Filed: September 21, 2023

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BAYER CROPSCIENCE LP AND MONSANTO COMPANY,
Petitioners,

v.

CORTEVA AGRISCIENCE LLC,
Patent Owner.

IPR2023-01037
U.S. Patent No. 11,149,283

PATENT OWNER'S PRELIMINARY RESPONSE

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EXHIBIT LIST

Exhibit	Description
2001	Fumiyasu Fukumori and Robert P. Hausinger, *Purification and Characterization of 2,4-Dichlorophenoxyacetate/α-Ketoglutarate Dioxygenase*, J. of Biol. Chem., Vol. 268, No. 32, pp. 24311-17 (1993) ("Fukumori").
2002	Sealed Version of Defendants' Counterclaims to Plaintiff's Second Amended Complaint, *Corteva Agriscience LLC v. Monsanto Co.*, No. 22-cv-1046-GBW (D. Del.), D.I. 143 (excerpted pages 38 to 65 and accompanying exhibits) (CONFIDENTIAL – FILED UNDER SEAL)
2003	Redacted Version of Defendants' Counterclaims to Plaintiff's Second Amended Complaint, *Corteva Agriscience LLC v. Monsanto Co.*, No. 22-cv-1046-GBW (D. Del.), D.I. 143 (excerpted pages 38 to 65 and accompanying exhibits)
2004	Protein sequences (CONFIDENTIAL – FILED UNDER SEAL)
2005	Protein sequences (CONFIDENTIAL – FILED UNDER SEAL)
2006	Protein presentation (CONFIDENTIAL – FILED UNDER SEAL)
2007	Protein presentation (CONFIDENTIAL – FILED UNDER SEAL)
2008	Protein sequences (CONFIDENTIAL – FILED UNDER SEAL)
2009	Protein assay analysis (CONFIDENTIAL – FILED UNDER SEAL)
2010	Protein presentation (CONFIDENTIAL – FILED UNDER SEAL)
2011	Protein sequences and correspondence (CONFIDENTIAL – FILED UNDER SEAL)
2012	GenBank Accession No. MH043112
2013	GenBank Accession No. MH043114
2014	GenBank Accession No. MH043115

I. Introduction

The invention of Corteva's U.S. Patent No. 11,149,283 ("the '283 patent") concerns transgenic maize (corn) plant cells (and plants) that produce AAD-1 proteins that degrade two different classes of herbicides (phenoxy auxin herbicides and (*R*)-aryloxyphenoxypropionate (abbreviated as "AOPP" or "FOP") herbicides) and render the maize plant cells tolerant to those herbicides as compared to an untransformed maize plant cell. The specification discloses exemplary AAD-1 proteins by amino acid sequence, including the common motif of their active site defined by particular conserved amino acid residues and their relative spacing. The specification also discloses examples including *in vitro* testing and genetic transformation of maize plants that produce AAD-1 enzymes. Corteva's invention, commercialized in Corteva's Enlist® corn products, thus enables growers to use multiple classes of herbicides to control weeds. Before Corteva's groundbreaking invention, no other proteins within AAD-1's class of αKG-dependent dioxygenases were reported to degrade FOP herbicides, let alone also exhibit dual activity against a second herbicide class.

The Petition essentially repeats two alleged grounds of unpatentability that the Office addressed during prosecution of the predecessor '406 Application: anticipation/obviousness based on a priority challenge (Grounds IA and IB) and obviousness (Grounds IIA and IIB) based on references either considered during

prosecution of both the ’406 Application and the ’283 patent or that are cumulative (e.g., substituting one reference disclosing an amino acid sequence for another disclosing the same sequence).

The Board should deny institution for at least three reasons. *First*, Petitioners’ priority challenge in Grounds IA and IB based on written description is legally flawed and fails to establish that the asserted PCT publication (WO ’437 or Corteva ’437, Ex. 1021) within the ’283 patent’s priority chain qualifies as prior art. Contradicting Petitioners’ characterization of the claims as functionally defined and overly broad, the ’283 patent claims contain significant structural limitations correlated to the claimed dual enzymatic activity against phenoxy auxin and FOP herbicides. These limitations restrict the AAD-1 proteins to those having (i) at least 85% sequence identity to SEQ ID NO: 9, *and* (ii) the specific AAD-1 active site motif: $HX_{112}D(X)_{114\text{-}137}T(X)_{139\text{-}269}H(X)_{271\text{-}280}R$.

Petitioners primarily contend, for example, that the ’283 patent’s priority applications do not describe the claimed AAD-1 active site motif. Pet., 24-31. But Petitioners (1) fail to dispute that the claimed motif is *literally embodied* in SEQ ID NO: 9, (2) concede that skilled artisans *would have recognized* the active site motif in SEQ ID NO: 9, and (3) fail to address evidence that skilled artisans had *already recognized* that functionally essential motif by the time of Corteva’s 2005 PCT filing

date. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (written description is assessed from the perspective of a skilled artisan).

Petitioners' structure-function arguments are also legally deficient under *Ajinomoto Co. v. ITC*, 932 F.3d 1342 (Fed. Cir. 2019). Petitioners concede that the AAD-1 motif is "important to the function," and skilled artisans contemporaneously recognized the motif as "functionally important" and "functionally essential." Ex. 1054, ¶ 95; Ex. 1042, Abstr., 5357, 5362. Further, Petitioners fail to address the specification's disclosure that the claimed minimum level of at least 85% sequence identity to SEQ ID NO: 9 is "highly identical" in this technical field, and that such proteins "*would be expected to retain similar properties.*"[1] Ex. 1002, 43:63-44:9; Exs. 1005-1009, 1021, ¶ [0171]. Disregarding these disclosures, Petitioners advance the type of perfect-correspondence argument for structure-function correlation that *Ajinomoto* squarely rejected. 932 F.3d at 1360 (requiring only a "*correlation* between structure and function") (emphasis in original) (quoting *Ariad*, 598 F.3d at 1350). Petitioners' remaining written-description arguments, advancing the same type of bare numerosity theory (i.e., alleging 20^{44} possible species) that the Board and courts have repeatedly rejected, are similarly premised on a misapplication of written-description law.

[1] All emphases are added unless otherwise noted.

Second, Petitioners' Grounds IIA and IIB attempt to skirt the required obviousness analysis under *Graham*. Rather than identifying the differences between the claimed invention and the cited references or addressing the claimed invention as a whole, Petitioners conduct a hindsight-driven analysis. They first selectively address only a *subset* of claim limitations in an effort to combine the references. Then they circle back to contend that the "*remaining limitations* are obvious" based on that purported combination. Pet., 54-56. The law, however, requires evaluating the claimed invention "as a whole"—not in piecemeal fashion—and thus Grounds IIA and IIB are legally deficient.

Petitioners also fail to establish that the cited references disclose all limitations of the claims, even if combined. For example, Petitioners do not identify any prior art disclosure of AAD-1 proteins (or any other proteins) having the ability to degrade FOP herbicides, much less two distinct classes of herbicides, as claimed. Instead, Petitioners present a legally deficient, single-sentence assertion that the claimed activity is inherent. *In re Spormann*, 363 F.2d 444, 448 (CCPA 1966) ("[T]he inherency of an advantage and its obviousness are *entirely different questions*."). Such superficial inherency assertions are insufficient as a matter of law. *Honeywell Int'l Inc. v. Mexichem Amanco Holding S.A. de C.V.*, 865 F.3d 1348, 1354-55 (Fed. Cir. 2017) (use of inherency in the context of obviousness must be "carefully circumscribed"); *Millennium Pharms., Inc. v. Sandoz Inc.*, 862 F.3d 1356, 1367

(Fed. Cir. 2017) ("The mere fact that a certain thing may result from a given set of circumstances is not sufficient….").

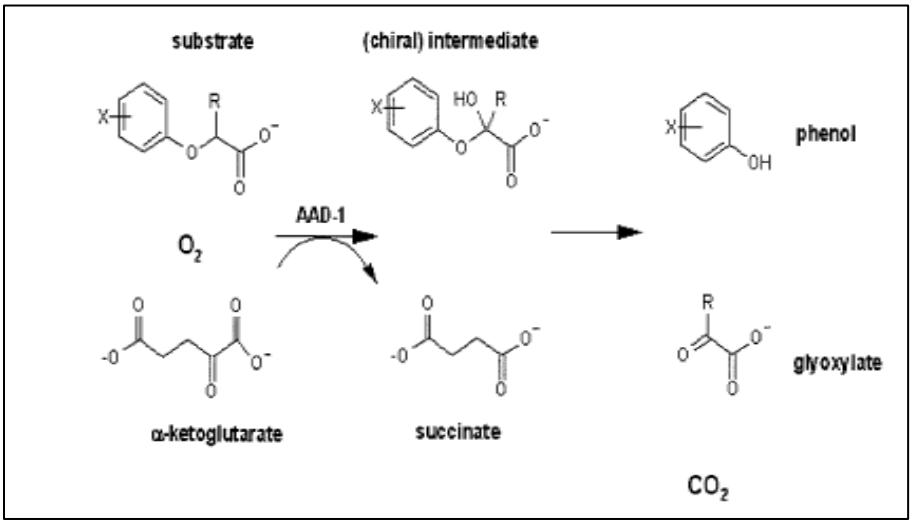
Third, the Board should also exercise its discretion to deny institution under 35 U.S.C. § 325(d). The same or similar cited references were before the Office and used in rejections that were overcome during prosecution of the '283 patent's predecessor application and were resubmitted to the Office during the '283 patent prosecution. Petitioners, for example, simply substitute one reference from prosecution disclosing the native AAD-1 sequence (Kohler, Ex. 1016) for another (Schleinitz, Ex. 1013). Petitioners similarly substitute one reference from prosecution disclosing transformation of plants expressing a TfdA enzyme (Jepson, Ex. 1030) for another (Streber, Ex. 1043), while still continuing to rely on Jepson in Ground IIB. Petitioners also appear to acknowledge that Saari 1998 is cumulative of the Saari 1999 reference considered during prosecution, as they address them together as "Saari 1998 or Saari 1999" or collectively as the "Saari References." Pet., 54, 58. Petitioners also fail to establish that the Office erred in evaluating priority (Grounds IA and IB) or obviousness (Grounds IIA and IIB) during prosecution.

Accordingly, Corteva respectfully requests that the Board deny institution.

II. Background

A. α-Ketoglutarate-Dependent Dioxygenase Enzymes and RdpA (AAD-1)

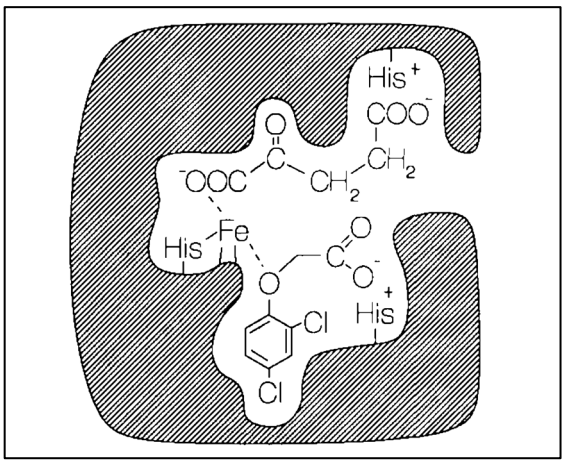
α-Ketoglutarate-dependent ("αKG-dependent") dioxygenase enzymes that degrade phenoxy auxin herbicides, such as 2,4-D, were known in the art by 2004-2005. Examples include the enzymes TfdA, RdpA, and SdpA. *See, e.g.*, Ex. 1027; Ex. 1047. To degrade 2,4-D, these enzymes generally require the presence of Fe(II) as the metallocenter, as well as oxygen (O_2) and α-ketoglutarate as a co-substrate. Ex. 2001, 24311. When 2,4-D is the substrate, the enzymatically catalyzed oxidation reaction produces carbon dioxide, succinate, 2,4-DCP (a phenol), and glyoxylate.



