

Filed on behalf of Petitioner by:

Paper No. ____

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INARI AGRICULTURE, INC.,
Petitioner,

v.

CORTEVA AGRISCIENCE LLC,
Patent Owner.

Case No. PGR2023-00022
Patent No. 11,371,055

**PETITIONER'S REPLY TO PATENT OWNER'S
PRELIMINARY RESPONSE**

The POPR flouts the Supreme Court’s recent admonition in *Amgen* that “the more one claims, the more one must enable,” and further that “advice to engage in trial and error” cannot substitute for an enabling disclosure. *Amgen Inc. v. Sanofi*, 143 S. Ct. 1243, 1254, 1257 (2023). The ’055 patent exemplifies the over-claiming practices plaguing U.S. agricultural development and harming American farmers.¹

PO does not dispute that claim 1 covers transgenic plant cells encoding over 2.4×10^{106} different “AAD-12 proteins”—all satisfying the claim requirements that the protein’s amino acid sequence (1) be at least 85% identical to SEQ ID NO: 2 and (2) include specific residues at 5 locations within the 292 amino acid chain. Pet., 30. PO also silently concedes that this “85% sequence identity constraint is an arbitrary number lacking any experimental support” (Silverstone, ¶80 (cited in Pet., 24)), and further that it permits any 43 of the other 287 locations in the chain to include any of the 20 canonical amino acids rather than the actual residue the sequence recites (Pet., 39-40). *See Amgen*, 143 S. Ct. at 1257 (analogizing protein to a “combination lock” incorporating “tumblers, each of which can be set to 20 different positions”).

Nor does PO dispute that many proteins otherwise satisfying claim 1 do **not** achieve the claimed functions of degrading two different herbicides; one must test each protein to assess if they do so. Pet., 58-59 (citing Silverstone, ¶¶76-79).

Despite this vast but uncertain scope of the challenged claims, PO also silently

¹ Director Vidal is prioritizing effort to combat such practices. Ex. 1009, 74-81.

concedes that the '055 patent only discloses *two* AAD-12 proteins satisfying the claimed requirements. Pet., 38. One has the exact 292 amino acid sequence of SEQ ID NO: 2, and the second is identical to the first aside from adding a 293rd amino acid at one end, making it 99.7% identical to SEQ ID NO:2. *Id.* Indeed, as compared to Amgen's patent, the '055 Patent discloses an "order of magnitude fewer embodiments" (2 as opposed to 26) despite claiming "a genus approximately one hundred orders of magnitude larger in size" (over 2.4×10^{106} proteins). *Id.* See also *Amgen*, 143 S. Ct. at 1257 (analogizing Amgen's patent to 26 "lock combinations").

PO attempts to side-steps *Amgen* by touting the '055 patent's "twenty-four examples." POPR at 1, 10, 12, 50, 53. None concerns any proteins aside from the two noted above. Even PO concedes that the examples merely offer a "**roadmap** for making and **evaluating** other AAD-12 proteins." POPR at 50. PO's concession parallels Amgen's own unsuccessful argument that Amgen's specification provided a "**roadmap**" for identifying all proteins satisfying Amgen's claimed functions. 143 S. Ct. at 1256. The Supreme Court dismissed Amgen's "roadmap" as mere "research assignments." *Id.* PO's "examples" fail for the same reason.

For example, PO's example 1 merely suggests "min[ing] current public databases" to identify potential proteins. Ex. 1001 at 31:55-32:22. Others concern the numerous steps required to refine and test candidate proteins once selected—for example, "reengineer[ing] the protein encoding sequence of the genes so that they

are more efficiently expressed in plant cells” (*id.* at 32:29-31), cloning vectors to insert the genes (*id.* at 41:5-45:49), conducting “in vitro assays” (*id.* at 45:50-48:60), and ultimately progressing to in vivo experiments (*id.* at 48:61-102:49).

In sum, much like Amgen’s patent, the ’055 Patent “call[s] on scientists to create a wide range of candidate [proteins] and then screen each to see which happen to” perform the claimed functions. *Amgen*, 143 S. Ct. at 1256. And just like Amgen, PO maintains that such synthesis and screening is “routine.” POPR at 51; compare with Amgen’s Supreme Court Reply Brief, 2023 WL 2431330, at *13 (“undisputed that making individual variants was ***routine***”). But no matter how readily POSAs could screen individual proteins as of 2017,² PO’s claims are not adequately enabled for the same reason Amgen’s claims failed: both specifications offer “little more than advice to engage in trial and error.” *Amgen*, 143 S. Ct. at 1257. Indeed, as Petitioner

² PO wrongly faults Petitioner for analyzing the disclosure as of 2017 instead of PO’s pre-AIA filing dates. POPR at 21-25. Given that the claims were not enabled even as of 2017, they plainly were not enabled by PO’s earlier applications. By contrast, the petitioners in *Merck* and *Biogen* (POPR at 24) had only analyzed the ***earliest*** applications in the priority chains—ignoring the prospect that later developments could have rendered disclosures adequate under § 112 as of subsequent filing dates still within the pre-AIA timeframe. The situation here is fundamentally different.

