IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

IMPOSSIBLE FOODS INC., *Plaintiff*, v. MOTIF FOODWORKS, INC., and GINKGO BIOWORKS, INC., *Defendants*.	§ § § § § § § § §	Civil Action No. 22-311-WCB **FILED UNDER SEAL**

CLAIM CONSTRUCTION ORDER

In this patent case, plaintiff Impossible Foods Inc. has asserted numerous claims from U.S. Patent No. 10,273,492 ("the '492 patent") and U.S. Patent No. 10,689,656 ("the '656 patent") against defendants Motif Foodworks, Inc. and Gingko Bioworks, Inc.[1] The asserted patents are directed to the expression of heme-containing proteins in genetically engineered yeast, as well as other proteins that assist in that goal.

The parties disagree about the proper construction of a number of claim terms from the asserted patents.[2] They have filed numerous briefs outlining their positions with respect to each disputed term. Dkt. Nos. 106, 120, 142, 148, 333, 338, 340, 346, 351, 352. Several of those briefs,

[1] Impossible has also asserted claims against Motif from Impossible's U.S. Patent Nos. 9,943,096; 10,039,306; 10,863,761; 11,013,250; and 11,224,241, which are directed to food products designed to mimic the taste of meat. On July 24, 2023, I ordered the portion of the case involving Impossible's claims of infringement of the food product patents to be tried separately from the portion of the case involving Impossible's claims of infringement of the yeast patents. Dkt. No. 161 at 1. Although I characterized that action as a "severance of the two cases," it is more properly characterized as an order providing for separate trials for claims found in the two groups of patents, pursuant to Rule 43 of the Federal Rule of Civil Procedure. In this order I have addressed only the claim construction issues relating to the yeast patents.

[2] The parties have provided competing approaches for numbering the disputed claim terms. For simplicity, I have adopted Ginkgo's system of numbering the claim terms.

Dkt. Nos. 106, 120, 142, and 148, were filed prior to my order directing that the yeast patent claims be tried separately from the food product claims. Those briefs address terms from the food products patents as well as from the yeast patents. Dkt. Nos. 333, 338, 340, 346, 351, and 352 address only terms from the yeast patents. On March 18, 2024, I held a claim construction hearing. I address below each of the disputes identified in the parties' briefing and at the hearing.

Term 1: "Promoter Element"

The first term disputed by the parties is "promoter element," which is found in all the asserted claims. Impossible argues that a "promoter element" is a polynucleotide that regulates transcription of another polynucleotide sequence. Impossible further argues that the promoter element is upstream of, and adjacent to the gene.

Ginkgo and Motif argue that the term "promoter element" is indefinite. To avoid invalidity for indefiniteness, a patent claim must "inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 901 (2014). Indefiniteness is a question of law dependent on subsidiary questions of fact. *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 325 (2015). The meaning to a person of ordinary skill in the art of "technical words or phrases not commonly understood" is one such factual question. *Id.* at 326.

"Promoter" is a term of art. It refers to a portion of a gene with binding sites for transcriptional activators to bind and regulate gene expression. Dkt. No. 341 at ¶ 62. The claim term, however, is "promoter element," and "promoter element" is not a term of art.[3] As used in

[3] Impossible's expert, Dr. Hal Alper, argues that "promoter element" is a term of art, and in support he cites two articles referring to a "promoter element." Dkt. No. 339 at ¶ 27. The two articles he cites, however, both use "promoter element" to mean "promoter." A promoter is one element of a gene, which is why the articles Dr. Alper cites refer to the promoter portion of the gene as a "promoter element."

the asserted claims, the term "promoter element" refers to a part of a promoter sequence. Put differently, a promoter element is simply an element of a promoter. The specification[4] makes clear that a "promoter element" is part of a promoter by repeatedly referencing a "promoter or promoter element therefrom" and equating that phrase to a "promoter, or a portion thereof." '656 patent at 4:54–60; *see also id.* at 7:5–6 ("[A] single promoter, or promoter element therefrom can be used to drive transcription . . . ."); *id.* at 6:60–61 ("Other methanol-inducible promoter elements therefrom, however, can be used . . . ."). Ginkgo and Motif concede that a promoter element is part of a promoter, Dkt. No. 333 at 3; Dkt. No. 340 at 5, so this aspect of the term is not at issue.

Ginkgo and Motif argue, however, that a person of ordinary skill in the art would not know which parts of a promoter would constitute a promoter element. In other words, they assume that only certain parts of a promoter can constitute a promoter element, and that the failure to identify which parts of the promoter contribute the promoter element renders the claims indefinite.

The intrinsic record does not expressly state which parts of a promoter constitute a promoter element, but it describes the characteristics of a promoter element. Namely, it makes clear that a promoter element must be able to perform the functions of a promoter. For example, the specification of the '656 patent describes the use of a specific methanol-inducible promoter that is "strongly transcribed in response to methanol." '656 patent at 4:56–60. It goes on to explain that the specific promoter can be substituted for other methanol-inducible promoters or promoter elements therefrom with similar characteristics. '656 patent at 4:60–5:11. Thus, a "promoter element" is a part of a promoter capable of performing the functions of a promoter.

[4] The specifications of the two patents in suit are almost identical. Accordingly, statements in this opinion regarding the specification refer to the common language in each of the specifications.

Although "promoter element" may be an imprecise term, it is not indefinite, as Ginkgo and Motif argue. "[A] patentee need not define his invention with mathematical precision in order to comply with the definiteness requirement." *Niazi Licensing Corp. v. St. Jude Med. S.C., Inc.*, 30 F.4th 1339, 1347 (Fed. Cir. 2022) (quoting *Guangdong Alison Hi-Tech Co. v. Int'l Trade Comm'n*, 936 F.3d 1353, 1359 (Fed. Cir. 2019). It is not necessary, therefore, that the patents delineate exactly what portion of a promoter can constitute a promoter element. All that is required is that the term reasonably inform a person of ordinary skill in the art about the scope of the invention. *Nautilus*, 572 U.S. at 901.

A person of ordinary skill in the art would certainly understand that the term "promoter element" covers a full promoter. Dr. Carl Batt, for example, one of Motif and Ginkgo's technical experts, identified the AOX1, TEF1, and GAP promoters as promoter elements. Dkt. No. 142-1, Ex. 23 at ¶¶ 44–45, 141–144. Likewise, a person of ordinary skill in the art would understand that a short, dysfunctional, region of the promoter would not be a promoter element within the meaning of the claims, even if it were taken from a promoter, because such a sequence could not be used in the ways contemplated by the specification. As such, a person of ordinary skill would have a reasonable understanding of the scope of the invention. Here, "the language is as precise as the subject matter permits," so the term is not indefinite. *PPG Industries, Inc. v. Guardian Industries Corp.*, 75 F.3d 1558, 1562–63 (Fed. Cir. 1996).

Although I agree with Impossible's indefiniteness position, Impossible's proposed construction of "promoter element" reads in definitions from other patents, which define a promoter element as something that "stimulates transcription but constitutes a sub-fragment of a larger promoter sequence." Dkt. No. 339 at ¶ 28; *see also id.* at ¶ 29 (referring to unrelated U.S. Patent No. 9,133,463, which uses "promoter element" interchangeably with "promoter" to require

regulation of transcription). Based on the use of definitions found in other patents, Impossible arrived at a proposed construction requiring that the promoter element "regulates (e.g., drives) transcription." Nothing in the intrinsic record supports the degree of specificity associated with that additional limitation.

I therefore reject both sides' positions and construe "promoter element" to mean "a functional part of a promoter."