Ex. 1002, Fig. 1; Ex. 2001, 24311.

In 1993, researchers published initial structural characterizations of TfdA. They predicted the presence of essential histidine residues that form at least a part

of the enzyme's binding pocket and assist in the binding of the Fe(II) metallocenter, α-ketoglutarate, and the substrate (e.g., 2,4-D). Ex. 2001, 24316. At that time, without identifying the locations of specific amino acid residues, researchers depicted the active site of TfdA that accommodates the Fe(II), α-ketoglutarate, and 2,4-D substrate as follows:



Id. (Fig. 11: Model of the TfdA active site indicating potential roles of essential histidine residues).

By 2000, researchers had categorized enzymes within the αKG-dependent dioxygenase family into groups, identifying particular histidines and other amino acid residues as forming a "consensus sequence" or "motif" for their active sites. Ex. 1027, 12400. For example, TfdA and TauD were classified as Group II αKG-dependent dioxygenases based on their common $HX(D/E)X_nHX_{10\text{-}13}R$ motif, confirmed via sequence alignment. *Id.*, 12408, 12401 (Table I). Other groups of αKG-dependent dioxygenases had different motifs and acted on different substrates.

Id. Thus, skilled artisans understood that different amino acid motifs led to different substrate specificities within the αKG-dependent dioxygenase family. *Id.*, 12408.

TABLE I
Consensus motifs for subgroups within the α-KG-dependent dioxygenase superfamily

Group I (IPNS, DAOCS, and related enzymes)	HXD	X_{50-70}	HX_{10}(R/K)XS
Group II (TfdA, TauD, clavaminate synthase and related enzymes)	HX(D/E)	$X_{128-207}$	HX_{10-12}R
Group III (Phytanoyl-CoA hydroxylase, proline hydroxylase and related enzymes)	HXD	X_{72-101}	HX_{10}(R/K)XS

Id., 12401 (Table I).

Using site-directed mutagenesis, Hogan et al. identified the specific locations of likely Fe(II)-coordinating residues in TfdA: H_{113}, D_{115}, and H_{262}. *Id.*, 12401. Hogan disclosed that the HX(D/E) portion of the motif is "strictly conserved" in enzymes related to TfdA, as shown by sequence alignment. *Id.*, 12406-07; *e.g.*, *id.*, 12406 ("[T]hese data indicate that Asp-115 is very likely a metal-binding residue and may also be involved in formation of the proper catalytic conformation.").

In 2002, Hotopp et al. identified two additional important, conserved residues of TfdA, T_{141} and R_{274}, believed to bind the α-KG co-substrate. Ex. 1029, 9792-93; Ex. 1027, 12407 (Fig. 8). Thus, as reflected in Hogan and Hotopp, skilled artisans understood the structure-function relationships of Group II αKG-dependent dioxygenases and had identified five common, conserved residues (H, D, T, H, R) in those enzymes' active sites with variable spacing, depending on the specific enzyme.

Researchers had also discovered additional enzymes produced by soil bacteria (not plants) that had been reported to degrade phenoxy auxin herbicides, such as 2,4-D. These included RdpA enzymes having identical sequences from the bacteria *Sphingobium herbicidovorans* MH and *Delftia acidovorans* MC1. Ex. 1015, 1; Ex. 1042, 5360 (Fig. 2); Ex. 1013. By 2004, researchers had identified the specific active-site motif residues in RdpA. Ex. 1042, Abstr., 5362 ("The functionally important motif … is present in both RdpA and SdpA.").[2]

Accordingly, as of Corteva's 2004 and 2005 filing dates, skilled artisans had substantial knowledge of the structure and function of αKG-dependent dioxygenases, including RdpA and TfdA.

B. The '283 Patent

The '283 patent specification provides extensive disclosures relating to the claimed invention; for example, it describes AAD-1 enzymes, their common active

[2] Citing Hogan (Ex. 1027), Petitioners' declarant, Dr. Hausinger, contemporaneously reported in 2006 that the high degree of active site sequence identity and strong orientation of key side chains by interactions with the Fe^{II} were "supportive of the *active site being the most conserved and structurally accurate part of the RdpA and SdpA models*." Ex. 1035, 1358.

site motif, the significance of the claimed 85% sequence identity limitation, and *twenty-six* examples, including examples of AAD-1-transformed maize plants.

1. AAD-1 Enzymes

The inventors' creation of transgenic plants expressing the bacterial αKG-dependent dioxygenase enzyme RdpA from *Sphingobium herbicidovorans* (i.e., AAD-1) led to a unique discovery—these novel transgenic plants exhibited dual activity against two different classes of herbicides: phenoxy auxins (e.g., 2,4-D) and aryloxyphenoxypropionates ("FOP" herbicides, such as quizalofop). Ex. 1002, 4:12-16, 4:45-5:2. In light of this dual herbicide-tolerance activity, the enzymes and genes of the '283 patent are called "AAD-1" (**A**ryloxy **A**lkanoate **D**ioxygenase) proteins and genes. *Id.*, 4:49-57.

The '283 patent discloses the amino acid sequence of AAD-1 (v1) as SEQ ID NO: 9, which is the native amino acid sequence expressed by the *rdpA* gene from *Sphingobium herbicidovorans*. *Id.*, 7:3-5. The '283 patent also discloses two AAD-1 variants, SEQ ID NO: 10 (AAD-1 (v2)) and SEQ ID NO: 11 (AAD-1 (v3)), with SEQ ID NO: 11 representing a plant-optimized version of AAD-1 (v1). *Id.*, 7:6-10. The '283 patent discloses that preferred proteins of the invention variants having 85% (or higher) sequence identity and the same or similar activity. *Id.*, 37:16-36.

For αKG-dependent dioxygenases, the '283 patent discloses that amino acid sequences having 85% to 98% identity are "highly identical" and that such enzymes

are "expected to retain similar properties." *Id.*, 43:63-44:8; *see also id.*, 19:57-59 ("Many homologues are quite similar to tfdA (>85% amino acid identity) and have similar enzymatic properties to tfdA.").

The '283 patent also describes the location of the known active site motif in Group II αKG-dependent dioxygenases such as AAD-1. It states: "This family of proteins is characterized by three conserved histidine residues in a 'HX(D/E)X_{23-26}(T/S)$X_{114-183}$HX_{10-13}R' motif which comprises the active site." *Id.*, 18:44-50 (citing Hogan, Ex. 1027).

The specification also provides techniques for modifying AAD-1 genes and proteins to create AAD-1 homologues. *Id.*, 33:1-38:32. For example, it states that proteins and genes for use in the invention can be rapidly identified using oligonucleotide probes. *Id.*, 33:1-58. It also discloses that variant enzymes can be made with conservative amino acid substitutions and, in some instances, nonconservative substitutions. *Id.*, 37:54-38:12.

2. The Specification's Twenty-Six Examples

Written description "does not demand either examples or an actual reduction to practice." *Ariad*, 598 F.3d at 1352. The '283 patent nonetheless discloses twenty-six examples. Ex. 1002, 22:1-3 ("The transgenic expression of the subject AAD-1

genes is exemplified in, for example, *Arabidopsis*, corn (maize), tobacco, cotton, rice, soybean, and canola."), 43:57-129:29.

The '283 patent discloses examples of high-throughput *in vitro* assays for measuring AAD-1 activity, including a 96-well microplate format for performing enzyme assays measuring degradation activity against 2,4-D and FOP herbicides using 15-minute incubation times. *Id.*, 45:27-54:57 (Examples 2-4). The '283 patent presents *in vitro* testing data showing that AAD-1 degrades "aryloxyphenoxypropionate [i.e., FOP] herbicides as well as phenoxy auxins." *Id.*, 51:56-52:7, Figs. 6A, 6B. The '283 patent also describes how to plant-optimize the gene sequences for efficient expression of AAD-1 proteins in plant cells. *Id.*, 54:59-63:42 (Example 5).

The '283 patent describes transformation of *Arabidopsis* plants with an AAD-1 gene. *Id.*, 63:43-78:8 (Example 6). The '283 patent reports test data confirming that AAD-1-transformed *Arabidopsis* exhibited tolerance to 2,4-D as well as the FOP herbicides tested. *Id.*, 69:18-35 ("This provides the first in planta data that AAD-1 (v3) will provide [FOP] resistance.").

The '283 patent also discloses comparative testing of AAD-1-transformed *Arabidopsis* against *Arabidopsis* transformed to express a different αKG-dependent dioxygenase enzyme (AAD-2). *Id.*, 108:37-115:55 (Example 17). AAD-2 has a substantially different amino acid sequence than AAD-1 and has a different active

site motif. *See id.*, 108:41-44, SEQ ID NOs: 9, 13. In this testing, AAD-1 transformed plants exhibited stronger 2,4-D resistance than AAD-2-transformed plants, whereas their relative activities *in vitro* were reversed (i.e., AAD-2 was stronger). *Id.*, 113:27-31, 115:27-55.

The ’283 patent provides examples of maize plants transformed with AAD-1 genes, as well as examples of other AAD-1-transformed monocot and dicot plants. *Id.*, Examples 7-9, 12-15, 19-20, 24-26. For instance, the specification discloses field testing of AAD-1-transformed corn and compared the tolerance of the transformed plants to herbicides as compared to untransformed plants, reporting that the “results indicate AAD-1 (v3) not only provides robust field level resistance to 2,4-D and quizalofop individually, but also to exaggerated rates of multiple combinations of the two chemistries.” *Id.*, Example 8, 90:1-14. The ’283 patent further discloses stacking AAD-1 traits with other herbicide-tolerance traits (e.g., genes providing resistance to glyphosate, glufosinate, and/or imidazolinone herbicides) to confer multiple herbicide-tolerance traits in transformed plants. *Id.*, Examples 16, 21-23.

3. The Claims

The ’283 patent claims are directed to novel transgenic maize plants and plant cells comprising a recombinant polynucleotide encoding a structurally well-defined class of AAD-1 proteins. The claims require the recited AAD-1 proteins to have a combination of two structural limitations. First, the AAD-1 protein must have at least

85% sequence identity with SEQ ID NO: 9. Second, the AAD-1 protein must also have the defined AAD-1 motif with each of the specified active site amino acid residues and their required spacing. Claim 1, for example, recites:

1. A transgenic maize 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:

    $\boldsymbol{HX_{112}D(X)_{114\text{-}137}T(X)_{139\text{-}269}H(X)_{271\text{-}280}R}$ (SEQ ID NO:34), wherein

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

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

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

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

    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.

Ex. 1002, *see also id.*, claim 29. The dependent claims recite additional features, including:

- An AAD-1 motif of the general formula $HX_{112}D(X)_{114\text{-}137}T(X)_{139\text{-}269}H(X)_{271\text{-}280}R(X)_{282\text{-}284}R$ (claim 2);
- A transgenic maize plant comprising a plurality of the maize plant cells of claim 1, wherein expression of the polynucleotide renders the plant tolerant to an aryloxyalkanoate herbicide (claim 3);
- Tolerance to particular herbicides or herbicide classes (claims 4-6);
- A transgenic plant having a second herbicide resistance gene (claims 7, 8);
- Methods of controlling at least one weed in a field, wherein the field contains at least one plant of claim 6 and the methods require certain herbicide resistance genes or applying certain herbicides (claims 9-24, 26); and
- Seeds, plants, progeny, etc., comprising a plurality of the plant cells of claim 1 (claims 25, 27, 28).

