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THE REGENTS OF THE UNIVERSITY OF CALIFORNIA,
UNIVERSITY OF VIENNA, AND EMMANUELLE CHARPENTIER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA, UNIVERSITY OF VIENNA, AND EMMANUELLE CHARPENTIER
Junior Party

Applications 15/947,680; 15/947,700; 15/947,718; 15/981,807; 15/981,808; 15/981,809; 16/136,159; 16/136,165; 16/136,168; 16/136,175; 16/276,361; 16/276,365; 16/276,368; and 16/276,374

v.

TOOLGEN, INC.
Application 14/685,510

Patent Interference No. 106,127 (DK)
(Technology Center 1600)

CVC MOTION 2 (to deny ToolGen P1 benefit)

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I. INTRODUCTION

The PTAB should deny ToolGen accorded benefit to its first provisional application. ToolGen cannot be accorded benefit to its first provisional application because, by its own admissions, the application does not disclose an embodiment of the count. According to ToolGen, a codon-optimized Cas9 nucleic acid is required for CRISPR-Cas9 to function in eukaryotic cells. Moreover, according to ToolGen, a skilled artisan would have no idea what the outcome may be if one were to codon optimize a Cas9 nucleic acid.[1] These positions were central to its argument to the Patent Office in obtaining allowance of its involved claims over the prior art. But there is no embodiment in ToolGen's P1 of a codon-optimized Cas9 nucleic acid in ToolGen's P1 and no disclosure that would fill the gaps that ToolGen claimed would prevent a skilled artisan from codon-optimizing a Cas9 nucleic acid. Having successfully persuaded the Patent Office to issue its involved claims on these bases, ToolGen cannot now renounce those positions and argue in reply to this motion that its P1 described an embodiment of the count even though it lacked any disclosure of a codon-optimized Cas9 nucleic acid.

ToolGen's representations to the Patent Office regarding the requirement for codon optimization are unambiguous. It stated that the Cas9 nucleic acid "has to be codon optimized." Ex. 2012, 510 Appl. Pros. History, 8604:1-3 (Oral Hr., Mar. 11, 2020). When an earlier PTAB panel asked what was the "secret sauce" that distinguished its claims over the prior art, ToolGen

[1] While CVC disagrees, ToolGen argued during prosecution that there was no reasonable expectation of success because obtaining a functional codon-optimized Cas9 nucleic acid was unpredictable, and a skilled artisan "would have no idea what the outcome may have been if one were to apply codon optimization . . . to CRISPR/Cas9." Ex. 2012, 510 Appl. Pros. History, 8531 (Reply Br., Jan. 8, 2019).

averred that the "nucleic acid has been engineered . . . with codon optimization." *Id.*, 8604:24-8605:25. And it insisted codon optimization was "required in the science to get it to work." *Id.*, 8606:5-11. ToolGen's position during prosecution is clear and unmistakable: **its invention required a codon-optimized Cas9 nucleic acid, codon-optimizing the Cas9 nucleic acid was unpredictable, and one would have "no idea" of the outcome of codon optimizing.**

ToolGen's insistence that codon-optimization is required is fatal to any argument in reply that it should be accorded benefit of its first provisional application. ToolGen's first provisional application fails to describe the supposedly required codon-optimization of a Cas9 nucleic acid. It does not even mention codon optimization generically, let alone provide a single codon-optimized sequence. Because ToolGen's application does not disclose the very thing it deemed critical for function, its application cannot serve as a constructive reduction to practice of the Count. "Proof of a reduction to practice, absent an adequate description in the specification of what is reduced to practice, does not serve to describe or identify the invention for purposes of the written description requirement." *In re Alonso*, 545 F.3d 1015, 1021 (Fed. Cir. 2008).

Moreover, given ToolGen's unequivocal and repeated assertions during *ex parte* prosecution and appeal, it does not matter that CVC's half of the count does not require a codon-optimized Cas9 nucleic acid. ToolGen cannot now switch positions and argue the opposite—that disclosure of a codon-optimized sequence is not required. Principles of judicial estoppel preclude a party from taking clearly inconsistent positions on the same issue before different tribunals. *See Zedner v. United States*, 547 U.S. 489 (2006).[2]

[2] To be clear, ToolGen's position does not apply to CVC because CVC has not taken the position that codon optimization is required or that codon optimization is unpredictable. In fact,

Accordingly, the PTAB should deny ToolGen benefit to its first provisional application.