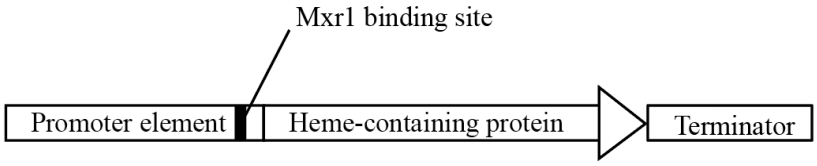
Term 2a: "A Mxr1 transcriptional activator sequence"

The second term the parties address is "a Mxr1 transcriptional activator sequence," which appears in all the claims of the '492 patent. In the absence of context, an "Mxr1 transcriptional activator sequence" could mean either of two things. Because every protein is translated from a DNA sequence, one potential meaning of "a Mxr1 transcriptional activator sequence" is a nucleic acid sequence encoding the Mxr1 protein itself.[5] In addition to being translated from a DNA sequence, however, a transcriptional activator such as Mxr1 also binds to different DNA sequences from the ones that encode the Mxr1 protein. Thus, the second potential meaning of "a Mxr1 transcriptional activator sequence" is a DNA sequence to which Mxr1 binds. Ginkgo and Motif argue for the first meaning. Impossible argues for the second. Impossible's construction is correct.

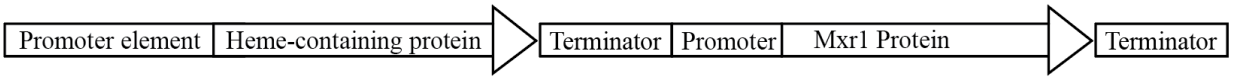
The first part of claim 1 of the '492 patent recites "a nucleic acid molecule encoding a heme-containing protein operably linked to a promoter element from *P. pastoris* and a Mxr1 transcriptional activator sequence from *P. pastoris*." Under Impossible's construction, that part of claim 1 calls for a DNA sequence encoding a heme-containing protein operably linked to a promoter element and an Mxr1 binding site. One role of a promoter is to bind transcription factors

[5] Nucleic acids (DNA and RNA) use three base-pair long "codons" to encode each amino acid. Multiple codons will correspond with the same amino acid, so various combinations of codons will result in the same amino acid sequence. Thus, many different nucleic acid sequences can encode the same protein.

such as Mrx1, so an Mxr1 binding site would be on the promoter element in most embodiments. A visual representation of the first nucleic acid sequence called for by claim 1 under Impossible's construction is shown below:



Under Ginkgo and Motif's construction,[6] the first part of claim 1 of the '492 patent calls for a heme-containing protein operably linked to a promoter element, and a sequence encoding an Mxr1 protein. A visual representation of the first DNA sequence called for by claim 1 under Ginkgo and Motif's constructions is shown below:[7]



Although Ginkgo and Motif present reasonable arguments favoring their position, a skilled artisan would not understand their construction to be correct for two reasons. First, the claims are directed to the invention described in the specification under Impossible's construction, but not under Ginkgo and Motif's. Second, Impossible's construction makes more sense in context, particularly when considering the dependent claims. Therefore, as explained in more detail below,

[6] Ginkgo and Motif propose differently worded constructions that carry the same meaning. Because they are equivalent for purposes of this analysis, I treat Ginkgo and Motif's construction as singular.

[7] Ginkgo and Motif's construction does not expressly call for a second promoter and terminator. I have included them in the figures and annotations because they are the most standard way of ensuring that the DNA sequence is translated into two separate proteins, rather than a single dysfunctional construct. *See, e.g.,* '492 patent at Figure 2 (showing each coding region under a separate promoter). The inclusion of those additional elements does not affect any of the analysis in this section.

the court construes the term "a Mxr1 transcriptional activator sequence" to mean "a DNA sequence to which the Mxr1 transcriptional activator protein binds."

A. The Patented Invention

Impossible's construction is consistent with what is described in the figures and the specification of the '492 patent, whereas Ginkgo and Motif's construction is not. Put differently, if Impossible's construction is applied, the claims cover only what was actually invented. Figures 2 and 4 of the '492 patent depict embodiments consistent with Impossible's construction, and the claims, as construed by Impossible, correspond exactly with those figures. By contrast, the specification discloses no embodiments following Ginkgo and Motif's construction. "[I]n case of doubt or ambiguity it is proper in all cases to refer back to the descriptive portions of the specification to aid in solving the doubt or in ascertaining the true intent and meaning of the language employed in the claims." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1315 (Fed. Cir. 2005) (quoting *Bates v. Coe*, 98 U.S. 31, 38 (1878)). The fact that the specification aligns with the claims under Impossible's construction, but not Ginkgo's or Motif's, strongly suggests that Impossible's construction is correct.

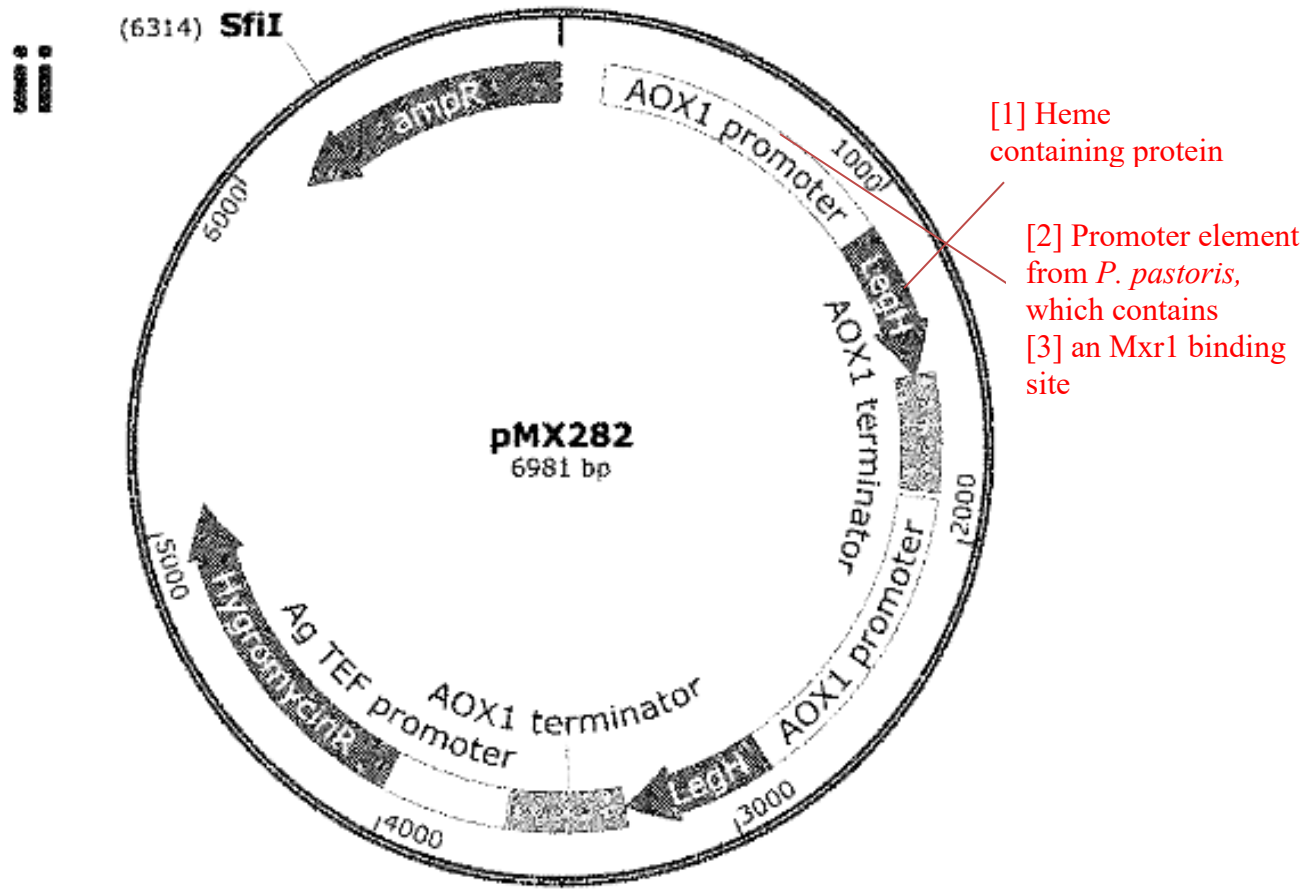
Figure 2 of the '492 patent depicts five plasmids (circular pieces of DNA) each containing an "AOX1 promoter." The AOX1 promoter has six binding sites for Mxr1, *see* Dkt. No. 334 at ¶ 128, which are "Mxr1 transcriptional activator sequence[s]" under Impossible's construction. Because it is a full promoter, AOX1 necessarily includes a promoter element. In other words, the AOX1 promoter is one embodiment of the claimed "promoter element from *P. pastoris* and [] Mxr1 transcriptional activator sequence. . . ." Under Impossible's construction, the plasmids in Figures 2 and 4 of the asserted patents depict various embodiments of the '492 claims. Under Ginkgo and Motif's construction, on the other hand, none of the embodiments in the specification

correspond with the claims, because all of the depicted plasmids lack a sequence encoding the Mxr1 protein.[8]

