Trials@uspto.gov
571-272-7822

Paper 11
Entered: October 13, 2023

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 B2

Before MICHAEL J. FITZPATRICK, ZHENYU YANG, and DEVON ZASTROW NEWMAN, *Administrative Patent Judges*.

NEWMAN, *Administrative Patent Judge*.

DECISION
Granting Institution of Post-Grant Review
35 U.S.C. § 324

I. INTRODUCTION

A. Background and Summary

Inari Agriculture, Inc. ("Petitioner"), filed a Petition requesting post-grant review of claims 1–33 ("the challenged claims") of U.S. Patent No. 11,371,055 B2 (Ex. 1001, "the '055 patent"). Paper 2 ("Pet."), 1. Corteva Agriscience LLC ("Patent Owner") filed a Preliminary Response to the Petition. Paper 6 ("Prelim. Resp."). With authorization, Petitioner filed Petitioner's Reply to Patent Owner's Preliminary Response (Paper 9, "Reply") and Patent Owner filed Patent Owner's Sur-Reply (Paper 10, "PO Sur-reply").

Under 35 U.S.C. § 324(a), a post-grant review may be instituted only if "the information presented in the petition . . . demonstrate[s] that it is more likely than not that at least 1 of the claims challenged in the petition is unpatentable." Post-grant review is available for patents that issue from applications that at one point contained at least one claim with an effective filing date on or after March 16, 2013. *See* Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) ("AIA"), §§ 3(n)(1), 6(f)(2)(A).

After considering the briefing and the evidence of record, for the reasons set forth below, we determine that Petitioner has sufficiently shown that it is more likely than not that at least one challenged claim of the '055 patent is unpatentable under § 324(a). Accordingly, we institute a post-grant review of the challenged claims of the '055 patent.

B. Real Parties in Interest

The parties identify themselves as real parties-in-interest. Pet. 3; Paper 4, 1 (Mandatory Notice).

C. Related Matters

Petitioner identifies no related matters. Pet. 4. Patent Owner states that there are no related litigation matters. Paper 4, 1. Patent Owner also cites the '055 patent's priority applications and states that a patent (U.S. Patent No. 8,283,522) that issued from one of the priority applications is involved in an *ex parte* reexamination proceeding, Control No. 90/019,131, which was requested by Petitioner. *Id.*

D. The '055 Patent (Ex. 1001)

The '055 patent, titled "Herbicide Resistance Genes," issued on June 28, 2022, from U.S. Application No. 15/468,494 ("the '494 application"), filed on March 24, 2017. Ex. 1001, codes (21), (22), (45), (54). The '494 application claims priority to U.S. Application No. 14/491,197, filed on September 19, 2014, which is a continuation of U.S. Application No. 13/647,081, filed on October 8, 2012, which is a continuation of U.S. Application No. 12/091,896, which was filed as application No. PCT/US2006/042133 on October 27, 2006, and U.S. Provisional Application No. 60/731,044, filed on October 28, 2005. *Id.* at codes (60), (63).

The '055 patent relates to a transgenic plant that is resistant to both 2,4-dichlorophenoxyacetic acid ("2,4-D") and pyridyloxyacetate herbicides. *Id.* at code (57). The Specification explains that 2,4-D has been used for broad spectrum, broadleaf weed control and that "2,4-D remains one of the most widely used herbicides globally." *Id.* at 2:27–34. However, the Specification further explains that the use of 2,4-D is limited because "its selectivity in dicot crops like soybean or cotton is very poor," and 2,4-D can injure grass crops. *Id.* at 2:34–49. The Specification states that 2,4-D can be

used in combination with glyphosate for a burndown treatment prior to planting no-till soybeans and cotton, but the treatment must be done at least 14–30 days prior to planting. *Id.* at 2:39–44. In addition, the Specification describes the use of pyridyloxyacetic acid herbicides, namely triclopyr and fluroxypyr. *Id.* at 2:52–54.

The '055 patent states that *Ralstonia eutropha* has the ability to degrade 2,4-D due to the gene tfdA. *Id.* at 3:8–11. The Specification explains that "[t]fdA catalyzes the conversion of 2,4-D acid to dichlorophenol (DCP) via an α-ketoglutarate-dependent dioxygenase reaction" and that DCP has little herbicidal activity in comparison to 2,4-D. *Id.* at 3:12–17. The Specification further states that "[t]fdA has been used in transgenic plants to impart 2,4-D resistance to dicot plants (e.g., cotton and tobacco) normally sensitive to 2,4-D." *Id.* at 3:17–19.

According to the '055 patent, "[n]o α-ketoglutarate-dependent dioxygenase enzyme has previously been reported to have the ability to degrade herbicides of both the phenoxyacetate and pyridyloxyacetates auxin herbicides." *Id.* at 4:50–54. The '055 patent states that its "invention relates to the use of an enzyme that is capable of degrading both 2,4–D and pyridyloxyacetate herbicides." *Id.* at 4:48–50. The '055 patent identifies its preferred enzyme and gene as AryloxyAlkanoate Dioxygenase ("AAD-12"). *Id.* at 4:55–57. The '055 patent states that the AAD-12 gene "is able to degrade the pyridyloxyacetates auxins (e.g., triclopyr, fluroxypyr) in addition to achiral phenoxy auxins," such as 2,4-D. *Id.* at 6:41–46.

E. Challenged Claims

Petitioner challenges claims 1−33. Pet. 1. Claim 1 is independent and 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:
>
> $HX_{109}D(X)_{111-134}\ T(X)_{136-261}H(X)_{263-272}R$, wherein
>
> X_{109} represents a single amino acid at position 109, relative to the sequence of SEQ ID NO: 2;
>
> $(X)_{111-134}$ represents a sequence of 24 amino acids;
>
> $(X)_{136-261}$ represents a sequence of 126 amino acids; and
>
> $(X)_{263-272}$ represents a sequence of 10 amino acids.

Ex. 1001, 125:2–18.

Claim 32 is identical to claim 1 but adds the limitation "wherein said AAD-12 motif has 90% sequence identity with corresponding amino acids of position 108 to 273 of SEQ ID NO: 2." *Id*. at 126:52–127:4.

The remaining challenged claims are all dependent on claim 1 and recite further limitations for the plant cell; transgenic plants including the cell; methods using the cell; and a part, progeny, or asexual propagate of a plant including cell. *Id.* at 125:19–127:26.

F. Asserted Grounds

Petitioner asserts that claims 1−33 are unpatentable on the following grounds:

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1–33	112(a)[1]	Lack of Written Description
1–33	112(a)	Lack of Enablement

Pet. 7. Petitioner relies on the Declaration of Aron Silverstone, Ph.D., (Exhibit 1003) in support of these grounds.

II. ANALYSIS

A. Person of Ordinary Skill in the Art

Petitioner contends that a person having ordinary skill in the art (POSA) "at the time the '055 was filed, had 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" and that "[a]dditional graduate education could substitute for professional experience, or significant experience in the field could substitute for formal education." Pet. 23 (citing Ex. 1003 ¶¶ 16–18).

Patent Owner argues that "Petitioner proposes a high level of ordinary skill in the art." Prelim. Resp. 20. According to Patent Owner, "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." *Id.* at 20–21 (citing Exs. 1019, 1020). Patent Owner asserts that "Petitioner's declarant appears to have no meaningful background with that family of enzymes." *Id.* at 21 (citing Ex. 1003 ¶¶ 6–15; *Kyocera Senco Indus. Tools Inc. v. Int'l Trade Comm'n*, 22

[1] The Leahy-Smith America Invents Act, Pub. L. No. 112–29, 125 Stat. 284 (2011) ("AIA"), amended 35 U.S.C. § 112. Because we determine that the challenged claims of the '055 patent have an effective filing date after the effective date of the applicable AIA amendment, we refer to post-AIA § 112(a).

F.4th 1369, 1377 (Fed. Cir. 2022)). Patent Owner argues that, should we "define a level of ordinary skill at this stage of the proceeding, familiarity with αKG-dependent dioxygenases such as SdpA should be included." *Id.* However, Patent Owner contends that "it is not necessary at this stage to define a specific level of ordinary skill, which is reflected in the art." *Id.* at 20.

Based on the information presented, we agree with Patent Owner that the asserted prior art itself is sufficient to demonstrate the level of skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (prior art itself can reflect the appropriate level of ordinary skill in the art). We do not find it necessary to define the level of skill in the art at the time of the invention at this time. However, for purposes of deciding whether to institute trial, we find that Dr. Silverstone is qualified to provide helpful opinion testimony on the issues regarding which we cite his testimony in this decision. *See* Ex. 1003 ¶¶ 6–15.

B. Claim Interpretation

The parties do not propose any specific claim constructions at this stage. Pet. 23; Prelim. Resp. 21.

We construe terms in controversy only to the extent necessary to resolve the controversy. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)). We do not find it necessary to expressly interpret any claim term for purpose of deciding whether to institute trial.

If either party intends to further argue claim construction at trial it should do so in a clearly designated section of its brief so as to expressly

identify such arguments. *See, e.g.*, 37 C.F.R. § 42.104(b)(3) (content of petition); *see also* Patent Trial and Appeal Board Consolidated Trial Practice Guide (Nov. 2019), 46, 48–49) (*available at* https://www.uspto.gov/sites/default/files/documents/tpgnov.pdf?MURL=). Critical claim construction arguments should not be relegated to or hidden within patentability arguments on the facts.

III. DISCRETIONARY DENIAL UNDER 35 U.S.C. § 325(D)

Patent Owner argues we should exercise discretion under § 325(d) and deny institution of review because the USPTO previously considered substantially the same arguments during prosecution of the '055 patent. Prelim. Resp. 54–65. Petitioner provides opposing arguments. *See* Pet. 8–15. For the reasons discussed below, we decline to invoke our discretion to deny institution under § 325(d).

A. Legal Framework

Pursuant to 35 U.S.C. § 325(d), when determining whether to institute a post-grant review, we "*may* take into account whether, and reject the petition . . . because, the same or *substantially the same* prior art or *arguments previously were presented to the Office*."[2] 35 U.S.C. § 325(d) (emphases added). In this case, only the "arguments" portion of § 325(d) is at issue. The parties do not argue that the "prior art" portion is at issue, and we discern no reason to address that portion.

When applying § 325(d), we utilize a two-part framework. *See Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 8 (PTAB Feb. 13, 2020) (precedential) ("*Advanced Bionics*"). First, we determine "ether the same or substantially

[2] The Board institutes trial on behalf of the Director. 37 C.F.R. § 42.4(a).

the same arguments previously were presented to the Office." *Id.* Second, if the same or substantially the same arguments previously were presented to the Office, we determine "whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims." *Id.* We consider several non-exclusive factors as set forth in *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 (Dec. 15, 2017) (precedential as to § III.C.5, first paragraph) ("*Becton, Dickinson*"), which "provide useful insight into how to apply the framework" under § 325(d). *Id.* at 9.

