicide is selected from the group consisting of glyphosate, glufosinate, dicamba, acetolactate synthase (ALS) inhibitors, protoporphyrinogen oxidase (PPO) inhibitors, and 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD) inhibitors.
22. The method of claim 17, wherein said first herbicide is 2,4-D and said	18. The method of claim 13, wherein said first herbicide is 2,4-D and said

second herbicide is glyphosate or glufosinate.	second herbicide is glyphosate or glufosinate.
23. The method of claim 17 , wherein said first herbicide is an (R)-aryloxyphenoxypropionate and said second herbicide is glyphosate or glufosinate.	19. The method of claim 13 , wherein said first herbicide is an (R)-aryloxyphenoxypropionate and said second herbicide is glyphosate or glufosinate.

537. These claims should be deemed anticipated based on Corteva '437 for the reasons discussed in connection with claim 13 of the '745 patent and claims 21-23 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.k, IX.A.2.i.

k. Claims 20-21

538. Claims 20-21 refer, directly or indirectly, back to claim 13.

539. Claim 20 recites: “The method of claim 13 wherein said plant further comprises a second herbicide resistance gene that renders said plant resistant to said second herbicide.”

540. Claim 21 recites: “The method of claim 20 wherein said second gene is selected from the group consisting of a modified acetolactate synthase (ALS) gene, a glyphosate resistance gene, a glufosinate resistance gene, and a dicamba-degrading enzyme gene.

541. Claims 20-21 of the '745 patent and claims 25-24 of the '555 patent recite similar additional limitations. Claim 25 of the '555 patent states that the second gene is a “second herbicide resistance gene,” a limitation that is required by claim 20 of the '745 patent and claim 24 of the '555 patent.

<u>'555 Patent, Claims 24-25</u>	<u>'745 Patent, Claims 20-21</u>
24. The method of claim 17 wherein said plant further comprises a second herbicide resistance gene that renders said plant resistant to said second herbicide.	20. The method of claim 13 wherein said plant further comprises a second herbicide resistance gene that renders said plant resistant to said second herbicide.
25. The method of claim 24 wherein said second <i>herbicide resistance</i> gene is selected from the group consisting of a modified acetolactate synthase (ALS) gene, a glyphosate resistance gene, a glufosinate resistance gene, and a dicamba-degrading enzyme gene.	21. The method of claim 20 wherein said second gene is selected from the group consisting of a modified acetolactate synthase (ALS) gene, a glyphosate resistance gene, a glufosinate resistance gene, and a dicamba-degrading enzyme gene.

542. These claims should be deemed anticipated based on Corteva '437 for the reasons discussed in connection with claim 13 of the '745 patent and claims 24-25 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.1-VII.A.2.m, IX.A.2.i.

I. Claims 22-24

543. Claims 22-24 refer, directly or indirectly, back to claim 13.

544. Claim 22 recites: “The method of claim 13 wherein said method further comprises applying a third herbicide.”

545. Claim 23 recites: “The method of claim 22, wherein said third herbicide is selected from the group consisting of glyphosate, glufosinate, HPPD-inhibitors, PPO-inhibitors, ALS inhibitors, and dicamba.”

546. Claim 24 recites: “The method of claim 23 wherein said first, second and third herbicides are 2,4-D, quizalofop, and glyphosate.”

547. Claims 22-24 of the '745 patent and claims 27-29 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 27-29</u>	<u>'745 Patent, Claims 22-24</u>
27. The method of claim 17 wherein said method further comprises applying a third herbicide.	22. The method of claim 13 wherein said method further comprises applying a third herbicide.
28. The method of claim 27, wherein said third herbicide is selected from the group consisting of glyphosate, glufosinate, HPPD-inhibitors, PPO-inhibitors, ALS inhibitors, and dicamba.	23. The method of claim 22, wherein said third herbicide is selected from the group consisting of glyphosate, glufosinate, HPPD-inhibitors, PPO-inhibitors, ALS inhibitors, and dicamba.
29. The method of claim 28 wherein said first, second and third herbicides are 2,4-D, quizalofop, and glyphosate.	24. The method of claim 23 wherein said first, second and third herbicides are 2,4-D, quizalofop, and glyphosate.

548. These claims should be deemed anticipated based on Corteva '437 for the reasons discussed in connection with claim 13 of the '745 patent and claims 27-29 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.n, IX.A.2.i.

m. Claim 25

549. Claim 25 refers back to claim 1 and recites: “A seed comprising a plurality of the plant cell of claim 1.”

550. Claim 25 of the '745 patent and claim 30 of the '555 patent recite similar additional limitations. Claim 30 of the '555 patent requires a plurality of plant cells. Claim 25 of the '745 patent requires a plurality of “plant cell.”

<u>'555 Patent, Claim 30</u>	<u>'745 Patent, Claim 25</u>
30. A seed comprising a plurality of the plant cells of claim 1.	25. A seed comprising a plurality of the plant cell of claim 1.

551. Claim 25 is anticipated, irrespective of this difference in language. If a seed contains a “plurality of the plant cells” (*i.e.*, multiple plant cells) it also includes at least a “plurality of the plant cell.”

552. Thus, the claim should be deemed anticipated based on Corteva '437 for the reasons discussed in connection with claim 1 of the '745 patent and claim 30 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.o, IX.A.2.b.

n. Claim 26

553. Claim 26 refers back to claim 25 and recites: “A method of controlling weeds in a field, wherein said method comprises applying an aryloxyalkanoate herbicide to said field and planting a seed of claim 25 in said field within 14 days of applying said aryloxyalkanoate herbicide.”

554. Claim 26 of the '745 patent and claim 31 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claim 31</u>	<u>'745 Patent, Claim 26</u>
31. A method of controlling weeds in a field, wherein said method comprises applying an aryloxyalkanoate herbicide to said field and planting a seed of claim 30 in said field within 14 days of applying said aryloxyalkanoate herbicide.	26. A method of controlling weeds in a field, wherein said method comprises applying an aryloxyalkanoate herbicide to said field and planting a seed of claim 25 in said field within 14 days of applying said aryloxyalkanoate herbicide.

