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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INARI AGRICULTURE, INC.,
Petitioner,

v.

CORTEVA AGRISCIENCE LLC,
Patent Owner.

PGR2023-00022
Patent 11,371,055

PATENT OWNER'S PRELIMINARY RESPONSE

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EXHIBIT LIST

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2002	Tina A. Müller et al., *Structural basis for the enantiospecifics of R- and S-specific phenoxypropionate/α-ketoglutarate dioxygenases*, Protein Sci., Vol. 15, No. 6, pp. 1356-68 ("Müller") (library stamped copy of Ex. 1020).
2003	Julie C. Dunning Hotopp and Robert P. Hausinger, *Probing the 2,4-Dichlorophenoxyacetate/α-Ketoglutarate Dioxygenase Substrate-Binding Site by Site-Directed Mutagenesis and Mechanism-Based Inactivation*, Biochem., Vol. 41, No. 31, pp. 9787-94 (2002) ("Hotopp").
2004	U.S. Patent No. 9,125,357 ("the '357 patent").
2005	United States Environmental Protection Agency, Types of Pesticide Ingredients, *available at* https://www.epa.gov/ingredients-used-pesticide-products/types-pesticide-ingredients (last accessed July 12, 2023).

I. Introduction

The invention of Corteva's U.S. Patent No. 11,371,055 ("the '055 patent") concerns transgenic plants and plant cells that produce AAD-12 proteins that degrade two different classes of herbicides: phenoxy auxin herbicides and pyridyloxy auxin herbicides. The specification discloses exemplary AAD-12 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 twenty-four examples that include *in vitro* testing, genetic transformation of crop plants that produce AAD-12 enzymes (e.g., in *Arabidopsis*, tobacco, soybean, cotton, rice, corn, and canola), as well as test results demonstrating that the transgenic plants of the invention exhibit resistance to phenoxy auxin and/or pyridyloxy auxin herbicides.

The Board should deny institution for three independent reasons. *First*, Inari Agriculture Inc. ("Petitioner" or "Inari") fails to establish that the '055 patent is PGR-eligible as an AIA patent. The '055 patent claims priority to a series of pre-AIA patent applications, including a provisional application filed October 28, 2005, and a nonprovisional application filed October 27, 2006. The Examiner also determined during prosecution that the application would be examined under pre-AIA law. Petitioner, however, fails to analyze written description or enablement as of *any* pre-AIA filing date. Instead, the Petition only addresses a post-AIA 2017 filing date,

which is legally insufficient to show lack of written description or enablement in Corteva's priority applications filed before the PGR-eligibility cutoff of March 16, 2013. Ex. 1003 at ¶ 16 (Dr. Silverstone conducting his analysis as of "March 24, 2017—the filing date of the application that issued as the '055 patent"); *id.* at ¶¶ 17, 28, 33-34, 47, 80, 87 (similarly conducting his analysis as of March 24, 2017). Thus, on its face, the Petition is legally deficient and cannot establish PGR eligibility. *See, e.g.*, *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1355 (Fed. Cir. 2010) (en banc) (written description must be analyzed "as of the filing date sought"). Institution should be denied for this dispositive reason alone.

Second, even if Petitioner could establish PGR eligibility (which it cannot), Petitioner has not shown that it is more likely than not that any challenged claim is unpatentable. 35 U.S.C. § 324(a). Petitioner's written description arguments are fundamentally flawed. Petitioner, for example, cites Corteva's commercial product materials to allege that AAD-12-transformed soybeans do not have activity against pyridyloxy auxin herbicides. Pet. at 1-2, 12-14, 24-25, 34-36. But there is not yet any Environmental Protection Agency ("EPA") registration for post-burndown use of pyridyloxy auxin herbicides with Corteva's commercial AAD-12-transformed soybeans and therefore Corteva *cannot* advertise that currently unapproved use as a matter of law. Corteva's commercial product materials thus are not pertinent to written description. Moreover, Petitioner concedes that Corteva's AAD-12-

transformed soybeans *would have tolerance* to commercial levels of pyridyloxy auxin herbicides. Ex. 1003 at ¶ 78.

Petitioner also incorrectly contends that the challenged claims are functionally defined and encompass a wide variety of species. The '055 patent's claims contain significant structural limitations, restricting the AAD-12 proteins to those having (i) at least 85% sequence identity to SEQ ID NO: 2, ***and*** (ii) the specific AAD-12 active site motif: $HX_{109}D(X)_{111\text{-}134}T(X)_{136\text{-}261}H(X)_{263\text{-}272}R$. Relying on a biochemistry textbook and later developments in protein analysis software (dated even after 2017), Petitioner dismisses the high degree of sequence identity and common active site motif required by the claims and contends that the specification was required to disclose the protein's three-dimensional configuration (e.g., spatial coordinates). But that is not the law. *Ajinomoto Co. v. Int'l Trade Comm'n*, 932 F.3d 1342, 1360 (Fed. Cir. 2019) ("Adequate written description does not require a perfect correspondence between the members of the genus and the asserted common structural feature . . . we have spoken more modestly of a '*correlation* between structure and function.'" (quoting *Ariad*, 598 F.3d at 1350, emphasis in original)).[1] Petitioner concedes that (1) AAD-12 is "very efficient" in degrading phenoxy auxin herbicides (e.g., 2,4-D); (2) AAD-12 has "significant activity" on pyridyloxy auxin herbicides; and (3) the

[1] Unless otherwise noted, all emphases are added.

AAD-12 motif is "necessary" for the claimed activity. Ex. 1003 at ¶¶ 48, 70. The law requires nothing more to satisfy the written description requirement. *Ajinomoto*, 932 F.3d at 1360.

Petitioner's enablement arguments, based on the same incorrect allegations about functionally defined claims and widely variant species, are similarly deficient. Petitioner identifies no species within the claims that could not be made using routine experimentation. *Sandoz Inc. v. Boehringer Ingelheim Int'l GmbH*, PGR2022-00037, Paper 11 at 28-29 (PTAB Nov. 7, 2022) ("*Sandoz*") (citing *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577 (Fed. Cir. 1984)). Indeed, Petitioner does not contend that making a transgenic plant or plant cell within the scope of the claims would require more than routine experimentation in view of the specification's disclosures and the level of skill in the art. *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564 (Fed. Cir. 1996) (even a "considerable amount of experimentation is permissible, if it is merely routine"); *Cephalon, Inc. v. Watson Pharms., Inc.*, 707 F.3d 1330, 1338-39 (Fed. Cir. 2013) ("repetition of known or commonly used techniques" does not amount to undue experimentation).

Third, a discretionary denial of institution under 35 U.S.C. § 325(d) is also appropriate because Petitioner's unpatentability arguments are substantially the same as those previously considered by the Office. Petitioner repeats, essentially

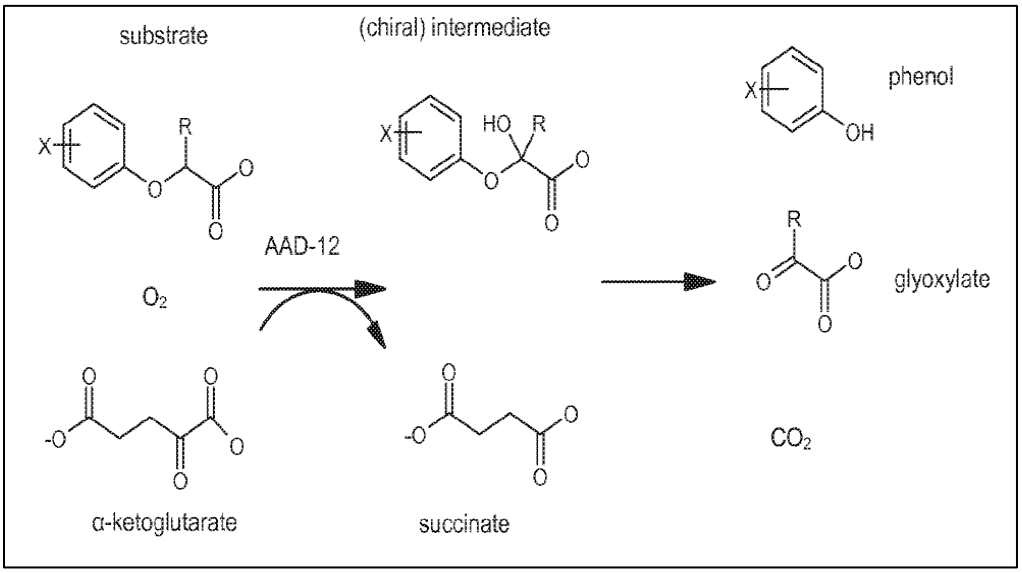
verbatim, statements made by the Examiner in written description rejections that Corteva overcame during prosecution. Petitioner also fails to address the *Ajinomoto* decision and its precedential holding regarding common structure and written description that Corteva cited to the Office during prosecution.

Accordingly, for the reasons detailed below, the Board should deny institution.

II. Background

A. α-Ketoglutarate-Dependent Dioxygenase Enzymes and SdpA (AAD-12)

α-Ketoglutarate-dependent ("αKG-dependent") dioxygenase enzymes that degrade phenoxy auxin herbicides, such as 2,4-D, were known in the art by 2005. Examples include the enzymes TfdA, SdpA, and RdpA. *See, e.g.*, Ex. 1025; Ex. 1027 at 15. To degrade 2,4-D, these enzymes generally require the presence of Fe(II) as the metallocenter, as well as oxygen and α-ketoglutarate as a co-substrate. Ex. 2001 at 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. 1001 at Fig. 1; Ex. 2001 at 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 at 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:

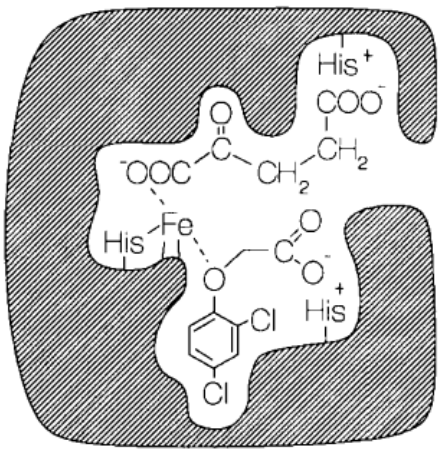


FIG. 11. **Model of the TfdA active site indicating potential roles of essential histidine residues.** The varied abilities of 2,4-D, α-KG, Fe(II), and mixtures of these compounds to protect against TfdA modification by DEP is interpretted in terms of a model that includes three distinct roles for histidine residues: assisting in the binding of 2,4-D, facilitating the binding of α-KG, and ligation of the metallocenter. The illustration is not meant to depict the Fe(II) coordination number or geometry, and the indicated Fe(II) coordination by the α-ketoacid group and the phenoxy oxygen is purely speculative at this time.

Id. at 24316 (Fig. 11).