4. Relevant Prosecution History

The ’283 patent was filed as U.S. Application No. 17/175,966 on February 15, 2021. It claims priority to a series of applications that originate from U.S. Provisional Patent Application No. 60/567,052, filed April 30, 2004, and PCT Application PCT/US2005/014737, filed May 2, 2005, including Application No. 15/288,406 (“the ’406 Application”), which issued as U.S. Patent No. 10,947,555 and is the subject of copending IPR2023-01036. Ex. 1002, cover.

During prosecution of the predecessor ’406 Application, the Office issued a November 13, 2018 Non-Final Office Action asserting that the pending claims (1) lacked written-description support for the claimed AAD-1 motif; (2) were obvious over US 2003/0041357 (“Jepson”; Ex. 1030) and GenBank Accession No: Q8KSC8 (“Kohler”; Ex. 1016); and (3) were anticipated by US 2016/0108422 (“Ellis”; Ex. 1017) and EP1740039B1 (European counterpart of WO ’437). Ex. 1008, COR-AAD1-00000267-78. The Office based its anticipation rejections on an alleged lack of priority to the earliest filing date. *Id.*, COR-AAD1-00000270-71.

On April 12, 2019, Corteva filed a Response and declaration by inventor Dr. Terry Wright traversing the rejection. *Id.*, COR-AAD1-00000457-74, -479-94. The Response asserted that the specification disclosed the “necessary common attributes possessed by … each member of the genus.” *Id.*, COR-AAD1-00000490. The Response also cited information in Examples 1 and 17 (unexpected results) as

evidence of the "surprising advantages that neither Jepson nor Kohler taught." *Id.*, COR-AAD1-00000491-92.

The Office issued a July 12, 2019, Final Office Action. *Id.*, COR-AAD1-00000496-515. Corteva then filed a Response and declaration by Dr. Satish Nair (a professor at the University of Illinois) explaining that there was "a clear single maximal alignment of the general motif with the AAD-1 proteins [SEQ ID NO: 9]" that was "readily apparent" to a skilled artisan. *Id.*, COR-AAD1-00000594, ¶ 9. In the next action, the Examiner withdrew the priority-based anticipation rejections. *Id.*, COR-AAD1-00000557-622, -629-41.

On September 9, 2020, Corteva filed a Response and second declaration by Dr. Wright.[3] *Id.*, COR-AAD1-00000655-70, -676-93. The Response explained that the "specification describes the common structure of the catalytic core of α-ketoglutarate-dependent dioxygenases." *Id.*, COR-AAD1-00000678-79. The Response also argued that the Federal Circuit's precedential *Ajinomoto* decision

[3] Petitioners assert that Dr. Wright's declarations are "irrelevant" to the issues of written description and priority. Pet., 32. But they then attempt to fault Dr. Wright for not disclosing the amino acid sequences used in his second declaration. *Id.*, 33. Either way, those sequences are provided herewith. *See* Ex. 2002 at 941-42.

supported the sufficiency of the specification's disclosure of common, function-correlated structural features. *Id.*, COR-AAD1-00000679-80.

The Office withdrew the written description and obviousness rejections and allowed the claims of the '406 Application on January 4, 2021. *Id.*, COR-AAD1-00003844, -4686-91. The Office credited the evidence of unexpected results, citing "the ability of the AAD-1 gene to produce herbicide tolerance in a transgenic plant cell to two distinct type[s] of herbicides." *Id.*, COR-AAD1-000003844.

During prosecution of the '283 patent, the Examiner reconsidered prior art submitted during prosecution of the predecessor '406 Application, including EP1740039, Jepson (Ex. 1030), Kohler (Ex. 1016), Saari 1999 (Ex. 1041), and Streber (Ex. 1043). The Examiner confirmed patentability of the pending claims without issuing any rejections. In the reasons for allowance, the Examiner concluded that the prior art did "not suggest that rdpA enzyme would degrade a phenoxy auxin herbicide nor that transforming a maize plant cell therewith would produce tolerance to both a phenoxy auxin herbicide and an (*R*)-aryloxyphenoxypropionate herbicide." Ex. 1010, COR-AAD1-00005670, -00006195-211, -00006177.

III. Level of Ordinary Skill in the Art

Petitioners propose a vague level of ordinary skill in the art: an "advanced degree in a relevant [unspecified] discipline and several years of advanced academic (*e.g.*, post-doc or higher) and/or professional experience" in an unspecified field, with background knowledge focused on protein biochemistry, aspects of enzymology, and amino acid sequences. Pet., 18.

The challenged claims, however, are more broadly directed to transgenic plants and plant cells, and also include features relating to plant seeds and progeny, herbicide tolerance, methods of controlling weeds, and herbicide-resistance gene stacking. *Supra* § II(B)(3). Despite purporting to provide opinions on such subject matter, Petitioners' declarant, Dr. Hausinger, appears to have no meaningful background in these technical areas. Ex. 1054, ¶¶ 9-19. Petitioners' vague definition and failure to address these aspects of the claims in their proposed level of ordinary skill further demonstrates their failure to meet their burden at institution on their proposed obviousness grounds. *See infra* § V(B)(1); *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966) (the level of ordinary skill in the "pertinent art" must be resolved).

Corteva reserves the right to define an appropriate level of ordinary skill, if necessary, later in this proceeding.

IV. Claim Construction

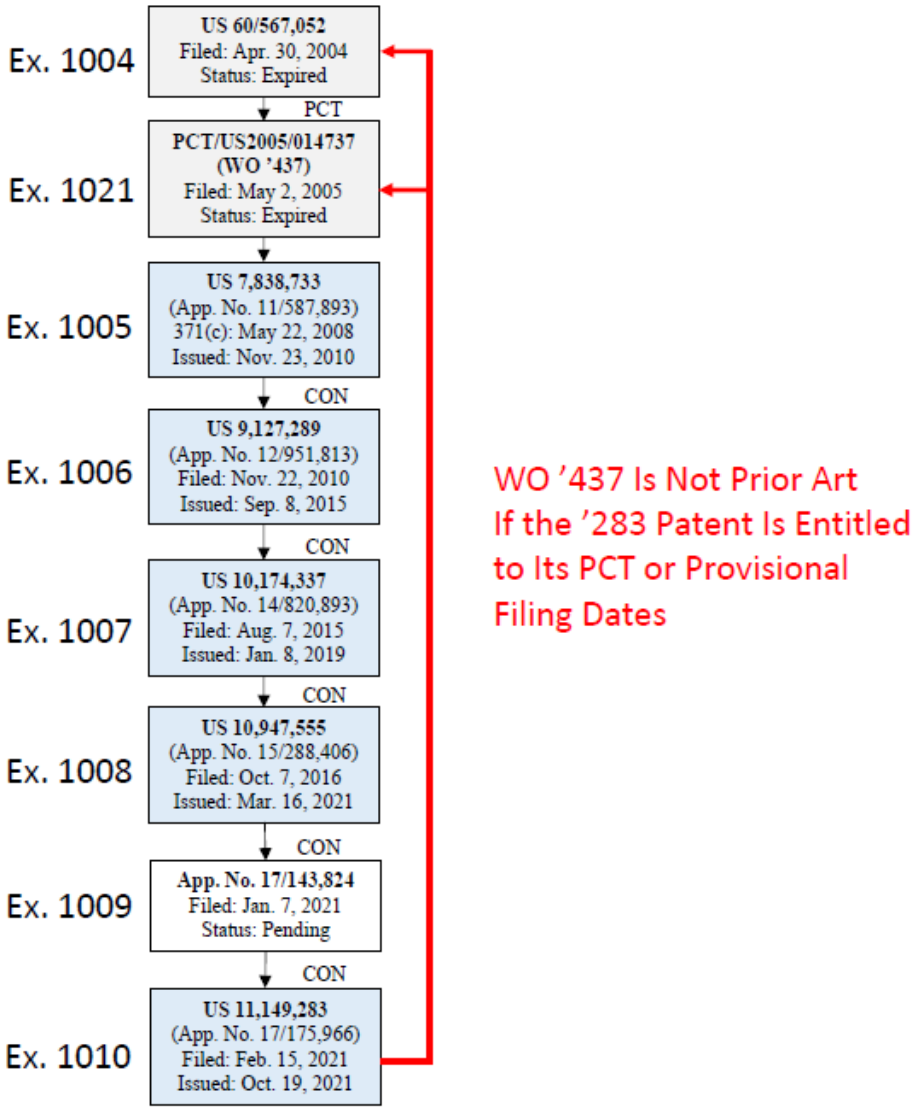
Petitioners propose no specific constructions of any terms of the ’283 patent claims.[4] For purposes of this POPR, Corteva also does not propose any specific constructions at this time.

V. Petitioners Have Not Established a Reasonable Likelihood that Any Challenged Claim Is Unpatentable

A. Grounds IA and IB: Petitioners’ Written Description-Based Priority Challenge Fails to Establish that WO ’437 Is Prior Art

Grounds IA and IB, asserting anticipation and obviousness based on the published PCT application within the ’283 patent’s priority chain (i.e., WO ’437, published November 17, 2005), depend on Petitioners’ written description-based priority challenge. The Petition, however, fails to establish that any challenged claim of the ’283 patent lacks priority benefit of the Priority Applications (Exs. 1004-1009, 1021), including the PCT application, filed May 2, 2005, and provisional application, filed April 30, 2004.

[4] In the copending district court litigation, the court issued a *Markman* memorandum opinion and order adopting Corteva’s proposed constructions and rejecting Bayer’s constructions for all disputed claim terms. *See Corteva Agriscience LLC v. Monsanto Co.*, No. 1:22-cv-01046-GBW, D.I. 191, 192 (D. Del. Sept. 18, 2023).



The written-description requirement is met when the specification "*reasonably conveys* to those skilled in the art that the inventor had possession of the claimed subject matter." *Ariad*, 598 F.3d at 1351. The "hallmark" of written description is disclosure, which must be read from a skilled person's perspective. *Id.*; *Sandoz Inc. v. Biogen MA Inc.*, PGR2022-00054, Paper 16, 25-27 (PTAB Feb. 2, 2023) ("[T]he state of knowledge is relevant in evaluating sufficiency of written-

description support in the specification."). For genus claims, the written-description requirement is satisfied when the specification discloses a representative number of species within the scope of the genus or structural features common to the members of the genus such that a skilled person can visualize or recognize the members of the genus. *Ariad*, 598 F.3d at 1350.

The Petition presents a mix of common structure, representative species, and literal disclosure arguments in its priority challenge. Pet., 23-41. As detailed below, those written-description arguments are legally and factually flawed. Petitioners have no other arguments for challenging priority other than written description, as they do not dispute enablement of the full scope of the '283 patent claims.

Petitioners thus have failed to meet their burden of establishing that the inventors' own WO '437 publication qualifies as prior art and this deficiency is dispositive of Grounds IA and IB. 35 U.S.C. § 102(a)(1) (AIA) (a reference can only be prior art if patented or described in a printed publication "before the effective filing date"); *see also* 35 U.S.C. § 102(b)(1)(A) (a disclosure by the inventors one year or less before the effective filing date is not prior art).