555. The claim should be deemed anticipated based on Corteva '437 for the reasons discussed in connection with claim 25 of the '745 patent and claim 31 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.p, IX.A.2.m.

o. Claims 27-28

556. Claims 27-28 refer, directly or indirectly, back to claim 25.

557. Claim 27 recites: “A plant grown from the seed of claim 25 comprising said polynucleotide.”

558. Claim 28 recites: “A part, progeny, or asexual propagate of the plant of claim 27, wherein said part, progeny, or sexual propagate comprises said polynucleotide.”

559. Claims 27-28 of the '745 patent and claims 32-33 of the '555 patent recite similar additional limitations. Claim 27 of the '745 patent states that the seed comprises “said polynucleotide,” a limitation that is required by claim 1 of the '745 patent, from which claim 25 depends.

<u>'555 Patent, Claim 32-33</u>	<u>'745 Patent, Claims 27-28</u>
32. A plant grown from the seed of claim 30 .	27. A plant grown from the seed of claim 25 <u>comprising said polynucleotide.</u>
33. A part, progeny, or asexual propagate of the plant of claim 32 , wherein said part, progeny, or sexual propagate comprises said polynucleotide.	28. A part, progeny, or asexual propagate of the plant of claim 27 , wherein said part, progeny, or sexual propagate comprises said polynucleotide.

560. These claims should be deemed anticipated based on Corteva '437 for the reasons discussed in connection with claim 25 of the '745 patent and claims 32-33 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.A.2.q, IX.A.2.m.

p. Claim 29

561. Claim 29 is similar to claim 1, but requires (1) the transgenic soybean plant cell to be an “(R)-aryloxyphenoxypropionate herbicide tolerant soybean transgenic plant cell” and (2) the “AAD-1 motif” to have “90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9.”

562. Claim 29 of the '745 patent is also similar to claim 34 of the '555 patent. The only differences are also present in claim 1 of the '745 patent.

<u>'555 Patent, Claim 34</u>	<u>'745 Patent, Claim 29</u>
34. An (R)-aryloxyphenoxypropionate herbicide tolerant transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of:	29. An (R)-aryloxyphenoxypropionate herbicide tolerant transgenic <u>soybean</u> plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of:

$HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$, wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(X)_{114-137}$ represents a sequence of 24 amino acids; $(X)_{139-269}$ represents a sequence of 131 amino acids; and $(X)_{271-280}$ represents a sequence of 10 amino acids, wherein said motif has 90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9.	$HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$ <u>(SEQ ID NO: 34)</u>, wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(X)_{114-137}$ represents a sequence of 24 amino acids; $(X)_{139-269}$ represents a sequence of 131 amino acids; and $(X)_{271-280}$ represents a sequence of 10 amino acids, wherein said motif has 90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9 <u>wherein said AAD-1 protein when expressed in a soybean plant cell renders said soybean plant cell tolerant to a phenoxy auxin herbicide and an (R)- aryloxyphenoxypropionate</u>
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	<u><i>herbicide, as compared to an untransformed soybean plant cell.</i></u>
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563. The claim should be deemed anticipated based on Corteva '437 for the reasons discussed in connection with claim 1 of the '745 patent and claim 34 of the '555 patent (which are incorporated here by reference). *See supra* Section VII.A.2.r, IX.A.2.b.

3. Claims 1-29 Should Be Deemed Obvious Based on Corteva '437.

564. I understand that if a claim is anticipated based on a given reference, it also would have been obvious based on that reference. As I explain above, claims 1-29 of the '745 patent should be deemed anticipated based on Corteva '437. Claims 1-29 should therefore be deemed obvious based on Corteva '437.

B. Invalidity Analysis as of April 30, 2004

565. As explained in Section VII.A.1, which is incorporated here by reference, the challenged claims of the Corteva patents are not entitled to a priority date earlier than October 7, 2016. Even if the challenged claims were entitled to the earliest possible priority date of April 30, 2004, however, claims 1-29 should be deemed obvious based on the prior art and the knowledge of the POSA.

1. Claims 1-6, 9-12, and 29 Should Be Deemed Obvious Based on Saari 1999 or Saari 1998 in Combination with Schleinitz and Streber.

566. As I explain above in Sections VII.B.1-VII.B.2, which are incorporated here by reference, even as of April 2004, the POSA would have regarded it as obvious based on either of the Saari References in combination with Schleinitz or Streber to express RdpA in transgenic plant cells and plants. As such, and as discussed in detail below, claims 1-6, 9-12, and 29 should be deemed obvious.

b. Claim 1

567. Claim 1 of the '745 patent is similar to claim 1 of the '283 patent, but requires (1) the transgenic plant cell to be a transgenic soybean plant cell and (2) the transgenic plant cell to be compared to an untransformed soybean plant cell.

<u>'283 Patent, Claim 1</u>	<u>'745 Patent, Claim 1</u>
1. A transgenic <u>maize</u> plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide which are aryloxyalkanoate herbicides, further wherein said AAD-1 protein comprises:	1. A transgenic <u>soybean</u> plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, which are aryloxyalkanoate herbicides, further wherein said AAD-1 protein comprises:

i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $\text{HX}_{112}\text{D}(\text{X})_{114-137}\text{T}(\text{X})_{139-269}\text{H}(\text{X})_{271-280}\text{R} \text{ (SEQ ID NO: 34),}$ wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(\text{X})_{114-137}$ represents a sequence of 24 amino acids; $(\text{X})_{139-269}$ represents a sequence of 131 amino acids; and $(\text{X})_{271-280}$ represents a sequence of 10 amino acids, wherein said AAD-1 protein when expressed in a <u>maize</u> plant cell renders said <u>maize</u> plant cell tolerant to a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide, as compared to an untransformed <u>maize</u> plant cell.	i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $\text{HX}_{112}\text{D}(\text{X})_{114-137}\text{T}(\text{X})_{139-269}\text{H}(\text{X})_{271-280}\text{R} \text{ (SEQ ID NO: 34),}$ wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(\text{X})_{114-137}$ represents a sequence of 24 amino acids; $(\text{X})_{139-269}$ represents a sequence of 131 amino acids; and $(\text{X})_{271-280}$ represents a sequence of 10 amino acids, wherein said AAD-1 protein when expressed in a <u>soybean</u> plant cell renders said <u>soybean</u> plant cell tolerant to a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide,
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	as compared to an untransformed <u>soybean</u> plant cell.
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568. The claim should be deemed obvious based on either of the Saari References in combination with Schleinitz and Streber.