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. 1019 at 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.* at 12408, 12401. 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.* at 12408.

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

Group I (IPNS, DAOCS, and related enzymes)	HXD	X_{60-70}	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. at 12401 (Table I).

Using site-directed mutagenesis, Hogan et al. also identified the specific locations of likely Fe(II)-coordinating residues in TfdA: H_{113}, D_{115}, and H_{262}. *Id.* at 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.* at 12406-07; *e.g.*, *id.* at 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. 2003 at 9792-93; Ex. 1019 at 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 that had been reported to degrade phenoxy auxin herbicides, such as 2,4-D. These

enzymes included SdpA and RdpA from the bacteria *Delftia acidovorans* MC1, as well as SdpA and RdpA from *Sphingomonas herbicidovorans* MH. Ex. 1027; Ex. 1023.

Before the October 27, 2006 filing date of Corteva's nonprovisional application, Müller et al. had identified the specific motif residues in SdpA and RdpA from *Sphingomonas herbicidovorans*. Ex. 1020; Ex. 2002. Citing Hogan (Ex. 1019) and its active site motif disclosures, Müller reported 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. 1020 at 1358; Ex. 2002 at 1358.

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

B. The '055 Patent

The '055 patent specification provides extensive disclosures relating to the claimed invention; for example, it describes AAD-12 enzymes, their common active

site motif, the significance of the claimed 85% sequence identity limitation, and *twenty-four* examples.

1. AAD-12 Enzymes

The inventors' creation of transgenic plants expressing the bacterial αKG-dependent dioxygenase enzyme SdpA from *Delftia acidovorans* (i.e., AAD-12) 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 pyridyloxy auxins (e.g., triclopyr and fluroxypyr). Ex. 1001 at 12:23-58. In light of this dual herbicide-tolerance activity, the enzymes and genes of the '055 patent are called "AAD-12" (**A**ryloxy **A**lkanoate **D**ioxygenase) proteins and genes. *Id.* at 4:48-61.

The '055 patent discloses the amino acid sequence of AAD-12 as SEQ ID NO: 2, which is the native protein expressed by the SdpA gene from *Delftia acidovorans*. *Id.* at 5:48-51. The '055 patent also discloses a plant-optimized sequence of AAD-12 as SEQ ID NO: 4. *Id.* at 5:55-56. The '055 patent discloses that proteins of the invention include homologues having 85% or greater sequence identity to AAD-12. *Id.* at 21:41-60.

For αKG-dependent dioxygenases, the '055 patent discloses that amino acid sequences having 85% to 98% identity are "highly identical" and such enzymes are "expected to retain similar properties." *Id.* at 31:61-32:6; *see also id.* at 3:22-34

("Many homologues are similar to tfdA (>85% amino acid identity) and have similar enzymatic properties to tfdA.").

The '055 patent also discloses the location of the known active site motif in Group II αKG-dependent dioxygenases such as AAD-12. 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.* at 10:61-11:14 (citing Hogan, Ex. 1019).[2] The '055 patent further provides a sequence alignment of five αKG-dependent dioxygenases, including AAD-12, highlighting the highly conserved residues across these enzymes. *Id.* at Fig. 2.

The specification also provides techniques for modifying AAD-12 genes and proteins to create AAD-12 homologues. *Id.* at 17:6-22:56. For example, it states that proteins and genes for use in the invention can be rapidly identified using

[2] The paragraph at column 11, lines 15-34, of the '055 patent was incorporated via amendment to the specification to provide antecedent basis for the claim terms. MPEP § 608.01(o) (recognizing that, with claim language, "an applicant is not limited to the nomenclature used in the application as filed," but an amendment to the specification may be made to provide antecedent basis for terms appearing in the claims); Ex. 1002 at 229, 238-39 (amending specification pursuant to MPEP § 608.01(o)). Petitioner takes no position on this amendment. Pet. at 6 n.4.

oligonucleotide probes. *Id.* at 17:6-62. It also discloses that homologous enzymes can be made with conservative amino acid substitutions and, in some instances, non-conservative substitutions. *Id.* at 22:11-37. The '055 patent also discloses high-throughput assays for verifying the activity of AAD-12 proteins. *Id.* at 45:50-48:60. Citing protein-design references, the '055 patent also discloses that variant proteins can be designed that differ at the sequence level but "*retain the same or similar overall essential three-dimensional structure*." *Id.* at 28:57-29:10.

2. The Specification's Twenty-Four Examples

Written description "does not demand either examples or an actual reduction to practice." *Ariad*, 598 F.3d at 1352. The '055 patent nonetheless discloses twenty-four examples. *See, e.g.*, Ex. 1001 at 13:42-44 ("The transgenic expression of the subject AAD-12 genes is exemplified in, for example, *Arabidopsis*, tobacco, soybean, cotton, rice, corn and canola."), 31:55-102:49.

The '055 patent discloses examples of high-throughput *in vitro* assays for measuring AAD-12 activity. *Id.* at 45:50-48:60 (Examples 5 and 6). For example, the specification describes a 96-well microplate format for performing enzyme assays measuring degradation activity against 2,4-D and triclopyr using incubation times of 5 to 10 minutes. *Id.* at 45:50-46:45. The '055 patent presents *in vitro* testing data "show[ing] that AAD-12 (v2) is able to effectively degrade pyridyloxy-alkanoate herbicides such as triclopyr" and 2,4-D. *Id.* at 47:4-48:60, Fig. 3.

The ’055 patent describes how to plant-optimize the gene sequences for efficient expression of AAD-12 proteins in plant cells, including cells of monocot crops (e.g., corn) and dicot crops (e.g., soybeans). *Id.* at 32:24-41:2 (Example 2). It discloses preparation of expression and transformation vectors for AAD-12 (v2). *Id.* at 41:4-43:20 (Example 3). The ’055 patent states that a wide variety of methods were available for introducing genes encoding desired proteins into target host cells under conditions that allow for stable maintenance and expression of the genes. *Id.* at 23:57-62, 24:25-26 (“A large number of techniques are available for inserting DNA into a plant host cell.”). The specification instructs the skilled artisan to take advantage of events that were “known to be excellent locations in a plant genome for insertions” of recombinant nucleotides. *Id.* at 29:11-25.

The ’055 patent describes the transformation of *Arabidopsis* plants with an AAD-12 gene. *Id.* at 48:62-50:33. Seeds from those transformed plants were collected, and first-generation plants grown from that seed (i.e., T_1 seed) were tested for dual herbicidal activity. *Id.* at 50:32-56:38. The ’055 patent discloses that “AAD-12-transformed plants were . . . clearly protected from the triclopyr and fluroxypyr herbicide injury that was seen in the transformed non-resistant controls . . . .” *Id.* at 54:13-16, 54:23-45 (Table 13). It reports that the AAD-12 (v1) gene imparted herbicide resistance to *Arabidopsis* plants against 2,4-D. *Id.* at 51:35-52:38 (Table 11).

The ’055 patent also discloses comparative testing of AAD-12-transformed *Arabidopsis* against *Arabidopsis* transformed to express a different αKG-dependent dioxygenase enzyme (AAD-2). *Id.* at 83:22-85:23. AAD-2 has a substantially different amino acid sequence than AAD-12 and has a different active site motif. *See id.* at Fig. 2. In this testing, AAD-12-transformed plants exhibited stronger 2,4-D resistance than AAD-2-transformed plants. *Id.* at 84:49-85:23. Additionally, the ’055 patent discloses that, “unlike all tfdA homologues characterized to date, AAD-12 is able to degrade the pyridyloxyacetates auxins (e.g., triclopyr, fluroxypyr) in addition to achiral phenoxy auxins (e.g., 2,4-D . . .).” *Id.* at 6:40-46, 4:48-55.

The ’055 patent provides examples of monocot and other dicot plants transformed with AAD-12 genes, including soybeans, tobacco, cotton, corn, rice, and canola. *Id.* at Examples 8, 10-12, 16, 17, 21, 22. For example, the specification describes how to prepare AAD-12 expression cassettes and transform soybean plants using (1) *Agrobacterium*-mediated transformation, (2) aerosol-beam-mediated transformation, (3) biolistic bombardment using mature seed, (4) WHISKERS-mediated transformation, and (5) particle bombardment using embryogenic callus tissue. *Id.* at 72:48-79:61. In Example 11, transformed soybean plants were tested for tolerance to the herbicide 2,4-D. *Id.* The ’055 patent discloses that “[a]ll AAD-12 (v1)-containing plants were clearly resistant to the herbicide application,” while “control plants were severely injured” or killed, depending on the 2,4-D application

rate. *Id.* at 76:40-50 ("These data are consistent with the fact that AAD-12 (v1) can impart high tolerance (>2x field rates) to a sensitive crop like soybeans."). The '055 patent also discloses the use of combinations of 2,4-D, triclopyr, and fluroxypyr with dicot crops such as soybeans. *Id.* at 86:23-87:20 ("One skilled in the art of weed control will now recognize that use of various commercial phenoxy or pyridyloxy auxin herbicides alone or in combination with a herbicide is enabled by AAD-12 (v1) transformation."); *see also id.* at 71:4-9 ("AAD-12 (v1) transformed event lines [in tobacco] displayed a high level of tolerance to 2,4-D, triclopyr and fluroxypyr . . . ."). The '055 patent also describes successful testing of AAD-12-transformed corn, rice, and canola to both classes of herbicides. *Id.* at 64:28-65:53, 94:19-95:15, 98:32-99:20.

The '055 patent further discloses stacking AAD-12 traits with other herbicide tolerance traits (e.g., genes providing resistance to glyphosate, glufosinate, and imidazolinone herbicides) and insect resistance traits to confer multiple tolerance traits in plants. *Id.* at Examples 18-20, 23.

3. The Claims

The '055 patent claims are directed to novel transgenic plants and plant cells comprising a recombinant polynucleotide encoding a structurally well-defined class of AAD-12 proteins. The claims' definition of AAD-12 proteins has two structural limitations. First, the AAD-12 protein must have at least 85% sequence identity with

SEQ ID NO: 2. Second, the AAD-12 protein must have the defined AAD-12 motif having each of the specified active site amino acid residues and their required spacing. Claim 1, for example, recites:

> 1. A transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-12 protein that exhibits aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and a pyridyloxy auxin herbicide, further wherein said AAD-12 protein comprises:
>
> i) ***an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 2***; and
>
> ***ii) an AAD-12 motif having the general formula of:***
>
> $\boldsymbol{HX_{109}D(X)_{111\text{-}134}T(X)_{136\text{-}261}H(X)_{263\text{-}272}R}$, wherein
>
> X_{109} represents a single amino acid at position 109, relative to the sequence of SEQ ID NO: 2;
>
> $(X)_{111\text{-}134}$ represents a sequence of 24 amino acids;
>
> $(X)_{136\text{-}261}$ represents a sequence of 126 amino acids; and
>
> $(X)_{263\text{-}272}$ represents a sequence of 10 amino acids.