1. Sequence encoding a heme-containing protein

Consistent with Impossible's construction, Figure 2(ii) of the '492 patent (below) depicts exactly what is described in the first part of claim 1 of the '492 patent. As stated above, that part of claim 1 recites "a nucleic acid molecule encoding [1] a heme-containing protein operably linked to [2] a promoter element from *P. pastoris* and [3] a Mxr1 transcriptional activator sequence. . . ." Figure 2(ii) shows exactly that. LegH, shorthand for Leghemoglobin, is a heme-containing protein. And, as explained above, the promoter element and Mxr1 transcriptional activator sequence are both found in the AOX1 promoter. Claim 2, which depends from claim 1, specifies that "the heme-containing protein is Leghemoglobin," as in Figure 2(ii). And claim 6, which also depends from claim 1, specifies that the nucleic acid molecule further includes "a promoter element from a transcriptional elongation factor EF-1 (TEF1) gene." The promoter element of claim 6 is labeled in Figure 2(ii) as the Ag TEF promoter. The sole portion of Figure 2(ii) that is unaccounted for by the claims is the section labeled AmpR, which refers to a gene conferring resistance to ampicillin, a common antibiotic. *See* '492 patent at 22:63–65 (discussing plating colonies containing the plasmids of Figure 2 on agar plates with ampicillin to eliminate cells not containing the plasmid).

[8] Figure 4 shows a plasmid with a sequence encoding the Mxr1 protein, but one would expect it to contain two such sequences. *See infra* at 13.

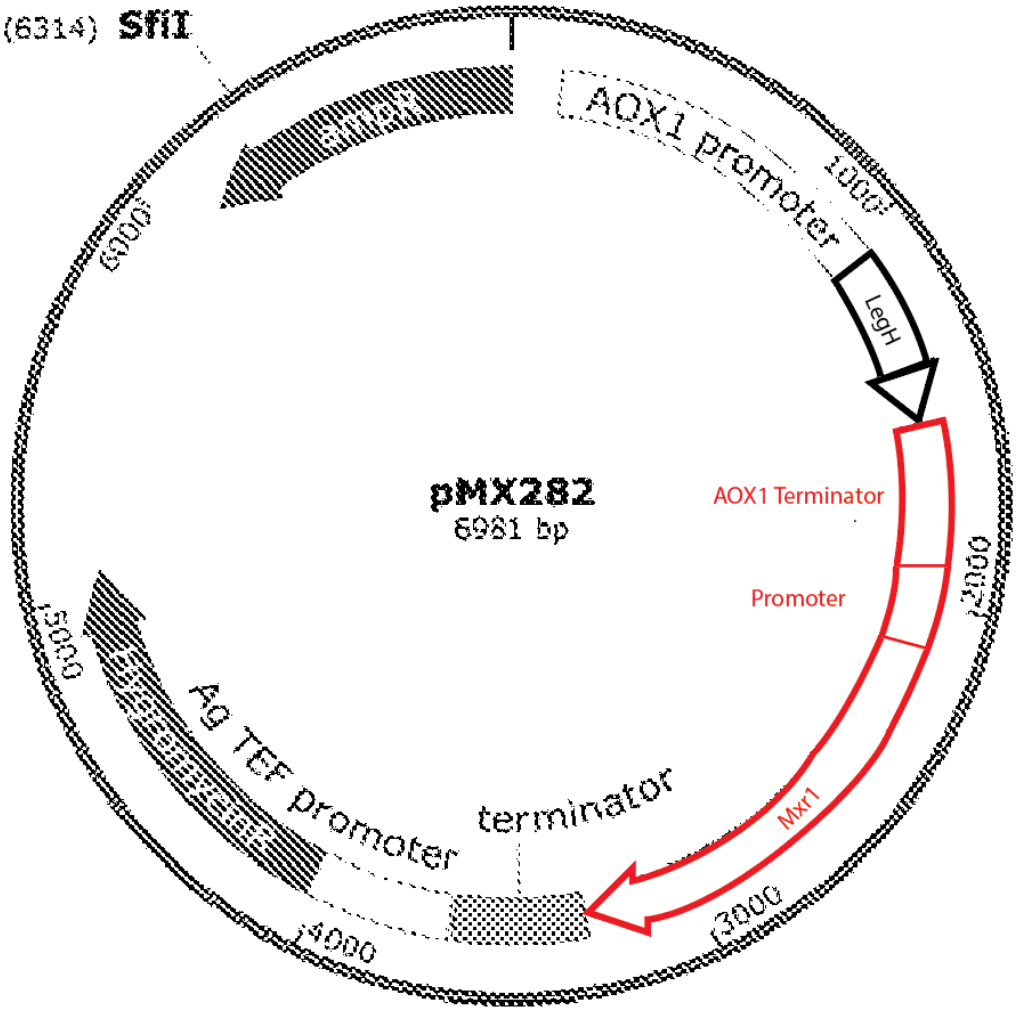


If Ginkgo and Motif's construction were correct, the corresponding embodiment would also contain a sequence encoding the Mxr1 protein linked to a separate promoter. An annotated version of Figure 2(ii) embodying the first part of claim 1 under Ginkgo and Motif's construction is shown below: [9]

[9] None of the annotated figures are to scale. All of the plasmids would be much larger if they were to embody Ginkgo and Motif's construction because they would contain an additional Mxr1 gene. The DNA sequence encoding Mxr1 alone is almost 3500 base pairs. *See* '492 patent at 29:1–30:55. In order to show modifications on the same background image, the modified genes are depicted as shorter than they would be in reality.

Annotations adding new components to the plasmids are shown in red. Annotations moving existing components on the plasmids to make space for new material are shown in black.