569. The POSA would have understood soybeans were commonly grown as an agricultural crop. The POSA would have also understood that although researchers had developed soybeans that were resistant to glyphosate, overuse of glyphosate had led to the development of glyphosate-resistant weeds. *See, e.g.*, EX1003 ('745 Pat.), 1:37-45, 2:12-35. As a result, the POSA would have desired to use alternative herbicides, including phenoxy (*i.e.*, “aryloxyalkanoate”) herbicides, in combination with soybeans and would have been motivated to transform soybean plant cells to express RdpA, which each of the Saari References disclosed to degrade those herbicides.

570. The '745 patent states that dicots, which include soybeans, “are generally considered naturally tolerant to AOPP herbicides.” EX1003 ('745 Pat.), 69:21-22. Nevertheless, as noted previously, I understand that Corteva has admitted that Corteva '437 discloses that AAD-1 v1 (RdpA) when expressed in a soybean renders the soybean tolerant to an (R)-aryloxyphenoxypropionate as compared to an untransformed soybean. *Supra* ¶ 497. Given that it would have been obvious to transform soybeans to express RdpA (based on Saari 1998 or Saari 1999 in

combination with Schleinitz and Streber, as I have explained), the claim should be deemed obvious.

571. I address the remaining limitations of this claim in connection with claim 1 of the '555 patent and claim 1 of the '283 patent (the discussions of which are incorporated here by reference). *See supra* Sections VII.B.3.a, VIII.B.1.a.

c. Claim 2

572. Claim 2 refers back to claim 1 and recites: “The plant cell of claim 1 wherein said AAD-1 motif has the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R(X)_{282-284}R$ (SEQ ID NO: 35), wherein $(X)_{282-284}$ represents a sequence of 3 amino acids.”

573. Claim 2 of the '745 patent and claim 2 of the '555 patent recite similar additional limitations. Claim 2 of the '745 patent parenthetically assigns a sequence identity number to the AAD-1 motif (which does not affect whether Corteva '437 disclosure of AAD-1 proteins, such as AAD-1 v1 and v2, satisfies this limitation), and the claims have slightly different formatting.

<u>'555 Patent, Claim 2</u>	<u>'745 Patent, Claim 2</u>
2. The plant cell of claim 1 wherein said AAD-1 motif has the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R(X)_{282-284}R$, wherein $(X)_{282-284}$	2. The plant cell of claim 1 wherein said AAD-1 motif has the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R(X)_{282-284}R$ <u>(SEQ ID NO: 35)</u>,

represents a sequence of 3 amino acids.	wherein (X) ₂₈₂₋₂₈₄ represents a sequence of 3 amino acids.
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574. The claim should be deemed obvious based on either of the Saari References in combination with Schleinitz and Streber for the reasons discussed in connection with claim 1 of the '745 patent and claim 2 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.3.b, IX.B.1.b.

d. Claim 3

575. Claim 3 refers back to claim 1 and recites: “A transgenic soybean plant comprising a plurality of the soybean plant cell of claim 1, wherein expression of said polynucleotide renders said plant tolerant to said aryloxyalkanoate herbicide.”

576. Claim 3 of the '745 patent and claim 6 of the '555 patent recite similar additional limitations. Claim 3 of the '745 patent requires the plant cell to be a soybean plant cell, a limitation that is required by claim 1 of the '745 patent. Claim 3 of the '745 patent also uses the term “said,” rather than the term “an,” to refer to the term “aryloxyalkanoate herbicide,” a term that is used in claim 1 of the '745 patent.

<u>'555 Patent, Claim 6</u>	<u>'745 Patent, Claim 3</u>
6. A transgenic plant comprising a plurality of the plant cells of claim 1, wherein expression of said polynucleotide renders said plant	3. A transgenic <u>soybean</u> plant comprising a plurality of the <u>soybean</u> plant cell of claim 1, wherein expression of said polynucleotide renders said

tolerant to <i>an</i> aryloxyalkanoate herbicide.	plant tolerant to <i>said</i> aryloxyalkanoate herbicide.
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577. The claim should be deemed obvious based on either of the Saari References in combination with Schleinitz and Streber for the reasons discussed in connection with claim 1 of the '745 patent and claim 6 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.3.e, IX.B.1.b.

e. Claims 4-6

578. Claims 4-6 refer back to claim 3.

579. Claim 4 recites: “The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop.”

580. Claim 5 recites: “The plant of claim 3 wherein said aryloxyalkanoate herbicide is an (R)-aryloxyphenoxypropionate.”

581. Claim 6 recites: “The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofof.”

582. Claims 4-6 of the '745 patent and claims 8-10 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 8-10</u>	<u>'745 Patent, Claims 4-6</u>
8. The plant of claim 6 wherein said aryloxyalkanoate herbicide is selected from the group consisting of 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop.	4. The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of 2,4-dichlorophenoxyacetic acid, MCPA, dichlorprop, and mecoprop.
9. The plant of claim 6 wherein said aryloxyalkanoate herbicide is an (R)-aryloxyphenoxypropionate.	5. The plant of claim 3 wherein said aryloxyalkanoate herbicide is an (R)-aryloxyphenoxypropionate.
10. The plant of claim 6 wherein said aryloxyalkanoate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofofop.	6. The plant of claim 3 wherein said aryloxyalkanoate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofofop.

583. These claims should be deemed obvious based on either of the Saari References in combination with Schleinitz and Streber for the reasons discussed in connection with claim 3 of the '745 patent and claims 7-10 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.3.e, IX.B.1.d.

f. Claim 9

584. Claim 9 refers back to claim 3 and recites: “A method of controlling at least one weed in a field, wherein said field contains at least one plant of claim 3, wherein said method comprises applying to at least a portion of said field a first

herbicide selected from the group consisting of a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide.”

585. Claim 9 of the '745 patent and claim 13 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claim 13</u>	<u>'745 Patent, Claim 9</u>
13. A method of controlling at least one weed in a field, wherein said field contains at least one plant of claim 6, wherein said method comprises applying to at least a portion of said field a first herbicide selected from the group consisting of a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide.	9. A method of controlling at least one weed in a field, wherein said field contains at least one plant of claim 3, wherein said method comprises applying to at least a portion of said field a first herbicide selected from the group consisting of a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide.