1. Petitioners' Analysis of Common Structure Is Incorrect Under *Ariad* and *Ajinomoto*

As the Federal Circuit has held, disclosure of "structural features common to the members of the genus so that one of skill in the art can 'visualize or recognize' the members of the genus" provides adequate written description. *Ajinomoto*, 932 F.3d at 1358-59 (quoting *Ariad*, 598 F.3d at 1350). Petitioners fail to meet their burden of establishing that the Priority Applications' disclosure of common, function-correlated AAD-1 protein structure is insufficient.

a. Petitioners Fail to Show Lack of Disclosure of the AAD-1 Motif

Petitioners' argument that the Priority Applications disclose only a prior art αKG motif, rather than the claimed AAD-1 motif, fails for several reasons. Pet., 24-30.

First, each of the Priority Applications discloses the amino acid sequence of RdpA as SEQ ID NO: 9 (AAD-1 (v1)), as well as where to identify the active site motif residues in enzymes like RdpA. Ex. 1004, ¶¶ [0059], [0040], SEQ ID NO: 9; Exs. 1005-1009, 1021, ¶¶ [0085], [0050], SEQ ID NO: 9 (*see e.g.,* stamped pages 255-57 in Ex. 1005). Petitioners present no challenge to Dr. Nair's explanation in his declaration submitted during prosecution that there is only *one fit* for the αKG motif in SEQ ID NO: 9—i.e., the claimed AAD-1 motif—and that it was "readily apparent" to a skilled artisan. Ex. 1008, COR-AAD1-00000594, ¶ 9 ("As there is a

clear single maximal alignment of the general motif with the AAD-1 proteins (SEQ ID NO: 9 only contains a single instance of the tripeptide HX(D/E)), the specific AAD-1 motif … is readily apparent….").

Second, Petitioners concede that a skilled artisan *would have recognized* the αKG motif residues in SEQ ID NO: 9 (i.e., the claimed AAD-1 motif), where each of the required residues and their relative spacing are literally described. *Ariad*, 598 F.3d at 1351 (written description is analyzed from the perspective of a skilled artisan). Petitioners cite no case holding such literal disclosure insufficient. Petitioners, for example, acknowledge:

- "*[T]he POSA would have appreciated that RdpA's amino acid sequence shares* certain characteristics with other αKG dioxygenases like TfdA, including *the consensus, prior art αKG dioxygenase motif*…." Ex. 1054, ¶ 214.
- "*[T]he prior art already taught[] that RdpA shares the canonical active site residues characteristic of αKG dioxygenases*." *Id.*, ¶ 95.
- "[T]he POSA would have expected to see similarities between RdpA/AAD-1 and other αKG dioxygenases, *including the defined residues in the consensus motif*…." *Id.*, ¶ 89.
- "Corteva '437 also *discloses and claims proteins having the claim 1 AAD-1 motif*…. SEQ ID NO[s]: 9-10 have 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." Pet., 44.

Third, before the filing of Corteva's PCT application in 2005, skilled artisans had already identified where the αKG general motif residues are located in the RdpA/SEQ ID NO: 9 sequence (i.e., the claimed AAD-1 motif). Schleinitz 2004, for example, discloses that "[t]he functionally important motif $HX(D/E)X_{23\text{-}26}(T/S)X_{114\text{-}183}HX_{10\text{-}13}R/K$ . . . *is present in* . . . *RdpA*." Ex. 1042, 5362. Accordingly, not only have Petitioners conceded that a skilled artisan would have recognized the AAD-1 motif in SEQ ID NO: 9—their evidence submitted with the Petition confirms that skilled artisans in fact had *already done so*.[5] *Biogen*, PGR2022-00054, Paper 16, 25-27 ("[T]he state of knowledge is relevant in evaluating sufficiency of written description support in the specification.").

Petitioners' position therefore boils down to a legally flawed argument that the Priority Applications did not contain an *in ipsis verbis* description of the AAD-1

[5] Petitioners fail to reconcile their argument that a "convoluted analysis" would be necessary to identify the AAD-1 motif in SEQ ID NO: 9 (*see* Pet., 35) with their admissions that a skilled artisan would have recognized the αKG motif residues in RdpA (i.e., the AAD-1 motif) and Schleinitz's disclosure that those motif residues had *already* been identified.

motif outside of SEQ ID NO: 9. The law, however, does not require such disclosure. *Martin v. Johnson*, 454 F.2d 746, 751 (CCPA 1972) (rejecting written-description challenge related to a structural formula, explaining that "the description need not be in *ipsis verbis*"); *Union Oil Co. of Cal. v. Atl. Richfield Co.*, 208 F.3d 989, 1000 (Fed. Cir. 2000) ("[T]he invention claimed does not have to be described *in ipsis verbis* in order to satisfy the description requirement of § 112….").

Fourth, Petitioners incorrectly seek to erase the "background knowledge" of a skilled artisan as purportedly irrelevant to written description. Pet., 31. As the Board has explained, however, "controlling case law … holds that the state of knowledge *is relevant* in evaluating sufficiency of written description support in the specification," including the "existing knowledge in the particular field [and] the extent and content of the prior art." *Biogen*, PGR2022-00054, Paper 16, 25-27 (quoting *Ariad*, 598 F.3d at 1351). Petitioners' legal error is particularly glaring with respect to claim 2, which recites an additional arginine residue in the claimed motif. Pet., 34; Ex. 1002, claim 2. Petitioners do not dispute that SEQ ID NO: 9 expressly discloses that arginine residue, or that a skilled artisan would have recognized its importance as such skilled artisans had done in Hotopp 2002 (Ex. 1029). *See* Pet., 34. Thus, this case is unlike *Rivera* or *L.A. Biomedical*, which both involved subject matter that was only allegedly *obvious* from the specification, rather than disclosed. *Rivera v. ITC*, 857 F.3d 1315, 1322-23 (Fed. Cir. 2017); *L.A. Biomed. Rsch. Inst. at*

Harbor-UCLA Med. Ctr. v. Eli Lilly & Co., 849 F.3d 1049, 1058 (Fed. Cir. 2017). Refuting Petitioners' position, *Rivera* confirms that it is proper for a skilled artisan's knowledge "to *inform* what is actually in the specification," such as appreciating the significance of the arginine in SEQ ID NO: 9. 857 F.3d at 1322.

Fifth, Petitioners' arguments based on Patent Owner's amendment to the specification during prosecution of the '406 Application and the '283 patent are also misplaced. *See* Pet., 28. Petitioners omit that Patent Owner's amendment originally responded to the Examiner's objection under MPEP § 608.01(o). Ex. 1008, COR-AAD1-00000271, -480, -488. Section 608.01(o) instructs examiners to require antecedent basis in the specification for nomenclature used in the claims to provide clarity for, e.g., claim construction purposes. MPEP § 608.01(o). It thus specifies that "the application should be scrutinized not only for new matter but also for new terminology." *Id.* (recognizing that, with claim language, "an applicant is *not limited* to the nomenclature used in the application as filed"). The Examiner's issuance and withdrawal of a § 608.01(o) objection during prosecution of the '406 Application confirms that the amendment was proper and did not constitute new matter in view of the specification's original disclosures. Ex. 1008, COR-AAD1-00000498. Patent Owner thus properly carried the amendment forward in prosecution of the '283 patent. Ex. 1010, COR-AAD1-00006134-42. Accordingly, Petitioners are merely

retreading old ground that the Examiner already addressed. *See also infra* § VI (addressing 35 U.S.C. § 325(d)).

b. Petitioners Disregard the 85% Sequence Identity Limitation

Petitioners' common-structure arguments are also fatally flawed because they fail to meaningfully address the 85% sequence identity limitation for the AAD-1 proteins recited in the challenged claims. The specification discloses that preferred proteins of the invention may have 85% (or higher) sequence identity and have the same or similar activity. Ex. 1002, 37:16-35; Ex. 1004, ¶ [0116]; Exs. 1005-1009, 1021, ¶ [0142]. The May 2, 2005, PCT and later Priority Applications also disclose 85% and greater sequence identity among αKG-dependent dioxygenases as a "highly identical" level of sequence identity, and that such sequences having "high homology would be expected to retain similar properties." Ex. 1002, 44:5-8; Exs. 1005-1009, 1021, ¶ [0171]. Petitioners nowhere address these important disclosures in the specification. *See* Pet., 30-31, 38-41.

Instead, Petitioners improperly address the at least 85% sequence identity limitation in isolation, alleging that three exemplary proteins having "nearly 100% sequence identity"—i.e., AAD-1 v1, v2, and v3—are not representative of a genus of AAD-1 proteins having 85% or greater sequence identity. Pet., 38-39. But a sufficient description requires "the disclosure of *either* a representative number of

species … or structural features common to the members of the genus"—not both. *Ajinomoto*, 932 F.3d at 1358-59 (quoting *Ariad*, 598 F.3d at 1350). Here, the at least 85% sequence identity and AAD-1 motif limitations are inseparable and must be addressed together in a common-structure analysis, as both features limit the scope of the claims and are correlated to function.

Petitioners also raise a literal-disclosure argument, contending that the express disclosure of at least 85% sequence identity in the Priority Applications is insufficient based on a "laundry list" theory. Pet., 39; *see* Ex. 1004, ¶ [0116]; Exs. 1005-1009, ¶ [0142]. Here again, Petitioners fail to meet their burden. As *Snitzer v. Etzel* held, the express listing of a claimed element represents a literal disclosure, and thus no blaze marks are required. 465 F.2d 899, 902-03 (CCPA 1972) (holding that listing of a Yb ion for use in a claimed laser within a broader list was sufficient, as "we see no reason to hold that which is plainly described not to be described"); *In re Driscoll*, 562 F.2d 1245, 1249-50 (CCPA 1977). Consistent with this longstanding authority, the Board has rejected similar literal-disclosure arguments directed to sequence identity limitations based on listings of sequence identities. *See Lifescan Glob. Corp. v. Ikeda Food Rsch., Ltd.*, PGR2019-00032, Paper 11, 25 (PTAB Aug. 15, 2019).

Petitioners' cited cases do not hold to the contrary. *See* Pet., 30, 39. In *Regents*, the patentee asserted written-description support by tracing a "maze-like" path

through numerous original claims in a provisional application—not literal description of options within a single list, as here. *Regents of Univ. of Minn. v. Gilead Scis., Inc.*, 61 F.4th 1350, 1357-58 (Fed. Cir. 2023). *Purdue* also does not support Petitioners' position. Pet., 39. There, the patentee claimed a gelling agent comprising a combination of two or more compounds from a list that did not identify or describe any particular combination or mixture of those compounds. *Purdue Pharma L.P. v. Iancu*, 767 F. App'x 918, 920, 924 (Fed. Cir. 2019).

Regardless, to the extent any blaze-mark requirement applies, the Priority Applications contain more than ample disclosure. They disclose a genus of AAD-1 proteins and genes as the "invention," referring to AAD-1 more than ***four hundred times*** throughout the specification. *See, e.g.*, Ex. 1002, 20:29-31 ("[P]roteins and genes of the subject invention are referred to herein as AAD-1 proteins and genes."); Ex. 1004, ¶ [0069], Examples 2-4, 6-9, 12-15, 17, 19-20; Exs. 1005-1009, 1021, ¶ [0095], Examples 2-4, 6-9, 12-15, 17, 19-20, 24-26. For such a genus, the specification expressly lists minimum sequence identities including 85%, as claimed, for variant proteins "having the same or similar activity of the exemplified

proteins." Ex. 1002, 37:16-36; Ex. 1004, ¶ [0116]; Exs. 1005-1009, 1021, ¶ [0142].[6] The specification further calls out 85% sequence identity as a "highly identical" level of identity within this technical field that would lead one to expect "similar properties." Ex. 1002, 44:5-8; Exs. 1005-1009, 1021, ¶ [0171]. The law requires no further blaze marks than these, and indeed Petitioners cite no authority to the contrary. Accordingly, Petitioners' blaze-marks written-description challenge fails as a matter of law.

c. Petitioners Fail to Establish that the Disclosed Common Structures Lack Correlation to the Claimed Function

Petitioners further fail to meet their burden of establishing that the Priority Applications' disclosure of common structural features lacks a reasonable correlation to the claimed dual enzymatic activity of degrading the two specified classes of herbicides (phenoxy auxins and FOPs). As *Ajinomoto* explained, adequate written description does not require a *perfect correspondence* between the members of the genus and a common structure. 932 F.3d at 1360. Rather, the Federal Circuit has "spoken more modestly of a '*correlation* between structure and function.'" *Id.*

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[6] Petitioners' assertion that there are more than "1,000 possible combinations" of sequence identity values (Pet., 12) is exactly the type of "hopelessly exaggerated" argument *Snitzer* rejected. 465 F.2d at 903.