In the first part of the *Advanced Bionics* framework, we consider the extent of the overlap between the arguments made during examination and those made by Petitioner. *Id.* at 10 (citing factors (a), (b), and (d) of *Becton, Dickinson*). "If, after review of factors (a), (b), and (d), it is determined that the same or substantially the same art or arguments previously were presented to the Office, then factors (c), (e), and (f)[3] relate to whether the petitioner has demonstrated a material error by the Office." *Advanced Bionics*, Paper 6 at 10.

B. Whether the Arguments Are the Same or Substantially the Same

Patent Owner argues that Petitioner's written description and enablement challenges raise substantially the same arguments as the Office's written description arguments that Applicant (now Patent Owner)

[3] Factors (c), (e), and (f) are: (c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection; (e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and (f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the prior art or arguments. *Becton, Dickinson*, Paper 8 at 17–18.

successfully overcame during prosecution. Prelim. Resp. 55–60. Patent Owner provides charts comparing Petitioner's arguments to Examiner's rejections, and argues that all of Examiner's issues were overcome. *Id.* (citing Ex. 1002, 214, 315, 317). Patent Owner argues, for instance, that the Examiner rejected the claims because Applicant's disclosure lacked identification of a structural/functional relationship between the AAD-12 motif and the enzyme degradation function, but that the Examiner ultimately withdrew the rejection in light of Applicant's arguments. *Id.* at 56–57; *see also* Ex. 1002, 342–348 (Applicant's final argument challenging the written description rejection), 355 (Examiner's withdrawal of the rejection "in view of Applicant's remarks").

Further with regard to enablement, Patent Owner argues that although the Examiner issued no rejection for non-enablement, the Examiner is presumed to have evaluated this issue, and that Petitioner presents no evidence that the Examiner failed to do so. *Id.* at 57.

Petitioner argues that both the written description and enablement arguments are not the same as those made during prosecution because the Examiner's rejection focused on the Specification's failure to describe the genus of the AAD-12 proteins because "AAD-12 motif" did not appear in the Specification, and the Examiner's rejections were conclusory.[4] Pet. 8–9.

[4] Petitioner's § 325(d) analysis fails to address the discussions in the prosecution history at Ex. 1003, 342–348 following Applicant's amendment to add "AAD-12 motif," and we are not persuaded by Petitioner's characterization of Applicant's arguments.

Petitioner also argues that the Examiner did not analyze the *Wands*[5] factors or consider arguments directly related to the enablement of the claims. *Id.*

Our review of the evidence reveals that most, though not all of Petitioner's arguments in this proceeding overlap with arguments raised during examination. Because Petitioner raises arguments not adequately addressed during prosecution, we conclude the arguments are not sufficiently similar to support a discretionary denial of institution.

A brief recitation of the relevant prosecution history is warranted. The Examiner issued a written description rejection because the claims recited a genus of the AAD-12 proteins, yet the recited "AAD-12 motif" did not appear in the Specification. Ex. 1002, 213–214. In response to the rejection, Applicant argued that the Specification contained sufficient information to support the genus reciting the AAD-12 motif because of the disclosed SEQ ID NOS: 2 and 4 and additional guidance in the Specification. *Id.* at 240–241.

The Examiner mailed a Final Rejection, maintaining the written description rejection for lack of sufficient information in the Specification supporting the breadth of the genus recited in the claims. *Id.* at 253–257. Appellant argued against the rejection, without amendment, arguing, e.g., that the structure/function of the gene tfdA and related α-ketoglutarate dependent dioxygenases provided a substantial amount of the structure of

[5] *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (Factors considered in weighing undue experimentation include "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

the members of the claimed genus and would guide the ordinary artisan in preparing derivatives of the disclosed sequence for testing to confirm the required activity of herbicide degradation. *Id.* at 276–284.

In response to Applicant's filing a Request for Continued Examination, the Examiner again maintained the written description rejection, citing a lack of description of a structural/functional relationship between the AAD-12 motif and the enzymatic degradation of the recited herbicides, noting that specific features in the AAD-12 motif were "critical to the recited function." Ex. 1002, 315. The Examiner also found the Applicant did not "describe a representative number of species that would represent the variation within the claimed genus." *Id.* at 317.

Without amendment to claim 27, which issued as claim 1, Applicant argued that the skilled artisan's knowledge of the AAD-12 motif and its involvement in dioxygenase activity, along with the disclosure of SEQ ID Nos. 2 and 4 in the Specification provided sufficient written description. Ex. 1002, 345–348. Applicant described the Specification as containing a "roadmap to readily identify the corresponding positions in the AAD-12 proteins of SEQ ID Nos: 2 and 4 to generate a 'AAD-12 motif' of $HX_{109}D(X)_{111\text{-}134}T(X)B_{6\text{-}261}H(X)_{263\text{-}212}R$, that is specific to the claimed genus of AAD-12 proteins." *Id.* at 344.

Applicant further stated "[b]ecause the claimed common structure of the $HX_{109}D(X)_{111\text{-}134}T(X)B_{6\text{-}261}H(X)_{263\text{-}212}R$ motif corresponds to the recognized active site of dioxygenases, a skilled artisan would have readily appreciated that *the disclosed AAD-12 common structural motif confers the specific activity of the claimed dioxygenases, including the phenoxy auxin and pyridyloxy auxin degrading activity*." *Id.* at 347 (emphasis added).

Applicant further argued that known crystal structure and sequence information on dioxygenases provided additional information on dioxygenase structure and, with the disclosures of the Specification, the skilled artisan would have been "able to envision the structure of variants that meet the limitations of the claimed invention and would thus understand that applicant was in possession of the invention as claimed." *Id.* The Examiner, relying on the accuracy of Applicant's statement, withdrew the rejection "in view of Applicant's Remarks." *Id.* at 355.

Based on the above, we agree with Patent Owner that many of the arguments raised by the Examiner are highly similar to the challenges in this proceeding, particularly the written description challenge. However, some arguments differ. For instance, Petitioner's enablement argument identifies that, contrary to Applicant's statement during prosecution reproduced above, amino acids and protein structure *outside* the disclosed AAD-12 motif can also affect the activity of the claimed dioxygenases to degrade phenoxy auxin and pyridyloxy auxin. *See* Ex. 1003 ¶¶ 42–50, 79 (Dr. Silverstone describing the mechanics of protein binding and explaining why the '055 patent disclosure fails to provide sufficient information to the skilled artisan to know which amino acids could be changed while retaining the ability to enzymatically degrade both phenoxy and pyridyloxy auxin herbicides). *See also* Pet. 27–34 (asserting, e.g., 85% homology to AAD-12 motif alone is insufficient to predict enzymatic degradation activity). While the Examiner's rejections regarded the disclosure corresponding to the ability to degrade herbicides, the Examiner plainly relied on Applicant's statements that the AAD-12 motif's structure *alone* was responsible when deciding to withdraw the rejection. Ex. 1002, 355. The Examiner did not have the

additional testimony supplied by the Silverstone declaration explaining otherwise. *See* Ex. 1003 ¶¶ 42–50, 79.

Petitioner, through Dr. Silverstone, also addresses the effort the skilled artisan would have needed to undertake to determine what proteins outside of the AAD-12 motif would affect the ability of homologues to enzymatically degrade the recited herbicides, and provides evidence for consideration regarding the lack of a clear link between the AAD-12 motif and the ability to enzymatically degrade both phenoxy and pyridyloxy auxin herbicides. Ex. 1003, 347. Therefore, the arguments are not entirely overlapping. And while these issues do in part overlap with Petitioner's arguments pertaining to enablement, we agree with Petitioner that the Examiner did not complete a written *Wands* analysis. Although we conclude that the arguments are not entirely overlapping, we proceed to the second step in the analysis, for completeness.

C. Whether Petitioner Has Demonstrated Material Error

We next consider whether Petitioner has demonstrated that the Examiner materially erred in a manner material to the patentability of challenged claims. *Advanced Bionics*, Paper 6 at 8.

Petitioner alleges that, to the extent we conclude the arguments are the same, "the Examiner erred in withdrawing the written description rejection" and that such error extended to enablement to the extent the arguments overlap. Pet. 9, 13. Petitioner argues that the Examiner erred in not considering how the skilled artisan would have practiced the claimed invention, and that this information is described in detail in its declarant's testimony. *Id*. at 14–15.

Patent Owner argues that Petitioner fails to meet its burden to show error and that none of Petitioner's alleged new evidence warrants reconsideration. Prelim. Resp. 60–65. Patent Owner argues that the examination of section 112 support for the claims was sufficient to encompass enablement and that Petitioner's analysis does not address the appropriate dates and applied an incorrect standard. *Id.* at 62–63. Patent Owner alleges that Dr. Silverstone's analysis is deficient and does not support Examiner error. *Id.* at 63–65.

After consideration of the evidence in the briefs and arguments of the parties, we conclude that the Examiner erred in reversing the written description rejection and in not issuing a rejection for enablement. Though the Examiner articulated concerns in his written description rejection similar to those presented here, the arguments made to the Examiner focused heavily on the AAD-12 motif and its central role in enzymatically degrading phenoxy and pyridyloxy auxin herbicides. Ex. 1003, 347. The Examiner relied on Applicant's representations in finding the disclosures sufficient to provide written description of the full genus. *Id.* at 355. With the benefit of Dr. Silverstone's Declaration, it is evident that the rejection should not have been withdrawn. In addition, consideration of recent Supreme Court precedent confirms the Examiner should have issued a rejection for lack of enablement due to insufficient examples and over-reliance on trial and error by a skilled artisan. *See Amgen Inc. v. Sanofi*, 143 S. Ct. 1243, 1256 (2023) (affirming district court finding and holding patent claims not enabled where the disclosure claimed a group of antibodies defined by their function but specification disclosed only "step-by-step [patentee's] own trial-and-error method for finding functional antibodies—calling on scientists to create a

wide range of candidate antibodies and then screen each to see which [was functional])." Accordingly, we decline to exercise our discretion to deny institution under 35 U.S.C. § 325(d).

IV. ELIGIBILITY FOR POST-GRANT REVIEW

As a threshold matter, we must determine whether the '055 patent is eligible for post-grant review.

A. Legal Framework

First, post-grant review is only available if the petition is filed within nine months of the issuance of the challenged patent. 35 U.S.C. § 321(c) (2018). Here, the Petition was filed on March 28, 2023, which is within nine months of the '055 patent's June 28, 2022, issue date. Ex. 1001, code (45).