The dependent claims recite additional features, including:

- At least 90% sequence identity with SEQ ID NO: 2 (claim 2);

- A dicot plant cell selected from cotton, tobacco, canola, soybean, and *Arabidopsis* cells (claim 3);
- A transgenic plant comprising a plurality of the plant cells of claim 1, wherein expression of the polynucleotide renders the plant tolerant to an aryloxyalkanoate herbicide (claim 4);
- Tolerance to particular herbicides or herbicide classes (claims 5-9);
- A transgenic plant having a second herbicide resistance gene (claims 10 and 11);
- Methods of controlling at least one weed in a field, wherein the field contains at least one plant of claim 4 and the method comprises applying a first herbicide selected from the group of a phenoxy auxin herbicide and a pyridyloxy herbicide, as well as other herbicides and herbicide tolerances (claims 12-27 and 29);
- A seed comprising a plurality of the plant cell of claim 1 (claim 28);
- A plant grown from the seed of claim 28, wherein the plant comprises the polynucleotide (claim 30); and
- A part, progeny, or asexual propagate of the plant of claim 30 comprising the polynucleotide (claim 31).

Independent claim 32 recites similar features as independent claim 1 but requires the AAD-12 motif to have 90% sequence identity with corresponding amino

acids of position 108 to 273 of SEQ ID NO: 2. Independent claim 33 generally recites a method of controlling at least one weed in a field planted with seeds that comprise an AAD-12 recombinant polynucleotide, and the method comprises applying to the field a pyridyloxy auxin herbicide.

4. Relevant Prosecution History

The ’055 patent was filed as U.S. Application No. 15/468,494 (“the ’494 application”) on March 24, 2017. It claims priority to a series of applications, including U.S. Provisional Patent Application No. 60/731,044 filed October 28, 2005, and nonprovisional Application No. 12/091,896 filed October 27, 2006 as PCT/2006/042133. Ex. 1001 at cover, 1:5-15.

On April 24, 2019, the Office issued a Non-Final Office Action stating that the application was being “examined under the pre-AIA first to invent provisions.” Ex. 1002 at 210-19. The Office issued a written description rejection asserting that the application did not describe a structural/functional relationship between the AAD-12 motif and enzymatically degrading a phenoxy auxin herbicide and a pyridyloxy auxin herbicide. *Id.* at 213-14.

Applicant responded that the specification provided a sufficient description of the claimed invention such that one of ordinary skill in the art would have recognized that Applicant was in possession of the invention. *Id.* at 240-41. Applicant also summarized the specification’s disclosure of the “key amino acid residues of

aryloxyalkanoate dioxygenases by providing the structure of a motif comprising the active site of the enzyme" and its location in the sequence of AAD-12 (SEQ ID NO: 2). *Id.* at 240.

On December 20, 2019, the Office issued a Final Office Action maintaining the written description rejection. *Id.* at 251-64. In response to Applicant's arguments, the Office asserted that the general structure known in an enzyme family did not adequately describe the specific structure required to produce activity that enzymatically degrades a phenoxy auxin herbicide and a pyridyloxy auxin herbicide. *Id.* at 256.

Applicant filed an Amendment and Response on April 17, 2020, explaining how the specification complies with the written description requirement. *Id.* at 270-88. The Response addressed *Ajinomoto*, 932 F.3d 1342, and its holding regarding disclosure of common structure for providing written description support for a genus of proteins. Ex. 1002 at 279-80. Applicant also cited to Müller (Ex. 1020) as evidence that persons skilled in the art were familiar with the structure of αKG-dependent dioxygenases. Ex. 1002 at 280-81.

The Office maintained the written description rejection on July 24, 2020 (*id.* at 312-26), stating that the "claimed motif represents the family of α-ketoglutarate dioxygenases . . . hav[ing] a broad genus of substrates" (*id.* at 317).

On January 21, 2021, Applicant filed an Amendment and Response, explaining that the specification's disclosure of a common structure, in view of the state of the art, provided adequate support for the claims. *Id.* at 336-51. Applicant pointed out that the specification describes the amino acid sequence of AAD-12 proteins that exhibit the claimed dual herbicidal activity and teaches how to prepare species that retain that desired activity. *Id.* at 343.

The Office then withdrew the written description rejection and, after Applicant overcame a remaining obviousness rejection, allowed the claims. *Id.* at 355, 485-91.

III. Level of Ordinary Skill in the Art

Petitioner proposes a high level of ordinary skill in the art: "a Ph.D. in biochemistry, cell biology, genetics, or a related field, and 3-5 years of experience in the design or development of transgenic plants including genomics, proteomics, biochemistry, plant transformation and crop science, or the equivalent." Pet. at 23. Petitioner further states that "[a]dditional graduate education could substitute for professional experience, or significant experience in the field could substitute for formal education." *Id.*

Corteva submits that it is not necessary at this stage to define a specific level of ordinary skill, which is reflected in the art. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001). However, Petitioner's definition omits any background

in enzymology, including familiarity with αKG-dependent dioxygenases, which a skilled artisan would have possessed in view of Petitioner's cited references (e.g., Ex. 1019; Ex. 1020). Petitioner's declarant appears to have no meaningful background with that family of enzymes. *See* Ex. 1003 at ¶¶ 6-15; *see Kyocera Senco Indus. Tools Inc. v. Int'l Trade Comm'n*, 22 F.4th 1369, 1377 (Fed. Cir. 2022) (when an expert does not have ordinary skill in the art, his "opinions are neither relevant nor reliable"). To the extent the Board believes it is appropriate to define a level of ordinary skill at this stage of the proceeding, familiarity with αKG-dependent dioxygenases such as SdpA should be included.

IV. Claim Construction

Petitioner proposes no specific constructions of any terms of the '055 patent claims. For purposes of this POPR, Corteva also does not propose any specific constructions at this time. As detailed below in Section V(B)(2)(a), however, Petitioner fundamentally misconstrues the scope of the '055 patent claims, particularly in view of their structural limitations.

V. Petitioner Has Not Established That It Is More Likely Than Not that Any Challenged Claim Is Unpatentable

A. Petitioner Has Not Shown that the '055 Patent Is PGR-Eligible

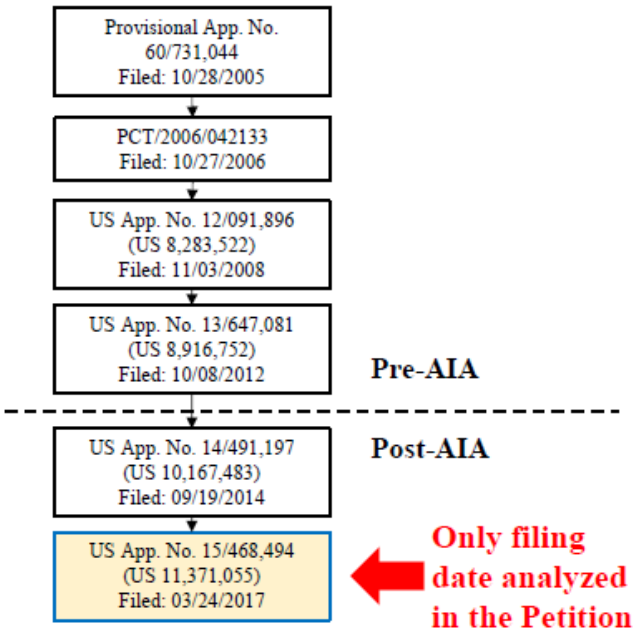
The Petition is legally deficient on its face because Petitioner failed to analyze written description or enablement as of the filing date of any pre-AIA application in

the priority chain of the '055 patent. Petitioner thus has not established PGR eligibility, as PGRs are unavailable for challenging pre-AIA patents. *Sandoz*, PGR2022-00037, Paper 11 at 14-16 (citing AIA, Pub. L. No. 112-29, 125 Stat. 284, 305-11, §§ 6(d), 6(f)(2)(A) (2011)). Institution should be denied for this reason alone.

A written description or enablement analysis requires evaluating the specification from the perspective of those skilled in the art *as of the filing date*. *Ariad*, 598 F.3d at 1355 ("[A] written description analysis occurs 'as of the filing date sought.'" (citation omitted)); *Union Carbide Chems. & Plastics Tech. Corp. v. Shell Oil Co.*, 308 F.3d 1167, 1185 (Fed. Cir. 2002) ("Enablement is determined as of the filing date . . . ."). Accordingly, to establish that the '055 patent is eligible for post-grant review, Petitioner had to show that at least one challenged claim lacks written description and enablement support in the '055 patent's pre-AIA priority applications filed before March 16, 2013. *Sandoz Inc. v. Biogen MA Inc.*, PGR2022-00054, Paper 16 at 25-28 (PTAB Feb. 2, 2023) ("*Biogen MA*") (denying institution where Petitioner failed to "demonstrate that the priority applications' respective written descriptions were insufficient in view of the state of the art as of the filing date of each of [the] three pre-AIA applications").

The Petition, however, provides no § 112 analysis with respect to *any* of the '055 patent's pre-AIA priority applications. Instead, Petitioner and its declarant, Dr.

Silverstone, performed their analysis only as of the post-AIA March 24, 2017, filing date of the '494 application that issued as the '055 patent. Ex. 1003 at ¶¶ 16, 17, 28, 33-34, 47, 80, 87 (analyzing the state of the art as of "March 24, 2017"); Pet. at 52, 56 (analyzing the state of the art "as of March 24, 2017"). Indeed, Dr. Silverstone took the March 24, 2017 date as an *assumption*, rather than conducting any analysis at all. Ex. 1003 at ¶ 28 ("I have been informed that the assessment of undue experimentation is based on the state of the art as of the earliest filing date . . . . In this case, *I have been informed* that date is March 24, 2017"). Petitioner's written description and enablement analyses are thus legally deficient on their face and cannot meet Petitioner's burden because they do not address the relevant pre-AIA filing dates and applications for assessing PGR eligibility.



See Merck Sharp & Dohme Corp. v. Wyeth LLC, PGR2017-00016, Paper 9 at 14 (PTAB Oct. 20, 2017) ("Petitioner's failure to address each relevant date bolsters our holding that Petitioner fails to show sufficiently that the [challenged] patent is post grant review eligible."); *Biogen MA*, PGR2022-00054, Paper 16 at 26 (denying institution where Petitioner did not analyze § 112 "in light of . . . the then-current state of the art" as of the pre-AIA filing dates).

Petitioner's argument that Corteva's priority applications have the same disclosures as the '055 patent cannot remedy the Petition's fatal deficiency. *See* Pet. at 6. By using the wrong March 24, 2017 time frame (as well as relying on numerous references dated even after 2017), Petitioner legally erred by assessing the specification against later developments in the art, including in the areas of protein folding and structure modeling (Exs. 1015, 1016, 1021, 1022), crop transformation (Exs. 1013, 1034), and USDA- and EPA-approved product launches and associated labeling and literature (Exs. 1004, 1006, 1011, 1012, 1029).