(emphasis in original) (quoting *Ariad*, 598 F.3d at 1350). Although Corteva addressed *Ajinomoto* during prosecution of the '406 Application (Ex. 1008, COR-AAD1-00000677-78), Petitioners never cite *Ajinomoto*, much less attempt to apply its legal standard for function-correlated structure to the challenged claims.

Petitioners concede that the five conserved residues of the AAD-1 motif in SEQ ID NO: 9 correspond to "canonical active site residues" that are important to enzymatic function. Ex. 1054, ¶ 95 (acknowledging that "the five or six active site residues required by the consensus motif and AAD-1 motifs *are important to the function*"), ¶ 53 ("*critical interactions* exist between the enzyme's active site and the carboxyl end of the substrate"); Ex. 1004, ¶ [0059]; Exs. 1005-1009, 1021, ¶ [0085] (Priority Applications disclosing that the "active site" is "*essential for catalytic activity*"). Skilled artisans had also recognized that the active site motif "is present in . . . RdpA" and described it as "*functionally important*" and "*functionally essential*." Ex. 1042, Abstr., 5357, 5362. The Priority Applications further disclose that 85% is a "highly identical" level of sequence identity. Ex. 1002, 44:5-8; Exs. 1005-1009, 1021, ¶ [0171]. Sequences with such high identity to an input sequence (i.e., AAD-1) "*would be expected to retain similar properties*"—a disclosure of the specification that Petitioners nowhere address. Ex. 1002, 44:5-8; Exs. 1005-1009, 1021, ¶ [0171]. The law requires no more, as these common structural features would permit a skilled artisan to visualize or recognize the AAD-1

proteins recited in the claims by their AAD-1 active site motif and high homology to SEQ ID NO: 9, and those features are correlated with the claimed enzymatic activity. *Ajinomoto*, 932 F.3d at 1358-60 (affirming adequate written description based on a link between a consensus sequence and promoter strength).

In *Ajinomoto*, the Federal Circuit also held that a skilled artisan could "identify more potent [claimed] promotors given the well-known link between consensus sequence and promoter strength" as further supporting adequate disclosure of common structural features. 932 F.3d at 1359-60. Here, this factor also weighs against Petitioners' priority challenge, as Petitioners nowhere dispute that the specification enables a skilled artisan to make and use AAD-1 proteins across the full scope of the challenged claims.

Notwithstanding their acknowledgement of the importance of the claimed active site motif to the claimed function, Petitioners assert that the AAD-1 motif is insufficient because it represents only 5 or 6 amino acids within the claimed AAD-1 sequences. Pet., 30. But the law does not require disclosure of *all amino acids* relevant to function, which would amount to the "perfect correspondence" standard that *Ajinomoto* held was not legally required. 932 F.3d at 1360. Indeed, the Federal Circuit and the Board have credited disclosures of partial, function-correlated amino acid sequences as sufficient to meet the written-description requirement. *See, e.g.*, *id.* at 1359-61 (crediting a "consensus sequence" as sufficient disclosure); *Lifescan*,

PGR2019-00032, Paper 11, 29 (rejecting written-description challenge where the evidence suggested that a six-amino-acid sequence or a close variation of it was necessary for activity). Further, Petitioners' narrow focus on the AAD-1 motif fails to account for the 85% sequence identity limitation, which is a "highly identical" level of sequence identity described as correlated to having similar properties. *See* Exs. 1005-1009, 1021, ¶¶ [0085], [0142], [0171]; Ex. 1004, ¶¶ [0059], [0116]; *Ex parte Campbell*, No. 2021-000865, Decision on Appeal, 15 (PTAB July 20, 2021) (finding claims with a structural 90% sequence identity limitation adequately described).

Petitioners also erroneously focus their structure-function arguments on the αKG motif residues in general terms, rather than on the specific AAD-1 motif claimed. *E.g.*, Pet., 26 (asserting that "many proteins that have the prior-art motif do not have the claimed functional activities"). Such arguments address only proteins *outside* the scope of the claims, which have neither the AAD-1 motif residues at their required relative spacing nor at least 85% sequence identity to SEQ ID NO: 9, as claimed. *Campbell*, No. 2021-000865, Decision on Appeal, 15 (reversing written-description rejection based on the Examiner's failure to appropriately address the invention *as claimed*); *Ajinomoto*, 932 F.3d at 1360 (rejecting challenger's argument that failed to address the "genus at issue" in the claims).

Petitioners' argument that other amino acid residues outside the AAD-1 motif may also be necessary for the claimed activity is misplaced. Petitioners, for example, contend that an additional arginine residue in the claim 2 motif is important, that some proteins having the AAD-1 motif may be insoluble, and that other residues in the AAD-1 sequence later identified in 2019 are also important.[7,8] Pet., 32-33, 37-38. As in *Ajinomoto*, however, Petitioners' allegations at most seek to establish that proteins having the AAD-1 motif do not *always* have the claimed function (the specified dual enzymatic activity). *Ajinomoto*, 932 F.3d at 1360 (criticizing challenger's evidence as "at most establish[ing] that, starting with the consensus sequence, deviations … do not *always* decrease promoter strength" (emphasis in original)). The law, however, "does not require a perfect correspondence between the members of the genus and the asserted common structural feature"—only a more modest *correlation* between structure and function is required. *Id.*

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[7] Protein variants and insolubility have been a focus of Petitioners' counterclaims in the copending district court litigation. *See* Exs. 2002-2003. Protein sequences and analyses have also been submitted as Exs. 2004-2011.

[8] Petitioners' reliance on Ex. 1019 fails to address AAD-1 proteins specifically, much less AAD-1 proteins having the conserved AAD-1 motif and at least 85% sequence identity to SEQ ID NO: 9, as recited in the challenged claims. Pet., 37-38.

Here, there is no dispute that the AAD-1 motif residues are important to the claimed dual enzymatic activity, and the law requires no further description. *Id.*; Ex. 1042, Abstr., 5357, 5362; Ex. 1054, ¶ 95; Ex. 1002, 44:5-8; Ex. 1004, ¶ [0059]; Exs. 1005-1009, 1021, ¶¶ [0085], [0171]; *Lifescan*, PGR2019-00032, Paper 11 at 29 (rejecting written-description argument where the evidence suggested that a six-amino-acid sequence or close variation thereof was common to a claimed genus and was necessary for the claimed activity); Ex. 1035, 1358 (Dr. Hausinger reporting in his work outside this IPR that the "active site" is "*the most conserved and structurally accurate part of the RdpA* and SdpA models").

Accordingly, for at least these reasons, Petitioners fail to meet their burden of establishing that WO '437 is prior art, as their legally flawed priority challenge fails in view of the disclosed common, function-correlated AAD-1 motif and minimum 85% sequence identity features of all challenged claims.

2. Petitioners' Numerosity Theory Fails to Establish that AAD-1 and Its Variants Are Nonrepresentative of the Claimed Genus

Petitioners' priority challenge also fails for an independent reason: Petitioners have not met their burden of establishing that the Priority Applications' disclosed species are nonrepresentative of the claimed genus. *Ajinomoto*, 932 F.3d at 1358-59 (disclosure of a "representative number of species falling within the scope of the

genus" satisfies the written-description requirement (quoting *Ariad*, 598 F.3d at 1350)).

The challenged claims are directed to, among other things, *transgenic maize plants and plant cells* comprising a recombinant polynucleotide that encodes an AAD-1 protein. Ex. 1002, claim 1. The '283 patent discloses extensive examples of transgenic plants and plant cells and related testing, including in maize. *See supra* § II(B)(2). Petitioners are thus incorrect in characterizing the '283 patent as only allegedly disclosing three AAD-1 protein examples, reflecting their failure to consider the claimed subject matter and the specification's disclosures as a whole. *E.g.*, Pet., 30-31, 38; *Sandoz Inc. v. Boehringer Ingelheim Int'l GmbH*, PGR2022-00037, Paper 13 at 7 (PTAB Feb. 23, 2023) (denying institution for failure to analyze enablement of the claimed subject matter "as a whole").

Petitioners' assertion that the disclosed AAD-1 (v1), (v2), and (v3) enzymes are insufficiently representative of the genus of AAD-1 enzymes is also incorrect. Petitioners do not dispute that the specification contains examples of transgenic maize plants that express an AAD-1 enzyme meeting the structural and functional (i.e., dual enzymatic activity) requirements of the claims. *See supra* § II(B)(2). Petitioners thus have not established that AAD-1 (v1), (v2), and (v3) fail to represent the structures and functions of the genus of AAD-1 proteins encoded by the recombinant polynucleotides of the claimed transgenic plants and plant cells.

Indeed, Petitioners notably fail to identify any written-description decision holding unpatentable structurally defined claims that recite a high level of sequence identity—much less with an active site motif limitation—as the ’283 patent claims have here. *Regents of Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997) (“[S]uch a formula is normally an adequate description of the claimed genus.”). Petitioners instead present a numerosity theory that the Board and courts have rejected. *See* Pet., 30 (alleging that the AAD-1 motif “cover[s] at least 20^{44} amino acid sequences”).

In *Ex parte Campbell*, for example, the Board reversed a written-description rejection that was based on an allegation—like Petitioners’ here—that there were an essentially “unlimited number” of antibodies encompassed by claims requiring 90% sequence identity to a particular amino acid sequence. No. 2021-000865, Decision on Appeal, 4-5. The Board found that the claimed antibodies were “not exclusively claimed functionally, but are also claimed structurally” by the 90% sequence identity limitation. *Id.*, 15. Similar to the ’283 patent’s description of AAD-1 (v1), (v2), and (v3) enzymes, the Board found that the specification’s disclosure of two exemplary antibodies provided sufficient written-description support. *Id.*; *see also Alcon Rsch. Ltd. v. Barr Lab’ys, Inc.*, 745 F.3d 1180, 1190-91 (Fed. Cir. 2014) (rejecting written-description argument that the claims encompassed “innumerable” species); *Bilstad v. Wakalopulos*, 386 F.3d 1116, 1122, 1124, 1126 (Fed. Cir. 2004) (vacating Board’s

decision that a claimed range up to infinity lacked written-description support, explaining that it was "of no moment" that a claim may be broader than an embodiment disclosed in the specification); *Sandoz Inc. v. Boehringer Ingelheim Int'l GmbH*, PGR2022-00037, Paper 11 at 22, 26, 28-29 (PTAB Nov. 7, 2022) (denying institution and rejecting petitioner's argument that claims encompassing "millions of potential formulations" lacked adequate written description).