Second, post-grant review is available only for patents that issue from applications that at one point contained at least one claim with an effective filing date of March 16, 2013 or later. The post-grant review provisions set forth in section 6(d) of the Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (September 16, 2011) ("AIA"), apply only to patents subject to the first-inventor-to-file provisions of the AIA. *See* AIA § 6(f)(2)(A) (stating that the provisions of section 6(d) "shall apply only to patents described in section 3(n)(1)"). Patents subject to the first-inventor-to-file provisions are those that issue from applications that contain or contained at any time—

> (A) a claim to a claimed invention that has an effective filing date as defined in section 100(i) of title 35, United States Code, that is on or after [March 16, 2013]; or
>
> (B) a specific reference under section 120, 121, or 365(c) of title 35, United States Code, to any patent or application that contains or contained at any time such a claim.

AIA § 3(n)(1).

Our rules require that a petitioner for post-grant review certify that the challenged patent is available for post-grant review. 37 C.F.R. § 42.204(a) ("The petitioner must certify that the patent for which review is sought is available for post-grant review . . . ."). Petitioner has the burden of establishing eligibility for post-grant review. *See Mylan Pharms. Inc. v. Yeda Res. & Dev. Co.*, PGR2016-00010, Paper 9 at 10 (PTAB Aug. 15, 2016).

The application that matured into the '055 patent is a transition application, as it claims priority to applications filed before March 16, 2013. Specifically, the '055 patent issued June 28, 2022 from the '494 application, filed on March 24, 2017, which claims priority to U.S. Application No. 14/491,197, filed on September 19, 2014, which is a continuation of U.S. Application No. 13/647,081, filed on October 8, 2012, which is a continuation of U.S. Application No. 12/091,896, which was filed as application No. PCT/US2006/042133 on October 27, 2006, and U.S. Provisional Application No. 60/731,044, filed on October 28, 2005. Ex. 1001, codes (21), (22), (60), (63).

To show that the '055 patent is eligible for post-grant review, Petitioner bears the burden of proving that at least one of the challenged claims lacks the benefit of the filing date of the earliest application that supports the claim. In particular, Petitioner must show that at least one of the challenged claims "was not disclosed in compliance with the written description and enablement requirements of § 112(a) in the earlier application for which the benefit of an earlier filing date prior to March 16,

2013 was sought." *Inguran, LLC v. Premium Genetics (UK) Ltd.*, PGR2015-00017, Paper 8 at 11 (PTAB Dec. 22, 2015).

B. Petitioner's Eligibility Allegations

In alleging that the '055 patent is eligible for post-grant review, Petitioner asserts that the '055 patent "is entitled to a priority date no earlier than 3/27/2017 (the actual filing date of the '494 Application, which issued as the '055 patent)" because "the '055 claims include limitations that both lack a proper written description and are not enabled." Pet. 5–6. In support of this argument, Petitioner cites to its arguments on Grounds 1 and 2 for lack of written description support and lack of enablement. *Id.* Petitioner argues that "because the '055 specification was amended during prosecution of the '494 Application, all the disclosures of the parent applications (to which the '055 claims to be continuations) are, *at best*, the same as the '055." Pet. 6 (footnote omitted). Thus, if the '055 Specification fails to adequately describe and enable any claim of the '055 patent, then the '055 patent is eligible for post-grant review.[6] We, therefore, turn to Petitioner's arguments as to why the challenged claims lack written description and enablement.

[6] Because we find that Petitioner is likely to show that one or more of the challenged claims lacks written descriptive support and is not enabled by the Specification of the '055 patent, we are not persuaded by Patent Owner's argument that the Petitioner failed to demonstrate PGR eligibility by failing to analyze written description and enablement support "as of the filing date of any pre-AIA application in the priority chain of the '055 patent." Prelim. Resp. 21–22.

C. Alleged Lack of Written Description

Petitioner argues that the challenged claims lack sufficient written descriptive support in the Specification for several reasons, which we discuss below. Pet. 25–36.

1. Legal Standard

To satisfy the written description requirement under 35 U.S.C. § 112(a), the specification must "reasonably convey[] to those skilled in the art that the inventor had possession" of the claimed invention as of the filing date based on an "objective inquiry into the four corners of the specification." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351–52 (Fed. Cir. 2010) (en banc). If this test fails, the '055 patent is not entitled to the benefit of the earlier filing date of the priority application and we would have jurisdiction under 35 U.S.C. § 324 to institute post-grant review.

The written description requirement is satisfied when the specification "set[s] forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed." *University of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 928 (Fed. Cir. 2004). The specification does not have to provide exact or *verbatim* textual support for the claimed subject matter at issue. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570 (Fed. Cir. 1996). The Federal Circuit has clarified that

> [a]lthough [the applicant] does not have to describe exactly the subject matter claimed, . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed . . . . The test for sufficiency of support . . . is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter."

Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563 (Fed. Cir. 1991) (citations omitted). Moreover, "the written description requirement does not demand either examples or an actual reduction to practice." *Ariad Pharms.*, 598 F.3d at 1351. "[A]n applicant is not required to describe in the specification every conceivable and possible future embodiment of his invention." *Cordis Corp. v. Medtronic AVE, Inc.*, 339 F.3d 1352, 1365 (Fed. Cir. 2003). Furthermore, "[a] specification may . . . contain a written description of a broadly claimed invention without describing all species that [the] claim encompasses." *Id.*

Finally, the written description inquiry is a question of fact, is context specific, and must be determined on a case-by-case basis. *Ariad Pharms.*, 598 F.3d at 1351 (citing *Ralston Purina Co. v. Far-Mar-Co, Inc.*, 772 F.2d 1570, 1575; *Capon v. Eshhar*, 418 F.3d 1349, 1357–1358 (Fed. Cir. 2005)); *see also Vas-Cath*, 935 F.2d at 1562 ("Precisely how close the [original] description must come to comply with [the description requirement of] § 112 must be [determined on a] case-by-case basis.") (quoting *In re Smith*, 258 F.2d 1389, 1395 (CCPA 1972)). "[T]he level of detail required to satisfy the written description requirement varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology." *Ariad Pharms.* 598 F.3d at 1351 (citing *Capon*, 418 F.3d at 1357–1358). Factors used to evaluate the sufficiency of a disclosure include: 1) "the existing knowledge in the particular field"; 2) "the extent and content of the prior art"; 3) "the maturity of the science or technology"; and 4) "the predictability of the aspect at issue" (the "*Ariad* factors"). *Id.* (citing *Capon*, 418 F.3d at 1359).

2. Petitioner's Allegations

Petitioner alleges three areas in which the Specification fails to provide written descriptive support for the challenged claims: (1) lack of structure-function correlation or representative number of species commensurate with the scope of the claim; (2) insufficient support for AAD-12 proteins having less than 99.7% identity to SEQ ID NO: 2; and (3) the two disclosed species do not function across the claimed genus of transgenic plants. Pet. 27–36. We address these arguments in turn, below.

a) Insufficient Support for the Claimed Genus

According to Petitioner, "[t]he claims of the '055 patent are overly broad and functionally defined, and the specification fails to disclose either a representative number of species commensurate with the scope of the claim or establish a reasonable structure-function correlation." *Id.* at 27 (citing Ex. 1003 ¶¶ 41–55). Petitioner asserts that "[t]he claimed genus encompasses up to 2.4 x 10^{106} species" but

> the specification discloses only two species, and tests only one, that meet[s] the structural requirements of the claims and possess the required functional features; the native AAD-12, and an AAD-12 variant that differs only by the addition of a single alanine residue near the N-terminus of the protein, 99.7% identical to the native AAD-12.

Id. at 27–28 (citing Ex. 1001, SEQ ID NOs: 2, 4; Ex. 1003 ¶ 80 n.1). According to Petitioner, this falls short of the claims, "which allow up to 43 mutations, including in the recited 'AAD-12 motif' structure." *Id.* at 28.

Petitioner further argues that "[t]he '055 patent provides no information, testing, data, or discussion of species with less than 99.7% sequence identity to SEQ ID NO: 2." *Id.* (citing Ex. 1003 ¶¶ 80–82). Petitioner contends that "given the unpredictable nature of protein folding

and structure/function correlation," "the 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." *Id.* (citing Ex. 1003 ¶¶ 42–50; *Regents of the Univ. of Cal. v. Eli Lilly*, 119 F.3d 1559, 1568 (Fed. Cir. 1997)).

Petitioner asserts that:

> Aside from the requirement that AAD-12 proteins of the invention have at least 85% identity to SEQ ID NO: 2, the only structural definition of the genus disclosed was the five conserved residues of the 166 amino acid long "AAD-12 motif" and the lengths of amino acid sequences around and between them.

Id. (citing Ex. 1001, claim 1; Ex. 1003 ¶ 79). Petitioner contends that, although the claimed genus is functionally defined to include only those sequences exhibiting activity that enzymatically degrades certain herbicides, "no clear link between the recited 'AAD-12' motif and the novel ability to enzymatically degrade both phenoxy and pyridyloxy auxin herbicides is disclosed." *Id.* at 28–29 (citing Ex. 1003 ¶¶ 42–50, 79). Petitioner argues that "the defined residues of the 'AAD-12 motif' are conserved in, for example tfDa as well, yet it does not exhibit claimed functionality." *Id.* at 29 (citing Ex. 1001, Fig. 2). According to Petitioner, chain lengths alone cannot confer this functionality to a protein because a protein's function "is dependent on its folded, tertiary structure, which depends far more on amino acid sequence than on sequence length." *Id.* (citing Ex. 1003 ¶¶ 42–50). In view of this, Petitioner contends that "five isolated residues of a protein and the lengths of sequences between them are insufficient to impart said tertiary structure, more is needed to establish 'a reasonable structure-function correlation.'" *Id.* (citing Ex. 1003 ¶¶ 42–50; *AbbVie*, 759 F.3d at 1300–01).

In reply, Petitioner argues that the disclosure of the '055 patent, like that of the patent owner in *Amgen*, provides merely a "roadmap" for identifying the claimed subject matter, that instructs the skilled artisan through "the numerous steps required to refine and test candidate proteins once selected," and is invalid for the same reasons. Reply, 2–3 (citing *Amgen*, 143 S. Ct. 1243). Petitioner argues that Patent Owner concedes that "many proteins satisfying claim 1's structural elements will lack the claimed functions; instead, both '*in vitro* and *in vivo*' testing is needed." *Id.* at 4 (citing Prelim. Resp., 51). Petitioner argues that the structural information Patent Owner claims to provide, the 5 conserved amino acids and sequence lengths in between these residues, is necessary to the claim subject matter yet insufficient to reliably describe or enable the entire range of the such subject matter. *Id.* at 5–6.