586. The claim should be deemed obvious based on either of the Saari References in combination with Schleinitz and Streber for the reasons discussed in connection with claim 3 of the '745 patent and claim 13 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.3.f, IX.B.1.d.

g. Claims 10-12

587. Claims 10-12 refer back to claim 9.

588. Claim 10 recites: “The method of claim 9 wherein said phenoxy auxin herbicide is an R-enantiomer of a chiral phenoxy auxin.”

589. Claim 11 recites: “The method of claim 9 wherein said phenoxy auxin herbicide is an achiral phenoxy auxin selected from the group consisting of 2,4-D and MCPA.”

590. Claim 12 recites: “The method of claim 9 wherein said (R)-aryloxyphenoxypropionate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-metamifop, (R)-cyhalofop, and (R)-clodinofop.”

591. Claims 10-12 of the '745 patent and claims 14-16 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 14-16</u>	<u>'745 Patent, Claims 10-12</u>
14. The method of claim 13 wherein said phenoxy auxin herbicide is an R-enantiomer of a chiral phenoxy auxin.”	10. The method of claim 9 wherein said phenoxy auxin herbicide is an R-enantiomer of a chiral phenoxy auxin.”
15. The method of claim 13 wherein said phenoxy auxin herbicide is an achiral phenoxy auxin selected from the group consisting of 2,4-D and MCPA.	11. The method of claim 9 wherein said phenoxy auxin herbicide is an achiral phenoxy auxin selected from the group consisting of 2,4-D and MCPA.
16. The method of claim 13 wherein said (R)-aryloxyphenoxypropionate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-	12. The method of claim 9 wherein said (R)-aryloxyphenoxypropionate herbicide is selected from the group consisting of (R)-fluazifop, (R)-haloxyfop, (R)-diclofop, (R)-quizalofop, (R)-fenoxaprop, (R)-

metamifop, (R)-cyhalofop, and (R)-clodinofof.	metamifop, (R)-cyhalofop, and (R)-clodinofof.
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592. These claims should be deemed obvious based on either of the Saari References in combination with Schleinitz and Streber for the reasons discussed in connection with claim 9 of the '745 patent and claims 14-16 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.3.f, IX.B.1.f.

h. Claim 29

593. Claim 29 is similar to claim 1, but requires (1) the transgenic soybean plant cell to be an “(R)-aryloxyphenoxypropionate herbicide tolerant soybean transgenic plant cell” and (2) the “AAD-1 motif” to have “90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9.”

594. Claim 29 of the '745 patent is also similar to claim 34 of the '555 patent. The only differences are also present in claim 1 of the '745 patent.

<u>'555 Patent, Claim 34</u>	<u>'745 Patent, Claim 29</u>
34. An (R)-aryloxyphenoxypropionate herbicide tolerant transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-	29. An (R)-aryloxyphenoxypropionate herbicide tolerant transgenic <u>soybean</u> plant cell comprising a recombinant polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-

aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R,$ wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(X)_{114-137}$ represents a sequence of 24 amino acids; $(X)_{139-269}$ represents a sequence of 131 amino acids; and $(X)_{271-280}$ represents a sequence of 10 amino acids, wherein said motif has 90% sequence identity with corresponding amino acids of position 111 to 281 of SEQ ID NO: 9.	aryloxyphenoxypropionate herbicide, further wherein said AAD-1 protein comprises: i) an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 9; and ii) an AAD-1 motif having the general formula of: $HX_{112}D(X)_{114-137}T(X)_{139-269}H(X)_{271-280}R$ <u>(SEQ ID NO: 34)</u>, wherein X_{112} represents a single amino acid at position 112, relative to the sequence of SEQ ID NO: 9; $(X)_{114-137}$ represents a sequence of 24 amino acids; $(X)_{139-269}$ represents a sequence of 131 amino acids; and $(X)_{271-280}$ represents a sequence of 10 amino acids, wherein said motif has 90% sequence identity with corresponding amino acids of
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	position 111 to 281 of SEQ ID NO: 9 <u>wherein said AAD-1 protein when expressed in a soybean plant cell renders said soybean plant cell tolerant to a phenoxy auxin herbicide and an (R)- aryloxyphenoxypropionate herbicide, as compared to an untransformed soybean plant cell.</u>
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595. The claim should be deemed obvious based on either of the Saari References in combination with Schleinitz and Streber for the reasons discussed in connection with claim 1 of the '745 patent and claim 34 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.3.g, IX.B.1.b.

2. Claims 7-8 and 13-28 Should Be Deemed Obvious Based on Saari 1999 or Saari 1998 in Combination with Schleinitz, Streber, and Jepson.

596. The remaining challenged claims of the '745 patent should be deemed obvious based on the references discussed in the prior section and Jepson.

b. Claims 7-8

597. Claims 7 and 8 refer, directly or indirectly, back to claim 3.

598. Claim 7 recites: "The plant of claim 3 wherein said plant further comprises a second herbicide resistance gene."

599. Claim 8 recites: “The plant of claim 7 wherein said second herbicide resistance gene renders said plant resistant to an herbicide selected from the group consisting of glyphosate, glufosinate, acetolactate synthase (ALS) inhibitors, inhibitors of 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD), dicamba, and inhibitors of protoporphyrinogen oxidase (PPO).”

600. Claims 7-8 of the '745 patent and claims 11-12 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 11-12</u>	<u>'745 Patent, Claims 7-8</u>
11. The plant of claim 6 wherein said plant further comprises a second herbicide resistance gene.	7. The plant of claim 3 wherein said plant further comprises a second herbicide resistance gene.
12. The plant of claim 11 wherein said second herbicide resistance gene renders said plant resistant to an herbicide selected from the group consisting of glyphosate, glufosinate, acetolactate synthase (ALS) inhibitors, inhibitors of 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD), dicamba, and inhibitors of protoporphyrinogen oxidase (PPO).	8. The plant of claim 7 wherein said second herbicide resistance gene renders said plant resistant to an herbicide selected from the group consisting of glyphosate, glufosinate, acetolactate synthase (ALS) inhibitors, inhibitors of 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD), dicamba, and inhibitors of protoporphyrinogen oxidase (PPO).