ii

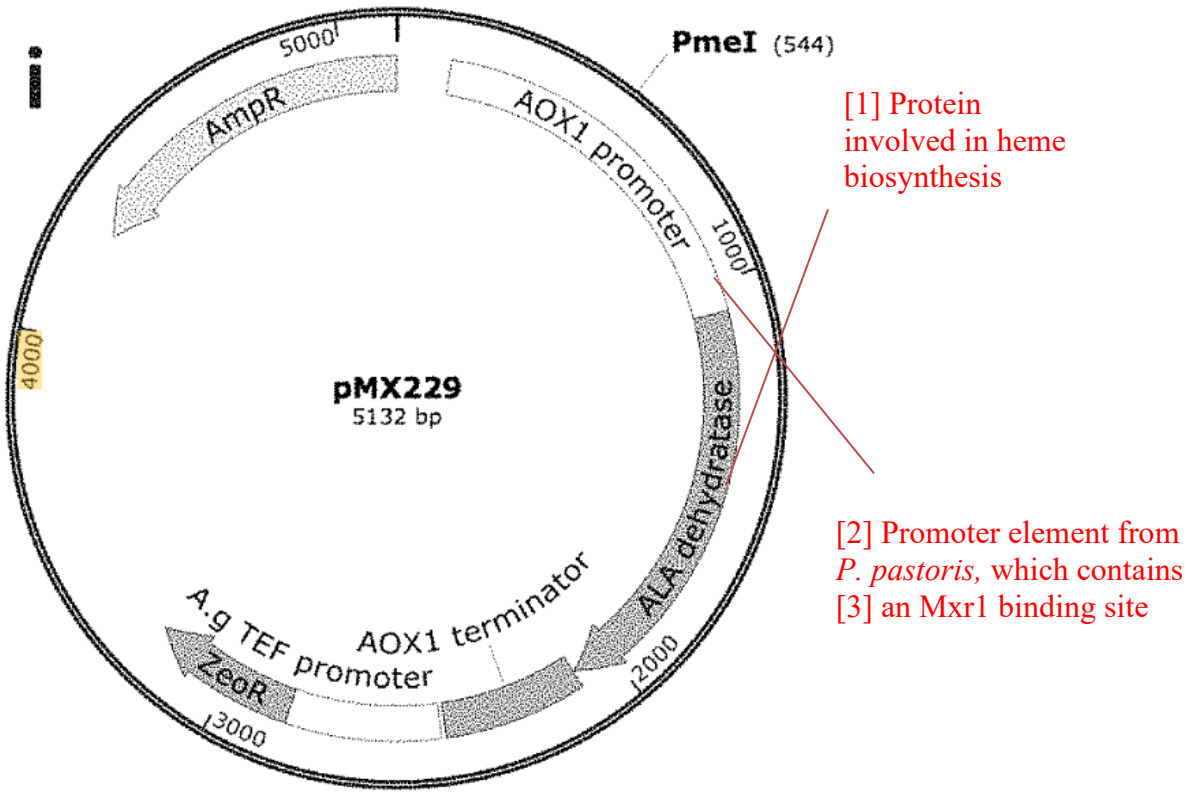


No such embodiment is present in either of the asserted patents.

2. Sequence encoding a protein involved in heme biosynthesis

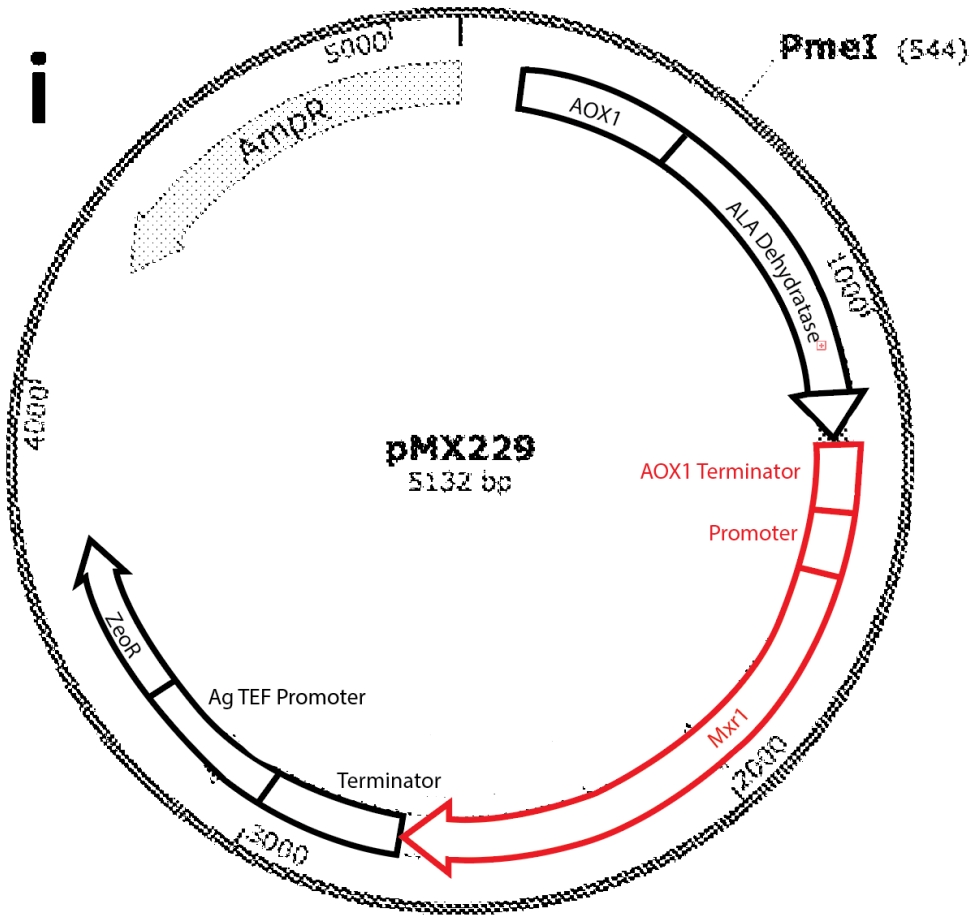
Figures 2(i), (iii), (iv), and (v) of the '492 patent all depict embodiments of the second nucleic acid molecule described in claim 1. That molecule contains "a nucleic acid molecule encoding [1] at least one polypeptide involved in heme biosynthesis . . . [2] a promoter element from *P. pastoris* and [3] a Mxr1 transcriptional activator sequence . . . ." Figure 2(i) (below) is representative and contains all three sequences called for by the claim under Impossible's construction. ALA dehydratase is a polypeptide involved in heme biosynthesis. *See e.g.*, '492

patent at cl. 4 ("[T]he at least one polypeptide involved in heme biosynthesis is selected from the group consisting of ALA synthase, ALA dehydratase . . . ."). As noted, under Impossible's construction, the AOX1 promoter contains both a promoter element and a Mxr1 transcriptional activator sequence. Figures 2(iii), (iv), and (v) show plasmids encoding different combinations of proteins involved in heme synthesis.. The nucleic acid encoding an Mxr1 protein, which is required by Ginkgo and Motif's constructions, is not present in any of Figures 2(i), (iii), (iv), or (v).



As in the case of the heme-containing protein, the corresponding embodiment of the portion of claim 1 that is directed to a protein involved in heme biosynthesis would also differ from the one described in the patent following Ginkgo and Motif's construction. In addition to everything found in Figure 2(i), the corresponding embodiment under Ginkgo and Motif's

construction would also contain a sequence encoding the Mxr1 protein linked to a separate promoter. An annotated version of Figure 2(i) embodying the second part of claim 1 under Ginkgo and Motif's construction is shown below:

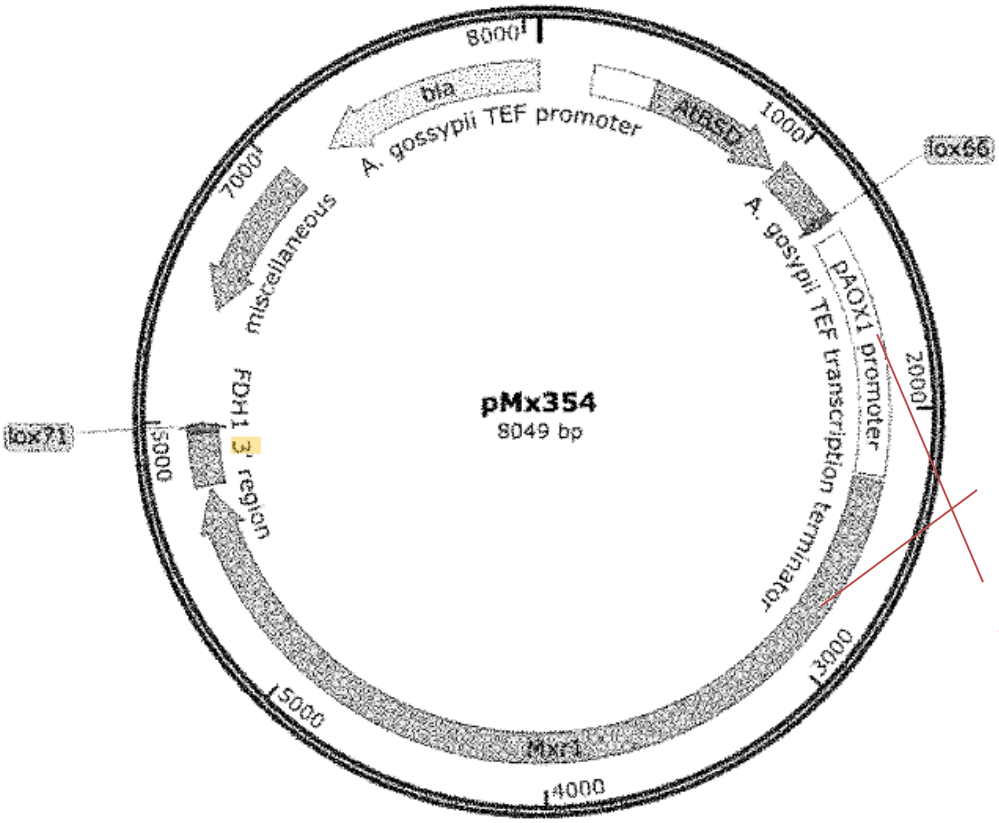


No such embodiment can be found in either asserted patent.