II. STATEMENT OF PRECISE RELIEF REQUESTED

CVC requests that the PTAB deny ToolGen the benefit with respect to Count 1 to the October 23, 2012, filing date of its first provisional application, Application No. 16/717,324.

III. ARGUMENT

The PTAB's December 14, 2020 Declaration of Interference accorded ToolGen benefit of its first provisional application, Application No. 16/717,324, filed on October 23, 2012 ("P1"). Paper 1, 10. During prosecution, ToolGen represented to the Patent Office that codon-optimized Cas9 nucleic acid is required and sufficiently inventive to render its claims patentable. MF2, 10, 11, 32-33, 43-44. The Patent Office relied on those representations in allowing the claims. MF12-13. However, ToolGen's P1 fails to demonstrate a constructive reduction to practice of an embodiment of the count consistent with its prior arguments to the Patent Office.

a. Through repeated and unequivocal assertions during prosecution, ToolGen persuaded the Patent Office that a codon-optimized Cas9 nucleic acid is required for CRISPR-Cas9 to function in eukaryotic cells.

ToolGen's involved claims all require a Cas9 nucleic acid that "is codon-optimized for expression in mammalian cells." Paper 6; MF1. ToolGen added this limitation to the involved claims to distinguish the prior art and to overcome the examiner's anticipation and obviousness rejections. Ex. 2012, 510 Appl. Pros. History, 6745-6749 (Resp., Mar. 3, 2017); MF2. ToolGen argued that its invention required a codon-optimized Cas9 nucleic acid and it even argued that

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neither is true. But, ToolGen represented the contrary to the Patent Office to obtained allowance and should be held that representation.

CRISPR-Cas9 would not function in eukaryotic cells without it. MF2, 10, 11, 32-33, 43-44. It further argued codon-optimizing the Cas9 nucleic acid was unpredictable, and not all codon optimized Cas9 nucleic acids would be functional. MF34-38, 45. These arguments were central to its successful efforts to obtain allowance of its claims over the prior art. MF12-13.

ToolGen was unequivocal in its arguments that codon-optimization was essential to its alleged invention. During the oral argument appealing the obviousness rejection, ToolGen explained "you have to introduce the nucleic acid [encoding Cas9] into the mammalian cell, and then in our case, we're explicitly claiming it has to have a nuclear localization signal, and **it has to be codon optimized.**" Ex. 2012, 510 Appl. Pros. History, 8604:1-3 (Oral Hr., Mar. 11, 2020) (emphasis added); MF9. And when the PTAB asked what the "secret sauce" was in ToolGen's claimed invention that made it distinguishable from the prior art, ToolGen doubled-down and told the PTAB that the "nucleic acid [that] has been engineered with . . . codon optimization" is the "main distinction" from the prior art.

> JUDGE FLAX: So what is it that's specifically different about this claimed method, that is different from more generalized disclosure of CRISPR in the prior art that allows you to do it in a mammalian -- even say, eukaryotic cell? What is it that you claimed here that's the secret sauce?

* * *

> MR. INSOGNA: Well, the main distinction is recited in Section A, where we are providing a nucleic acid into the mammalian cell, and that nucleic acid has been engineered with both the nuclear localization signal and codon optimization. So, in order to express a protein in the mammals of prokaryotic protein or bacterial protein in a eukaryotic cell, number one, there's lots of evidence in the record from Dr. Cullen (phonetic) that that's not an easy task. It doesn't always work.

Ex. 2012, 510 Appl. Pros. History, 8604:24-8605:25 (Oral Hr., Mar. 11, 2020) (emphasis added); MF10, 43.

And to leave no doubt as to the importance of codon optimization, ToolGen confirmed to the PTAB that codon optimization was one of two things that "were required in the science to get [CRISPR-Cas9] to work."