This legal error permeates Petitioner's written description and enablement analyses. For example, Dr. Silverstone repeatedly demands disclosure of three-dimensional structural features to satisfy the written description requirement, stating that "[t]he active site is usually determined by crystallizing the protein" (Ex. 1003 at ¶ 45) or "us[ing] software the [sic] predicts protein folding" (*id.* at ¶ 46). He contends that even using later-developed software such as AlphaFold would not have

"*guarantee[d]* the ability to accurately predict the substrates of an enzyme" "on or around March 24, 2017." *Id.* at ¶ 47. But he fails to meaningfully analyze the body of scientific literature regarding αKG-dependent dioxygenases as it existed, e.g., as of Corteva's 2005 provisional and 2006 nonprovisional filing dates. Indeed, Petitioner's own evidence shows that skilled artisans described enzymes within the relevant family by their amino acid sequence and their *active site motifs*—just as Corteva described and claimed them in the '055 patent. Ex. 1019; Ex. 1020 at 1358 ("The high degree of *active-site sequence identity* and strong orientation of key side chains by interactions with the Fe^{II} are supportive of the *active site being the most conserved and structurally accurate part of the RdpA and SdpA models*."); Ex. 2002 at 1358.

The state of the art as of Corteva's pre-AIA priority applications is thus entirely consistent with and supportive of how Corteva described and claimed AAD-12 proteins in the '055 patent—i.e., by their specific, conserved active site motif and high level of sequence identity to SEQ ID NO: 2. Petitioner's criticism that "Patent Owner could *better define* the active site through a set of spatial coordinates" as of 2017 or later is thus legally irrelevant and has no bearing on the sufficiency of Corteva's disclosure in 2005, 2006, or any of Corteva's other pre-AIA filing dates. Ex. 1003 at ¶¶ 79-80; Pet. at 5-7.

Accordingly, the Board should deny institution because the Petition fails to establish that the '055 patent is PGR-eligible, which is dispositive of the Petition in its entirety. *Biogen MA*, PGR2022-00054, Paper 16 at 25-28.

B. Ground 1: Petitioner Fails to Show that Any Challenged Claim Lacks Written Description Support

In addition to the Petition's fundamental failure to establish PGR eligibility, the Petition also fails to establish that it is more likely than not that any challenged claim of the '055 patent lacks written description support as of its 2017 filing date. 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.* 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. *Id.* at 1350.

As detailed below, Petitioner's arguments for lack of written description are legally and factually flawed, and thus Petitioner has failed to meet its burden.

1. Petitioner Fails to Demonstrate that the Inventors Lacked Possession of the Claimed Transgenic Plants

From its opening pages, the Petition repeatedly cites Corteva's Technology Use Agreement ("TUA") (Ex. 1004) and other commercial product and stewardship materials (Exs. 1006, 1011, 1012) to allege that AAD-12 does not have the claimed activity against pyridyloxy auxin herbicides. Pet. at 1-2, 12-14, 24-25, 34-36. Petitioner primarily bases this argument on Corteva's TUA listing post-burndown use of pyridine auxin herbicides as a "prohibited activity." *Id.* at 2 (citing Ex. 1004 at 2). Petitioner's interpretation of these materials is incorrect.

Petitioner omits that herbicides and their uses are comprehensively regulated by the EPA. Under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA") and the EPA's implementing regulations, it is unlawful to "place or sponsor advertisements which recommend or suggest the purchase or use of: . . . [a] pesticide product for an unregistered use . . . ." 40 C.F.R. § 168.22(b)(5).[3] Here, for example, Corteva has registered its 2,4-D herbicide product with the EPA for post-

[3] For clarity, herbicides, which "kill weeds and other plants that grow where they are not wanted" (i.e., weedy plants are considered pests), are covered by the EPA's regulation of pesticides under FIFRA. *See* Ex. 2005 ("Well known pesticides (terms defined below) include: . . . herbicides").

burndown use with transgenic AAD-12 soybeans (sold under the trade name Enlist E3® soybeans), which is reflected in Corteva's TUA. Ex. 1004 at 1 (referencing Corteva's 2,4-D choline herbicides "specifically designed to provide ultra-low volatility, minimized potential for physical drift, decreased odor and improved handling characteristics").

Until the EPA registers triclopyr, fluroxypyr, or other pyridyloxy auxin herbicides for post-burndown use with Enlist E3® soybeans, however, Corteva *cannot*, under FIFRA, suggest or advertise pyridyloxy auxin herbicides for use with Enlist E3® soybeans. Corteva's TUA thus appropriately warns farmers against running afoul of EPA regulations by using those herbicides off-label for unregistered uses. Accordingly, Corteva's commercial product and stewardship materials simply are not pertinent to Petitioner's proposed written description ground. Indeed, the Petition cites no authority indicating that a patent specification should be analyzed for written description through the prism of such later-dated materials for products subject to independent and complex regulatory regimes.

Moreover, contradicting Petitioner's position, the specification repeatedly discloses and reports test data showing tolerance to pyridyloxy auxin herbicides as well as phenoxy auxin herbicides. *See supra* § II(A)-(B). Despite acknowledging that "the specification provides experimental results for seven species of plants comprising the AAD-12 variant," Petitioner asserts that *test data* against both

pyridyloxy auxin and phenoxy auxin herbicides were not reported for two of those transgenic plants: soybeans and cotton. Pet. at 34-35 ("*[N]o data* is presented for . . . transgenic soybeans comprising the AAD-12 variant against pyridyloxy auxin herbicides."), 35 ("*[N]o data* is presented for the herbicide resistance of transgenic cotton . . . ."); Ex. 1003 at ¶ 53 (Dr. Silverstone demanding that Patent Owner "perform *all experiments* with *each species* of transgenic plant").

As the en banc Federal Circuit and the PTAB have held, however, no such data are required to satisfy the written description requirement. *Ariad*, 598 F.3d at 1352 ("[T]he written description requirement does not demand either examples or an actual reduction to practice . . . ."); *Biogen MA*, PGR2022-00054, Paper 16 at 17, 22, 28 (denying institution and explaining that "data and studies are not required"); *Sandoz*, PGR2022-00037, Paper 11 at 17-18, 23-24, 29 (denying institution and explaining that "there is no legal requirement that a patent specification must include test results or working examples").

Petitioner's argument is further undercut by Dr. Silverstone's admission that the '055 patent's disclosed AAD-12-transformed cotton and soybean plants *would have tolerance* to commercial levels of both pyridyloxy auxin and phenoxy auxin herbicides:

> The invention disclosed in the '055 patent includes five different crops (*cotton*, tobacco, canola, *soybean* and Arabidopsis), that are expressing a transgenic protein that is at least 85% identical

> to AAD-12 and contains the "AAD-12 motif". *These crops would be tolerant of commercial levels of the synthetic phenoxy auxin herbicide 2,4-D as well as commercial levels of the synthetic pyridyloxy auxin herbicides, like triclopyr and fluroxypyr*.

Ex. 1003 at ¶ 78.

Further, the '055 patent discloses that "AAD-12 is able to degrade the pyridyloxyacetates auxins (e.g., triclopyr, fluroxypyr) in addition to . . . 2,4-D." Ex. 1001 at 6:41-46; Ex. 1003 at ¶ 70 (Dr. Silverstone conceding that AAD-12 was "found to have significant activity on the pyridyloxy auxin herbicides"). The '055 patent also discloses that "[s]oybeans are a preferred crop for transformation according to the subject invention," discloses AAD-12-transformed soybeans in Example 11, and discloses combinations of triclopyr and fluroxypyr for use with dicots such as soybeans in Example 16. Ex. 1001 at 13:42-45, 72:48-79:61, 86:23-87:20. Petitioner fails to demonstrate how these disclosures in the '055 patent are insufficient to meet the written description requirement.

2. Petitioner Fails to Demonstrate that Patent Owner Lacked Possession of the AAD-12 Proteins Recited in the Challenged Claims

a. Petitioner Misconstrues the Scope of the Claims

Contending that the recited AAD-12 proteins are "overly broad and functionally defined" (Pet. at 27) and embrace "widely variant species" (*id.* at 26), Petitioner fundamentally misconstrues the scope of the '055 patent claims, which

contain significant structural limitations. The challenged claims bear no resemblance to those at issue in the cases Petitioner relies on, which contained *no* structural limitations. *Id.* at 25-36 (citing *Ariad*, *AbbVie*, and *Lilly*).

First, each claim of the '055 patent requires that the AAD-12 protein have an amino acid sequence with at least 85% sequence identity with SEQ ID NO: 2. *See, e.g.*, Ex. 1001 at claims 1, 2, 32, 33. This is a specific structural limitation, not a functional limitation. Moreover, the '055 patent discloses that those levels of sequence identity would be considered "highly identical" within this technical field—not widely variant as Petitioner contends. *Id.* at 31:61-32:4 (differentiating between "highly identical (85-98%)" and "low identity (23-32%) at the amino acid level" of αKG-dependent dioxygenases). Dr. Silverstone failed to address this disclosure of the '055 patent.

Second, each claim of the '055 patent requires that the AAD-12 protein have a motif of five conserved amino acid residues located at specified distances from each other, as in SEQ ID NO: 2: $\boldsymbol{HX_{109}D(X)_{111\text{-}134}T(X)_{136\text{-}261}H(X)_{263\text{-}272}R}$. This is also a structural limitation, not a functional limitation. The '055 patent explains that these conserved motif residues comprise "the active site that is essential for catalytic activity." *Id.* at 11:1-6.

In contrast, in the cases Petitioner relies on, the challenged claims contained no structural limitations. In *Ariad*, the claims were functionally defined in terms of

"altering NF-κB activity" in cells, with no structural elements. 598 F.3d at 1340-41. In *AbbVie*, the claims defined the claimed antibodies "by their function . . . rather than by structure," broadly encompassing *all antibodies regardless of amino acid sequence* that exhibited the claimed activity. *AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1292 (Fed. Cir. 2014). In *Lilly*, the claims were generically directed to vertebrate or mammalian insulin cDNA that—again—did "not distinguish the claimed genus from others, except by function." *Regents of Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997).

As the *Lilly* court explained, generic formulas in claims "usually indicate with specificity what the generic claims encompass" such that skilled persons can identify many species within the claims. *Id.* Thus, with structural formulas and other limitations—e.g., here, the AAD-12 motif and high sequence identity to SEQ ID NO: 2—the written description requirement is normally met. *Id.* ("Accordingly, such a formula is normally an adequate description of the claimed genus."). Accordingly, if anything, Petitioner's cited cases *distinguish* cases like this one, which supports denial of institution.

Petitioner's generalized arguments about protein folding and tertiary, three-dimensional structure fail to account for the disclosed and claimed high level of sequence identity (85%) to SEQ ID NO: 2. *See* Pet. at 29; Ex. 1003 at ¶¶ 42-50. For example, Petitioner repeatedly relies on a generic biochemistry textbook chapter.