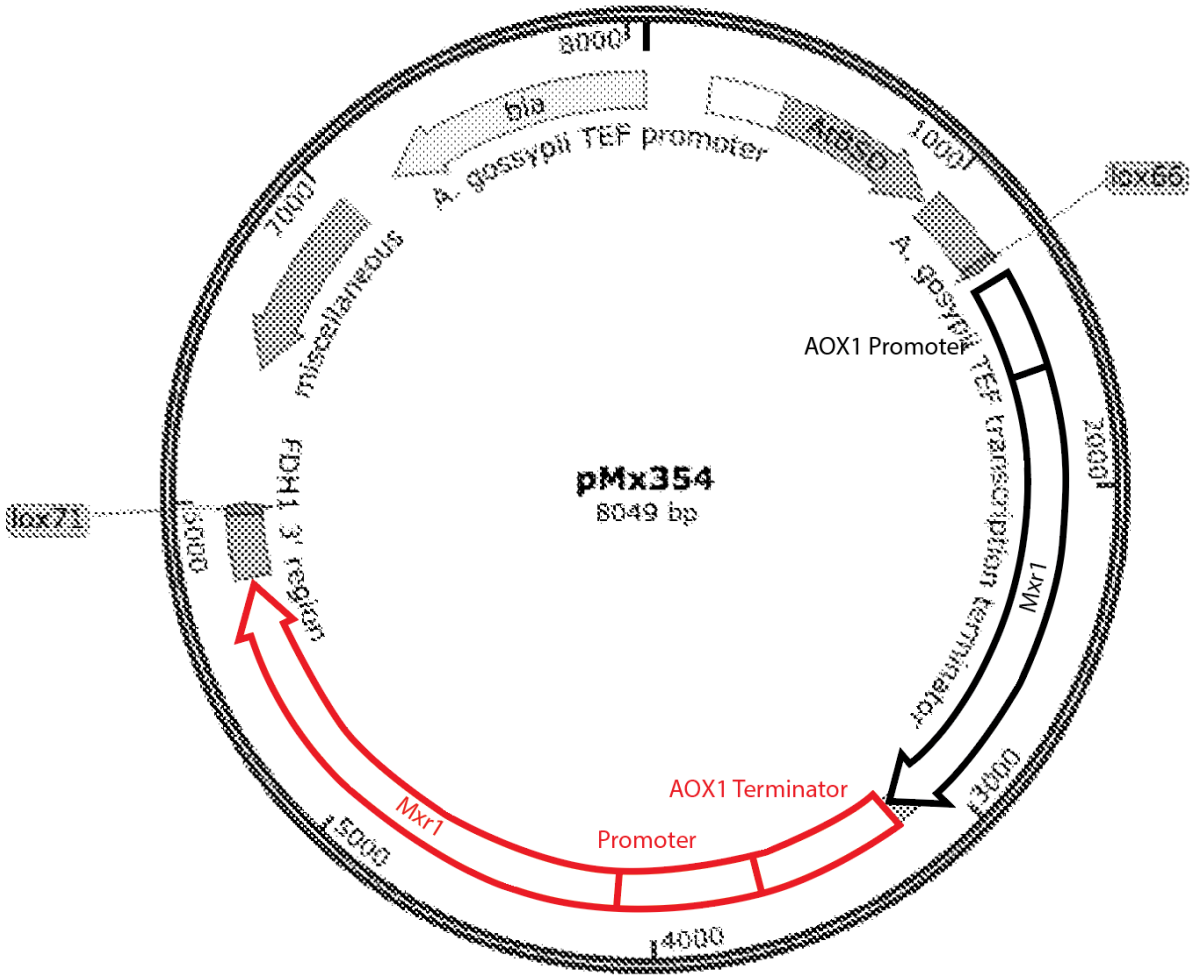
3. Sequence encoding the Mxr1 protein

Figure 4 of the '492 patent (below) depicts an embodiment of the additional nucleic acid molecule described in dependent claim 14. The additional nucleic acid molecule of claim 14 contains "a nucleic acid molecule encoding [1] a Mxr1 transcriptional activator . . . [2] a promoter element from *P. pastoris* and [3] a Mxr1 transcriptional activator sequence from *P. pastoris*." The "nucleic acid molecule encoding a Mxr1 transcriptional activator" is the large portion labeled

Mxr1. And the promoter element and Mxr1 transcriptional activator sequences are found in the AOX1 promoter.



At the claim construction hearing, counsel for Ginkgo argued that Figure 4 supports Ginkgo's construction because it shows a plasmid containing the Mxr1 gene, i.e., a sequence encoding the Mxr1 protein. But if Figure 4 were to embody any of the claims under Ginkgo and Motif's construction, it would need to contain both the Mxr1 gene and a second gene encoding a heme-containing protein (claim 1), protein involved in heme biosynthesis (claim 1), or a second Mxr1 protein (claim 14). Thus, it is clear that Figure 4 is an embodiment of claim 14 under Impossible's construction, but does not embody any claims under Motif and Ginkgo's construction. A version of Figure 4 that has been annotated to embody claim 14 under Ginkgo and Motif's construction is shown below:



As in the case of the other claimed elements, there is no embodiment following Ginkgo and Motif's construction of claim 14 in either of the asserted patents.

In sum, under Impossible's proposed construction, every nucleic acid molecule called for by the claims can be found in the embodiments described in the specification. By contrast, nothing in either of the asserted patents embodies the '492 claims under Ginkgo and Motif's construction. I decline to adopt Motif and Ginkgo's construction because it would result in the claims being directed to something other than what Impossible invented. The intrinsic record makes clear that Impossible's construction is correct and that Motif and Ginkgo's is not. *See Phillips*, 415 F.3d at 1315.

B. Context of Use

In addition to aligning closely with the specification, Impossible's construction also makes more sense in context than Ginkgo and Motif's. Context therefore provides a second reason supporting Impossible's position. *See Phillips*, 415 F.3d at 1314 (explaining that "the context in which a term is used in the asserted claim" is often "highly instructive" in determining the correct construction). As explained above, claim 14 of the '492 patent depends from claim 1 and recites:

> 14. The yeast cell of claim 1, further comprising a nucleic acid molecule encoding a Mxr1 transcriptional activator operably linked to a promoter element from *P. pastoris* and a Mxr1 transcriptional activator sequence from *P. pastoris*.

Claim 14 refers separately to "a nucleic acid molecule encoding a Mxr1 transcriptional activator" and "a Mxr1 transcriptional activator sequence." The structure of claim 14 therefore indicates that those components are two different things. "A nucleic acid encoding a Mxr1 transcriptional activator" unambiguously refers to the nucleic acid encoding the Mxr1 protein. As such, "a Mxr1 transcriptional activator sequence" must refer to something else. And the only other thing to which it could reasonably refer is the DNA sequence to which Mxr1 binds, which is what Impossible's construction dictates.