> JUDGE FLAX: So are those two recited features, sub-steps, is that what's allowing it to happen, the use of an NLS, and the codon optimization?
> MR. INSOGNA: In this claim 66, yes.
> JUDGE FLAX: Even not claimed. Just let's talk in a broader sense, were these the two things that were required in the science to get it to work?
> MR. INSOGNA: Yes.
> JUDGE FLAX: Okay.

Ex. 2012, 510 Appl. Pros. History, 8606:5-11 (Oral Hr., Mar. 11, 2020) (emphasis added); MF11, 44. According to ToolGen, a codon-optimized Cas9 nucleic acid was required for CRISPR-Cas9 to function in eukaryotic cells. ToolGen never retracted this assertion post-appeal; and it may not do so now.

The technique of codon optimization was known in the art as of the filing date of ToolGen's P1. Ex. 2015, Bailey Decl., ¶39; Ex. 2075, Sandhu 2008, 187. It allows for the replacement of existing codons with a set of more suitable codons for enhancing the "expression of the foreign gene in the host cell." *Id*. But ToolGen argued during prosecution that codon optimization was required and that codon optimization of the Cas9 nucleic acid so as to obtain a functional protein was not predictable. For example, in its appeal brief, ToolGen emphasized the codon-optimization limitation when traversing the obviousness rejection and argued that it was not "predictable" whether the Cas9 protein would "preserve its functionality" when expressed from a codon-optimized nucleic acid:

> Bacterial proteins may not fold properly in mammalian cells, and alteration of codons (which occurs as a result of codon optimization) can result in altered translation kinetics leading to misfolding. Since improperly folded proteins can lack activity, exhibit aberrant function or be degraded in cells, it would not have been predictable, whether a bacterial protein such as Cas9 and, in particular, codon-optimized Cas9 would fold in a mammalian cell in a way that would preserve its functionality.

Ex. 2012, 510 Appl. Pros. History, 6895-6896 (Appeal Br., Jun. 13, 2018) (internal citations omitted); MF6. Similarly, it argued that "it was not known or reasonably expected in the art that a prokaryotic Type II CRISPR/Cas system with codon-optimized Cas9 would successfully function in mammalian cells." Ex. 2012, 510 Appl. Pros. History, 6899 (Appeal Br., Jun. 13, 2018); MF7. And it argued that a skilled artisan "would have had no idea what the outcome may have been even if one were to apply codon optimization and NLS addition to CRISPR/Cas9." Ex. 2012, 510 Appl. Pros. History, 8531 (Reply Br., Jan. 8, 2019); MF8. ToolGen made similar codon optimization-based arguments throughout prosecution. *See* Ex. 2012, 510 Appl. Pros. History, 6758, 6761-6762, 6767 (Resp., Mar. 3, 2017); MF4-8, 34-38, 45. For example, ToolGen stated that a skilled artisan "would ***not*** have reasonably expected that a Type II CRISPR/Cas9 system could successfully have been used . . . in eukaryotic (e.g., mammalian) cells" because of the "challenges presented by modification (*e.g.*, tagging and codon-optimization) of nucleic acids to be expressed in eukaryotic/mammalian cells." *Id.*, 6758 (emphasis in original) (internal citations omitted); *see also id.*, 6761-6762, 6767; MF4-5.

Relying on ToolGen's representations and accepting its arguments, the PTAB reversed the examiner's obviousness rejection of ToolGen's involved claims. Ex. 2012, 510 Pros. History, 8638, 8642, 8643, 8645, 8646 (PTAB Decision, Jun. 22, 2020); MF12. On remand, the examiner merely stated ToolGen's claims "are in condition for allowance." *Id.*, 8651 (Office Comm., Oct. 23, 2020); MF13.

b. ToolGen should be bound and estopped from now arguing that its first provisional application is a constructive reduction to practice of the count despite failing to disclose a codon-optimized Cas9 nucleic acid.

ToolGen represented during prosecution that codon-optimized Cas9 nucleic acid is required for CRISPR-Cas9 to function in eukaryotic cells and for patentability of its involved claims. MF2, 10, 11, 32-33, 43-44. Under party admission and judicial estoppel doctrines, the PTAB should hold ToolGen to its representations. ToolGen's P1 lacks a constructive reduction to practice of either half of the count because P1 fails to disclose a codon-optimized Cas9 nucleic acid.

i. ToolGen's representations are binding admissions.