Ex. 1003 at ¶¶ 42-50 (citing Ex. 1033). That textbook, however, reports that three-dimensional structure is *even more conserved* than amino acid sequence. Ex. 1033 at 141 (disclosing that "protein tertiary structure *is more reliably conserved* than primary sequence," and that "*Protein Motifs* Are the Basis for Protein Structural Classification"); *see also* Ex. 1028 at 6 ("[T]hree-dimensional structures of proteins *are more conserved* during evolution time than are the primary amino-acid sequences."). Moreover, Petitioner nowhere addresses the specification's disclosure, citing known protein-design references, that variant proteins can be designed that differ at the sequence level but "*retain the same or similar overall essential three-dimensional structure*." Ex. 1001 at 28:57-29:10.

Petitioner notably fails to identify any written description case holding structurally defined claims unpatentable, much less any case involving claims requiring a high degree of sequence similarity and an active site motif, as the '055 patent claims have here. Petitioner instead rests its arguments on a speculative numerosity theory that the PTAB and other courts have rejected. *See* Pet. at 30 n.7 (alleging that the '055 patent claims encompass more species than the number of atoms in the universe).

In *Ex parte Campbell*, the PTAB reversed a written description rejection that was based on an allegation—like Petitioner's 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 at 4-5 (PTAB July 20, 2021) (also noting similar arguments that particular three-dimensional "conformations" were allegedly needed for activity). The PTAB found that the claimed antibodies were "not exclusively claimed functionally, but are also claimed structurally" by the 90% sequence identity limitation, and were supported by disclosure of two species. *Id.* at 15; *see also Alcon Rsch. Ltd. v. Barr Lab'ys, Inc.*, 745 F.3d 1180, 1190 (Fed. Cir. 2014) (rejecting written description challenge on the basis 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 "infinit[y]" lacked written description, explaining that "a claim may be broader than the specific embodiment disclosed in a specification *is in itself of no moment*"); *Sandoz*, PGR2022-00037, Paper 11 at 22, 26, 28-29 (denying institution and rejecting petitioner's argument that claims encompassing "millions of potential formulations" lacked adequate written description).

Similarly, in *Lifescan*, the PTAB 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 5×10^{76} unique sequences. *Lifescan Glob. Corp. v. Ikeda Food Rsch., Ltd.*, PGR2019-00032, Paper 11 at 21, 18-19 (PTAB Aug. 15, 2019). The PTAB noted that the petitioner's argument, like Inari's here, inappropriately focused

on the number of sequences encompassed by the 90% limitation. *Id.* at 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 PTAB 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.* at 29. The PTAB thus refused to adopt the written description argument in *Lifescan* that parallels Petitioner's position here.[4]

Accordingly, Petitioner's written description challenge is fundamentally flawed in view of Petitioner's disregard of the scope and structural features of the challenged claims and reliance on nonanalogous cases and a numerosity theory repeatedly rejected by the PTAB and other courts.

b. Petitioner's 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'

[4] In *Lifescan*, the PTAB appears to have granted institution solely based on an enablement ground where the challenged claim did not recite the common six amino acid sequence, deemed to be an "essential" feature. *Id.* at 17-18. Here, by contrast, the AAD-12 motif is expressly recited in the '055 patent claims.

the members of the genus" provides adequate written description. *Ajinomoto*, 932 F.3d at 1358-59 (quoting *Ariad*, 598 F.3d at 1350). Petitioner fails to meet its burden of establishing that the '055 patent's disclosure of common structural features is insufficient.

Petitioner concedes that the five conserved residues of the AAD-12 motif in SEQ ID NO: 2 correspond to "*key active site residues*" that are "*necessary for the claimed activity*." Pet. at 32-33. The '055 patent also discloses that 85% is a "highly identical" level of sequence identity. Ex. 1001 at 32:1-6. It further discloses that "*sequences with high homology would be expected to retain similar properties*"—a disclosure that Petitioner nowhere addresses. *Id.* The law requires no more, as these common structural features permit a skilled artisan to visualize or recognize the AAD-12 proteins recited in the claims by their active site motif and high homology to SEQ ID NO: 2, 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).

Despite conceding that the AAD-12 motif is "necessary" for the claimed enzymatic activity, Petitioner contends that the active site motif is "not sufficient" because the "function of AAD-12 proteins of the invention depends on the correct 3-D structure of the active site." Pet. at 33. Dr. Silverstone, for example, suggests that "the Patent Owner *could better define* the active site through a set of spatial

coordinates." Ex. 1003 at ¶ 79. But Petitioner applies an incorrect legal standard in demanding stricter structure-function correlation. As the Federal Circuit explained in *Ajinomoto*, "[a]dequate written description does not require a perfect correspondence between the members of the genus and the asserted common structural feature . . . we have spoken more modestly of a '*correlation* between structure and function.'" 932 F.3d at 1360 (emphasis in original) (quoting *Ariad*, 598 F.3d at 1350). 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 1360-61 (crediting a "consensus sequence" as sufficient disclosure); *Lifescan*, PGR2019-00032, Paper 11 at 29 (rejecting written description challenge where the evidence suggested that a six amino acid sequence was necessary for activity). Petitioner cites no authority requiring disclosure of 3-D spatial coordinates of amino acid residues to satisfy the written description requirement.

Moreover, for his 3-D coordinate theory, Dr. Silverstone repeatedly relies on a generic textbook chapter discussing protein folding in general (Ex. 1033), which nowhere mentions αKG-dependent dioxygenase enzymes, much less AAD-12 (SdpA) enzymes specifically. Ex. 1003 at ¶¶ 42-50; Ex. 1033, 120 (providing an "overview" of protein structure). He thus disregards Petitioner's own evidence indicating that skilled artisans as of the '055 patent's pre-AIA filing dates described

enzymes in this field by their amino acid sequences and active site motifs, without using 3-D coordinates. *See* Ex. 1019 at 12401; Ex. 1020 at 1358 (Müller reporting that the "*high degree of active-site sequence identity* and strong orientation of key side chains by interactions with the Fe^{II} are supportive of the *active site being the most conserved and structurally accurate part of the RdpA and SdpA models*"); Ex. 2002 at 1358.

Petitioner's other criticisms of the AAD-12 motif are also deficient. For example, Petitioner contends that the conserved amino acids of the AAD-12 motif are present in other αKG-dependent dioxygenases that do not have the claimed dual activity. Pet. at 32-33. But Petitioner ignores that the *location and spacing* of those residues in other αKG-dependent dioxygenases differ from those in the AAD-12 motif. *Id.*; *see also* Ex. 1003 at ¶ 48 (Dr. Silverstone analyzing "the general motif attributed to the family" of enzymes, rather than the AAD-12 motif).

Petitioner's speculation that additional amino acids could be important to the dual activity of degrading phenoxy auxin and pyridyloxy auxin herbicides is also irrelevant. For example, Dr. Silverstone points to residues later identified in 2019 (in a different enzyme than AAD-12). Ex. 1003 at ¶ 49 (citing Ex. 1015). He also cites literature from 2000 and 2006 as identifying additional residues potentially

important to TfdA's activity. *Id.* at ¶ 90 (citing Exs. 1019, 1020, 1023).[5] 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 required in upholding claims supported by disclosure of a consensus sequence. 932 F.3d at 1360 ("[W]e have spoken more modestly of a '*correlation* between structure and function.'" (emphasis in original) (quoting *Ariad*, 598 F.3d at 1350)); *Lifescan*, PGR2019-00032, Paper 11 at 29 (crediting a sequence of six amino acids).

Accordingly, Petitioner's common-structure arguments are legally deficient and fail to establish that the '055 patent's disclosure of common structural features is insufficient.

[5] If anything, the identification of particular residues relevant to function in enzymes related to AAD-12 by 2000 and 2006 would further support written description as of the '055 patent's pre-AIA filing dates, which would render the '055 patent PGR-ineligible. *Biogen MA*, PGR2022-00054, Paper 16 at 25-27 ("[T]he state of knowledge is relevant in evaluating sufficiency of written description support in the specification.").

c. Petitioner Fails to Demonstrate that AAD-12 and Its Variants Are Nonrepresentative of the Claimed Genus

Petitioner's written description challenge also fails for another independent reason: Petitioner has not met its burden of establishing that the '055 patent's disclosed species are nonrepresentative of the genus claimed. *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 plants and plant cells* comprising a recombinant protein that encodes an AAD-12 protein. Ex. 1001 at claim 1; Pet. at 17-18. As detailed above, the '055 patent discloses extensive examples of such transgenic plants and plant cells and related testing, including in *Arabidopsis* (Example 7), corn (Example 8), tobacco (Example 10), soybeans (Example 11), cotton (Example 12), rice (Example 21), canola (Example 22), and other crops (Examples 13, 16, and 17). *See supra* § II(B)(2). Indeed, Dr. Silverstone acknowledges the various crops exemplified in the '055 patent and their dual herbicide tolerance. Ex. 1003 at ¶ 78. Petitioner is thus incorrect in characterizing the '055 patent as only allegedly disclosing one or two species, reflecting Petitioner's failure to consider the claimed subject matter and the disclosures of the specification as a whole. *E.g.*, Pet. at 34-36, 31-32.

Petitioner's assertion that the disclosed AAD-12 enzyme and a variant (AAD-12 (v1)) are insufficiently representative of the genus of AAD-12 enzymes is also incorrect. Petitioner does not dispute that the specification contains many examples of transgenic plants that express an AAD-12 enzyme meeting the structural and functional (i.e., dual activity) requirements of the claims. *See supra* § II(B)(2). Petitioner thus has not established that AAD-12 and AAD-12 (v1) are not representative of the structures and functions of the genus of AAD-12 proteins encoded by the recombinant polynucleotides of the claimed transgenic plants and plant cells.

Instead, Petitioner argues lack of representativeness by rehashing its flawed numerosity theory. Pet. at 27-28, 30 n.7 (asserting that claims encompass a greater number of species than the number of atoms in the universe). *See supra* § V(B)(2)(a); *see Lifescan*, PGR2019-00032, Paper 11 at 30 (criticizing similar written description arguments that "derive purely from the size of the genus rather than from consideration of all of the facts informing the written description analysis").

Petitioner's argument that the requirement for 85% sequence identity to SEQ ID NO: 2 "embraces widely variant species" (Pet. at 28) also contradicts the specification's express disclosure that enzymes having at least 85% sequence identity are "highly identical"—a disclosure Petitioner never addresses. Ex. 1001 at 32:1-6. This case is thus far different than the *AbbVie* decision Petitioner relies on

(Pet. at 29), where the claims encompassed *all antibodies regardless of amino acid sequence* that exhibited the claimed activity, including an accused product having only 50% sequence identity. *AbbVie*, 759 F.3d at 1292, 1301 (the "patents do not describe any common structural features of the claimed antibodies"). Nor was any evidence presented in *AbbVie* regarding any motif, consensus sequence, or other common structure. Petitioner thus fails to establish that the disclosed AAD-12 proteins are not representative of AAD-12 proteins within 85% amino acid sequence identity (i.e., "highly identical" proteins) that also have the AAD-12 motif. Ex. 1001 at 32:1-6.