Petitioner argues that "[t]he '055 patent discloses two species, native AAD-12 and the AAD-12 variant, the only species tested," and the aryloxyalkanoate dioxygenase activity that degrades both phenoxy and pyridyloxy auxin herbicides is attributed to these species. Pet. 30 (citing Ex. 1003 ¶ 80). According to Petitioner, "[t]hese species, with 99.7% sequence identity, differ by the insertion of a single alanine at the N-terminus of the protein, 107 amino acids removed from the 'AAD-12 motif' and not indicated to have any significant affect upon the tertiary structure of the protein." *Id.* (citing Ex. 1001, 35:8–13; Ex. 1003 ¶ 80). Petitioner asserts this is a negligible degree of variations between proteins that exhibits the claimed functionality, which is not informative of the structural features to impart this functionality to proteins. *Id.* (citing Ex. 1003 ¶¶ 42–50). Petitioner argues that "[t]he claims place no limits on the types of mutations

that can be made, or where in the sequence they can be made, aside from the 5 conserved amino acids of the 'AAD-12 motif' and the chain lengths around and between them." *Id.* at 30–31 (citing Ex. 1003 ¶ 79).

Petitioner contends that the final three-dimensional "'tertiary' structure of a protein cannot be accurately predicted solely from the primary amino acid sequence," enzymes "require a specific spatial arrangement of amino acids to form the active site," and any alteration to the shape of an enzyme's active site "can have significant effects on the substrate specificity, catalytic activity, and other biochemical parameters thereof, or abrogate activity altogether." *Id.* at 31 (citing Ex. 1003 ¶¶ 42–47). Petitioner argues that, "[b]ecause the '055 patent does not disclose any species with less than 99.7% sequence identity to SEQ ID NO: 2, it does not provide any direction or guidance as to species with any greater degree of variation than that." *Id.* According to Petitioner, the '055 patent describes "only two, nearly identical species of a genus encompassing up to 2.4×10^{106} species." *Id.* at 32 (citing Ex. 1003 ¶ 80 n.1).

Petitioner further asserts that "[t]he '055 patent also fails to describe 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." *Id.* (citing Ex. 1003 ¶¶ 48–50). According to Petitioner, "[t]he '055 patent also fails to describe 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" but "no other members of the family of α-ketoglutarate-dependent dioxygenases have been shown to exhibit the claimed

functionality; thus the maintenance of these active site residues alone cannot explain the novel functionality of the claimed genus." *Id.* at 32–33 (citing Ex. 1001, Fig. 2; Ex. 1003 ¶ 48). Petitioner contends that "[w]hile the conserved amino acids of the 'AAD-12 motif' are necessary for the claimed activity, they are not sufficient to determine substrate specificity or activity" because that depends on the amino acids being in the correct spatial configuration. *Id.* at 33 (citing Ex. 1003 ¶¶ 48–49). According to Petitioner, "[i]t would be nearly impossible for a POSITA to predict whether a species other than the disclosed AAD-12 or AAD-12 variant would function as claimed from the disclosure of the '055 patent, even in view of the state of the art at the time of filing." *Id.* (citing Ex. 1003 ¶¶ 48–50).

Petitioner asserts that their experimental evidence and Patent Owner's own publications show that the claimed invention does not function. Pet. 34 (citing Ex. 1004, 2; Ex. 1003 ¶¶ 51–55). Petitioner argues that "the specification provides experimental results for seven species of plants comprising the AAD-12 variant, with some, but not all, of the tested plant species showing herbicide resistance to both phenoxy and pyridyloxy auxin herbicides." *Id.* (citing Ex. 1001, 48:62–102:49). According to Petitioner, "no data is presented for the herbicide resistance of transgenic soybeans comprising the AAD-12 variant against pyridyloxy auxin herbicides" and "no data is presented for the herbicide resistance of transgenic cotton comprising the AAD-12 variant against any herbicides; the data concerns transformation efficiency, and provides only prophetic experiments to test for phenoxy, but not pyridyloxy, auxin herbicide resistance." *Id.* at 34–35 (citing Ex. 1001, 31:55–102:49; Ex. 1003 ¶ 53).

Petitioner contends that "Patent Owner's own Technology Use Agreement (the 'Agreement') for Pioneer® Brand Enlist E3 Soybeans—transgenic soybeans comprising the AAD-12 variant—expressly prohibits use, following burndown, of 'any pyridine auxin herbicides (e.g., triclopyr [sic], fluroxypyr) on emerged Enlist crop.'" *Id.* at 35 (citing Ex. 1004, 2; Ex. 1003 ¶ 54). Petitioner argues that "[t]he Agreement, the '055 patent, and indeed Patent Owner's marketing materials, make clear that transgenic soybeans comprising the AAD-12 variant show herbicide resistance only to phenoxy auxin herbicides such as 2,4-D." *Id.* (citing Ex. 1003 ¶¶ 53–54; Ex. 1004, 2; Ex. 1006; Ex. 1011, 6; Ex. 1012, 1, 11). According to Petitioner, the AAD-12 protein species disclosed and used by Patent Owner, which is one of only two species that allegedly support the claimed genus, fails to exhibit aryloxyalkanoate dioxygenase activity that degrades a phenoxy auxin herbicide and a pyridyloxy auxin herbicide, as claim 1 recites. *Id.* at 35–36.

3. Patent Owner's Arguments

Patent Owner argues that Petitioner misconstrues the scope of the claims. Prelim. Resp. 30–35. Patent Owner asserts that the claims "contain significant structural limitations" and "[t]he challenged claims bear no resemblance to those at issue in the cases Petitioner relies on, which contained *no* structural limitations." *Id.* at 30–31 (citing Pet. 25–36). Specifically, Patent Owner argues that "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" and this is a "specific structural limitation, not a functional limitation." *Id.* at 31 (citing Ex. 1001, Claims 1, 2, 32, 33). According to Patent Owner, "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" and Dr. Silverstone does not address this disclosure. *Id.* (citing Ex. 1001, 31:61–32:4).

Patent Owner contends that "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: ***HX*$_{109}$*D(X)*$_{111\text{-}134}$*T(X)*$_{136\text{-}261}$*H(X)*$_{263\text{-}272}$*R***" and this is also a structural limitation. *Id.* According to Patent Owner, "[t]he '055 patent explains that these conserved motif residues comprise 'the active site that is essential for catalytic activity.'" *Id.* (citing Ex. 1001, 11:1–6).

Patent Owner argues that the challenged claims are distinguished from the cases Petitioner cites because the claims in the cited cases contained no structural limitations. *Id.* at 31–32 (citing *Ariad*, 598 F.3d at 1340–41; *AbbVie*, 759 F.3d at 1291; *Lilly*, 119 F.3d at 1568). Patent Owner asserts that *Lilly* instead shows that "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.* at 32.

According to Patent Owner, "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." *Id.* (citing Pet. 29; Ex. 1003 ¶¶ 42–50). Patent Owner argues that Dr. Silverstone "repeatedly relies on a generic biochemistry textbook chapter" but "[t]hat textbook, however, reports that three-dimensional structure is *even more conserved* than amino acid sequence." *Id.* at 32–33 (citing Ex. 1003 ¶¶ 42–50; Ex. 1033, 141; Ex. 1028, 6). Patent Owner

further asserts that "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.*'" *Id.* at 33 (citing Ex. 1001, 28:57–29:10).

According to Patent Owner, the challenged claims require a high degree of sequence similarity and an active site motif and "Petitioner notably fails to identify any written description case holding such claims unpatentable." *Id.* Patent Owner argues that Petitioner's arguments rest on a numerosity theory that the Board and other courts have rejected. *Id.* at 33–35 (citing Pet. 30 n.7, *Ex parte Campbell,* Appeal No. 2021-000865 at 4–5 (PTAB July 20, 2021); *Alcon Rsch. Ltd. v. Barr Lab'ys, Inc.*, 745 F.3d 1180, 1190 (Fed. Cir. 2014); *Bilstad v. Wakalopulos*, 386 F.3d 1116, 1122, 1124, 1126 (Fed. Cir. 2004); PGR2022-00037, Paper 11 at 22, 26, 28–29 (PTAB Nov. 7, 2022); PGR2019-00032, Paper 11 at 18–19, 21, (PTAB Aug. 15, 2019)).

In addition, Patent Owner asserts that Petitioner's challenge fails because "Petitioner has not met its burden of establishing that the '055 patent's disclosed species are nonrepresentative of the genus claimed." *Id.* at 40 (citing *Ajinomoto Co. v. Int'l Trade Comm'n*, 932 F.3d 1342, 1358–59 (Fed. Cir. 2019)). According to Patent Owner, "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)." *Id.* (citing Prelim. Resp. 12–15). Patent Owner argues that "Dr. Silverstone

acknowledges the various crops exemplified in the '055 patent and their dual herbicide tolerance." *Id.* (citing Ex. 1003 ¶ 78). In view of this, Patent Owner contends that "Petitioner is thus incorrect in characterizing the '055 patent as only allegedly disclosing one or two species." *Id.* (citing Pet. 31–32, 34–37).

Patent Owner argues that "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." *Id.* at 41. According to Patent Owner, "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." *Id.* (citing Prelim. Resp. 12–15). Based on this, Patent Owner argues that "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" and Petitioner argues a lack of representativeness based on a flawed numerosity theory. *Id.* (citing Pet. 27–28, 30 n.7).

According to Patent Owner, "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." *Id.* (citing Ex. 1001, 32:1–6). Patent Owner argues that this case differs from *AbbVie*." *Id.* at 41–42 (citing *AbbVie*, 759 F.3d at 1292, 1301; Ex. 1011, 32:1–6). Patent Owner further asserts that the Board rejected arguments similar to Petitioner's in *Ex*

parte Campbell, Appeal No. 2021-000865 at 15, and the Board was unpersuaded by arguments similar to Petitioner's in PGR2019-00032, Paper 11 at 32 (PTAB Aug. 15, 2019). *Id.* at 42–43.

Patent Owner argues that Petitioner's analogy to *Amgen* is misplaced and not applicable to the challenged claims, because the claims recite high identity to the disclosed sequences and the disclosure in Amgen recited no similar information. PO Sur-reply 1–2. Patent Owner also argues that Dr. Silverstone's testimony is opinion without supporting evidence that should be given little weight. *Id.* at 3. Patent Owner urges us to reject Petitioner's "numerosity theory." *Id.* at 5–6.

Patent Owner argues that the Federal Circuit has held that the "disclosure of 'structural features common to the members of the genus so that one of skill in the art can "'visualize or recognize'" the members of the genus' provides adequate written description." Prelim. Resp. 35–36 (citing *Ajinomoto*, 932 F.3d at 1358–59). Patent Owner asserts that "Petitioner fails to meet its burden of establishing that the '055 patent's disclosure of common structural features is insufficient." *Id.* at 36.