Prosecution is suspended and ToolGen may not abandon its prosecution statements that led directly to this interference. *Springs Window Fashions LP v. Novo Industries, L.P.,* 323 F.3d 989, 995 (Fed. Cir. 2003); *Louis v. Okada*, 59 U.S.P.Q.2d 1073, 1075 (B.P.A.I. 2001) (precedential). "The public notice function of a patent and its prosecution history requires that a *patentee be held to what he declares during the prosecution* of his patent." *Springs Window*, 323 F.3d at 995 (emphasis added). To be binding, the party's prosecution statements "must be effected with reasonable clarity and deliberateness." *Id.* at 994. The *Springs Window* court found the party's prosecution statements "detailed, consistent, and repeated" and not "simply an inadvertent misstatement by the prosecuting attorney." *Id.* at 996. Therefore, it rejected the party's infringement argument that "would undercut the public's reliance on a statement that was in the public record and upon which reasonable competitors formed their business strategies." *Id.* at 995. Just like the *Springs Window* court held the patentee to its prosecution statements that led to the asserted patent, the PTAB should hold ToolGen to its prosecution statements that led to this interference.

The Board has previously held a party to its prosecution statements in an interference context. *See, e.g., Louis v. Okada*, 59 U.S.P.Q.2d 1073 (B.P.A.I. 2001) (precedential). In *Louis*, a party moved to change the count to remove a recited claim feature to better align with its best proofs. The Board denied the motion because that was the feature on which the party had relied during prosecution to overcome a prior art rejection and get the claims allowed. *Id.* at 1075. The Board further faulted the movant for not even addressing the examiner's prior art rejection after making "an apparent about-face with respect to arguments previously made to the examiner to overcome [the] rejection." *Id.*

ToolGen's efforts to distinguish prior art based on the codon-optimization claim limitation were "detailed, consistent, and repeated" and not "simply an inadvertent misstatement by the prosecuting attorney." *Springs Window*, 323 F.3d at 996. For example, ToolGen argued that Cas9 nucleic acid "has to be codon optimized" for CRISPR-Cas9 to function in eukaryotic cells. Ex. 2012, 510 Appl. Pros. History, 8604:1-3 (Oral Hr., Mar. 11, 2020). It led the PTAB to believe on appeal that the "secret sauce" that distinguished its claims over the prior art was that the "nucleic acid has been engineered . . . with codon optimization." *Id.*, 8604:24-8605:25 (Oral Hr., Mar. 11, 2020); MF10, 43. ToolGen also unequivocally represented to the PTAB that codon optimization was required "in the science" for CRISPR-Cas9 to function in eukaryotic cells. *Id*., 8606:5-11 (Oral Hr., Mar. 11, 2020). Thus, ToolGen argued "with reasonable clarity and deliberateness" that a codon-optimized Cas9 nucleic acid is required for CRISPR-Cas9 to function in eukaryotic cells. *Spring Window*, 323 F.3d at 994. As in *Louis*, ToolGen here would be doing "an apparent about-face with respect to [the] arguments previously made to the examiner to overcome a rejection" if it were permitted to argue a constructive reduction to

practice based upon a CRISPR-Cas9 system that does not include a codon-optimized Cas9 nucleic acid. *Louis,* 59 U.S.P.Q.2d at 1075.

The Board should not excuse ToolGen's binding prosecution admissions regarding the necessity of codon-optimization.

ii. Judicial estoppel precludes ToolGen from now taking a contrary position.