In *Ex parte Campbell*, the PTAB rejected arguments similar to those raised by Petitioner here and upheld claims under the written description requirement. Similar to the claims here, the PTAB found that Campbell's claimed antibodies were defined structurally, e.g., by 90% sequence identity to recited SEQ IDs. No. 2021-000865, Decision on Appeal at 15. Similar to the '055 patent's description of AAD-12 and AAD-12 (v1), the PTAB found that the specification's disclosure of two exemplary antibodies provided sufficient written description. *Id.* The PTAB further noted that a comparison of antibody sequences provided guidance to skilled persons as to where changes could be made in the amino acid sequence without significantly impairing antigen-binding functionality, which is analogous to the '055 patent's disclosures, including the sequence alignment in Figure 2 that Petitioner concedes

identifies "key active site residues." Pet. at 32; Ex. 1001 at Fig. 2, 22:11-37, 28:57-29:10.

Similarly, in *Lifescan*, the PTAB found unpersuasive written description arguments similar to Petitioner's, stating that three exemplary enzymes and description of a "portion of the claimed sequence believed to be critical to its activity" undercut petitioner's position. PGR2019-00032, Paper 11 at 32. In *Bilstad*, the Federal Circuit reaffirmed that it has "continued to apply the rule that disclosure of *a species* may be sufficient written description for a later claimed genus including that species." 386 F.3d at 1122-24 (vacating Board's decision that found a single disclosed embodiment insufficient to support a claimed range extending to infinity). Petitioner's arguments thus run afoul of the Federal Circuit's and the PTAB's admonition that there are no "bright line rules governing . . . the number of species that must be disclosed to describe a genus claim, as this number necessarily changes with each invention, and it changes with progress in the field." *Lifescan*, PGR2019-00032, Paper 11 at 28 (quoting *Ariad*, 598 F.3d at 1351-52).

Accordingly, Petitioner has failed to meet its burden of establishing that it is more likely than not that any challenged claim lacks written description support.

C. Ground 2: Petitioner Fails to Show that Any Challenged Claim Lacks Enablement

The Petition also fails to establish that it is more likely than not that any challenged claim of the '055 patent is unpatentable for lack of enablement. To establish that a claim is nonenabled, a challenger must show that a skilled artisan would be unable to practice the claimed invention without "undue experimentation." *Alcon*, 745 F.3d at 1188-89. In determining whether any alleged experimentation would be undue, the *Wands* factors may be considered, which include the: (1) quantity of experimentation necessary; (2) amount of direction or guidance presented; (3) presence or absence of working examples; (4) nature of the invention; (5) state of the prior art; (6) relative skill of those in the art; (7) predictability or unpredictability of the art, and (8) breadth of the claims. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

Petitioner's enablement challenge rehashes the same deficient positions it advanced for written description—e.g., its numerosity theory (Pet. at 38, 45-46, 59), 3-D protein structure and folding (*id.* at 47, 56-57), and Corteva's commercial product and stewardship materials (*id.* at 44-45). Thus, for similar reasons as those Corteva addressed above, Petitioner's enablement challenge lacks merit and does not justify institution.

1. Petitioner Identifies No Species Within the Challenged Claims that Could Not Be Made Using Routine Experimentation

Conducting an enablement analysis typically requires "concrete identification of at least some embodiment or embodiments asserted not to be enabled—including what particular products or processes are or may be within the claim, so that breadth is shown concretely and not just as an abstract possibility, and how much experimentation a skilled artisan would have to undertake to make and use those products or processes." *McRO, Inc. v. Bandai Namco Games Am. Inc.*, 959 F.3d 1091, 1100 (Fed. Cir. 2020).

Petitioner fails to make any such "concrete identification," instead relying on vague assertions that some proteins "will be worse," "equivalent," or "better" AAD-12 proteins depending on amino acid substitutions. Ex. 1003 at ¶ 82; Pet. at 39-40; *Alcon*, 745 F.3d at 1189 (unsubstantiated conclusory statements are not sufficient). Indeed, Petitioner fails to identify any embodiments within the scope of the claims that could not have been made using routine experimentation.[6] *See Atlas*

[6] As discussed above, Petitioner's interpretation of Corteva's TUA (Ex. 1004) and other commercial product materials (Exs. 1011, 1012) to allege that AAD-12 does not have the claimed activity against pyridyloxy auxin herbicides is flawed. Those materials concern the EPA's commercial regulation of Corteva's Enlist E3®

Powder, 750 F.2d at 1577 (upholding enablement of claims directed to an emulsion blasting agent comprising an emulsifying agent when the defendant failed to identify any nonenabled emulsifiers); *Union Carbide*, 308 F.3d at 1186 (finding "general and vague . . . statements" unpersuasive to support a claim of undue experimentation).

Because Petitioner has failed to make a threshold showing that any particular embodiments are nonenabled, its enablement ground fails for this reason alone. *Sandoz*, PGR2022-00037, Paper 11 at 22, 26, 28 (citing *Atlas Powder*, 750 F.3d at 1577, and denying institution because the petition did not provide "sufficient evidence of actual instability" to justify institution).

2. Petitioner Fails to Demonstrate that Any Experimentation Required to Practice the Claimed Invention Would Have Been Undue

Even if Petitioner had established that any particular embodiment was not enabled (which it has not), Petitioner fails to show that the amount of experimentation would have been undue. Experimentation alone does not preclude enablement, and even a considerable amount of experimentation may not be undue

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soybeans, not the adequacy of the specification's disclosure. *See supra* § V(B)(1); Pet. at 43-45; Ex. 1003 at ¶ 78 (Dr. Silverstone conceding that AAD-12-transformed soybeans *would* have tolerance to commercial levels of pyridyloxy auxin herbicides).

if it is merely routine. *In re Wands*, 858 F.2d at 736-37 ("Enablement is not precluded by the necessity for some experimentation such as routine screening.").

a. Petitioner Misconstrues the Scope of the Claims (*Wands* Factors 4 and 8)

As with its written description arguments, Petitioner misconstrues the scope of the claims as "extremely broad" and functionally defined, while ignoring their significant structural limitations. *See supra* § V(B)(2)(a); Pet. at 59. The challenged claims here bear no resemblance to those at issue in the only enablement case Petitioner relies on, which contained *no* structural limitations. Pet. at 37-38 (citing *Amgen Inc. v. Sanofi, Aventisub LLC*, 987 F.3d 1080 (Fed. Cir. 2021), *aff'd*, 143 S. Ct. 1243 (2023)).

In *Amgen*, the claims were "defined, not by structure, but by meeting functional limitations." 987 F.3d at 1087. The claims in *Amgen* thus encompassed "every antibody" that performed the claimed functions, without reciting any structural limitations. 143 S. Ct. at 1256.

In contrast, the '055 patent claims recite two structural limitations that are correlated to the claimed function—85% amino acid sequence identity and the AAD-12 active site motif. Ex. 1001 at 11:1-6, claims 1, 2, 32, 33. Petitioner admits that many sequences with 85% identity "would work at a level equivalent to the disclosed AAD-12" and that the "conserved amino acids of the 'AAD-12 motif' that

are present in the active site are necessary" for the claimed activity. Ex. 1003 at ¶¶ 48, 82. As the Supreme Court recently reaffirmed, disclosing a "general quality" across a genus may "reliably enable a person skilled in the art to make and use all of what is claimed." *Amgen*, 143 S. Ct. at 1254-55. Accordingly, the '055 patent claims bear no resemblance to the claims at issue in *Amgen*, which contained no structural limitations.

Petitioner's focus on the alleged potential number of species within the scope of the claims as compared to the number of embodiments disclosed in the specification also misses the mark. Pet. at 38. The PTAB and courts have rejected such arguments based on the sheer number of species encompassed by the claims. *See, e.g.*, *Sandoz*, PGR2022-00037, Paper 11 at 25, 28 (rejecting petitioner's argument that the claims were nonenabled because "the breadth of the claims is 'vast' and that the skilled artisan could only determine the stability of a formulation by way of testing"); *In re Depomed Pat. Litig.*, No. 13-4507 (CCC-MF), 2016 WL 7163647, at *44 (D.N.J. Sept. 30, 2016) (holding that enablement does not require "the making and testing of every one of the 11 million species" in an enabled genus claim and stating that, as "a practical matter, it would be 'absurd' to require" such testing), *aff'd sub nom. Grunenthal GmbH v. Alkem Lab'ys Ltd.*, 919 F.3d 1333 (Fed. Cir. 2019); *see also Amgen*, 143 S. Ct. at 1254-55 (for a genus claim, it suffices to give only one example where, as here, "the specification also discloses 'some

general quality . . . running through' the class that gives it 'a peculiar fitness for the particular purpose'" (quoting *Consol. Elec. Light Co. v. McKeesport Light Co.,* 159 U.S. 465, 475 (1895)).

Petitioner's enablement challenge is thus fundamentally flawed in view of Petitioner's misunderstanding of the scope of the '055 patent's claims and their structural limitations.

b. Petitioner Disregards Significant Disclosures of the Specification (*Wands* Factors 2 and 3)

Similar to its written description positions, Petitioner also contends that the '055 patent provides "no direction or guidance" regarding which proteins would exhibit the claimed enzymatic activity. Pet. at 46. These unsupported assertions fare no better in the context of enablement.

As discussed above, Petitioner concedes that the claimed AAD-12 motif in SEQ ID NO: 2 corresponds to "*key active site residues*" that are "*necessary for the claimed activity*." *Id.* at 32-33, 47. The '055 patent also discloses that 85% is a "highly identical" level of sequence identity. Ex. 1001 at 32:1-6. It further discloses that "*sequences with high homology would be expected to retain similar properties*." *Id.* The '055 patent further provides techniques for modifying AAD-12 genes and proteins to create AAD-12 homologues. *Id.* at 17:6-22:56. Citing known protein-design references, the '055 patent also discloses that "[v]ariant proteins can also be

designed that differ at the sequence level but that retain the same or similar overall essential three-dimensional structure, surface charge distribution, and the like." *Id.* at 28:57-29:10. Petitioner fails to address these disclosures or explain why they would provide insufficient guidance for a skilled artisan to routinely make additional AAD-12 proteins within the scope of the claims. *See* Pet. at 46-50 (discussing *Wands* factors 2 and 3).