601. These claims should be deemed obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson for the reasons

discussed in connection with claim 3 of the '745 patent and claims 11-12 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.a, IX.B.1.d.

c. Claims 13-16

602. Claims 13-16 refer, directly or indirectly, back to claim 9.

603. Claim 13 recites: “The method of claim 9 wherein said method comprises applying a second herbicide.”

604. Claim 14 recites: “The method of claim 13 wherein said first herbicide and said second herbicide are applied sequentially.”

605. Claim 15 recites: “The method of claim 13 wherein said first herbicide and said second herbicide are applied concurrently.”

606. Claim 16 recites: “The method of claim 13 wherein said first herbicide is a phenoxy auxin and said second herbicide is an (R)-aryloxyphenoxypropionate.”

607. Claims 13-16 of the '745 patent and claims 17-20 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 17-20</u>	<u>'745 Patent, Claims 13-16</u>
17. The method of claim 13 wherein said method comprises applying a second herbicide.	13. The method of claim 9 wherein said method comprises applying a second herbicide.

18. The method of claim 17 wherein said first herbicide and said second herbicide are applied sequentially.	14. The method of claim 13 wherein said first herbicide and said second herbicide are applied sequentially.
19. The method of claim 17 wherein said first herbicide and said second herbicide are applied concurrently.	15. The method of claim 13 wherein said first herbicide and said second herbicide are applied concurrently.
20. The method of claim 17 wherein said first herbicide is a phenoxy auxin and said second herbicide is an (R)-aryloxyphenoxypropionate.	16. The method of claim 13 wherein said first herbicide is a phenoxy auxin and said second herbicide is an (R)-aryloxyphenoxypropionate.

608. These claims should be deemed obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson for the reasons discussed in connection with claim 9 of the '745 patent and claims 17-20 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.b-VII.B.4.c, IX.B.1.f.

d. Claims 17-19

609. Claims 17-19 refer back to claim 13.

610. Claim 17 recites: “The method of claim 13 wherein said second herbicide is selected from the group consisting of glyphosate, glufosinate, dicamba, acetolactate synthase (ALS) inhibitors, protoporphyrinogen oxidase (PPO) inhibitors, and 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD) inhibitors.”

611. Claim 18 recites: “The method of claim 13, wherein said first herbicide is 2,4-D and said second herbicide is glyphosate or glufosinate.”

612. Claim 19 recites: “The method of claim 13, wherein said first herbicide is an (R)-aryloxyphenoxypropionate and said second herbicide is glyphosate or glufosinate.”

613. Claims 17-19 of the '745 patent and claims 21-23 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 21-23</u>	<u>'745 Patent, Claims 17-19</u>
21. The method of claim 17 wherein said second herbicide is selected from the group consisting of glyphosate, glufosinate, dicamba, acetolactate synthase (ALS) inhibitors, protoporphyrinogen oxidase (PPO) inhibitors, and 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD) inhibitors.	17. The method of claim 13 wherein said second herbicide is selected from the group consisting of glyphosate, glufosinate, dicamba, acetolactate synthase (ALS) inhibitors, protoporphyrinogen oxidase (PPO) inhibitors, and 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD) inhibitors.
22. The method of claim 17 , wherein said first herbicide is 2,4-D and said second herbicide is glyphosate or glufosinate.	18. The method of claim 13 , wherein said first herbicide is 2,4-D and said second herbicide is glyphosate or glufosinate.
23. The method of claim 17 , wherein said first herbicide is an (R)-aryloxyphenoxypropionate and said	19. The method of claim 13 , wherein said first herbicide is an (R)-aryloxyphenoxypropionate and said

second herbicide is glyphosate or glufosinate.	second herbicide is glyphosate or glufosinate.
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614. These claims should be deemed obvious based on either of the Saari References in Combination with Schleinitz, Streber, and Jepson for the reasons discussed in connection with claim 13 of the '745 patent and claims 21-23 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.d, IX.B.2.c.

e. Claims 20-21

615. Claims 20-21 refer, directly or indirectly, back to claim 13.

616. Claim 20 recites: “The method of claim 13 wherein said plant further comprises a second herbicide resistance gene that renders said plant resistant to said second herbicide.”

617. Claim 21 recites: “The method of claim 20 wherein said second gene is selected from the group consisting of a modified acetolactate synthase (ALS) gene, a glyphosate resistance gene, a glufosinate resistance gene, and a dicamba-degrading enzyme gene.

618. Claims 20-21 of the '745 patent and claims 25-24 of the '555 patent recite similar additional limitations. Claim 25 of the '555 patent states that the second gene is a “second herbicide resistance gene,” a limitation that is required by claim 20 of the '745 patent and claim 24 of the '555 patent.

<u>'555 Patent, Claims 24-25</u>	<u>'745 Patent, Claims 20-21</u>
24. The method of claim 17 wherein said plant further comprises a second herbicide resistance gene that renders said plant resistant to said second herbicide.	20. The method of claim 13 wherein said plant further comprises a second herbicide resistance gene that renders said plant resistant to said second herbicide.
25. The method of claim 24 wherein said second <u><i>herbicide resistance</i></u> gene is selected from the group consisting of a modified acetolactate synthase (ALS) gene, a glyphosate resistance gene, a glufosinate resistance gene, and a dicamba-degrading enzyme gene.	21. The method of claim 20 wherein said second gene is selected from the group consisting of a modified acetolactate synthase (ALS) gene, a glyphosate resistance gene, a glufosinate resistance gene, and a dicamba-degrading enzyme gene.

619. These claims should be deemed obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson for the reasons discussed in connection with claim 13 of the '745 patent and claims 24-25 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.e-VII.B.4.f, IX.B.2.c.

f. Claims 22-24

620. Claims 22-24 refer, directly or indirectly, back to claim 13.

621. Claim 22 recites: “The method of claim 13 wherein said method further comprises applying a third herbicide.”

622. Claim 23 recites: “The method of claim 22, wherein said third herbicide is selected from the group consisting of glyphosate, glufosinate, HPPD-inhibitors, PPO-inhibitors, ALS inhibitors, and dicamba.”