According to Patent Owner, "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*.'" *Id.* (citing Pet. 32–33). Patent Owner argues that "[t]he '055 patent also discloses that 85% is a 'highly identical' level of sequence identity" and "further discloses that '*sequences with high homology would be expected to retain similar properties*'—a disclosure that Petitioner nowhere addresses." *Id.* (citing Ex. 1001, 32:1–6). According to Patent Owner, "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." *Id.* (citing *Ajinomoto*, 932 F.3d at 1358–60).

Patent Owner argues that, "[d]espite 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.'" *Id.* (citing Pet. 33). As an example, Patent Owner cites Dr. Silverstone's statement that "the Patent Owner *could better define* the active site through a set of spatial coordinates." *Id.* at 36–37 (citing Ex. 1003 ¶ 79). According to Patent Owner, Petitioner applies an incorrect legal standard that demands a "stricter structure-function correlation" and "Petitioner cites no authority requiring disclosure of 3-D spatial coordinates of amino acid residues to satisfy the written description requirement." *Id.* at 37.

Patent Owner further contends that, "for his 3-D coordinate theory, Dr. Silverstone repeatedly relies on a generic textbook chapter discussing protein folding in general" that "nowhere mentions αKG-dependent dioxygenase enzymes, much less AAD-12 (SdpA) enzymes specifically." *Id.* (citing Ex. 1033, 120; Ex. 1003 ¶¶ 52–50). According to Patent Owner, Dr. Silverstone "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." *Id.* at 37–38 (citing Ex. 1019, 12401; Ex. 1020, 1358; Ex. 2022, 1358).

Patent Owner asserts that "Petitioner's other criticisms of the AAD-12 motif are also deficient." *Id.* at 38. Specifically, Patent Owner argues

"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," "[b]ut Petitioner ignores that the *location and spacing* of those residues in other αKG-dependent dioxygenases differ from those in the AAD-12 motif." *Id.* (citing Pet. 32–33; Ex. 1003 ¶ 48). Patent Owner further contends that Petitioner speculates about the importance of additional amino acids to the dual activity of degrading phenoxy auxin and pyridyloxy auxin herbicides but this is irrelevant because "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." *Id.* at 38–39 (citing Ex. 1003 ¶¶ 49, 90; *Ajinomoto*, 932 F.3d at 1360).

Patent Owner argues that Petitioner incorrectly interprets the Agreement and other commercial product and stewardship materials. Prelim. Resp. 27 (citing Exs. 1004, 1006, 1011, 1012). According to Patent Owner, "Petitioner omits that herbicides and their uses are comprehensively regulated by the EPA" and that "[u]nder 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.'" *Id.* (second alteration in original) (citing 40 C.F.R. § 168.22(b)(5)). Patent Owner asserts that its 2,4-D herbicide product is registered for post-burndown use with transgenic AAD-12 soybeans, which is reflected in the Agreement. *Id.* at 27–28 (citing Ex. 1004, 1).

Patent Owner contends that, until triclopyr, fluroxypyr, or other pyridyloxy auxin herbicides are registered by the EPA for post-burndown use with AAD-12 soybeans (particularly those under the trade name Enlist E3® soybeans), Patent Owner cannot suggest or advertise pyridyloxy auxin herbicides for use with those soybeans. *Id.* at 28. In view of this, Patent Owner argues that "Corteva's commercial product and stewardship materials simply are not pertinent to Petitioner's proposed written description ground" and "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." *Id.*

Patent Owner further asserts that "the specification repeatedly discloses and reports test data showing tolerance to pyridyloxy auxin herbicides as well as phenoxy auxin herbicides." *Id.* (citing Prelim. Resp. 5–20). According to Patent Owner, Petitioner argues "that *test data* against both pyridyloxy auxin and phenoxy auxin herbicides were not reported for" transgenic soybeans and cotton plants, yet Petitioner acknowledges "that 'the specification provides experimental results for seven species of plants comprising the AAD-12 variant.'" *Id.* at 28–29 (citing. Pet. 34–35; Ex. 1003 ¶ 53). Patent Owner argues that such data is not required to satisfy the written description requirement. *Id.* at 29 (citing *Ariad*, 598 F.3d at 1352; PGR2022-00054, Paper 16 at 17, 22, 28 (PTAB Feb. 2, 2023); PGR2022-00037, Paper 11 at 17–18, 23–24, 29 (PTAB Nov. 7, 2022)).

Patent Owner also contends that "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." *Id.* at 29–30 (citing Ex. 1003 ¶ 78). Patent Owner argues that "the '055 patent discloses that 'AAD-12 is able to degrade the pyridyloxyacetates auxins (e.g., triclopyr, fluroxypyr) in addition to . . . 2,4-D'" and "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." *Id.* at 30 (citing Ex. 1001, 6:41–46, 13:42–45, 72:48–79:61, 86:23–87:20; Ex. 1003 ¶ 70). According to Patent Owner, "Petitioner fails to demonstrate how these disclosures in the '055 patent are insufficient to meet the written description requirement." *Id.*

4. Analysis

We find that Petitioner has shown it is more likely than not that the claims[7] fail to comply with the written description requirement. As noted above, the '055 patent teaches the requirements of claim 1 of providing a recombinant 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, where the AAD-12 protein has at least 85% identity to SEQ ID NO: 2, with five conserved amino acids and recited chain lengths between them. Ex. 1001, 125:2–18. The '055 patent teaches that transgenic plant cells of the invention can be made by a series of *in vitro* and *in vivo* steps, namely making candidate polynucleotides, cloning them into a

[7] We analyze the issues regarding all claims together as the parties have not argued individual claims, but we address certain limitations that differ between the individual claims.

vector, introducing the polypeptides into plants through transformation, growing the plants, and then harvesting and analyzing the plant tissue. *See, e.g.*, *id*. at 56:40–62:68. The Specification provides several examples describing the various steps in this extensive process using different plants (e.g., tobacco, *id*. at 66:44–72: 45, and soybeans, *id.* at 72:48–79:61). However, the Specification provides examples of only two transgenic plant cells made using two individual recombinant polypeptides, AAD-12 (SEQ ID NO: 2) and a polypeptide with a single amino acid changed, such that the polypeptide is 99.3%[8] identical to AAD-12. *Id.* at 35:8–13 (describing a "plant-optimized" version of SEQ ID NO: 2, encoded as SEQ ID NO: 4).

Despite disclosing examples of multiple types of transgenic plant crops (e.g., corn, tobacco, and soybeans), the Specification provides no examples of any recombinant plant cell made using a sequence that has *less* than 99% identity to SEQ ID NO: 2, although the claim recites a sequence identity of at least 85%. Nor does the Specification provide any additional guidance in how to make a polypeptide that would lead to the claimed subject matter aside from the requirement of 85% or greater homology to SEQ ID NO: 2, the conserved 5 amino acids in the AAD-12 peptide, and the required chain lengths.[9] *See, e.g.*, Ex. 1003 ¶¶ 80–82. As a result, the '055

[8] We note that Petitioner alleges this embodiment is 99.7% identical (e.g., Pet. 10). We adopt the number provided in the Specification in this decision. Ex. 1001, 35:8–13

[9] The required amino acid chain lengths are "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." Ex. 1001, 125:13–19.

patent's Specification provides only the two embodiments disclosed, which both have over 99% identity despite that the claim recites as low as 85% identity ("at least 85%"). Yet, no species are disclosed to show that the recited plant cell can be made at 85% identity while retaining the recited function; the Specification provides only a set of instructions to potentially find more species.

At this stage of the proceeding, we are not persuaded by Patent Owner's argument (Prelim. Resp. 30–31) that the requirement of 85% identity to SEQ ID NO: 2, the recited 5 amino acids in the general formula of $HX_{109}D(X)_{111\text{-}134}T(X)_{136\text{-}261}H(X)_{263\text{-}272}R$, and the required chain lengths, which Patent Owner calls "structural" limitations, would "clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed." *Ariad*, 598 F.3d at 1351.

We acknowledge Patent Owner's arguments that the '055 patent lists 85% identity as "highly identical" in this field and that the "conserved motif residues comprise 'the active site that is essential for catalytic activity.'" Prelim. Resp. 31 (citing Ex. 1001, 11:1–6)). However, on the record before us, we are unpersuaded that this is sufficient because the Specification lacks disclosure supporting that a polypeptide of, for example, 86% identity to SEQ ID NO: 2 would retain the ability to degrade herbicides if the 5 amino acids in the general formula of $HX_{109}D(X)_{111\text{-}134}T(X)_{136\text{-}261}H(X)_{263\text{-}272}R$, and the required chain lengths are present. In this regard we are persuaded by the testimony of Dr. Silverstone (Ex. 1003 ¶¶ 48–93) regarding the limitations of the disclosure of the '055 patent and the lack of information supporting the skilled artisan in understanding that the inventor possessed the entire claimed genus (e.g., lack of example at lower end of sequence

identity and lack of information to assist the skilled artisan in predicting whether an α-ketoglutarate-dependent dioxygenase would interact with or degrade either phenoxy auxin herbicides and/or pyridyloxy auxin herbicides). Dr. Silverstone testifies, and we are persuaded on this record, that the skilled artisan would not have read the guidance in the disclosure and understood that the inventors possessed the ability to design a modified SEQ ID NO: 2 at the 85% identity level that retained the function of degrading the recited herbicides, let alone the full scope of the claimed genus. *Id.* Patent Owner argues that Dr. Silverstone's testimony that conserved amino acids of the AAD-12 motif are present in other α-ketoglutarate-dependent dioxygenases but do not have the claimed dual activity (Ex. 1003 ¶ 48) is misplaced because it "ignores that the *location and spacing* of those residues in other αKG-dependent dioxygenases differ from those in the AAD-12 motif." Prelim. Resp. 38. However, Patent Owner offers no evidence that supports its argument. *Id.* It is thus unpersuasive.

We acknowledge Patent Owner's argument that Dr. Silverstone's cited evidence relies on a textbook regarding protein function and that members of the field used protein-specific references to describe proteins. Prelim. Resp. 37–38. On the record before us, Dr. Silverstone's testimony is sufficient to identify reasons why the disclosure in the '055 patent regarding 85% identity is lacking. Patent Owner may test the strength of Dr. Silverstone's testimony at trial.