Moreover, although a "patentee is not required to provide actual working examples," *see Alcon*, 745 F.3d at 1189-90, the '055 patent discloses twenty-four examples providing additional guidance to a skilled artisan. The '055 patent's examples describe, *inter alia*, high-throughput *in vitro* assays for measuring AAD-12 activity (Examples 5 and 6), methods of optimizing gene sequences for expression of AAD-12 proteins in plant cells (Examples 2), preparation of expression and transformation vectors for AAD-12 (v2) (Example 3), and numerous examples transforming both monocot and dicot plants to incorporate AAD-12 genes (Examples 8, 10-12, 17, 21 and 22). *See supra* § II(B)(2). The examples thus provide a roadmap for making and evaluating other AAD-12 proteins and transgenic plants that produce AAD-12 proteins, which Petitioner glosses over. Petitioner's failure to address the significant enabling disclosures of the specification further undermines its enablement analysis.

c. Petitioner Fails to Establish that Any Required Experimentation Would Not Have Been Routine (*Wands* Factors 1 and 5-7)

Petitioner repeatedly argues that *in vitro* and *in vivo* testing would have been required for any amino acid sequence falling within the claims and that such testing "would be exceedingly time-consuming, laborious, expensive, and unpredictable," Pet. at 41, 45, 49, 58. However, even "extensive" testing does not constitute undue experimentation if it is routine and within the skill in the art. *Cephalon*, 707 F.3d at 1338-39 ("[E]xtensive experimentation does not necessarily render the experiments unduly extensive where the experiments involve repetition of known or commonly used techniques."); *Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.*, 276 F. Supp. 3d 629, 661 (E.D. Tex. 2017) (Bryson, J.) ("A patent must enable a skilled artisan to practice the full scope of the invention; it does not need to ensure that a skilled artisan can practice the entire scope of the invention within a short period of time."), *aff'd*, 739 F. App'x 643 (Fed. Cir. 2018).

Undermining Petitioner's enablement challenge, Dr. Silverstone previously represented to the Office that the various steps he addresses in his declaration were "routine" and "well known in the art" by 2008 (i.e., long before the 2017 priority date Petitioner relies upon).

Dr. Silverstone's PGR Testimony	Dr. Silverstone's Representations in his '357 Patent, Filed May 30, 2008 (Ex. 2004)
"Once a protein is chosen, the scientist needs to know how to choose the appropriate gene expression cassette, including promoter, terminator, other expression regulatory sequences, as well as how to codon optimize the coding portion of the gene for a given plant species." Ex. 1003 at ¶ 72.	"Plant Expression Cassettes A plant variety exhibiting a trait of interest can be obtained by introducing into the plant a nucleic acid sequence associated with a trait of interest. . . ." "It is a *routine matter* for one of skill in the art to modulate the expression of a sequence by appropriately selecting and positioning promoters and other regulatory regions relative to that sequence." Ex. 2004 at 20:15-21:29.
"[I]t often requires a *high degree of skill* to efficiently generate transgenic plants. Plant transformation is not completely predictable. *Id.* at ¶ 73.	"Transformation techniques for dicotyledons are *well known in the art* . . . ." *Id.* at 25:18-20 "Transformation of most monocotyledon species has now also become *routine*." *Id.* at 26:6-7.
"*[M]eticulous experimentation is required* to confirm the proper expression of the new protein. There are numerous processes that can impact successful expression of the protein." *Id.* at ¶ 74.	"It is a *routine matter* for one of skill in the art to modulate the expression of a sequence by appropriately selecting and positioning promoters and other regulatory regions relative to that sequence." *Id.* at 21:26-29.
"Once the transgenic plants are grown in the greenhouse or growth chamber, . . . [t]he plants need to be propagated for several generations to produce homozygous seed for testing of the herbicide tolerance in planta."	"The genetic properties engineered into the transgenic seeds and plants . . . are passed on by sexual reproduction or vegetative growth and can thus be maintained and propagated in progeny plants. Generally, maintenance and propagation *make use of known agricultural methods* . . . ." *Id.* at 28:61-67.

Id. at ¶ 75.	

Moreover, Petitioner acknowledges that the level of skill in the art is high and that a skilled artisan would have "specialized knowledge of protein engineering, expression, purification, and analysis, molecular cloning, genetic modification of plants, and crop science." Pet. at 55.

Petitioner notably fails to argue that any of the allegedly required testing would not have been routine. Instead, at most, Petitioner cites a declaration submitted during prosecution addressing the prior art in an obviousness rejection as indicating that "there is a high level of unpredictability associated with expressing bacterial genes in plant systems." *Id.* at 40 n.9, 42 n.10, 45 n.11, 49 n.12 (quoting Ex. 1010 at ¶ 9). Petitioner's reliance on this declaration is misplaced, however, because it focuses on the prior art, whereas "the enablement inquiry turns on whether the skilled artisan, *after reading the specification*, would be able to make and use the claimed invention . . . ." *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1310 (Fed. Cir. 2015). Petitioner's unpredictability argument is thus misplaced because it does not account for the "predictability of the aspect at issue"—i.e., a skilled artisan's ability to make and use AAD-12-transformed plants and plant cells within the scope of the claims in view of the '055 patent's roadmap disclosure of similar AAD-12 proteins, their sequences, the active site motif, and *twenty-four examples* including

high-throughput *in vitro* testing, crop transformation, and *in planta* testing. *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005).

Accordingly, Petitioner fails to establish that any alleged experimentation would have been beyond the routine skill of an ordinary artisan in view of the specification's disclosures, and thus fails to satisfy its burden of establishing that the claims of the '055 patent are not enabled.

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

The Board should also deny institution under 35 U.S.C. § 325(d) because Petitioner (1) presents the same or substantially the same art and arguments that were previously considered by the Office during prosecution, and (2) fails 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. Petitioner's Arguments Are the Same or Substantially the Same as Those Considered by the Office

Both of Petitioner's § 112(a) grounds raise the same or substantially the same arguments previously considered and overcome during prosecution. The Board should thus exercise its discretion to deny institution. *Hospira, Inc. v. Genentech, Inc.*, IPR2017-00739, Paper 16 at 17-19 (PTAB July 27, 2017) (informative)

(denying institution where the examiner considered the same arguments petitioner raised regarding written description and enablement).

1. Ground 1: Written Description

Petitioner concedes that the Examiner issued a written description rejection during prosecution but contends that it was "because Applicant amended the claims to recite an 'AAD-12 motif,' which was not literally recited in the original specification." Pet. at 8-9. The Office, however, substantively considered, and found persuasive, Applicant's arguments that claims reciting an AAD-12 motif were adequately described. *See supra* § II(B)(4). Petitioner provides no evidence that its arguments differ materially from those considered during prosecution.

As summarized below, Petitioner repeats, often verbatim, the Office's written description positions that Applicant successfully overcame during prosecution. *See Becton, Dickinson* factors (a), (b), and (d).

	Petitioner	**Examiner**
Claims	"The five conserved residues of the 'AAD-12 motif' correspond to *key active site residues* of homologous members of the family of *α-ketoglutarate-dependent dioxygenases*, as seen in [the] sequence alignment provided in the '055 patent." Pet. at 32.	"The 'AAD-12 motif' recited in the claims appears to be the specific motif in instant SEQ ID NO: 2 that represents the *general motif found in α-ketoglutarate-dependent dioxygenases* (paragraph 0053 on pages 12-13 of the instant Specification)." Ex. 1002 at 214.

	Petitioner	Examiner
Representative Number of Species	"[T]he minimal disclosure of the '055 patent's two species with 99.7% sequence identity *fails to provide a representative number of species* for the claimed genus, which embraces widely variant species." Pet. at 28.	"Applicant has *failed to describe a representative number of species* that would represent the variation within the claimed genus." Ex. 1002 at 317.
Common Structural Features	"The claimed genus . . . fails to establish a reasonable *structure-function correlation* between at least 85% sequence identity to SEQ ID NO: 2 and the 'AAD-12 motif', and the ability to enzymatically degrade both phenoxy and pyridyloxy auxin herbicides." Pet. at 26-27.	"Applicant does not describe a *structural/functional relationship* between the 'AAD-12 motif' and enzymatically degrading a phenoxy auxin herbicide and a pyridyloxy auxin herbicide. In particular, Applicant does not describe what specific features (amino acids) in the 'AAD-12 motif' are critical to the recited function." Ex. 1002 at 315.

Consistent with this substantial similarity of positions, Petitioner and its declarant rely on the same references (*e.g.*, Ex. 1019; Ex. 1020) and case law (*e.g.*, *AbbVie*) considered by the Office regarding the general structure of α-ketoglutarate dioxygenases and the claimed functional activity. *Compare* Ex. 1003 at ¶ 90 (discussing Müller (Ex. 1020), which found "several residues were likely responsible for mecocop binding," but not "critical for other auxin herbicides"), *with* Ex. 1002 at 316-17 (discussing Müller (Ex. 1020) as indicating there are amino acids outside of the AAD-12 motif that are critical to function), 256-57, 346-47, 355. The record thus shows that the Examiner fully considered the claimed features, including

the AAD-12 motif, sequence homology limitations, and state of the art with respect to similar enzymes, under the written description requirement of § 112. *See Boehringer Ingelheim Animal Health USA Inc. v. Kan. State Univ. Rsch. Found.*, PGR2022-00021, Paper 13 at 16-21 (PTAB Mar. 22, 2023) (denying institution under § 325(d) "based on the substantial overlap" between the petitioner's written description arguments and issues already presented to the examiner).

Thus, *Advanced Bionics* step 1 and *Becton, Dickinson* factors (a), (b), and (d) favor denial of institution with respect to written description Ground 1.

2. Ground 2: Enablement

Petitioner also cannot avoid discretionary denial based on its contention that the Examiner "never argued" that the claims lack enablement. Pet. at 13.

First, Petitioner presents no evidence that the Examiner did not evaluate the application for compliance with both the written description and enablement requirements. *See PowerOasis, Inc. v. T-Mobile USA, Inc*., 522 F.3d 1299, 1304 (Fed. Cir. 2008) (absent evidence to the contrary, a qualified government agency is presumed to have done its job properly); *see also* Ex. 1002 at 213 (the Examiner considering compliance with 35 U.S.C. § 112, setting forth the written description and enablement requirements).

Second, Petitioner's enablement arguments are substantially the same as those previously considered by the Office in the context of written description. Those

arguments are premised on Petitioner's inaccurate characterizations of the challenged claims as "functional" and of the specification as disclosing "limited" examples. *See* Pet. at 40-41, 49. As illustrated below, however, Petitioner's enablement analysis of the *Wands* factors is substantially the same as the Examiner's positions that were overcome during prosecution.