Judicial estoppel applies and precludes ToolGen from relying on an embodiment that does not include a codon-optimized Cas9 nucleic acid in arguing that its P1 provides a constructive reduction to practice. *Zedner v. United States*, 547 U.S. 489, 504 (2006); *New Hampshire v. Maine*, 532 U.S. 742, 742 (2001); *Wilson v. Martin,* 789 Fed. Appx. 861, 872 (Fed. Cir. 2019). Under the equitable doctrine of judicial estoppel, "[w]here a party assumes a certain position in a legal proceeding, and succeeds in maintaining that position, he may not thereafter, simply because his interests have changed, assume a contrary position . . . ." *Zedner*, 547 U.S. at 504; *New Hampshire*, 532 U.S. at 742; *see also Wilson,* 789 Fed. Appx. at 872. As the Supreme Court explained, "judicial estoppel, generally prevents a party from prevailing in one phase of a case on an argument and then relying on a contradictory argument to prevail in another phase." *Zedner*, 547 U.S. at 504; *New Hampshire*, 532 U.S. at 749. "The Board has authority and discretion to apply the doctrine of judicial estoppel." *Wilson,* 789 Fed. Appx. at 872. It "applies just as much when one of the tribunals is an administrative agency as it does when both tribunals are courts." *Trustees in Bankr. of N. Am. Rubber Thread Co. v. United States,* 593 F.3d 1346, 1354 (Fed. Cir. 2010).

Judges consider several factors in weighing whether to apply judicial estoppel. Foremost is their assessment of whether a party has taken a position that is "clearly inconsistent" with a prior position. *See Zedner*, 547 U.S. at 504. The new "position must be mutually exclusive and

directly inconsistent" with the earlier one. *Egenera, Inc. v. Cisco Sys.*, *Inc.,* 972 F.3d 1367, 1379 (Fed. Cir. 2020) (cleaned up). Whether the party had successfully persuaded a tribunal to accept its earlier position is another relevant factor. *See Zedner,* 547 U.S. at 504. Also relevant is whether the party "would derive an unfair advantage or impose an unfair detriment on the opposing part if not estopped." *Zedner*, 547 U.S. at 504. Here, these factors weigh strongly in favor of estopping ToolGen from now taking the directly inconsistent position that disclosure of a codon-optimized Cas9 nucleic acid is not required for a constructive reduction to practice.

A ToolGen argument that its P1 discloses a constructive reduction to practice would directly contradict its prosecution position that its invention required a codon-optimized Cas9 nucleic acid to get CRISPR Cas9 to function in eukaryotic cells. ToolGen cannot argue now that codon-optimized Cas9 nucleic acid is not required for a reduction to practice when it repeatedly argued that point of distinction.

Moreover, it is beyond reasonable dispute that ToolGen's codon-optimization requirement argument was necessary to the PTAB's decision reversing the obviousness rejection and the examiner's indication of allowance that led to this interference. Ex. 2012, 510 Pros. History, 8638, 8642, 8643, 8645, 8646 (PTAB Decision, Jun. 22, 2020); *see also id.*, 8651 (Office Comm., Oct. 23, 2020) (finding the claims "in condition for allowance, but [] pending a potential interference" on remand); MF12-13.

Judicial estoppel is further warranted here because ToolGen would derive an unfair advantage by being accorded the benefit of its P1 filing date notwithstanding the absence of a disclosure of codon-optimized Cas9 nucleic acid. Had ToolGen not been accorded benefit of its P1, CVC would have been the senior party as CVC's accorded benefit date (corresponding to its third provisional application) pre-dates ToolGen's subsequent applications. Senior party status

provides significant advantages in an interference. For example, it determines which party bears the burden to establish priority of invention in the priority phase and dictates which party files the first priority brief.

But for ToolGen's representations to the Patent Office, ToolGen's involved application would have never been allowed, and the present interference (and the parallel interference no. 106,126 with Broad) would have never been declared. Accordingly, the PTAB should estop ToolGen from now relying on an embodiment that does not include description of a codon-optimized Cas9 nucleic acid to argue a constructive reduction to practice irrespective of which half of the count is at issue.

c. In view of ToolGen's codon-optimization representations to the Patent Office, its first provisional application does not provide written description support for a codon-optimized Cas9 nucleic acid, and thus, it fails to qualify as a constructive reduction to practice of the count.