Ginkgo and Motif argue that the difference between the "Mxr1 transcriptional activator" and the "Mxr1 transcriptional activator sequence" is that the first must be "from *P. pastoris*," whereas the second refers to Mxr1 from any organism. That reading of claim 14 is unnatural. If that were the intended meaning of the claim language, one would expect the claim to refer to a "second" Mxr1 transcriptional activator, but it does not. As such, the structure of claim 14 favors Impossible's construction.

Impossible's construction is further supported by the patent's definition of the term "operably linked," which the patent uses to mean "positioned relative to a nucleic acid coding

sequence in such a way as to direct or regulate expression of the nucleic acid." '492 patent at 4:49–51; Dkt. No. 354 at ¶ 33, 42. A DNA sequence encoding the Mxr1 protein itself (Ginkgo and Motif's construction) would have nothing to do with directing or regulating the expression of "a heme-containing protein" or a "polypeptide involved in heme biosynthesis." A DNA sequence to which the Mxr1 protein binds (Impossible's construction), on the other hand, would regulate transcription by binding the Mxr1 transcriptional activator. Thus, only under Impossible's construction would the Mxr1 sequence be "operably linked" to a coding region. As such, Impossible's construction makes more sense in the context in which the term is used than the construction proposed by Motif and Ginkgo. Context therefore further supports Impossible's construction.

C. Ginkgo and Motif's Arguments

Ginkgo and Motif raise two points in support of their proposed construction. The first is that another patent in the same family uses "Mxr1 transcriptional activator sequence" to mean the DNA sequence encoding the protein, suggesting that it should be given the same meaning in the '492 patent. The second is that the Patent Trial and Appeal Board adopted Ginkgo and Motif's construction in its decision declining to institute review of the '492 patent. Both are reasonable arguments, but they are ultimately insufficient to overcome the evidence in Impossible's favor.

U.S. Patent No. 9,938,327 ("the '327 patent") claims priority to PCT/US2016031797, the same application as the '492 and '656 patents. The '327 patent also uses the phrase "Mxr1 transcriptional activator sequence," by which it means the DNA sequence encoding the Mxr1 protein. That meaning is unambiguous because dependent claim 17 further calls for an Mxr1 transcriptional activator sequence, wherein the sequence is a specific DNA sequence encoding the

Mxr1 protein. Thus, the '327 patent follows Motif and Ginkgo's construction.[10] It is well established that, "unless otherwise compelled, the same claim term in the same patent or related patents carries the same construed meaning." *In re Rambus Inc.*, 694 F.3d 42, 48 (Fed. Cir. 2012) (cleaned up) (quoting *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1334 (Fed. Cir. 2003)). Here, however, the meaning of "Mxr1 transcriptional activator sequence" is "otherwise compelled" by the figures and claims of the '492 patent itself, which make clear that Impossible's construction is the correct one. Although the meaning of the term "Mxr1 transcriptional activator sequence" in the '327 patent is a point in Motif and Ginkgo's favor, the usage of the term in the '327 patent does not overcome the intrinsic evidence in the '492 patent itself, which confirms Impossible's construction.

The second of Ginkgo and Motif's points is that the Patent Trial and Appeal Boardadopted their construction. *See* Dkt. No. 333-8, Ex. 8 at 13 (declining to institute inter partes review in part because "[p]etitioner has not sufficiently shown that a POSITA . . . would have been motivated to incorporate the nucleic acid sequence encoding a Mxr1 transcriptional activator"; referring to the disputed term as used in claim 1 of the '492 patent). But Ginkgo and Motif do not make a collateral estoppel argument, and this court is not bound by the Board's interpretation if it believes

[10] Impossible argues that the term's usage in the '327 patent is the product of a drafting error, because claim 18 of the patent requires that the same term have "the amino acid sequence shown in [a specific identified sequence]." Claim 1 of the '327 patent, from which claim 18 depends, recites a "nucleic acid molecule" comprising "a Mxr1 transcriptional activator sequence." According to Impossible, this discrepancy shows that the '327 patent's use of "a Mxr1 transcriptional activator sequence" must be a drafting error because a nucleic acid molecule cannot include an amino acid sequence as contemplated by claim 18. That argument is unpersuasive for two reasons. First, a person of ordinary skill in the art, recognizing the mismatch between claims 1 and 18, would understand that claim 18 requires the DNA sequence that *encodes* the specified amino acid sequence, rather than the sequence that "has" it. Second, claims 17 and 18 of the '327 patent both unambiguously call for sequences, whether nucleic acid or amino acid, encoding the Mxr1 protein, which is the crux of the immediate dispute. Errors aside, the '327 patent clearly uses the disputed term in the way Ginkgo and Motif propose that it be construed.

that interpretation to be incorrect. I am not persuaded that the construction of the term adopted by the Patent Trial and Appeal Board is correct.

For the foregoing reasons, the court construes "a Mxr1 transcriptional activator sequence" to mean "a DNA sequence to which the Mxr1 transcriptional activator protein binds."

Term 2b: "a first exogenous nucleic acid encoding a methanol expression regulator 1 (Mxr1) transcriptional activator"

The parties do not dispute that Term 2b refers to the sequence encoding the Mxr1 transcriptional activator protein. Dkt. No. 371 at 9. For consistency with the other terms, *see infra* Term 2c, I construe this term to mean "a first exogenous nucleic acid encoding a methanol expression regulator 1 (Mxr1) transcriptional activator protein."

Term 2c: "a nucleic acid encoding a Mxr1 transcriptional activator sequence"

The parties do not dispute that Term 2c refers to the sequence encoding the Mxr1 transcriptional activator protein. Dkt. No. 371 at 9. The word "sequence" is not specific, however, in that it can refer to the sequence to which Mxr1 binds or to the sequence encoding the Mxr1 protein. For clarity and consistency, I construe this term to mean "a nucleic acid encoding a Mxr1 transcriptional activator protein."

Term 3: "from *P. pastoris*" or "from *Pichia pastoris*"

The parties propose conflicting constructions of what it means to be "from *P. pastoris*." Impossible proposes that "from *P. pastoris*" "indicates that the sequence has its origins in the *P. pastoris* genome." Ginkgo and Motif's proposed constructions require that the thing be found in native *P. pastoris*, i.e., found naturally in *P. pastoris*. The main difference between the parties' constructions relates to whether "from *P. pastoris*" includes sequences that originated in the *P. pastoris* genome but have subsequently been modified. Impossible's construction would

encompass some such sequences; Ginkgo and Motif's would not. For the reasons set forth below, I adopt Impossible's proposed construction.

As an initial matter, Impossible argues that Motif's use of the term "native" contradicts the specification. The parties, however, appear to be speaking past one another on this issue. Synthetic biology, the field of the patents, often involves inserting one organism's DNA into a second "host" organism. Something is native if it is found naturally in a specified organism. Usually, the specified organism is the "host," but not always. In Motif's construction, it is clear that native refers to something found naturally in *P. pastoris*—not in the host cell. Dr. Alper, on the other hand, treats "native" as referring to whether "the relevant nucleic acid sequence" is found naturally in "the host organism." Dkt. No. 144 at ¶ 12; Dkt. No. 354 at ¶ 45 (incorporating Dkt. No. 144 at ¶ 12). Under this definition, Dr. Alper argues that the claims cannot require a native sequence because the claims call for a Mxr1 transcriptional activator sequence from *P. pastoris* to be inserted into a methylotrophic *Pichia* yeast cell, which could be a strain other than *P. pastoris*. Dkt. No. 107 at ¶¶ 57–59 (discussing claim 26 of the '656 patent). If the host cell is not *P. pastoris*, an Mxr1 sequence "from *P. pastoris*" would not be native under Dr. Alper's definition. Dkt. No. 107 at ¶ 59. Dr. Alper's argument is compelling as to why the court should not adopt a construction of "from *P. pastoris*" that would require the subject to be native to the host cell. But nobody has proposed such a construction. Motif's construction of "from *P. pastoris*" means that the subject is native to *P. pastoris*, so Impossible's argument addresses an issue that is not in contention.