623. Claim 24 recites: “The method of claim 23 wherein said first, second and third herbicides are 2,4-D, quizalofop, and glyphosate.”

624. Claims 22-24 of the '745 patent and claims 27-29 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claims 27-29</u>	<u>'745 Patent, Claims 22-24</u>
27. The method of claim 17 wherein said method further comprises applying a third herbicide.	22. The method of claim 13 wherein said method further comprises applying a third herbicide.
28. The method of claim 27 , wherein said third herbicide is selected from the group consisting of glyphosate, glufosinate, HPPD-inhibitors, PPO-inhibitors, ALS inhibitors, and dicamba.	23. The method of claim 22 , wherein said third herbicide is selected from the group consisting of glyphosate, glufosinate, HPPD-inhibitors, PPO-inhibitors, ALS inhibitors, and dicamba.
29. The method of claim 28 wherein said first, second and third herbicides are 2,4-D, quizalofop, and glyphosate.	24. The method of claim 23 wherein said first, second and third herbicides are 2,4-D, quizalofop, and glyphosate.

625. These claims should be deemed obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson for the reasons discussed in connection with claim 13 of the '745 patent and claims 27-29 of the

'555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.g, IX.B.2.c.

g. Claim 25

626. Claim 25 refers back to claim 1 and recites: “A seed comprising a plurality of the plant cell of claim 1.”

627. Claim 25 of the '745 patent and claim 30 of the '745 patent recite similar additional limitations. Claim 30 of the '555 patent requires a plurality of plant cells. Claim 25 of the '745 patent requires a plurality of “plant cell.”

<u>'555 Patent, Claim 30</u>	<u>'745 Patent, Claim 25</u>
30. A seed comprising a plurality of the plant cells of claim 1.	25. A seed comprising a plurality of the plant cell of claim 1.

628. Claim 25 is obvious, irrespective of this difference in language. If a seed contains a “plurality of the plant cells” (*i.e.*, multiple plant cells) it also includes at least a “plurality of the plant cell.”

629. Thus, the claim should be deemed obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson for the reasons discussed in connection with claim 1 of the '745 patent and claim 30 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.h, IX.B.1.b.

h. Claim 26

630. Claim 26 refers back to claim 25 and recites: “A method of controlling weeds in a field, wherein said method comprises applying an aryloxyalkanoate herbicide to said field and planting a seed of claim 25 in said field within 14 days of applying said aryloxyalkanoate herbicide.”

631. Claim 26 of the '745 patent and claim 31 of the '555 patent recite the same additional limitations.

<u>'555 Patent, Claim 31</u>	<u>'745 Patent, Claim 26</u>
31. A method of controlling weeds in a field, wherein said method comprises applying an aryloxyalkanoate herbicide to said field and planting a seed of claim 30 in said field within 14 days of applying said aryloxyalkanoate herbicide.	26. A method of controlling weeds in a field, wherein said method comprises applying an aryloxyalkanoate herbicide to said field and planting a seed of claim 25 in said field within 14 days of applying said aryloxyalkanoate herbicide.

632. The claim should be deemed obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson for the reasons discussed in connection with claim 25 of the '745 patent and claim 31 of the '555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.i, IX.B.2.g.

i. Claims 27-28

633. Claims 27-28 refer, directly or indirectly, back to claim 25.

634. Claim 27 recites: “A plant grown from the seed of claim 25 comprising said polynucleotide.”

635. Claim 28 recites: “A part, progeny, or asexual propagate of the plant of claim 27, wherein said part, progeny, or sexual propagate comprises said polynucleotide.”

636. Claims 27-28 of the '745 patent and claims 32-33 of the '555 patent recite similar additional limitations. Claim 27 of the '745 patent states that the seed comprises “said polynucleotide,” a limitation that is required by claim 1 of the '745 patent, from which claim 25 depends.

<u>'555 Patent, Claim 32-33</u>	<u>'745 Patent, Claims 27-28</u>
32. A plant grown from the seed of claim 30 .	27. A plant grown from the seed of claim 25 <u><i>comprising said polynucleotide.</i></u>
33. A part, progeny, or asexual propagate of the plant of claim 32 , wherein said part, progeny, or sexual propagate comprises said polynucleotide.	28. A part, progeny, or asexual propagate of the plant of claim 27 , wherein said part, progeny, or sexual propagate comprises said polynucleotide.

637. These claims should be deemed obvious based on either of the Saari References in combination with Schleinitz, Streber, and Jepson for the reasons discussed in connection with claim 25 of the '745 patent and claims 32-33 of the

'555 patent (which are incorporated here by reference). *See supra* Sections VII.B.4.j, IX.B.2.g.

X. SECONDARY CONSIDERATIONS OF NONOBVIOUSNESS

638. I understand that a patent owner may attempt to rely on what is referred to as secondary considerations of nonobviousness (also referred to as objective evidence of nonobviousness), such as unexpected properties, failure of others, and copying, to try to support the nonobviousness of a challenged patent claim. I am not aware of any secondary considerations of nonobviousness that would support the nonobviousness of the challenged claims as to any of the grounds discussed in any of Sections VII.A.3, VII.B, VIII.A.3, VIII.B, VIII.A.3, IX.B.

639. During prosecution of the '555 patent, the applicant argued that the inventors unexpectedly discovered that the claimed "AAD-1" proteins degraded both phenoxy auxin and (*R*)-aryloxyphenoxypropionate herbicides. *See, e.g.*, EX1008 ('406 Appl. & File History), COR-AAD1-00000492-493 (Response (Apr. 12, 2019) (pp. 14-15)). I disagree. As I explain above, the prior art reported that RdpA degraded phenoxy herbicides, including (*R*)-enantiomers; the POSA would not have viewed it as surprising that RdpA degraded structurally related (*R*)-phenoxy auxin and (*R*)-aryloxyphenoxypropionate herbicides. *See supra* Section VII.B.2. Moreover, I understand that for evidence of secondary considerations to be entitled to some weight, those secondary considerations must result from what is

both claimed and novel in the claim. In this case, RdpA's ability to degrade phenoxy-herbicides, including (*R*)-enantiomers, results directly from its known activity, rather than anything novel in the claims. *See supra* Section VII.B.2.