Further, we are unpersuaded by Patent Owner's argument (Prelim. Resp. 37–38) that "Petitioner's own evidence" supports a finding of sufficient written description because the cited references *do* provide the

types of detail that the '055 disclosure is lacking. *See, e.g.*, Ex. 1020, 1358 (describing high degree of active-site sequence identity of active site and orientation of key side chains to facilitate interactions with identified, specific amino acids and further identifying specific positively- and negatively-charged amino acids that are necessary to interact together coordinate to stabilize the reaction). In comparison, on the record before us, the disclosure of the '055 patent's Specification falls short.[10]

We acknowledge Patent Owner's argument (Prelim Resp. 33–34) that the Board has rejected certain arguments similar to Dr. Silverstone's that explain the high potential number of modifications that could be made within a claim range in support of § 112 arguments (e.g., a "numerosity theory"); here, as stated above, we are persuaded by the lack of disclosure particularly at the end of the range where more modifications from the natural protein (SEQ ID NO: 2) would occur. It may well be *possible* for a skilled artisan to design a protein using the guidance provided in the '055 patent's Specification by engaging in the lengthy steps disclosed, including using the design tools cited therein, but the question at hand is whether the disclosure "set[s] forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed." *Univ. of Rochester*, 358 F.3d at 928. At this point in the proceeding, we are not persuaded that it does.

[10] We are also unpersuaded by Patent Owner's argument (Prelim. Resp. 29–30) that Dr. Silverstone's testimony at Ex. 1003 ¶ 78 is an admission, as we read this paragraph to be his recounting of *what the '055 patent states* about the invention.

Also, we are unpersuaded by Patent Owner's argument that tertiary protein structure is more conserved than amino acid sequence (Prelim. Resp. 33, citing Ex. 1028, 6). The Specification does not support that, at 85% identity to SEQ ID NO: 2, the tertiary structure remains sufficient to support degradation of the recited herbicides, and it is Patent Owner's obligation to provide this information and sufficient guidance to the artisan to permit the artisan to understand the extent of and possession of the invention. "Merely drawing a fence around the outer limits of a purported genus is not an adequate substitute for describing a variety of materials constituting the genus and showing that one has invented a genus and not just a species." *Ariad*, 598 F3d. at 1349.

Nor are we persuaded that the two examples with 99.3% and 100% identity to SEQ ID NO: 2 are sufficient description for a genus of possible polypeptides with up to 15% sequence variation. It is clear that the disclosed SEQ ID NOs: 2 and 4 function as claimed, but it is unclear to the skilled artisan how far from 99.3% identity the polypeptide can deviate while still retaining the ability to degrade herbicides, including by stating design parameters that would indicate the inventors possessed this ability. For this reason we are unpersuaded by Patent Owner's citations to cases in which the court found that the genus was sufficiently disclosed in compliance with § 112 because sufficient structural limitations were recited. *See, e.g., Ajinomoto*, 932 F.3d at 1360 (patent disclosure containing four examples of potent promoters that provided guidance on methods for evaluation and strength, data about the relative strength of fourteen promoters, and a general methodology for determining promoter strength in E. coli bacteria found to contain "substantial evidence from which to find

that, starting from the native E. coli yddG promoter, deviations toward the consensus sequence generally increase promoter strength" despite that perfect correspondence between the members of the genus and the asserted common structural feature was not disclosed). Here, such guidance is missing, and as the *Ajinomoto* Court noted, the disclosure is "a research plan, leaving it to others to explore the unknown contours of the claimed genus." 932 F.3d at 1360 (citing *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1300 (Fed. Cir. 2014)).

D. Alleged Lack of Enablement

Petitioner argues that the challenged claims fail to meet the enablement requirement, which we discuss below. Pet. 36–60.

1. Legal Standard

"Enablement requires that 'the specification teach those in the art to make and use the invention without undue experimentation.'" *Idenix Pharm. LLC v. Gilead Sci. Inc.*, 941 F.3d 1149, 1154 (Fed. Cir. 2019) (quoting *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988)). The factors to be considered when determining if undue experimentation is required to practice the invention include: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims. *Wands*, 858 F.2d at 737.

The Supreme Court has further stated:

> If a patent claims an entire class of processes, machines, manufactures, or compositions of matter, the patent's specification must enable a person skilled in the art to make and

> use the entire class. In other words, the specification must enable the full scope of the invention as defined by its claims. The more one claims, the more one must enable.

Amgen, 143 S. Ct. at 1254). A specification need not "describe with particularity how to make and use every single embodiment within a claimed class," because, "[f]or instance, it may suffice to give an example (or a few examples) if the specification also discloses 'some general quality . . . running through' the class that gives it 'a peculiar fitness for the particular purpose.'" *Id.* at 1254–1255 (quoting *The Incandescent Lamp Patent*, 159 U.S. 465, 475 (1895)). "In some cases, disclosing that general quality may reliably enable a person skilled to make and use all of what is claimed, not merely a subset." *Id.* at 1255.

2. Petitioner's Arguments

Petitioner argues that "the '055 specification is too far removed from any reasonable level of disclosure and is not a reasonable analog to the *Amgen* fact pattern" because "Patent Owners here disclosed only two sequences, differing by a single amino acid at the N-terminus of the sequence, of up to 2.4×10^{106} species within the scope of the claim." Pet. 38. According to Petitioner, "the '055 patent discloses one order of magnitude fewer embodiments for a genus approximately one hundred orders of magnitude larger in size." *Id.* (emphases omitted).

Petitioner further argues that the *Wands* factors "demonstrate that undue experimentation would be required to practice the full scope of the claimed invention." *Id.* at 37–38. Petitioner provides specific arguments for each of the *Wands* factors, which we address below.

(1) Quantity of Experimentation

Petitioner asserts that "[r]eaching the full scope of claims 1-33 requires an extensive amount of experimentation to test for aryloxyalkanoate dioxygenase activity" that degrades herbicides as claimed. *Id.* at 39 (citing Ex. 1001, Claims 1, 32, 33; Ex. 1003 ¶¶ 57, 86–93). According to Petitioner, the full scope of the claims "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." *Id.*

Petitioner argues that SEQ ID NO: 2 is 292 amino acids in length so "a protein comprising an amino acid sequence having at least 85% sequence identity with SEQ ID NO: 2 can include up to 43 mutations." *Id.* (citing Ex. 1001, 109–110; Ex. 1003 ¶ 80 n.1). According to Petitioner, "[e]ven limiting the genus to proteins having 90% sequence identity with SEQ ID NO: 2, as in claims 2 and, in part, 32 of the '055 patent allows for up to 29 mutations." *Id.* at 39–40. Petitioner contends that each mutation permits 19 potential substitutions "(accounting for the 20 canonical amino acids), in addition to the insertion or deletion of an amino acid." *Id.* at 40 (citing Ex. 1001, 109–110; Ex. 1003 ¶ 80 n.1). Petitioner argues that, "because the claimed 'AAD-12 motif' comprises only 5 conserved amino acids, the mutations may be made at any of 286 positions in the sequence, accounting for the 'start' codon encoding methionine." *Id.* at 40 (citing Ex. 1001, Claim 1; Ex. 1003 ¶ 80 n.1). In view of this, Petitioner asserts that "[t]he broad claim allows for up to 2.4×10^{106} amino acid sequences that fall within the claims but without any meaningful disclosure as to whether or why such

would in fact work." *Id.* (citing Ex. 1003 ¶¶ 80–82, n.1). Petitioner argues that "it would be nearly impossible to reliably predict whether any other sequence within the scope of the claim would work" because "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.'" *Id.* (citing Ex. 1001, claim 1; Ex. 1003 ¶¶ 78–79).

Petitioner argues that the challenged claim's function of exhibiting aryloxyalkanoate dioxygenase activity to degrade phenoxy auxin and pyridyloxy auxin herbicides would have required each amino acid sequence "to be experimentally analyzed *in vitro* for its ability to enzymatically degrade a phenoxy auxin herbicide and a pyridyloxy auxin herbicide." *Id.* at 40–41 (citing Ex. 1003 ¶¶ 89–90). According to Petitioner, "this testing would be exceedingly time-consuming, laborious, expensive, and unpredictable" and "even the identification of species exhibiting the desired enzymatic activity could not reliably predict whether that enzymatic activity would be maintained in transgenic plants of interest." *Id.* at 41 (citing Ex. 1003 ¶¶ 86–91).

According to Petitioner, this experimental analysis would only be a starting point because, due to the unpredictability for the translation of *in vitro* expression and activity to *in vivo* expression and activity, "each amino acid sequence found functional via *in vitro* experimentation would additionally have to be experimentally analyzed *in vivo* for its ability to enzymatically degrade a phenoxy auxin herbicide and a pyridyloxy auxin herbicide as expressed in that transgenic plant." *Id.* at 41–42 (citing Ex. 1001, Claims 1, 32, 33, 48:62–88:14, 91:39–99:20; Ex. 1003 ¶¶ 91–93). Petitioner argues that such experimentation "would require creating a new

set of plant gene expression constructs, transforming and growing plant cells of interest, and expression analysis of those plants to determine which plants are producing the enzyme in sufficient quantities." *Id.* at 42 (citing Ex. 1003 ¶¶ 91–92). According to Petitioner, selected transgenic plants strains would be used to test herbicide resistance and "each step in the process would require the design and optimization of experimental conditions to identify variables impacting the desired activity and would need to be repeated and optimized for each amino acid sequence investigated," "[d]ue to the wide array of variables that could impact gene expression, protein folding, and enzyme activity." *Id.* (citing Ex. 1003 ¶¶ 86–93). Petitioner contends that the independent claims do not place any limitations on the transgenic plants so the experimentation would need to be repeated for each amino acid sequence of interest for each plant of interest. *Id.* at 43.

Petitioner further asserts that "Patent Owner's publications and product specifications appear to contradict the function of the claimed genus." *Id.* (citing Ex. 1003 ¶¶ 52–54, 79). Specifically, Petitioner argues that "Patent Owner's 2010 publication on transgenic plants expressing AAD-12 similarly . . . concludes that 'transgenic soybean plants expressing AAD-12 maintained field resistance to 2,4-D over five generations.'" *Id.* at 43–44 (citing Ex. 1005, Abstract; Ex. 1003 ¶ 54). According to Petitioner, "[u]nlike other transgenic plants in that publication, transgenic soybean was not shown to have resistance to pyridyloxy auxin herbicides." *Id.* at 44 (citing Ex. 1005, 20242; Ex. 1003 ¶ 54). Petitioner also contends that the Agreement "expressly prohibits the use of 'any pyridine auxin herbicides (e.g., triclopyr, fluroxypyr) on emerged Enlist crops' after burndown" and "only prohibits the use of phenoxy auxin herbicides 'NOT expressly labeled

for use in conjunction with Enlist crops' following burndown." *Id.* (citing Ex. 1004, 2). Petitioner further argues that "Patent Owner's website notes that '[t]he aad-12 protein in Enlist E3 soybeans and Enlist cotton metabolizes 2,4-D choline into a nonherbicide form, thus conferring 2,4-D choline tolerance in the plant[,]' while making no mention of pyridyloxy auxin herbicide resistance." *Id.* at 44–45 (alterations in original) (citing Ex. 1006; Ex. 1011, 6; Ex. 1012, 1, 11; Ex. 1003 ¶¶ 54, 81).