To be accorded the benefit of an earlier-filed application, the earlier application must provide a constructive reduction to practice—i.e. "a described and enabled anticipation" with respect to at least one embodiment within the scope of the count. *Falkner v. Inglis*, 448 F.3d 1357, 1362 (Fed. Cir. 2006); 37 CFR § 41.201. However, ToolGen's P1 fails to provide *any* description of a codon-optimized Cas9 nucleic acid. Ex. 2015, Bailey Decl., ¶¶9, 38-67, 143. Consequently, in view of ToolGen's binding prosecution arguments, P1 cannot disclose a constructive reduction to practice of a functioning embodiment of the count. *Id.*

"[T]he hallmark of written description is disclosure." *Ariad Pharms., Inc. v. Eli Lilly and Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (*en banc*). "[T]he description must clearly allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed." *Id.*; *see also In re Alonso*, 545 F.3d 1015, 1019 (Fed. Cir. 2008) ("To satisfy [the written description] requirement, the specification must describe the invention in sufficient detail so that one skilled

in the art can clearly conclude that the inventor invented the claimed invention as of the filing date sought."). The test for written description is "an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art." *Ariad*, 598 F.3d at 1351.

The specification must contain sufficient disclosure to "convey the detailed identity of an invention." *University of Rochester v. G.D. Searle & Co*., 358 F.3d 916, 923 (Fed. Cir. 2004). This means that "mere indistinct words" may not necessarily be sufficient to allow "one skilled in the art to visualize or recognize the identity of the subject matter purportedly described." *Id.* In *Rochester*, the court found that the specification lacked written description for the claimed treatment method because "no compounds that will perform the claimed methods [were] disclosed." *Rochester*, 358 F.3d at 927. In reaching its decision, the court reasoned that the disclosure of how to obtain the compounds or what can be done with the compounds that may be obtained does not help the specification satisfy the written description requirement because it did not disclose the "detailed identity" of the compounds. *Id.* at 924, 927.

As discussed above, ToolGen repeatedly argued during prosecution that a codon-optimized nucleic acid is unlikely to express a functional Cas9 protein in eukaryotic cells due to alleged unpredictability in protein folding. MF34-38, 45. For example, ToolGen argued that "it would not have been predictable, whether a bacterial protein such as Cas9 and, in particular, codon-optimized Cas9 would fold in a mammalian cell in a way that would preserve its functionality." Ex. 2012, 510 Appl. Pros. History, 6895-6896 (Appeal Br., June 13, 2018); MF6. According to ToolGen, a skilled artisan "would have had no idea what the outcome may have been even if one were to apply codon optimization . . . to CRISPR/Cas9" and which one of these

sequences would express a functional Cas9 protein in eukaryotic cells. Ex. 2012, 510 Appl. Pros. History, 8531 (Reply Br., Jan. 8, 2019); MF8.

If one accepts ToolGen's prosecution statements that a codon-optimized nucleic acid is unlikely to express a functional Cas9 protein in eukaryotic cells—which ToolGen now must—then its P1 fails to provide any identity, much less a detailed identity, for a codon-optimized Cas9 nucleic acid within its four corners. *Ariad*, 598 F.3d at 1351. As in *Rochester*, ToolGen's application does not provide a single codon-optimized Cas9 nucleic acid sequence. *Rochester*, 358 F.3d at 927; Ex. 2008, ToolGen's P1; Ex. 2015, Bailey Decl., ¶56; MF14. In fact, the application never even mentions "codon optimization." Ex. 2008, ToolGen's P1; Ex. 2015, Bailey Decl., ¶56; MF15. Instead, the application vaguely states that "[t]he Cas9-coding sequence (4,104 bp), derived from *Streptococcus pyogenes* strain M1 GAS (NC_002737.1), was reconstituted using the human codon usage table and synthesized using oligonucleotides." Ex. 2008, ToolGen's P1, 11; Ex. 2015, Bailey Decl., ¶56; MF16.