Similarly, in *Lifescan*, the Board declined to analyze written description and enablement according to the number of sequences encompassed by a limitation requiring 90% homology to a sequence of 593 amino acids, which the petitioner argued encompassed 5 x 10^{76} unique sequences. PGR2019-00032, Paper 11, 21, 18-19. The Board noted that the petitioner's argument, like Petitioners' here, inappropriately focused on the number of sequences encompassed by the 90% limitation. *Id.*, 28 ("Our concern with this approach is that the Federal Circuit has expressly declined to establish 'bright line rules….'" (quoting *Ariad*, 598 F.3d at 1351-52)). The Board instead found that the evidence suggested that a six-amino-acid sequence was a structural feature common to all members of the claimed genus,

supporting possession of the genus. *Id.*, 29. Thus, in *Lifescan*, the Board rejected a written-description argument that parallels Petitioners' position here.[9]

Petitioners' numerosity argument also overlooks the specification's express disclosure that enzymes having at least 85% sequence identity are "highly identical" and "expected to retain similar properties"—disclosures Petitioners never address. Ex. 1002, 44:5-8, 37:16-35; Exs. 1005-1009, 1021, ¶¶ [0142], [0171]. This described and claimed level of at least 85% sequence identity exceeds the level of identity that others in the field used to define related enzymes. *See* Ex. 1023, 5189 (Dr. Hausinger describing "closely related" enzymes as having "~30% sequence identity" in his work outside this IPR).

This case is thus distinguishable from the *AbbVie* decision Petitioners rely on (Pet., 31), where the claims encompassed *all antibodies regardless of amino acid sequence* that exhibited the claimed activity, including an antibody having only 50% sequence identity. *AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1292, 1301 (Fed. Cir. 2014) (the "patents do not describe any common

[9] In *Lifescan*, the Board appears to have granted institution based solely on an enablement ground where the challenged claim did not recite the common six-amino-acid sequence, deemed to be an "essential" feature. *Id.*, 17-18. Here, by contrast, the AAD-1 motif is expressly recited in all claims of the '283 patent.

structural features of the claimed antibodies"). Nor was any evidence presented in *AbbVie* regarding any motif, consensus sequence, or other common structure. Petitioners thus fail to establish that the disclosed AAD-1 proteins are not representative of AAD-1 proteins with 85% or higher amino acid sequence identity (i.e., "highly identical" proteins) that also have the AAD-1 motif.

Accordingly, Petitioners have failed to meet their burden of establishing that any challenged claim lacks written-description support in the Priority Applications. WO '437 therefore does not qualify as prior art, and Petitioners have failed to demonstrate a reasonable likelihood of prevailing as to any challenged claim in Grounds IA and IB.

B. Grounds IIA and IIB: Petitioners Have Not Established a Reasonable Likelihood that Any Challenged Claim Is Unpatentable for Obviousness

1. Petitioners' Obviousness Theory Is Legally Deficient

An obviousness analysis requires factual determinations of four general types: (1) the scope and content of the prior art; (2) the differences between the claimed invention and the prior art; (3) the level of ordinary skill in the pertinent art; and (4) any objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966). The *Graham* factors are mandatory: *all* of them must be considered by the trier of fact. *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 546 (Fed. Cir. 1998). As the Supreme Court held in *KSR*, "the [*Graham*] factors continue to define the

inquiry that controls." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406-07 (2007); *Graham*, 383 U.S. at 36 (warning courts against "slipping into use of hindsight").

Petitioners, however, fail to conduct a legally adequate *Graham* analysis. *See, e.g.*, Pet., 54-56. To illustrate, their cursory analysis in the Petition does not address *any* of the following nonexhaustive differences between the challenged claims and the asserted references. *See* Pet., 54-56, 58-59.

1. The Saari References (Exs. 1040, 1041) do not mention RdpA, much less "single[] out" RdpA as Petitioners contend. Pet., 55. Nor do they "refer to [it] as the TfdA-like gene from *S. herbicidivorans*." *See id*. Instead, the Saari References refer to a "tfdA-like gene" in *A. denitrificans*, which is a different gene from a different bacterium. Ex. 1041, 422 ("a tfdA-like gene is present in A. denitrificans"); Ex. 1040, 93 ("A potential application for *A. denitrificans* or the *tfdA*-like gene it contains…."); Ex. 1041, 427; Ex. 1054, ¶ 109 (Dr. Hausinger acknowledging that the *A. denitrificans* enzyme produced by the TfdA-like gene is different than RdpA). While the Saari References refer to studies with *S. herbicidivorans* as indicating that this bacterium may produce two αKG-dependent dioxygenases, they fail to mention RdpA and do not disclose (1) that RdpA has activity on FOP herbicides, (2) transforming maize cells, or (3) the claimed

herbicide tolerances against phenoxy auxin and FOP herbicides as compared to an untransformed maize plant cell, as required by all claims of the ’283 patent.

2. Schleinitz (Ex. 1013) does not disclose (1) that RdpA has any activity on FOP herbicides, (2) transforming maize cells, or (3) the claimed herbicide tolerances against phenoxy auxin and FOP herbicides as compared to an untransformed maize plant cell, as required by all claims of the ’283 patent.
3. Streber (Ground IIA, Ex. 1043) and Jepson (Ground IIB, Ex. 1030) do not disclose (1) RdpA, (2) that RdpA has any activity on FOP or phenoxy auxin herbicides, (3) transforming maize cells, or (4) the claimed herbicide tolerances against phenoxy auxin and FOP herbicides as compared to an untransformed maize plant cell, as required by all claims of the ’283 patent.

Accordingly, the cited references collectively fail to disclose at least three features of the challenged claims: (1) an AAD-1 protein’s dual herbicide degrading activity against FOP and phenoxy auxin herbicides, (2) transforming maize plant cells (much less RdpA-transformed maize cells), and (3) the claimed herbicide tolerances against phenoxy auxin and FOP herbicides as compared to an untransformed maize plant cell. Because Petitioners do not adequately address these

differences between the challenged claims and the prior art, Grounds IIA and IIB are legally deficient under the Board's rules and Supreme Court precedent. 37 C.F.R. § 42.104(b)(4) ("The petition *must specify where each element of the claim is found* in the prior art…."); *KSR*, 550 U.S. at 406-07; *ATD Corp.*, 159 F.3d at 546; *Apple Inc. v. ContentGuard Holdings, Inc.*, IPR2015-00443, Paper 9 at 10 (PTAB July 9, 2015).

In *ContentGuard*, for example, the Board denied institution where the petition failed "to identify sufficiently the differences between any claim of the [challenged] patent and the asserted prior art references." IPR2015-00443, Paper 9, 10. Rather than performing the required *Graham* analysis, the petition "obscure[d] any comparison of the individual prior art references to the claim limitations" and did "not explain with any particularity which claim limitations [were] absent from the asserted references." *Id.*, 10-11. The Board therefore denied institution. *Id.*; *Adaptics Ltd. v. Perfect Co.*, IPR2018-01596, Paper 20, 20 (PTAB Mar. 6, 2019) (informative) (denying institution where the Petition failed "to specify what Petitioner regards as the difference(s) between [the prior art] and the challenged claims"). The same rationale supports denying institution here.

Instead of a proper *Graham* analysis, Petitioners present a hindsight-driven argument that obfuscates the scope and content of the asserted references and their differences from the challenged claims. Petitioners begin by selectively addressing

only a *subset* of claim 1's limitations in an effort to combine the references. Pet., 54-55. Then they circle back to contend that the "*remaining limitations* are obvious" based on that purported combination. Pet., 56. This piecemeal analysis not only contravenes *Graham*—it violates § 103's requirement to analyze the claimed subject matter "as a whole." *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1086 (Fed. Cir. 2008) (obviousness is assessed as to "the subject matter as a whole, not separate pieces of the claim."). Indeed, the Board has repeatedly rejected this type of "piecemeal" analysis as inconsistent with the statute and *Graham*. 35 U.S.C. § 103(a); *Zhejiang Crystal-Optech Co. v. Viavi Sols. Inc.*, IPR2022-01184, Paper 8, 9, 27 (PTAB Feb. 7, 2023); *DIRECTTV, LLC v. Qurio Holdings, Inc.*, IPR2015-02006, Paper 6 at 8-9 (PTAB Apr. 4, 2016); *ContentGuard*, IPR2015-00443, Paper 9 at 10-11.

Grounds IIA and IIB thus present no basis for institution because they are legally deficient under *Graham* and § 103.

2. Petitioners Fail to Establish that the Asserted References Disclose All Limitations of the Claims

Grounds IIA and IIB are also deficient because the asserted references, even if combined, have not been shown to disclose all limitations of the challenged claims. This is a threshold requirement for establishing obviousness, as the Federal Circuit has repeatedly held that courts should "consider motivation and reasonable

expectation of success *only if* all the elements of an invention are found in a combination of prior art references." *Par Pharm., Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1194 (Fed. Cir. 2014) (quoting *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1164 (Fed. Cir. 2006)); *see also Dome Patent L.P. v. Lee*, 799 F.3d 1372, 1380 (Fed. Cir. 2015).

As discussed above, Petitioners fail to identify any prior art disclosing multiple limitations of claim 1, including (1) RdpA's dual activity on FOP and phenoxy auxin herbicides, (2) transforming maize cells (much less RdpA-transformed maize cells), and (3) the claimed herbicide tolerances against phenoxy auxin and FOP herbicides as compared to an untransformed maize plant cell. None of these features are disclosed in the Saari References, Schleinitz, Streber, or Jepson. Nor do Petitioners contend otherwise. *E.g.*, Ex. 1054, ¶ 219 (Petitioners conceding that the prior art "did not report testing of RdpA on (*R*)-aryloxyphenoxypropionate substrates").

Indeed, the Petition identifies no prior art disclosure of RdpA having dual activity—under *any* circumstances—against phenoxy auxin herbicides such as 2,4-D and the distinct class of FOP herbicides, as required by all challenged claims. *See* Pet., 55-57. Instead, after improperly skipping ahead to assert motivation and reasonable expectation of success based only on a *subset* of claim limitations, the Petition presents a single conclusory sentence asserting that the "recited

aryloxyalkanoate dioxygenase activities are inherent properties of RdpA." Pet., 56. Petitioners' conclusory inherency theory is legally flawed and factually unsupported. *KSR*, 550 U.S. at 418 ("obviousness grounds cannot be sustained by mere conclusory statements"); *Par*, 773 F.3d at 1195-96 ("A party must … meet a high standard in order to rely on inherency….").

For decades, the CCPA and Federal Circuit have cautioned that the use of inherency in the context of obviousness must be "carefully circumscribed." *Honeywell Int'l Inc. v. Mexichem Amanco Holding S.A. de C.V.*, 865 F.3d 1348, 1354-55 (Fed. Cir. 2017); *Spormann*, 363 F.2d at 448. That is because the "inherency of an advantage"—e.g., the claimed dual activity of AAD-1 proteins against two distinct classes of herbicides—"and its obviousness are *entirely different questions*." *Spormann*, 363 F.3d at 448 ("That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.").

In *Spormann*, the applicant claimed a process for producing alkali metal sulfite, which had the advantage of avoiding substantial production of sulfate byproducts. *Id.* at 444-45. The CCPA found that this advantage was unchallenged and reversed the Office's obviousness rejection because, "[s]o far as the disclosures of the references are concerned, we have found nothing to suggest it." *Id.* at 448. Similarly, in *Adams*, the claimed invention produced an unexpected and unsuggested increase in heat transfer efficiency, which the Office contended was inherent.

In re Adams, 356 F.2d 998, 1002 (CCPA 1966). Rejecting the Office's position as improperly based on hindsight, the court stated:

> Of course it is inherent, otherwise appellant's invention would not work. But patentability here does not hinge on inherency. It depends on the unexpected and unsuggested increase in heat transfer *efficiency*. No reference suggesting this has been produced, only *ex post facto* explanations….