	Petitioner	**Examiner**
Breadth of the Claims	"Reaching the full scope of the claims of the '055 patent would require the testing of all proteins comprising an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 2 and an AAD-12 motif having the general formula of: $HX_{109}D(X)_{111\text{-}134}T(X)_{136\text{-}261}H(X)_{263\text{-}272}R$ to determine whether they had aryloxyalkanoate dioxygenase activity as claimed." Pet. at 39.	"Applicant claims a transgenic plant cell comprising a recombinant polynucleotide that encodes an AAD-12 protein having at least 85% or 90% sequence identity with SEQ ID NO: 2 and an AAD-12 motif having the general formula of $HX_{109}D(X)_{111\text{-}134}T(X)_{136\text{-}261}H(X)_{263\text{-}272}R$. Applicant claims a transgenic plant comprising said plant cell and methods of using said transgenic plant." Ex. 1002 at 213.
State of the Prior Art	"The only possible 'guidance' comes from the background, where Patent Owner describes previous work done on sdpA from *Delftia acidivorans* (SEQ ID NO: 2) and on the *broad family of α-ketoglutarate dependent dioxygenases* . . . ." Pet. at 46.	"The claimed motif represents the *family of α-ketoglutarate dioxygenases which have a broad genus of substrates*. Further, the Muller *et al* (2006) document submitted by Applicant shows that there are critical amino acids outside of the 'AAD-12' motif that are critical to the claimed function as illustrated in Figure 2 on page 1360, critical structure not

	Petitioner	Examiner
		described in the instant Application." Ex. 1002 at 317.
Predictability	"Given that the '055 patent only structurally defines the genus based on 85% sequence identity to SEQ ID NO: 2 and the presence of the 'AAD-12 motif,' it would be *nearly impossible to reliably predict* whether any other sequence within the scope of the claim would work." Pet. at 40.	"The general structure described in the first line of instant page 13 shows said characteristic residues. This description of a general structure known in an enzyme family *does not adequately describe the specific structure required to produce activity* that enzymatically degrades a phenoxy auxin herbicide and a pyridyloxy auxin herbicide." Ex. 1002 at 256.
Working Examples	"[T]he working examples are limited to the AAD-12 variant comprising an alanine insertion at position 2 of the amino acid sequence (SEQ ID NO: 4), 99.7% identical to SEQ ID NO: 2." Pet. at 49 n.13.	"Applicant describes an AAD-12 protein in instant SEQ ID NO: 2 and a single variant having an additional amino acid at position 2 in instant SEQ ID NO: 4." Ex. 1002 at 214.

Thus, the Office fully considered the factual issues underpinning Petitioner's enablement arguments, as evidenced by the Office's statements regarding the scope of the claims, disclosures of the specification, state of the prior art, and the examples. *See Triplet Therapeutics, Inc. v. Bd. of Supervisors of La. State Univ.*, PGR2021-00059, Paper 12 at 33-40 (PTAB Sept. 8, 2021) (denying institution under § 325(d) because Petitioner's written description arguments were substantially the same as those considered by the Office in the context of an enablement rejection); *Pharmacosmos A/S v. Am. Regent, Inc.*, PGR2020-00009, Paper 17 at 20-21, 27-30

(PTAB Aug. 14, 2020) (denying institution under § 325(d) because the issues raised by a written description challenge had "substantial overlap" with those previously considered in an enablement rejection); *Novartis Pharms. Corp. v. Plexxikon, Inc*., IPR2018-01287, Paper 17 at 8-16(PTAB Jan. 16, 2019) (denying institution under § 325(d) because Petitioner relied on substantially the same arguments concerning whether a provisional application provided § 112 support for the challenged claims as those considered by the examiner during prosecution).

Finally, given that "§ 325(d) is sufficiently implicated" here—at least by written description Ground 1—instituting review on all grounds would undermine the purpose of this statutory provision. *Pharmacosmos*, PGR2020-00009, Paper 17 at 29-30 (denying institution based on § 112 and prior art grounds without reaching challenge for lack of written description); *see also Harmonic Inc. v. Avid Tech., Inc*., 815 F.3d 1356, 1367 (Fed. Cir. 2016) (explaining that "the PTO is permitted, but never compelled, to institute an IPR proceeding").

Thus, *Advanced Bionics* step 1 and *Becton, Dickinson* factors (a), (b), and (d) also favor denial of institution with respect to enablement Ground 2.

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

Petitioner fails to show that the Office erred in any material manner or that Petitioner's cited prior art and arguments would have led to a different result during

prosecution. *Advanced Bionics*, IPR2019-01469, Paper 6 at 8; *Becton, Dickinson* factors (c), (e). Nor does its "new evidence" (*Becton, Dickinson* factor (f)), including the Silverstone declaration (Ex. 1003) and commercial product and stewardship materials (e.g., Ex. 1004), warrant revisiting the Office's careful examination.

1. Petitioner Fails to Identify Any Material Error that Warrants Reconsideration

Advanced Bionics explains that the PTAB's § 325(d) framework reflects "a commitment to defer to previous Office evaluations of the evidence of record unless material error is shown." IPR2019-01469, Paper 6 at 8-11, 20-22 (discussing petitioner's burden to show material error by the Office where substantially similar art was considered). Petitioner's conclusory assertions that the Examiner "withdrew the written description rejection in error" (Pet. at 13-14) and "never considered how a POSITA would practice the claimed invention" (*id.* at 14) fail to establish any material error.

Petitioner does not allege any material error with respect to written description beyond asserting that the rejection was withdrawn "based on the Examiner's cursory analysis and conclusory statements . . . ." *Id.* at 9. Nor does Petitioner explain how the Examiner allegedly erred in finding persuasive Patent Owner's cited evidence in the specification of a common structure. *See supra* § V(B)(2)(b); *see also* Ex. 1019; Ex. 1020. Indeed, Petitioner *nowhere* addresses the precedential *Ajinomoto* decision

regarding common structure and written description that Corteva highlighted to the Examiner in overcoming the written description rejection. *See, e.g.*, Ex. 1002 at 345-46. While Petitioner may disagree with the Examiner's withdrawal of the rejection and allowance of the claims, that does not constitute an error material to patentability. *See Advanced Bionics*, IPR2019-01469, Paper 6 at 9 ("If reasonable minds can disagree regarding the purported treatment of the art or arguments, it cannot be said that the Office erred in a manner material to patentability.").

Nor can material error be established by arguing the absence of a particular new rejection—or else essentially any petitioner could contend "error" in view of some newly crafted and less relevant alleged ground of unpatentability. *See id.*; *Microsoft Corp. v. ThroughPuter, Inc.*, IPR2022-00757, Paper 10 at 20-22 (PTAB Nov. 1, 2022) (denying institution under § 325(d) where "the lack of a rejection itself" was not dispositive of whether there was material error). This is especially true here, where the Examiner extensively considered § 112 support for the claims and Petitioner identifies no error in the Examiner's allowance. *See supra* § II(B)(4); Ex. 1002 at 213-14, 253-57, 314-17.

Worse still, Petitioner's § 112 analysis fails to address the state of the art as of the appropriate filing dates. During prosecution, the Examiner determined that the application would be "examined under the pre-AIA first to invent provisions." Ex. 1002 at 212. Petitioner fails to address any of the '055 patent's pre-AIA filing

dates, much less show that the Examiner erred in examining the application under pre-AIA law. As detailed above, Petitioner applies the wrong standard and fails to establish that the challenged claims lack the benefit of the filing date of the earliest (pre-AIA) applications, which shows that Petitioner has not established PGR eligibility. *Biogen MA*, PGR2022-00054, Paper 16 at 25-28; *Sandoz*, PGR2022-00037, Paper 11 at 14-16; *see supra* § V(A).

Thus, Petitioner's disagreement with the Examiner's decision to allow the claims does not establish any error material to patentability.[7]

2. None of Petitioner's "New" Evidence Warrants Reconsideration

Petitioner contends that "new" evidence shows that the inventors did not possess or enable the claimed invention. Pet. at 12-15. Petitioner is incorrect.

[7] Nor do Petitioner's competition-related allegations, based on the position that the claimed invention "was squarely in the public domain," withstand scrutiny. Pet. at 2-3, n. 2. Petitioner presented no facts in support of its position. Nor did Petitioner submit any prior art showing that the claimed invention was in the public domain. Petitioner's challenge is limited to written description and enablement—the Petition presents no anticipation or obviousness ground.

Technology Use Agreement and Commercial Product Materials (e.g., Ex. 1004; Ex. 1011; Ex. 1012). As detailed above, Corteva's TUA and marketing literature are not relevant to a § 112 analysis. Those materials concern the EPA's commercial regulation of Corteva's Enlist E3® soybeans, not the adequacy of the specification's disclosure. *See supra* § V(B)(1).

Dr. Silverstone's Declaration (Ex. 1003). Petitioner's submission of a declaration is not a "super-factor" that overrides the Board's statutory discretion to deny institution. *See Boragen, Inc. v. Syngenta Participations AG*, IPR2020-00124, Paper 18 at 4-5 (PTAB Aug. 10, 2020). That is particularly true here, as Dr. Silverstone largely rehashes the same arguments already considered by the Office while incorrectly analyzing written description and enablement only as of the '055 patent's post-AIA 2017 filing date. *See Edge Endo, LLC v. Michael Scianamblo*, IPR2018-01321, Paper 15 at 19 (PTAB Jan. 14, 2019) ("[W]e do not find that inclusion of a declaration reflecting an opinion that the Examiner 'overlooked' something in McSpadden warrants a reconsideration of the McSpadden challenges as raised by Petitioner."); *Regeneron Pharms., Inc. v. Kymab Ltd.*, IPR2019-01579, Paper 9 at 18 (PTAB Mar. 20, 2020) ("[T]he fact that the Declaration of Petitioner's expert was not before the Examiner during prosecution does not itself demonstrate that the Examiner erred.").

Accordingly, *Advanced Bionics* step 2 and *Becton, Dickinson* factors (c), (e), and (f) also weigh in favor of discretionary denial with respect to Grounds 1 and 2. The totality of the factors therefore confirms that the same or substantially the same arguments were previously presented to the Office and that Petitioner has not demonstrated that the Office erred when considering those arguments. 35 U.S.C. § 325(d); *Advanced Bionics*, IPR2019-01469, Paper 6 at 22. Patent Owner thus respectfully requests that the Board exercise its discretion to deny institution under § 325(d).

VII. Conclusion

For these reasons, Petitioner has failed to establish that the '055 patent is PGR-eligible. Petitioner has also independently failed to establish that it is more likely than not that any challenged claim is unpatentable for lack of written description or enablement, and has only presented the same or substantially similar arguments to those Corteva overcame during prosecution. Accordingly, the Board should deny institution.

Respectfully submitted,

Dated: July 17, 2023

/Pier D. DeRoo/
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CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. § 42.24(d), I, Pier D. DeRoo, certify that **Patent Owner's Preliminary Response** contains 14,050 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: July 17, 2023

/Pier D. DeRoo/
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CERTIFICATE OF SERVICE

The undersigned certifies that a copy of the foregoing **Patent Owner's Preliminary Response** and **Exhibits 2001-2005** were served electronically via email on July 17, 2023, in their entirety on the following:

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Petitioner has consented to electronic service by email.

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