explained and PO does not dispute, the '055 patent provides “no information, testing, data, or discussion of species with less than 99.7% sequence identity to SEQ ID NO: 2”—despite claiming over 2.4×10^{106} candidates. Pet., 28. It is immaterial that '055 patent’s “twenty-four examples” may help expedite the “trial and error” involved in evaluating this unfathomable number of potentially relevant proteins. The claimed 85% identity requirement indeed is a mere unsupported hypothesis drawn from a laundry list of percentages from 49% to 99%. Ex. 1001 at 21:54-59.

PO again repackages Amgen’s unsuccessful arguments when faulting Petitioner for not “identify[ing] any embodiments within the scope of the claims that could not have been made using routine experimentation.” POPR at 45-46. Amgen likewise had complained that the challenger had not “identified even one actual antibody within the claims that could not be made following the patents’ roadmap.” Amgen’s Supreme Court Brief, 2022 WL 18108787, at *25. Despite such rhetoric, PO 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. POPR at 51. As *Amgen* confirms, such “trial and error” cannot substitute for an adequately enabled specification commensurate with the claims’ breadth. 143 S. Ct. at 1257.

In addition, PO seeks to add a non-existent loophole to *Amgen*. That is, PO wrongly dismisses *Amgen* because Amgen’s claims “contained no structural limitations,” whereas PO’s claims contain structural elements ***in addition to*** the

functional limitations critical for allowance. POPR at 47-48. As Petitioner explained and PO does not dispute, the purported structural limitations in claim 1 sweep so broadly as to cover over 2.4×10^{106} different “AAD-12 proteins”— 10^{26} times the number of atoms in the universe. Pet., 30. Under PO’s loophole, applicants could immunize themselves from *Amgen* by incorporating structural requirements so generic as to leave the functional limitations as the only actual basis for patentability.

PO’s loophole argument also contradicts the Federal Circuit’s holding in *Idenix Pharmaceuticals v. Gilead Sciences*, 941 F.3d 1149 (Fed. Cir. 2019) that claims to treating hepatitis C using an “effective amount of a purine or pyrimidine β -D-2’-methyl-ribofuranosyl nucleoside” were not enabled despite structural limitations requiring a methyl group in the nucleoside’s 2’-up position. The claims nevertheless encompassed “many, many thousands of 2’-methyl nucleosides,” which had to be tested for efficacy. *Id.* at 1159. Yet Idenix’s patent disclosed only four working examples—an “exceedingly narrow” number “relative to the claim scope.” *Id.* at 1161. It also lacked “meaningful guidance as to which 2’-methyl nucleosides are or are not effective.” *Id.* The Federal Circuit thus held that no reasonable factfinder could have found Idenix’s claims adequately enabled. *Id.* at 1162-63. The amount of experimentation required to practice the full scope of the claims was “excessive” and thus “undue,” notwithstanding that it was “routine” to screen individual compounds satisfying the structural elements. *Id.* at 1163.

Under PO's erroneous loophole theory, however, Idenix's claims would have been enabled because they had certain structural limitations (along with the required function of treating hepatitis C) and in particular because the methyl group at 2'-up constituted a "general quality...running through" the class. But the CAFC disagreed, as Idenix's specification lacked "meaningful guidance as to *which* 2'-methyl-up nucleosides are or are not effective" in treating hepatitis C. *Id.* at 1161 (emphasis added). While including a methyl group at 2'-up was a "key to curing hepatitis C" and "*necessary*" for effective treatment, the methyl alone was "*not sufficient.*" *Idenix Pharms. v. Gilead Scis.*, 2018 WL 922125, at *14 (D. Del. Feb. 16, 2018).

Here, likewise, Petitioner cites evidence—uncontradicted by PO—that while the five conserved residues of the "AAD-12 motif" are "*necessary* for the claimed activity, they are not *sufficient.*" Pet., at 33 (citing Silverstone, ¶¶ 48-49). The '055 patent thus does not disclose a "general quality" distinguishing working embodiments from non-functional ones and "*reliably* enabl[ing]" POSAs to practice "all of what is claimed." *Amgen*, 143 S. Ct. at 1255. The loophole theory fails.

The specification of the '055 patent is a mere research plan to identify and test proteins via trial and error. Claiming the results of unsatisfied research is repugnant to *Amgen*. The '055 patent does not provide adequate written description, or enable the vast scope of the challenged claims.

Date: August 18, 2023

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CERTIFICATE OF SERVICE UNDER 37 C.F.R. § 42.6 (e)(4)

I certify that on August 18, 2023, I will cause a copy of the foregoing document, including any exhibits filed therewith, to be served via electronic mail, as previously consented to by Patent Owner, upon the following:

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