Id. Thus, as the Federal Circuit has summarized, "[w]hat is important regarding properties that may be inherent, but unknown, is whether they are unexpected." *Honeywell*, 865 F.3d at 1355.

Policing the strict standard for inherency in obviousness analyses, the Federal Circuit has thus reversed decisions for "dismissing properties of the claimed invention as merely inherent, without further consideration as to unpredictability and unexpectedness." *Id.*; *Millennium*, 862 F.3d at 1367 (similar). But that is all Petitioners present here. The single conclusory sentence in the Petition alleging inherency addresses none of these issues. Pet., 56. Nor do Petitioners reconcile their unsupported assertions of inherency with their previous disclosure in their patent application that RdpA may not have activity under certain conditions. Ex. 1017, ¶ [0087] (stating that RdpA is "inactive" at 46°C under the conditions tested),

¶¶ [0015], [0093], Figs. 2A-2C.[10] *Par*, 773 F.3d at 1195 ("Inherency, however, may not be established by probabilities or possibilities."); *Millennium*, 862 F.3d at 1367 ("The mere fact that a certain thing may result from a given set of circumstances is not sufficient….").

Indeed, the Petition never identifies *any* αKG-dependent dioxygenase reported in the prior art to degrade FOP herbicides, much less two distinct classes of herbicides, as claimed. The unprecedented advantage of the claimed invention thus cannot be dismissed as purportedly inherent. *Spormann*, 363 F.3d at 448 ("Obviousness cannot be predicated on what is unknown."). The Petition's reliance on Dr. Hausinger's declaration also cannot remedy this deficiency.[11] Pet., 56 (citing Ex. 1054, ¶¶ 120, 227, 232, 418). Rather than addressing inherency, his paragraphs 227 and 232 improperly skip to later steps in an obviousness analysis. *Par*, 773 F.3d at 1194 (motivation and reasonable expectation are considered *only if* all elements are disclosed in the asserted references). In paragraph 120, Dr. Hausinger resorts to

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[10] The sequences of Petitioners' RdpA variants, publicly submitted in GenBank, are provided in Exs. 2012-2014.

[11] The Petition appears to improperly incorporate Dr. Hausinger's declaration as an attempted end-run around the Board's word count limits. *DIRECTTV*, IPR2015-02006, Paper 6, 10.

hindsight in contending that a POSA would have understood from WO '437 (i.e., Corteva's own specification) that the claimed activities are "a necessary and natural result of the disclosed AAD-1 v1 and v2 enzymes." Ex. 1054, ¶ 120. But Grounds IIA and IIB rely on the '283 patent's April 2004 provisional application filing date, and thus a POSA would *not* have had access to the inventors' insights from WO '437, which published in 2005 and is therefore irrelevant to obviousness. *Millennium*, 862 F.3d at 1367 (rejecting inherency and explaining that "[t]he inventor's own path itself never leads to a conclusion of obviousness; that is hindsight"); 35 U.S.C. § 103(a). Paragraph 418 of Dr. Hausinger's declaration merely incorporates his arguments concerning the '555 patent and does not provide any new argument for the '283 patent. Ex. 1054, ¶ 418.

Petitioners' inherency theory is thus legally deficient and factually unsupported and fails to demonstrate disclosure of all claim limitations in the asserted references.

3. Petitioners' Remaining Obviousness Arguments Are Conclusory and Impermissibly Tainted by Hindsight

Even assuming that Petitioners had established a reasonable likelihood that all claim limitations were expressly disclosed or inherent in the asserted references (which they did not), their cursory one-and-a-half pages of arguments devoted to motivation and reasonable expectation of success are fatally flawed and improperly

dependent on hindsight reasoning. Pet., 54-56; *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Pat. Litig.*, 676 F.3d 1063, 1070-71 (Fed. Cir. 2012) (courts should reject "hindsight claims of obviousness"); *KSR*, 550 U.S. at 418 ("obviousness grounds cannot be sustained by mere conclusory statements").

a. The Petition Fails to Establish Motivation

Petitioners' motivation arguments are tainted by impermissible hindsight. First, Petitioners seek to recast the Saari References through the lens of the claimed invention as having "singled out RdpA" by referring to it as the "TfdA-like gene from *S. herbicidovorans*." Pet., 55. The Saari References, however, do *not* use that language; they only refer to a *different enzyme* from a *different* bacterium, *A. denitrificans*. Ex. 1041, 422 ("a tfdA-like gene is present in A. denitrificans"), 426 (Fig. 5) ("an A. denitrificans TfdA-like sequence"); Ex. 1040, 93 ("*A. denitrificans* or the *tfdA*-like gene it contains"); Ex. 1054, ¶ 109 (Dr. Hausinger illustrating that the enzyme produced by the tfdA-like gene in *A. denitrificans* is different than RdpA). Petitioners provide no basis for how the Saari References could purportedly "single[] out" RdpA when that enzyme is never mentioned by name. Pet. 55. Petitioners' hindsight is further illustrated by their failure to cite any evidence that Dr. Saari, Dr. Hausinger, or anyone else ever attempted to develop genetically engineered crops expressing RdpA before Corteva developed the claimed invention. *Id.* (quoting Ex. 1041, 422); *Leo Pharm. Prods., Ltd. v. Rea*, 726

F.3d 1346, 1359 (Fed. Cir. 2013) (identifying "intervening time" between the prior art and development of the claimed invention as supporting nonobviousness).

Petitioners instead resort to tracing a hindsight-directed path through the asserted references. Dr. Hausinger, for example, states that the Saari References "would have led the POSA to Schleinitz," but the Saari References nowhere identify Schleinitz. Ex. 1054, ¶¶ 228, 412 (Dr. Hausinger incorporating his '555 patent analysis by reference). He then states that the Saari References "would have led the POSA to Streber," which again is not identified anywhere in the Saari References. *Id.*, ¶ 231; *see also* Pet., 55-56 (similar). During prosecution of the '406 Application, the Examiner considered and withdrew obviousness rejections based on similar references disclosing the RdpA sequence (*compare* Kohler, Ex. 1016, *with* Schleinitz, Ex. 1013) and generic transformation methods (*compare* Jepson, Ex. 1030, *with* Streber, Ex. 1043). Ex. 1008, COR-AAD1-00000638-41. Dr. Hausinger also relies on the '283 patent's own disclosures to support an alleged motivation to transform maize plant cells to express RdpA. Ex. 1054, ¶ 415. Petitioners thus appear to be using the '283 patent and its predecessor '406 Application's prosecution history as a roadmap to guide their hindsight-driven motivation theory. *Cheese Sys., Inc. v. Tetra Pak Cheese & Powder Sys., Inc.*, 725 F.3d 1341, 1352 (Fed. Cir. 2013) (courts must avoid "even a hint of hindsight").

Even at the end of Petitioners' hindsight path through the asserted references, the Petition only equivocally suggests that transformation methods "*could* be applied to RdpA," (Pet., 55), which is insufficient to demonstrate motivation. In *InTouch*, the Federal Circuit held that a patent challenger improperly "succumbed to hindsight bias" in presenting a similarly conclusory argument that a skilled artisan "*could* combine the[] references"—not that a skilled artisan "*would* have been motivated to do so." *InTouch Techs., Inc. v. VGo Commc'ns, Inc.*, 751 F.3d 1327, 1352 (Fed. Cir. 2014) (emphases in original). Accordingly, every step of Petitioners' motivation analysis is tainted by hindsight and thus is legally insufficient to establish obviousness.

b. The Petition Fails to Establish Reasonable Expectation of Success

A reasonable expectation of success must be based on the claimed invention "as a whole." 35 U.S.C. § 103(a); *Teva Pharms. USA, Inc. v. Corcept Therapeutics, Inc.*, 18 F.4th 1377, 1381 (Fed. Cir. 2021) (a petitioner is "required to prove a reasonable expectation of success in achieving the specific invention claimed"). Petitioners duck that required inquiry, rendering their reasonable-expectation analysis fatally flawed.

Rather than addressing the claimed invention as a whole, the Petition asserts that a POSA "would have reasonably expected success in transforming maize plant

cells to express RdpA." Pet., 55. Only later does the Petition purport to address the "remaining limitations" of claim 1, reflecting Petitioners' improper piecemeal analysis. 35 U.S.C. § 103(a) (requiring analysis of the claimed invention "as a whole"); *Teva*, 18 F.4th at 1382 (affirming nonobviousness where the Board correctly required a reasonable expectation of success tied "to the scope of the claimed invention").

Petitioners' analysis is also deficient because it includes only a single conclusory sentence regarding the required activity against FOP herbicides. Pet., 56 (alleging that "the Saari references disclosed that RdpA degraded (*R*)-dichlorprop and (*R*)-mecoprop; and the POSA would expect that RdpA would degrade other phenoxy auxin herbicides, as well as (*R*)-aryloxyphenoxypropionate [i.e., FOP] herbicides, via the same mechanism"). This single-sentence argument fails for at least three reasons.

First, Petitioners fail to identify *any* prior-art enzyme that was known to degrade FOP herbicides, let alone any evidence that RdpA was known to have this enzymatic activity. Indeed, Petitioners concede that no such knowledge existed in the art. Ex. 1054, ¶ 219 (the prior art "did not report testing of RdpA on (*R*)-aryloxyphenoxypropionate substrates"). Petitioners cite no authority for the proposition that achieving what was unknown can be obvious. The law is squarely

to the contrary. *See Spormann*, 363 F.3d at 448 ("Obviousness cannot be predicated on what is unknown.").

Second, Dr. Hausinger devotes a section of his declaration to a reasonable expectation of RdpA degrading FOP herbicides, but he cites no supporting prior art. Ex. 1054, ¶¶ 219-222, 416. He only cites the parent WO '437 application, the '555 patent, and the '555 patent's file history, which includes Corteva's post-filing discussion of the possible "implications" of the invention as suggesting that AAD-1 (v1) "is promiscuous enough to utilize chemicals with similar phenoxyalkanoate substructures." Ex. 1008, COR-AAD1-00000493; Ex. 1054, ¶¶ 219-220 (citing Ex. 1008), 221 (citing Exs. 1001, 1008), 416 (citing WO '437). But the "inventor's own path … never leads to a conclusion of obviousness; that is hindsight." *Millennium*, 862 F.3d at 1367 (quoting *Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1296 (Fed. Cir. 2012)); *id.* ("[T]he path that leads an inventor to the invention is expressly made irrelevant to patentability by statute." (citation omitted)).

Third, Petitioners' argument that activity against one class of (*R*)-enantiomeric substrates (e.g., (*R*)-dichlorprop and (*R*)-mecoprop) confers activity against *other classes* of (*R*)-enantiomeric substrates such as FOP herbicides lacks evidentiary support. Pet., 56-57; Ex. 1054, ¶ 219; 37 C.F.R. § 42.65(a) ("Expert testimony that does not disclose the underlying facts or data on which the opinion is based is entitled to little or no weight."). Petitioners contend that other (*R*)-specific

enzymes were known, such as from *A. denitrificans*, but they fail to identify any that were known to degrade multiple classes of (*R*)-enantiomeric substrates, let alone FOPs specifically. Moreover, Petitioners rely on Scheme 13 of the Saari thesis as allegedly showing the "same mechanism" that RdpA would use against FOP herbicides. Pet., 56-57; Ex. 1040, 71 (Scheme 13). But Scheme 13 shows a reaction "catalyzed by TfdA," which Petitioners admit has the *opposite* (*S*)-enantioselectivity than the (*R*)-enantioselectivity of RdpA. Ex. 1040, 71 (Scheme 13); Ex. 1054, ¶ 89. Petitioners fail to reconcile their position that the reaction mechanism of TfdA shows the "same mechanism" that RdpA would use against FOP herbicides with Dr. Hausinger's position that the "prior art *clearly taught* that RdpA/AAD-1 and TfdA were *not active* on [the same substrates]." *Id.*

c. The Petition Fails to Rebut the Evidence of Unexpected Results of Record

Objective evidence of nonobviousness, such as unexpected results, is not just "icing on the cake"—it must be considered before making any determination on obviousness. *See, e.g.*, *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380 (Fed. Cir. 1986).