Impossible also argues, based on normal usage of the term by skilled artisans, that a person of ordinary skill in the art would understand that an engineered sequence would still be "from *P. pastoris*" so long as it had its origins in the *P. pastoris* genome. For example, Impossible contends that a sequence would still be "from *P. pastoris*" even if it were subject to standard engineering

manipulations, such as codon optimization.[11] I credit Dr. Alper's assertion that persons of ordinary skill in the art often refer to sequences originating in the genome of a particular organism as being "from" that organism. Dkt. No. 354 ¶¶ 42–43 (collecting references to genetically modified sequences with origins in a species' genome as being "from" the species). I further credit Dr. Alper's opinion that this construction is consistent with the way engineered sequences are treated in the literature. *Id.*

Ginkgo and Motif argue that, if "from *P. pastoris*" only requires that the sequence originate in the *P. pastoris* genome, any sequence can be considered "from" *P. pastoris* regardless of how much it has been modified. I agree with Ginkgo and Motif that a sequence that has been modified to the point that it bears no resemblance to the original can no longer be considered "from *P. pastoris*," but I do not agree that such sequences would fall under Impossible's construction. Such a synthetic sequence would originate in the lab that created it—not in *P. pastoris.*

The court accordingly construes "from *P. pastoris*" to mean "originating in the *P. pastoris* genome."

Term 4: "wherein the recombinant nucleic acid molecule comprises [x], wherein the recombinant nucleic acid molecule comprises [y]"

Ginkgo and Motif argue that the two clauses of this term refer to the same recombinant nucleic acid molecule. Impossible does not argue that this reading is wrong; rather, Impossible argues that the term's plain and ordinary meaning is sufficient. The court adopts Ginkgo and Motif's construction.

[11] Codon optimization is a process by which a DNA sequence is modified to work more efficiently in a given host organism. Different organisms have different translation machinery, causing them to prefer different codons. Codon optimization accounts for these differences without changing the protein that is ultimately produced, and such optimization is standard practice when inserting an exogenous DNA sequence into an organism.

Impossible argued before the Patent Trial and Appeal Board that the two clauses of this phrase refer to the same recombinant nucleic acid molecule. The Board adopted that argument in its decision declining to institute *inter partes* review. *See* Dkt. No. 340, Ex. 6 at 23 ("As petitioner recognizes, claim 1 [of the '656 patent] requires that the same recombinant nucleic acid molecule comprises both the claimed first exogenous nucleic acid and the claimed second exogenous nucleic acid."). Impossible is estopped from changing its position now.

Impossible argues that it is not estopped from claiming that the recombinant nucleic acid molecule need not "reside entirely on a single chromosome in the yeast genome." Dkt. No. 338 at 19. That argument is confusing. The recombinant nucleic acid molecules contemplated by the claims and embodied in the specification are plasmids. Plasmids do not reside on chromosomes at all, much less on the "same chromosome." Ginkgo and Motif's construction means that [x] and [y] must be located on the same plasmid—not the same chromosome. Impossible's argument therefore appears to be beside the point.

Estoppel aside, Ginkgo's construction is correct and removes any potential ambiguity, so I will construe Term 4 to mean: "wherein the recombinant nucleic acid molecule comprises [x], wherein the same recombinant nucleic acid molecule comprises [y]."

Term 5: "a nucleic acid molecule encoding [x] and [y]"

Term 5 is used in claims 1 and 14 of the '492 patent. The dispute regarding its meaning is effectively the same as the dispute regarding Term 2a. As in the case of Term 2a, I agree with Impossible's construction.

The way Ginkgo has framed Term 5 term is loaded in its favor. Impossible rejects the premise of Ginkgo's construction and would instead read the claim as requiring "a nucleic acid molecule encoding [a], operably linked to [b] and [c]." Claim 1 is representative of the dispute and is reproduced below:

> 1. A methylotrophic *Pichia* yeast cell comprising:
>
> a nucleic acid molecule encoding a heme-containing protein operably linked to a promoter element from *P. pastoris* and a Mxr1 transcriptional activator sequence from *P. pastoris*; and
>
> a nucleic acid molecule encoding at least one polypeptide involved in heme biosynthesis operably linked to a promoter element from *P. pastoris* and a Mxr1 transcriptional activator sequence from *P. pastoris*.

Ginkgo and Motif propose that claim 1 be read as meaning:

> 1. A methylotrophic *Pichia* yeast cell comprising:
>
> [a] a nucleic acid molecule encoding [both]
>
> > [i] a heme-containing protein operably linked to a promoter element from P. pastoris and
> >
> > [ii] a Mxr1 transcriptional activator sequence from *P. pastoris*; and
>
> [b] a nucleic acid molecule encoding [both]
>
> > [i] at least one polypeptide involved in heme biosynthesis operably linked to a promoter element from P. pastoris and
> >
> > [ii] a Mxr1 transcriptional activator sequence from *P. pastoris*.

Impossible proposes that claim 1 be read as meaning:

> 1. A methylotrophic *Pichia* yeast cell comprising:
>
> [a] a nucleic acid molecule encoding a heme-containing protein operably linked to
>
> > [i] a promoter element from *P. pastoris* and
> >
> > [ii] a Mxr1 transcriptional activator sequence from *P. pastoris*; and
>
> [b] a nucleic acid molecule encoding at least one polypeptide involved in heme biosynthesis operably linked to
>
> > [i] a promoter element from *P. pastoris* and
> >
> > [ii] a Mxr1 transcriptional activator sequence from *P. pastoris*.

Claim 14, as construed under Ginkgo and Motif's convention would mean:

14. The yeast cell of claim 1, further comprising a nucleic acid molecule encoding

[i] a Mxr1 transcriptional activator operably linked to a promoter element from *P. pastoris* and

[ii] a Mxr1 transcriptional activator sequence from *P. pastoris*.

Claim 14, as construed under Impossible's convention, would mean:

14. The yeast cell of claim 1, further comprising

[a] a nucleic acid molecule encoding a Mxr1 transcriptional activator operably linked to

[i] a promoter element from *P. pastoris* and

[ii] a Mxr1 transcriptional activator sequence from *P. pastoris*.

For the same reasons discussed with respect to Term 2a, the court agrees with Impossible's reading of claims 1 and 14 of the '492 patent. Accordingly, Term 5 will be construed to mean "a nucleic acid molecule encoding [a], operably linked to [b] and [c]."

Term 6: "sequence to which [the/a] Mxr1 transcriptional activator binds"

Ginkgo and Motif argue that Term 6 is a means-plus-function term and therefore is indefinite because no corresponding structure is disclosed in the specification. Dkt. No. 333 at 10; Dkt. No. 340 at 24. But the claim term does not recite "means" anywhere, and the only argument raised as to why the subject language should be treated as a means-plus-function term is that the sequence is defined by whether it functions to bind Mxr1. But "the mere fact that the disputed limitations incorporate functional language does not automatically convert the words into means for performing such functions." *Zeroclick, LLC v. Apple Inc.*, 891 F.3d 1003, 1008 (Fed. Cir. 2018). Instead, Term 6 refers to a set of defined structures: DNA sequences to which Mxr1 is known to bind. *See* Dkt. No. 339 at 14 (explaining that such sequences were known in the art at the time of the invention). Term 6 is therefore not a means-plus-function term.

Ginkgo and Motif further argue that a person of ordinary skill in the art would not know whether Mxr1 would bind to a given sequence, referred to as a "consensus sequence," without knowing more about the context. Mxr1 consensus sequences were known in the art at the time of the invention. Dkt. No. 339 at 14 (identifying various prior art Mxr1 consensus sequences); *see also* Dkt. No. 340 at 24 (Motif conceding that Mxr1 consensus sequences were known in the art); Dkt. No. 334 at ¶ 126 (Ginkgo's expert conceding same). It was also known, however, that these consensus sequences would not bind Mxr1 in every context. Dkt. No. 334 at ¶ 130; Dkt. No. 339 at ¶ 15. But nothing in the claims requires binding to succeed in every instance. Even if a given consensus sequence does not bind Mxr1 in a particular context, a person of ordinary skill in the art would still understand it to be a "sequence to which [the/a] Mxr1 transcriptional activator binds." For that reason, Term 6 is not indefinite. *Nautilus*, 572 U.S. at 901. Its meaning is sufficiently clear as is, so Term 6 will be construed as following its plain language, i.e., a "sequence to which [the/a] Mxr1 transcriptional activator binds."