In addition, Petitioner asserts that:

> In order to practice the full scope of the invention claimed in the '055 patent, would require the experimental design and cloning of an expression vector for each of the up to 2.4 x 10_{106} amino acid sequences within the scope of the claim, analysis of expression and *in vitro* activity for each, and further experimental analysis of expression and activity of active sequences *in vivo* in a wide range of plant species.

Id. at 45 (citing Ex. 1001, Claims 1, 32, 33; Ex. 1003 ¶¶ 52–54, 80, 86–93).

(2) Amount of Direction of Guidance Presented

Petitioner contends that "[t]here is no direction or guidance provided by the specification as to which of the up to 2.4 x 10^{106} amino acid sequences encompassed by the claims would exhibit aryloxyalkanoate dioxygenase activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and a pyridyloxy auxin herbicide." *Id.* at 46 (citing Ex. 1003 ¶¶ 79–85). According to Petitioner, "[a] POSITA would not find direction or guidance from the specification as to which residues, or combinations thereof, within or without the claimed 'AAD-12 motif' to select for mutagenesis, or which mutations to select for those positions, without abrogating enzymatic activity." *Id.* (citing Ex. 1003 ¶¶ 79–85).

Petitioner asserts that the '055 patent only provides guidance in its background, which "describes previous work done on sdpA from *Delftia acidivorans* (SEQ ID NO: 2) and on the broad family of α-ketoglutarate dependent dioxygenases" and in the Examples, which involved testing of a single amino acid sequence. *Id.* (citing Ex. 1001, 5:48–51, 35:11–13; Ex. 1003 ¶ 90). According to Petitioner, the single amino acid is "an AAD-12 protein 99.7% identical to SEQ ID NO: 2" and is the only protein shown to possess the claimed activity for degrading herbicides. *Id.* at 46–47 (citing Ex. 1003 ¶¶ 48, 70). Petitioner argues that "the only unifying features of this 'guidance' are the conserved active site residues and the numbers of amino acids around and between them, as disclosed in the 'AAD-12 motif.'" *Id.* at 47 (citing Ex. 1003 ¶¶ 48, 79, 84, 90).

Petitioner further contends that "[t]he '055 patent, as described above, does not provide any guidance as to structural elements that confer the ability to degrade both phenoxy and pyridyloxy auxin herbicides and how mutations to the sequence might impact that ability." *Id.* at 47–48 (citing Ex. 1003 ¶¶ 42–50, 79–85). Petitioner also argues that the '055 patent does not provide direction or guidance as to which amino acid sequences would exhibit the claimed activity *in vitro* and *in vivo*. *Id.* at 48 (citing Ex. 1003 ¶¶ 79–85, 92). According to Petitioner, the claimed activity was not shown for all of the seven species of transgenic plants tested because transgenic soybeans and transgenic cotton were absent. *Id.* (citing Ex. 1003 ¶¶ 53, 81). Petitioner asserts that "the '055 patent proposes no more than a hypothesis that any protein having at least 85% sequence identity with SEQ ID NO: 2 and an 'AAD-12' motif" may have the claimed activity and there would be undue experimentation because "all amino acid sequences falling within the

scope of the claims would have to be meticulously tested over a period of years for activity with both phenoxy and pyridyloxy auxin herbicides, and further for activity in each species of plants." *Id.* at 49 (citing Ex. 1003 ¶¶ 42–50, 79–85).

(3) The Presence or Absence of Working Examples

Petitioner reiterates that the '055 patent's experimental studies are limited to testing SEQ ID NO: 4 and "*in vivo* experiments testing some properties of the same in seven species of transgenic plants." *Id.* at 49–50 (citing Ex. 1001, 47:4–102:49; Ex. 1003 ¶¶ 80–82). Petitioner also reiterates its argument that "the ability of the transgenic plants to enzymatically degrade both a phenoxy and a pyridyloxy auxin herbicide was not even described for all seven species of transgenic plants that are described." *Id.* at 50 (citing Ex. 1003 ¶¶ 53, 81).

(4) The Nature of the Invention

Petitioner asserts that "[c]laims 1, 3-31, and 33 only limit the AAD-12 protein by requiring that it have at least 85% sequence identity with SEQ ID NO: 2 and an 'AAD-12 motif.'" *Id.* (citing Ex. 1003 ¶ 78). According to Petitioner, the "'AAD-12 motif' defines only a 166 amino acid stretch of the protein fixed only with respect to the identities and positions of 5 amino acids therein." *Id.* (citing Ex. 1003 ¶¶ 78–79). Petitioner argues that the claims do not limit what mutations may be made or where they may be made, besides the five conserved residues of the "AAD-12 motif." *Id.* at 51 (citing Ex. 1003 ¶¶ 78, 84).

Petitioner contends that "[t]he predominantly prophetic '055 specification presents the hypothesis that amino acid sequences within the broad scope of the claims could exhibit the ability to enzymatically degrade

both phenoxy and pyridyloxy auxin herbicides, based on *in vitro* and *in vivo* experiments using a single amino acid sequence." *Id.* (citing Ex. 1003 ¶¶ 78–80).

(5) The State of the Prior Art

Petitioner argues that, although the prior art "identifies AAD-12 as an enzyme capable of degrading both phenoxy and pyridyloxy auxin herbicides *in vitro* and, in some plant species, *in vivo*," the prior art "also demonstrates that the wide array of activities catalyzed by the α-ketoglutarate dioxygenase superfamily of enzymes do not include other enzymes known to degrade pyridyloxy auxin herbicides." *Id.* at 52 (citing Ex. 1003 ¶¶ 65–70). In view of this, Petitioner asserts that the prior art "provides no guidance to a POSITA as to the key structural features of AAD-12 proteins responsible for the claimed function." *Id.*

According to Petitioner:

> The prior art demonstrates that enzyme function is largely unpredictable, even among enzymes in the same family, and despite there being the limited ability of AAD-12 to confer herbicide resistance to phenoxy and pyridyloxy auxin herbicides in some plants, the prior art does not probe or elucidate the key structural features of the enzyme responsible for its function.

Id. at 54 (citing Ex. 1003 ¶¶ 48, 65–70).

(6) The Relative Skill of Those in the Art

According to Petitioner, the level of ordinary skill in the art is high because "an ordinar[il]y skilled artisan needs specialized knowledge of protein engineering, expression, purification, and analysis, molecular cloning, genetic modification of plants, and crop science." *Id.* at 55 (citing Ex. 1003 ¶¶ 71–75). Petitioner contends that "[d]esigning, expressing, and testing protein variants is laborious, time-consuming, complicated, and

highly unpredictable due to the many effects, both direct and indirect, that a mutation can have on protein structure and function" and "progressing a protein variant to *in vivo* expression requires extensive work in codon optimization, transformation of target plants, and analysis of expression levels and *in vivo* efficacy." *Id.* (citing Ex. 1003 ¶¶ 71–75). Petitioner argues that only one protein variant had been shown to work and only in five of seven tested plant species. *Id.* (citing Ex. 1003 ¶¶ 53, 80–81). According to Petitioner, even though the level skill in the art was high, attempts to practice the claimed invention would still result in "nothing but a research idea for creating transgenic plant cells that degrade both phenoxy auxin herbicides and pyridyloxy auxin herbicides." *Id.* at 56.

(7) The Predictability or Unpredictability of the Art

Petitioner argues that "[t]he field of engineering enzymes for herbicide tolerance in plants is quite complex and unpredictable, as the number of variables involved in enzyme activity, both *in vitro* and *in vivo*, is high, and activity *in vitro* often does not correlate to activity *in vivo*." *Id.* (citing Ex. 1003 ¶¶ 71–77, 80). According to Petitioner, "detailed biochemical analyses are required to ascertain *in vitro* whether enzymes exhibit the target functionality." *Id.* (citing Ex. 1003 ¶¶ 86–93). Petitioner asserts that software, as of March 24, 2017 "could not accurately predict the three-dimensional structure of enzyme active sites based only on the primary sequence." *Id.* at 56–57 (citing Ex. 1003 ¶¶ 47, 87–88). In view of this, Petitioner contends that "prediction of enzyme function and substrate specificity based only on amino acid sequence was not possible." *Id.* at 57 (citing Ex. 1003 ¶¶ 87–88).

Petitioner further argues that "plant transformation is not completely predictable" because many variables can have a large effect on expression of the transgene. *Id.* (citing Ex. 1003 ¶¶ 72–77). Petitioner asserts that "[v]ariation of protein expression between independently transformed plants with the same gene expression cassette has been observed often in the art" and "off-target enzyme activities are rarely able to be predicted; they must be observed once a transgenic plant is generated." *Id.* (citing Ex. 1003 ¶¶ 74, 76). According to Petitioner, the '055 patent "demonstrates the variability of protein expression between transgenic lines" because "[t]he measured protein levels of AAD-12 in transgenic soybean, as shown in Table 25 (75-78), ranged from 4.65 ng/ml to 2657.36 ng/ml among the seven events reported; a 570-fold variance in protein expression." *Id.* (citing Ex. 1003 ¶ 77). Petitioner further argues that "the measured protein levels of AAD-12 in five sample strains of transgenic canola ranged from 41.36 ng/ml to 3879.09 ng/ml; a 94-fold variance in protein expression." *Id.* at 57–58 (citing Ex. 1003 ¶ 77).

Petitioner also contends:

> Patent Owner's declaration submitted in the course of prosecution, the inventor declared, *inter alia*, that "[t]hose skilled in the art appreciate that there is a high level of unpredictability associated with expressing bacterial genes in plant systems," such as in the case of AAD-2, which, despite having significantly higher activity with 2,4-D *in vitro* than AAD-1 (both tfdA homologs), "was surprisingly inactive when expressed in plants, while AAD-1 was very active."

Id. at 58 (citing Ex. 1010 ¶¶ 9–10; Ex. 1003 ¶ 52).

(8) The Breadth of the Claims

Petitioner asserts that "[t]he potential scope of the claims is extremely broad, covering up to 2.4×10^{106} different amino acid sequences, which

sequences would need to be tested for the capability to enzymatically degrade both a phenoxy auxin herbicide and a pyridyloxy auxin herbicide." *Id.* at 59 (citing Ex. 1003 ¶ 79–80, n.1). Petitioner further argues that the claims (except for claim 3) allow the use of the amino acid sequences in any plant. *Id.* (citing Ex. 1003 ¶¶ 78–79).