Here, as Corteva disclosed in the specification and established during prosecution, the claimed invention produced unexpected results with the AAD-1 dual activity of degrading two different classes of herbicides (FOPs and phenoxy

auxins), which was unprecedented in the agricultural biotechnology field. *See, e.g.*, Ex. 1002, 4:12-15, 4:45-5:2, 8:17-31 (AAD-1 is "unlike all tfdA homologues characterized to date"), 108:27-115:55 (Example 17); Ex. 1008, COR-AAD1-00000685-87, -576-77, -492-93. The Office credited this evidence of unexpected results during the prosecution of the '406 Application, citing "the ability of the AAD-1 gene to produce herbicide tolerance in a transgenic plant cell to two distinct type[s] of herbicides" in withdrawing its obviousness rejection. Ex. 1008, COR-AAD1-00003844. This is precisely the type of difference-in-kind from the prior art that strongly supports nonobviousness. *In re Albrecht*, 514 F.2d 1389, 1395-96 (CCPA 1975) (crediting a compound's unexpected dual activity of exhibiting antiviral and anesthetic properties).

Corteva's evidence of unexpected results strongly supports nonobviousness because it remains unrebutted by Petitioners. *In re Soni*, 54 F.3d 746, 751 (Fed. Cir. 1995) (when a patentee demonstrates substantially improved results and states that the results were unexpected, those results are established absent contrary evidence). Petitioners fail to identify *any* αKG-dependent dioxygenases in the prior art that degrade FOP herbicides, much less any that additionally degrade a second class of herbicides (e.g., phenoxy auxins). Ex. 1054, ¶ 219 (Dr. Hausinger conceding that the prior art "did not report testing of RdpA on (*R*)-aryloxyphenoxypropionate substrates"); Pet., 63.

Rather than disputing Corteva's evidence of unexpected results, Petitioners attempt to dismiss it as allegedly inherent "latent properties," which is incorrect as discussed above in Section V(B)(2). Pet., 64. Petitioners also fail to rebut the presumption of nexus for the claimed embodiments exhibiting the unexpected AAD-1 dual activity detailed above. *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1329, 1331 (Fed. Cir. 2016). Regarding nexus, Petitioners rehash their flawed numerosity theory (e.g., alleging "massive scope" of the claims) that fails to account for the AAD-1 dual activity and function-correlated structural features required by all challenged claims. Pet., 63; *see supra* § V(A)(2); Ex. 1002, 44:5-8 (disclosing that 85% or greater sequence identity is "highly identical" and such enzymes "would be expected to retain similar properties").

Accordingly, for at least these reasons, Grounds IIA and IIB fail to establish a reasonable likelihood of demonstrating obviousness for any challenged claim.

VI. The Board Should Deny Institution Under *Advanced Bionics* (35 U.S.C. § 325(d))

The Board should deny institution under 35 U.S.C. § 325(d) at least because Petitioners (1) present the same or substantially the same prior art and arguments previously considered by the Office, and (2) fail to demonstrate that the Office erred in a manner material to the patentability of the challenged claims. *See Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469,

Paper 6 at 8-9 (PTAB Feb. 13, 2020); *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 at 17-18 (PTAB Dec. 15, 2017) ("*Becton Dickinson*").

A. The Office Considered the Same or Substantially the Same Prior Art and Arguments Raised in the Petition

The Petition presents Grounds IA-IB (§§ 102/103) and Grounds IIA-IIB (§ 103). None of them are new. As shown in the table below, ***all*** of the asserted references were previously considered and overcome during prosecution or are plainly cumulative:

Reference	IPR Grounds	Status Before the Office
WO '437 (Ex. 1021)	IA, IB	Cumulative of EP1740039B1, which was before the Office and a focus of examination of the predecessor '406 Application and submitted to the Office again during prosecution of the '283 patent.
Jepson (Ex. 1030)	IIB	Before the Office and a focus of examination of the predecessor '406 Application and submitted to the Office again during prosecution of the '283 patent.

Schleinitz (Ex. 1013)	IIA, IIB	Cumulative of Kohler (Ex. 1016),[12] which was before the Office and a focus of examination of the predecessor '406 Application and submitted to the Office again during prosecution of the '283 patent.
Saari 1999 (Ex. 1041)	IIA, IIB	Submitted and considered during prosecution of the predecessor '406 Application and the '283 patent.
Streber (Ex. 1043)	IIA, IIB	Submitted and considered during prosecution of the predecessor '406 Application and the '283 patent.
Saari 1998 (Ex. 1040)	IIA, IIB	Cumulative of Saari 1999 (Ex. 1041), which was submitted and considered during prosecution.

Indeed, during prosecution of the predecessor '406 Application, the Office substantively considered EP1740039B1 (the European counterpart of WO '437) in the context of evaluating Corteva's entitlement to priority. Ex. 1008, COR-AAD1-00000267-78. Obviousness in view of Jepson and the RdpA sequence (disclosed in Kohler) was also a focus of examination. *Id.*; *see Apotex Inc. v. Auspex Pharms., Inc.*, IPR2021-01507, Paper 9 at 25-27 (PTAB Mar. 9, 2022) (finding references that were a focus of examination "previously presented to the Office"). Petitioners also appear to acknowledge that the Saari 1998 thesis is cumulative of the corresponding

[12] Petitioners acknowledge that Schleinitz (Ex. 1013) and Kohler ("Q8KSC8," Ex. 1016) disclose "the same nucleotide and amino acid sequences" as RdpA. Pet., 21.

Saari 1999 article previously before the Office, presenting them as alternative references in Grounds IIA and IIB. Pet., 54 ("Saari 1998 ***or*** Saari 1999"), 59 ("The Saari References"). *Bio-Rad Lab'ys, Inc. v. 10X Genomics, Inc.*, IPR2019-00566, Paper 21 at 7-11 (PTAB July 22, 2019) (denying institution because "Petitioner has not indicated, in the context of 35 U.S.C. §325(d), any material differences" from art presented in IDS); *Xilinx, Inc. v. Analog Devices, Inc.*, IPR2021-00294, Paper 9 at 26 (PTAB June 10, 2021) (denying institution because "Petitioner has not pointed [the Board] to any evidence or facts persuading" the Board that the petition's references "are particularly different" from art of record). Moreover, the Office had substantively considered written-description support for the claims across three Office Actions, three Responses, and three declarations during prosecution of the predecessor '406 Application. Ex. 1008, COR-AAD1-00000267-78, -457-74, -479-94, -496-515, -557-78, -590-98, -629-41, -655-70, -676-93.

Petitioners' attempt to justify their reliance on art cited during prosecution (e.g., Saari 1999) is unpersuasive. Pet., 64-65. Whether a reference was discussed in a rejection is not the standard under *Advanced Bionics*. Rather, the relevant inquiry is "whether proffered art or arguments are 'the same or substantially the same' as art or arguments previously presented to the Office," as they are here. *Advanced Bionics*, IPR2019-01469, Paper 6 at 7; *see also Palo Alto Networks, Inc. v. Centripetal Networks, Inc.*, IPR2021-01155, Paper 12 at 14-16, 19-20 (PTAB Jan.

20, 2022) (denying institution under § 325(d) in view of *Advanced Bionics*'s holding that previously presented art includes art provided to the Office by an applicant, such as on an IDS).

B. Petitioners Fail to Demonstrate that the Office Erred in a Manner Material to the Patentability of the Challenged Claims

Petitioners fail to show that the Office erred in any material manner or that their art and arguments would have led to a different result during prosecution. *Advanced Bionics*, IPR2019-01469, Paper 6, 8; *Becton Dickinson*, 17-18 (factors (c), (e)).

With respect to Grounds IA and IB, Petitioners allege that the Office materially erred by not "apply[ing] the correct priority date." Pet., 65. But Petitioners fail to address the Office's express evaluation of that issue during the prosecution of the '406 Application or dispute Dr. Nair's declaration explaining that there is only *one fit* for the αKG motif in SEQ ID NO: 9—i.e., the claimed AAD-1 motif—and that it was "readily apparent" to a skilled artisan. Ex. 1008, COR-AAD1-00000594, ¶ 9. Petitioners also concede that a skilled artisan *would have appreciated that* RdpA (SEQ ID NO: 9) shared the consensus αKG motif, i.e., the AAD-1 motif. Ex. 1054, ¶¶ 214, 95, 89. Petitioners also fail to distinguish the Federal Circuit's precedential *Ajinomoto* decision, which Corteva addressed during prosecution. Moreover, as detailed above, the same type of numerosity theory that Petitioners present in the

context of written description has been previously rejected by the Board. *See supra* § V(A)(2).

With respect to Grounds IIA and IIB, Petitioners present *no arguments* for material error in the Office's evaluation of the prior art, including the cumulative references they rely on. Pet., 65. Nor could they. Petitioners' piecemeal obviousness analysis fails to address the claimed invention "as a whole," as required. 35 U.S.C. § 103(a). It also fails to establish disclosure of all claim limitations in the prior art, including—as Petitioners concede—the claimed activity against FOP herbicides. Ex. 1054, ¶ 219 (the prior art "did not report testing of RdpA on *(R)*-aryloxyphenoxypropionate substrates"). Petitioners' own published patent application also contradicts their legally and factually deficient inherency theory. *Supra* § V(B)(2). Moreover, rather than demonstrating motivation, reasonable expectation of success, or addressing the evidence of unexpected results of record, Petitioners resort to hindsight reasoning. *Supra* § V(B)(2); *Adams*, 356 F.2d at 1002 ("ex post facto explanations" are insufficient).

Thus, while Petitioners may disagree with the Examiner's allowance of the claims, that disagreement does not demonstrate any error material to patentability. *See Advanced Bionics*, IPR2019-01469, Paper 6 at 9.

VII. Conclusion

For these reasons, Corteva respectfully requests that the Board deny institution.

Respectfully submitted,

Dated: September 21, 2023

/Pier D. DeRoo/
Pier D. DeRoo
Reg. No. 69,340

CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. § 42.24(d), I, Pier D. DeRoo, certify that **Patent Owner's Preliminary Response** contains 13,085 words, excluding those portions identified in 37 C.F.R. § 42.24(a), as measured by the word-processing system used to prepare this paper.

Dated: September 21, 2023

/Pier D. DeRoo/
Pier D. DeRoo
Reg. No. 69,340

CERTIFICATE OF SERVICE

The undersigned certifies that a copy of the foregoing **Patent Owner's Preliminary Response** and **Exhibits 2001-2014** were served electronically via email on September 21, 2023, in their entirety on the following:

Dov P. Grossman
Ben Picozzi
Williams & Connolly LLP
680 Maine Avenue SW
Washington, DC 20024
dgrossman@wc.com
bpicozzi@wc.com

Petitioners have consented to service by email.

Dated: September 21, 2023

/William Esper/
William Esper
Case Manager and PTAB Coordinator
Finnegan, Henderson, Farabow,
Garrett & Dunner, LLP