640. I further understand that, in order for evidence of secondary considerations to support nonobviousness, the evidence must be reasonably commensurate with the scope of the claims. Even if the patent owner could demonstrate that RdpA or the other examples it relied on during prosecution of the '555 patent (from the patent specification and the two declarations from Dr. Wright) demonstrated unexpected activity against both phenoxy auxins and (*R*)-aryloxyphenoxypropionate herbicides, the challenged claims of each of the '555, '283, and '745 patents encompass massive genera of proteins. *See supra* Section VII.A.1.c. Such a limited number of examples is not reasonably commensurate with the broad scope of those claims. If Corteva contends that the challenged claims are supported by one or more secondary considerations of nonobviousness, I reserve the right to respond.

* * *

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

I declare under penalty of perjury that the foregoing is true and correct.

Dated: 11/8/23



Aron Silverstone, Ph.D.

APPENDIX A

TABLE OF EXHIBITS

<u>Exhibit No.</u>	<u>Short Citation</u>	<u>Full Citation</u>
EX1001	'555 Pat.	U.S. Patent No. 10,947,555
EX1002	'283 Pat.	U.S. Patent No. 11,149,283
EX1003	'785 Pat.	U.S. Patent No. 11,299,745
EX1004	'052 Provisional Appl.	U.S. Provisional Application No. 60/567052
EX1005	'7893 Appl. & File History	U.S. Application No. 11/587893 and File History
EX1006	'813 Appl. & File History	U.S. Application No. 12/951813 and File History
EX1007	'0893 Appl. & File History	U.S. Application No. 14/820893 and File History
EX1008	'406 Appl. & File History	Certified U.S. Application No. 15/288,406 and File History
EX1009	'824 Appl. & File History	U.S. Application No. 17/143,824 and File History
EX1010	'966 Appl. & File History	Certified U.S. Application No. 17/175,966 and File History
EX1011	'476 Appl. & File History	Certified U.S. Application No. 17/403,476, and File History
EX1012		Accession No. AAS49436.1, submitted Feb. 04, 2004

<u>Exhibit No.</u>	<u>Short Citation</u>	<u>Full Citation</u>
EX1013	Schleinitz	Accession No. AF516751, published Aug. 6, 2002
EX1014		Accession No. AF516752, published Aug. 6, 2002
EX1015		Accession No. AJ628856, published March 3, 2004
EX1016		Accession No. Q8KSC8, published Oct. 1, 2002
EX1017		U.S. Patent Pub. No. 2016/0108422
EX1018	Bayley 1992	C. Bayley et al., <i>Engineering 2,4-D Resistance into Cotton</i> , 83 THEORETICAL & APPLIED GENETICS 645-649 (1992)
EX1019	Chekan 2019	J.R. Chekan et al., <i>Molecular Basis for Enantioselective Herbicide Degradation Imparted by Aryloxyalkanoate Dioxygenases in Transgenic Plants</i> , 27 PROC. NAT'L ACAD. SCI. 13299-13304 (2019)
EX1020	Chekan 2019 Suppl. Info.	J.R. Chekan et al., Supplementary Information, <i>Molecular Basis for Enantioselective Herbicide Degradation Imparted by Aryloxyalkanoate Dioxygenases in Transgenic Plants</i> , 27 PROC. NAT'L ACAD. SCI. 13299-13304 (2019)
EX1021	Corteva '437	U.S. Patent Pub. No. 2005/107437
EX1022	Cutler 1999	BIOLOGICALLY ACTIVE NATURAL PRODUCTS: AGROCHEMICALS (H.G. Cutler & S.J. Cutler, eds. 1999)
EX1023	Elkins 2002	J.M. Elkins, R.P. Hausinger et al., <i>X-ray Crystal Structure of Escherichia coli Taurine/α-</i>

<u>Exhibit No.</u>	<u>Short Citation</u>	<u>Full Citation</u>
		<i>Ketoglutarate Dioxygenase Complexed to Ferrous Iron and Substrates</i> , 41 BIOCHEMISTRY 5185-5192 (2002)
EX1024	Fukumori & Hausinger 1993	F. Fukumori & R.P. Hausinger, <i>Alcaligenes Eutrophus JMP134 "2,4-Dichlorophenoxyacetate Monooxygenase" Is an α-Ketoglutarate-Dependent Dioxygenase</i> , 175 J. BACTERIOLOGY 2083-2086 (1993)
EX1025	Hausinger 2004	R. Hausinger, <i>Fe(II)/α-Ketoglutarate-Dependent Hydroxylases and Related Enzymes</i> , 39 CRIT. REV. BIOCHEM. MOLECULAR BIO. 21-68 (2004)
EX1026	Hee 1981	S.S.Q. Hee & R.G. Sutherland, I PHENOXYALKANOIC HERBICIDES: CHEMISTRY, ANALYSIS, AND ENVIRONMENTAL POLLUTION (1981)
EX1027	Hogan 2000	D.A. Hogan, R.P. Hausinger et al., <i>Site-Directed Mutagenesis of 2,4-Dichlorophenoxyacetic Acid/α-Ketoglutarate Dioxygenase. Identification of Residues Involved in Metallocenter Formation and Substrate Binding</i> , 275 J. BIO. CHEM. 12400-12409 (2000)
EX1028	Hotopp 2001	J.C. Dunning Hotopp & R.P. Hausinger, <i>Alternative Substrates of 2,4-Dichlorophenoxyacetate/α-Ketoglutarate Dioxygenase</i> , 15 J. MOLECULAR CATALYSIS B: ENZYMATIC 155-162 (2001)
EX1029	Hotopp 2002	J.C. Dunning Hotopp & R.P. Hausinger, <i>Probing the 2,4-Dichlorophenoxyacetate/α-Ketoglutarate Dioxygenase Substrate Binding Site by Site-Directed Mutagenesis and Mechanism-Based Inactivation</i> , 41 BIOCHEMISTRY 9787-9794 (2002)