Petitioner also asserts that "[o]nly claims 2 and 32 further limit the sequence of the AAD-12 proteins of the invention" and, even with the additional limitations of claims 2 and 32, "the numbers of amino acid sequences falling within the scope of the claimed genera include up to 10^{76} species." *Id.* at 60 (citing Ex. 1003 ¶ 80, n.1).

3. Patent Owner's Arguments

Patent Owner argues that Petitioner has not identified any non-enabled embodiment of the challenged claims or embodiment that "could not have been made using routine experimentation." Prelim. Resp. 45. Patent Owner argues that the structural limitations in its claims make this case distinguishable from *Amgen*. *Id.* at 47–48. Patent Owner argues that Petitioner wrongly focuses "on the alleged potential number of species within the scope of the claims as compared to the number of embodiments disclosed" because the Board and courts have rejected such arguments. *Id.* at 48–49.

Patent Owner argues that twenty-four examples in the patent provide "a roadmap for making and evaluating other AAD-12 proteins and transgenic plants that produce AAD-12 proteins" that Petitioner ignores. *Id.* at 50. Patent Owner argues that the steps provided have not been shown to be non-routine, and that Dr. Silverstone himself stated so in a prior proceeding. *Id.* at 51–53. Patent Owner argues that, in light of the roadmap

provided, Petitioner has not shown that the process of making the claimed recombinant cells would have been beyond the routine skill of an skilled artisan or would have involved undue experimentation. *Id.* at 53–54.

4. Analysis

We find that Petitioner has shown it is more likely than not that one or more claims is not enabled by the Specification. As discussed above, on this record, we find that the Specification lacks information that would have led a skilled artisan to understand that the inventor had possession of recombinant plant cells made from an amino acid sequence with 85% identity to SEQ ID NO 2. This reasoning extends to enablement: without that understanding, and without the guidance that would have led the skilled artisan to envision this part of the claim scope, the artisan is likewise without the information needed to make and use that part of the claim scope. In this regard, we are persuaded by the testimony of Dr. Silverstone regarding the *Wands* factors and the details regarding the extensive effort required to identify embodiments at the 85% end of the claim scope in light of the guidance provided in the '055 patent's Specification. *See* Ex. 1003 ¶¶ 56–93. Dr. Silverstone testifies, and we are persuaded on this record, that with the guidance in the '055 patent's Specification, the skilled artisan would not have been able to predict whether a modified SEQ ID NO: 2 at the lower (e.g., 85% identity level) would have been able to retain the function of degrading the recited herbicides. *Id.*

We are further guided by the Supreme Court's holding in *Amgen* in which the patents claimed all antibodies that (1) bind to specific amino acid residues on a protein known as PCSK9; and (2) block PCSK9 from binding to LDL receptors. 598 U.S. at 602. The full scope of the claims covered

potentially millions of antibodies, but the specification only disclosed the amino acid sequences of twenty-six antibodies that performed the two claimed functions. *Id.* at 612–13. To make and use the undisclosed claimed antibodies, the skilled artisan could either follow the "roadmap" disclosed in the patent or attempt conservative substitution to seek a more likely result. *Id.* at 603. The roadmap directed skilled artisans to: (1) generate a range of antibodies in the lab; (2) test those antibodies to determine whether any bind to PCSK9 (the recited target); (3) test those antibodies that bind to PCSK9 to determine whether any bind to the "sweet spot" as described in the claims; and (4) test those antibodies that bind to the sweet spot as described in the claims to determine whether any block PCSK9 from binding to LDL receptors. *Id.*

Alternatively, the conservative substitution technique directed skilled artisans to: "(1) start with an antibody known to perform the described functions; (2) replace select amino acids in the antibody with other amino acids known to have similar properties; and (3) test the resulting antibody to see if it also performs the described functions." *Id.* The Supreme Court held these methods "amount[ed] to little more than two research assignments" and failed to enable the full scope of the claims. *Id.* at 612–15. The Court held that Amgen's roadmap "merely describes step-by-step Amgen's own trial-and-error method for finding functional antibodies—calling on scientists to create a wide range of candidate antibodies and then screen each to see" which practice the claims. *Id.* at 614. The Court found that the conservative substitution technique similarly required undue experimentation. *Id.* Such approaches leave skilled artisans to "engage in 'painstaking experimentation' to see what works," which "is not

enablement." *Id.* (quoting *Consol. Elec. Light Co. v. McKeesport Light Co.*, 159 U.S. 465, 475 (1895)). The Supreme Court acknowledged, however, that methods like a roadmap or conservative substitution might be sufficient to enable other claims under different circumstances, such as where the patent discloses "a quality common to every functional embodiment." *Id.*; *see also Baxalta Inc. v. Genentech, Inc.*, No. 2022-1461 2023 WL 6135930, at *4(Fed. Cir. Sept. 20, 2023) (claims reciting antibodies that bound to specified factors and increased the procoagulant activity of the factor found not to be enabled where the specification disclosed eleven antibody sequences with the two claimed functions and the specification instructed the artisan to (1) immunize mice with human Factor IX/IXa; (2) form hybridomas from the antibody-secreting spleen cells of those mice; (3) test those antibodies to determine whether they bind to Factor IX/IXa; and (4) test those antibodies that bind to Factor IX/IXa to determine whether any increase procoagulant activity; the court found the specification lacked sufficient disclosure to permit artisan to predict which antibodies would perform the claimed function and "simply directs skilled artisans to engage in the same iterative, trial-and error process the inventors followed to discover the eleven antibodies they elected to disclose").

While the genus in this case does disclose the AAD-12 motif with five conserved amino acids, recited chain lengths between them, and at least 85% identity to SEQ ID NO: 2, on this record the lack of other guiding information aside from the research plan described in the examples does not provide sufficient assistance to the skilled artisan in making and using the invention.

We address Patent Owner's arguments related to enablement below.

Patent Owner argues that Petitioner has not identified any non-enabled embodiment of the challenged claims or embodiment that "could not have been made using routine experimentation." Prelim. Resp. 45 (citing *McRO, Inc. v. Bandai Namco Games Am. Inc.*, 959 F.3d at 1100 (Fed. Cir. 2020)). We are not persuaded. In *McRO*, the court reviewed a judgment of invalidity of nonenablement. *Id.* at 1100. The court noted that, in a *Wands* analysis, the asserting party should concretely identify

> 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.

Id. The Court noted that this identification was necessary to permit evaluation of claim scope, but did not require an actual nonenabled product. *Id.* at 1100–01. Here, the testimony of Dr. Silverstone has articulated with specificity that the guidance in the '055 patent's Specification would not have permitted the skilled artisan to predict whether a modified SEQ ID NO: 2 at the lower (e.g., 85% identity) level would have been able to retain the function of degrading the recited herbicides. Ex. 1003 ¶¶ 56–93. On this record, we find this articulation sufficient for purposes of institution.

With regard to Patent Owner's argument regarding Petitioner's focus "on the alleged potential number of species within the scope of the claims as compared to the number of embodiments disclosed" (Prelim. Resp. 48–49), we are persuaded by the lack of disclosure particularly at the end of the range where more modifications from the natural protein (SEQ ID NO: 2) would occur. While it may have been *possible* for the skilled artisan to have

designed a protein using the roadmap provided in the '055 patent's Specification, on this record, we find that doing so would have required "engag[ing] in the same iterative, trial-and error process the inventors followed to discover the [two species] they elected to disclose." *Baxalta*, 2023 WL 6135930, at *4. For this reason, we are also unpersuaded by Patent Owner's argument that the Specification provides twenty-four examples with "a roadmap for making and evaluating other AAD-12 proteins and transgenic plants that produce AAD-12 proteins." Prelim. Resp. 50. As discussed above, only two of those examples provide embodiments, both of which have over 99% identity to SEQ ID NO: 2. The rest consist of "research assignments," not guidance. *Amgen*, 143 S. Ct. at 614.

We next turn to Patent Owner's arguments that Dr. Silverstone's testimony in a separate case regarding the various steps addressed in his declaration show that the examples in the '055 patent's Specification are routine and not unduly burdensome. Prelim. Resp. 51–53; *see also id*. at 53–54 (argument that the roadmap provided in the Specification has not been shown to be unpredictable or beyond the skill of the skilled artisan).

Dr. Silverstone testifies, *inter alia*, that these steps require a high degree of skill, comprise meticulous experimentation, and comprise significant work due to the relative unpredictability of the art. Ex. 1003, e.g., ¶¶ 72–75. Patent Owner argues this testimony contradicts with statements made in a separate case, submitted as Ex. 2004. We are not persuaded that this testimony alters our perception of the facts on this record. The parties do not appear to dispute that the skill level is high or that the steps required to obtain embodiments of the claims are known in the art; the

issue is whether the effort is unduly burdensome because of the lack of guidance provided in the Specification to permit the skilled artisan to make the claimed subject matter, such as the guidance Dr. Silverstone suggests would avoid undue burden. *See* Ex. 1003 ¶¶ 79–80 (suggesting "a set of spatial coordinates of key amino acids and distances, restricting mutations to conserved amino acids or predicted secondary or tertiary structures, and identifying 85% as a key threshold at which function is conserved"). On this record, we find Petitioner has demonstrated that it is more likely than not that the guidance was insufficient to avoid undue burden.

Because Petitioner has shown that it is more likely than not that Petitioner will prevail in showing that at least one claim lacks sufficient written description and is not enabled, we conclude the challenged claims are eligible for post-grant review.

V. CONCLUSION

After considering the evidence and arguments presently before us, we determine Petitioner has shown it is more likely than not that at least one challenged claim of the '055 patent lacks written description and is unpatentable. Accordingly, we institute a post-grant review.

VI. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 324(a), a post-grant review of claims 1–33 of the '055 patent is *instituted* with respect to all grounds set forth in the Petition; and

FURTHER ORDERED that, pursuant to 35 U.S.C. § 324(c) and 37 C.F.R. § 42.4(b), post-grant review of the '055 patent shall commence on the

entry date of this Order, and notice is hereby given of the institution of a trial.

FOR PETITIONER:

Scott A. McKeown
Victor Cheung
ROPES & GRAY LLP

FOR PATENT OWNER:

Pier DeRoo
Michael Flibbert
Jessica Roberts
Constance Lee
FINNEGAN, HENDERSON, FARABOW,
GARRTETT & DUNNER, LLP
pier.deroo@finnegan.com
michael.flibbert@finnegan.com
jessica.roberts@finnegan.com
constance.lee@finnegan.com