Term 7: "wherein each nucleic acid is operably linked to a methanol-inducible promoter element"

The parties disagree as to the meaning of this term in two respects. First, although the parties agree that "each nucleic acid" refers to sequences encoding (1) an Mxr1 protein, (2) a member of globin family PF00042, and (3) a polypeptide involved in heme biosynthesis, they disagree about whether those three sequences must be present on the same recombinant nucleic acid molecule. Second, they disagree about whether all three nucleic acid molecules must be operably linked to the same "methanol-inducible promoter element." I adopt Motif and Ginkgo's construction with respect to the first issue, and I therefore construe Term 7 as requiring all three sequences to be on the same plasmid. I adopt Impossible's construction with respect to the second

issue, and I further construe Term 7 as requiring that each nucleic acid molecule be linked to one or more methanol-inducible promoter elements, rather than to the same one.

As to the first issue, Impossible argues that the three nucleic acid molecules recited in claim 26 of the '656 patent do not need to be on the same nucleic acid molecule, and that the proposed construction is an improper attempt to read additional limitations into the claims. Impossible, however, argued for Ginkgo's construction in its preliminary IPR response, and it is now estopped from changing its position. Impossible previously argued that "claim [26] requires all three nucleic acids to be present on the same recombinant nucleic acid molecule." Dkt. No. 333-6, Ex. 6 at 32. The PTAB relied on that construction in its decision denying institution of *inter partes* review. Dkt. No. 333-7, Ex. 7 at 23 (addressing "the requirement that all three nucleic acids be on the same nucleic acid molecule"). "Statements made by a patent owner during an IPR proceeding, whether before or after an institution decision, can be relied upon to support a finding of prosecution disclaimer." *Aylus Networks, Inc. v. Apple Inc.*, 856 F.3d 1353, 1364 (Fed. Cir. 2017). Impossible has disavowed embodiments in which the three nucleic acid sequences are not located on the same molecule. Accordingly, I adopt Ginkgo and Motif's construction as to this issue.

The second argument is based on dependent claim 28, which refers to "the methanol-inducible promoter element," specifying that it be an alcohol oxidase 1 (AOX1) promoter." According to Ginkgo and Motif, that language suggests that there cannot be multiple methanol-inducible promoters. Otherwise, they contend, claim 28 would be indefinite because a person of ordinary skill in the art would not know which promoter needs to be an AOX1 promoter.

Ginkgo and Motif's argument is at odds with the default rule is that "a" or "an" means "'one or more' in open-ended claims containing the transitional phrase 'comprising.'" *Baldwin Graphic Sys., Inc. v. Siebert, Inc.*, 512 F.3d 1338, 1342 (Fed. Cir. 2008) (citing *KCJ Corp. v.*

Kinetic Concepts, Inc., 223 F.3d 1351, 1356 (Fed. Cir. 2000)); *01 Communique Lab'y, Inc. v. LogMeIn, Inc.*, 687 F.3d 1292, 1297 (Fed. Cir. 2012); *TiVo, Inc. v. EchoStar Commc'ns Corp.*, 516 F.3d 1290, 1303 (Fed. Cir. 2008). "The subsequent use of . . . 'the' or 'said' in a claim to refer back to the same claim term does not change the general plural rule, but simply reinvokes that non-singular meaning." *Baldwin*, 512 F.3d at 1342. "The exceptions to this rule are extremely limited: a patentee must evince a clear intent to limit 'a' or 'an' to 'one.'" *Id.* (cleaned up). If one were to substitute "one or more methanol-inducible promoter elements" for "a" and "the" "methanol-inducible promoter element," claims 26–28 would read perfectly naturally. Nothing mandates an alternative construction. As such, the plurality presumption expressed in *Baldwin* applies. I therefore adopt Impossible's construction with respect to this issue.

For the foregoing reasons, the court construes Term 7 to mean "wherein the nucleic acid encoding a Mxr1 transcriptional activator sequence, the nucleic acid encoding a member of the globin family PF00042, and the nucleic acid encoding the at least one polypeptide are all present on the same recombinant nucleic acid molecule and are operably linked to one or more methanol-inducible promoter elements."

Term 8: "the [at least one] methanol-inducible promoter element"

The independent claims refer to multiple methanol-inducible promoter elements, and the dependent claims further refer to "the" methanol-inducible promoter element. Ginkgo and Motif argue that this term is indefinite because it is not clear which of the promoter elements the dependent claims refer to.

To the extent that Ginkgo and Motif argue that reference to "the" methanol-inducible promoter element is inherently singular, that argument is foreclosed by *Baldwin*. 523 F.3d at 1342 ("The subsequent use of . . . "the" or "said" in a claim to refer back to the same claim term . . .

simply reinvokes [the] non-singular meaning" of "a" or "an" as meaning "one or more."). That is Ginkgo and Motif's only argument as to why claim 28 of the '656 patent is indefinite.

The other claims, however, call for multiple promoter elements and refer back to "the" promoter element. In those claims, the phrases used in the dependent claims directly match the antecedent phrases in the independent claims. As such, the phrases in the dependent claims refer to all the promoter elements called for in the independent claims. That is:

1. "the promoter element from *P. pastoris*" in claim 5 of the '492 patent refers to both instances of that phrase in claim 1;
2. "the methanol-inducible promoter element from *P. pastoris*" in claim 7 of the '492 patent refers to that same phrase in claim 5; and
3. "the at least one methanol-inducible promoter element" in claims 10 and 11 of the '656 patent refers to both instances of that phrase in claim 1.

Ginkgo cites *Bushnell Hawthorne, LLC v. Cisco Systems, Inc.*, 813 F. App'x 522, 526 (Fed. Cir. 2020) and § 2173.05(e) of the Manual of Patent Examining Procedure (MPEP), as support for the proposition that a dependent claim's reference to "the" promoter element is indefinite when the independent claim refers to multiple promoter elements. In *Bushnell*, however, the later reference was "without explanation or antecedent basis." 813 F. App'x at 526. Here, the antecedent basis is clearly laid out every time Term 8 is used, so a person of ordinary skill in the art would understand that any limitations following Term 8 apply to every antecedent instance. For the same reason, MPEP § 2173.05 does not apply. As was explained in *Baldwin*, "MPEP § 2173.05(e) is inapposite because the limitations in claim 32 all relate to proper antecedent bases." 512 F.3d at 1343.

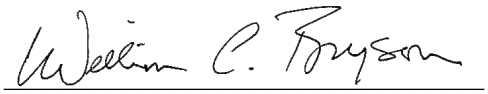
Ginkgo bears the burden of proving indefiniteness by clear and convincing evidence. *Ironburg Inventions Ltd. v. Valve Corp.*, 64 F.4th 1274, 1284 (Fed. Cir. 2023). Ginkgo has not demonstrated that a person of ordinary skill in the art would not understand the meaning of Term 8, and it therefore has not met its burden. Accordingly, I adopt Impossible's construction of Term 8, which follows the plain language of the term, and I construe Term 8 to mean "the [at least one] methanol-inducible promoter element."

* * * * *

I note that many of the parties' materials pertaining to claim construction have been filed under seal. Accordingly, in an abundance of caution, this order has been filed under seal. Within three business days of the issuance of this order, the parties are directed to advise the court by letter whether they wish any portions of the order to remain under seal, and if so which portions. Any request that portions of the order should remain under seal must be supported by a particularized showing of need to limit public access to those portions of the order.

IT IS SO ORDERED.

SIGNED this 22nd day of March, 2024.



WILLIAM C. BRYSON
UNITED STATES CIRCUIT JUDGE