<u>Exhibit No.</u>	<u>Short Citation</u>	<u>Full Citation</u>
EX1030	Jepson	U.S. Patent Pub. No. 2003/0041357
EX1031	Kohler 1999	H.P.E. Kohler, <i>Sphingomonas herbicodovorans MH: A Versatile Phenoxyalkanoic Acid Herbicide Degradar</i> , 23 J. INDUS. MICROBIO. & BIOTECH. 336-340 (1999)
EX1032	Lyon 1989	B.R. Lyon et al., <i>Expression of a Bacterial Gene in Transgenic Tobacco Plants Confers Resistance to the Herbicide 2,4-Dichlorophenoxyacetic Acid</i> , 13 PLANT MOLECULAR BIO. 533-540 (1989)
EX1033	Lyon 1993	B.R. Lyon et al., <i>Cotton Plants Transformed with Bacterial Degradation Gene Are Protected from Accidental Spray Drift Damages by the Herbicide 2,4-Dichlorophenoxyacetic Acid</i> , 2 TRANSGENIC RES. 162-169 (1993)
EX1034	Müller 2001	R.H. Müller et al., <i>Physiological and Genetic Characteristics of Two Bacterial Strains Utilizing Phenoxypropionate and Phenoxyacetate Herbicides</i> , 156 MICROBIO. RES. 121-131 (2001)
EX1035	Müller 2006	T.A. Müller, R.P. Hausinger et al., <i>Structural Basis for the Enantiospecificities of R- and S-Phenoxypropionate/α-Ketoglutarate Dioxygenases</i> , 15 PROTEIN SCI. 1356-1368 (2006)
EX1036	Nickel 1997	K. Nickel et al., <i>Involvement of Two α-Ketoglutarate-Dependent Dioxygenases in Enantioselective Degradation of (R)- and (S)-Mecoprop by Sphingomonas herbicidovorans MH</i> , 179 J. BACTERIOLOGY 6674-6679 (1997)
EX1037	Otoxby 1990	E. Otoxby & M.A. Hughes, <i>Engineering Herbicide Tolerance into Crops</i> , 8 TIBTECH 61-65 (1990)

<u>Exhibit No.</u>	<u>Short Citation</u>	<u>Full Citation</u>
EX1038	Perkins 1987	E.J. Perkins et al., <i>Use of Alcaligenes eutrophus as a Source of Genes for 2,4-D Resistance in Plants</i> , 35 WEED SCI. 12-18 (1987)
EX1039	Rao 2000	PRINCIPLES OF WEED SCIENCE (V.S. Rao, ed., 2d ed. 2000)
EX1040	Saari 1998	R.E. Saari, Substrate Specificity and Spectroscopic Properties of 2,4-Dichlorophenoxyacetic Acid/ α -Ketoglutarate Dioxygenase, Doctoral Thesis, Mich. State Univ. (July 6, 1998)
EX1041	Saari 1999	R.E. Saari, R.P. Hausinger, et al., <i>Stereospecific Degradation of the Phenoxypropionate Herbicide Dichlorprop</i> , 6 J. MOLECULAR CATALYSIS B: ENZYMATIC 6 421-428 (1999)
EX1042	Schleinitz 2004	K.M. Schleinitz et al., <i>Localization and Characterization of Two Novel Genes Encoding Stereospecific Dioxygenases Catalyzing 2(2,4-Dichlorophenoxy)Propionate Cleavage in Delftia acidovorans MCI</i> , 70 APPLIED & ENVTL. MICROBIO. 5357-5365 (2004)
EX1043	Streber	U.S. Patent No. 6,153,401
EX1044	Streber 1987	W.R. Streber et al., <i>Analysis, Cloning, And High-Level Expression of 2,4-Dichlorophenoxyacetate Monooxygenase Gene tfdA of Alcaligenes eutrophus JMP134</i> , 169 J. BACTERIOLOGY 2950-2955 (1987)
EX1045	Streber 1989	W.R. Streber & L. Willmitzer, <i>Transgenic Tobacco Plants Expressing a Bacterial Detoxifying Enzyme Are Resistant to 2,4-D</i> , 7 BIOTECHNOLOGY 811-816 (1989)

<u>Exhibit No.</u>	<u>Short Citation</u>	<u>Full Citation</u>
EX1046	Vedler 2004	E. Vedler et al., <i>The Completely Sequenced Plasmid pEST4011 Contains a Novel IncP1 Backbone and a Catabolic Transposon Harboring tfd Genes for 2,4-Dichlorophenoxyacetic Acid Degradation</i> , 186 J. BACTERIOLOGY 7161-7174 (2004)
EX1047	Westendorf 2002	A. Westendorf et al., <i>The Two Enantiospecific Dichlorprop/α-Ketoglutarate Dioxygenases from Delftia acidovorans MCI-Protein and Sequence Data of RdpA and SdpA</i> , 157 MICROBIO. RES. 317-322 (2002)
EX1048	Westendorf 2003	A. Westendorf et al., <i>Purification and Characterization of the Enantiospecific Dioxygenases from Delftia acidovorans MCI Initiating the Degradation of Phenoxypropionate and Phenoxyacetate Herbicides</i> , 23 ACTA BIOTECHNOLOGY 3-17 (2003)
EX1050		First Amended Complaint, <i>Corteva Agriscience LLC v. Monsanto Co.</i> , No. 1:22-cv-1046-GBW (D. Del.), D.I. 68, excluding exhibits
EX1051	Krausz 1993	R.F. Krausz et al., <i>Soybean (Glycine max) Tolerance to 2,4-D Ester Applied Preplant</i> , 7 WEED TECH. 906-910 (1993)
EX1052	Larue 2019	C.T. Larue et al., <i>Development of Enzymes for Robust Aryloxyphenoxypropionate and Synthetic Auxin Herbicide Tolerance Traits in Maize and Soybean Crop</i> , 75 PEST MGMT. SCI. 2086-2094 (2019)
EX1055		Curriculum Vitae of Aron Silverstone, Ph.D.

<u>Exhibit No.</u>	<u>Short Citation</u>	<u>Full Citation</u>
EX1056		Joint Claim Construction Chart, <i>Corteva Agriscience LLC v. Monsanto Co.</i> , No. 1:22-cv-1046-GBW (D. Del.), D.I. 82
EX1062	MSU Library Website	<i>Finding Dissertations and Theses: Home</i> , MICH. STATE UNIV., https://libguides.lib.msu.edu/dissertations (accessed October 18, 2023)