But, in light of ToolGen's representations of unpredictability in codon optimization, this limited disclosure is not sufficient to support that feature. Ex. 2015, Bailey Decl., ¶¶9, 38-67, 143. NC_002737.1 is merely the accession number for the nucleic acid sequence record of the complete genome of M1 GAS strain of *S. pyogenes* in the NCBI database, which at best includes the nucleotide range of the location of the Cas9 gene in the genome. Ex. 2015, Bailey Decl., ¶59; Ex. 2447; Ex. 2448; MF17. Thus, the disclosure at best identifies the location and sequence of the Cas9 gene in the nucleic acid sequence of the *S. pyogenes* genome and vaguely states that the gene was "reconstituted using the human codon usage table." Ex. 2015, Bailey Decl., ¶59; Ex. 2447; Ex. 2448; MF17. ToolGen's P1 does not provide a single human codon-usage table. Ex. 2015, Bailey Decl., ¶60; Ex. 2008, ToolGen's P1; MF18. Without knowing the specific codon-

usage table or the process or set of rules for selecting codons from the table, numerous sequences could be "reconstituted" from a table, not all of which, according to ToolGen, are in fact codon optimized to express a functional Cas9 protein as compared to the native *S. pyogenes* sequence. Ex. 2015, Bailey Decl., ¶¶60, 64; MF19. But, ToolGen's P1 does not disclose what the reconstituted sequence was or whether the reconstituted sequence was in fact optimized for enhanced expression vis-à-vis the wild-type *S. pyogenes* Cas9 nucleic acid. Ex. 2015, Bailey Decl., ¶57; Ex. 2008, ToolGen's P1; MF20.

As Dr. Bailey explains, by October 23, 2012, multiple human codon-usage tables were known in the art, and these tables often identified a different codon as the most frequent codon for certain amino acids. Ex. 2015, Bailey Decl., ¶¶41-46, 61; Ex. 2449, Kazusa 2007; Ex. 2077, Jorgensen 2005, Table 8; Ex. 2078, Alff-Steinberger 1987, Table 1; MF21-22. ToolGen's P1 does not provide any human codon-usage information or indicate which human codon-usage table should be used to reconstitute the Cas9 sequence. Ex. 2008, ToolGen's P1; Ex. 2015, Bailey Decl., ¶60; MF23-24. Because the codon-usage frequencies for as many as 12 of the 20 possible amino acids differed from table to table, even if the most frequent codon for each amino acid were picked from multiple possible human codon-usage tables, ToolGen's P1 "reconstituted" myriad different Cas9 nucleic acids from the native *S. pyogenes* nucleic acid sequence. Ex. 2015, Bailey Decl., ¶¶39-46, 60-61, 63-65; MF25-26.

Further, although several codon-optimization programs were known in the art by October 23, 2012, these programs relied on codon-usage data from different tables and applied different criteria to select codons to generate a codon-optimized nucleic acid sequence. Ex. 2015, Bailey Decl., ¶¶47-49, 62; Ex. 2084; Ex. 2088; Ex. 2094; Ex. 2089; Ex. 2087; Ex. 2085; Ex. 2086; Ex. 2091; Ex. 2074; Ex. 2073; MF28-30. ToolGen's P1 does not disclose a particular codon-

optimization program. Ex. 2008, ToolGen's P1; Ex. 2015, Bailey Decl., ¶62; MF27. As with the codon-usage tables, different programs would have generated a myriad of different nucleic acid sequences. Ex. 2015, Bailey Decl., ¶¶47-49, 62-64; MF31.

According to ToolGen's prosecution argument, codon optimization was unpredictable; thus, a skilled artisan reading its P1 would not have been able to discern a codon-optimized Cas9 nucleic acid that ToolGen alleged its invention requires. Ex. 2015, Bailey Decl., ¶¶50-67; MF34-39. For example, its P1 does not describe *which* of the myriad Cas9 nucleic acid sequences obtained using human codon-usage tables or codon-optimization programs would express a functional Cas9 protein in eukaryotic cells. Ex. 2015, Bailey Decl., ¶¶60-65; MF34-38, 40-41. Thus, all ToolGen's P1 provides is "generalized language" that is insufficient to satisfy written description as "it does not convey the detailed identity of [the] invention" under ToolGen's own representations. *Rochester*, 358 F.3d at 923; Ex. 2015, Bailey Decl., ¶¶9, 38, 55-67, 143.

ToolGen's P1 purportedly demonstrates target DNA cleavage using CRISPR-Cas9 in human cells; but, that does not remedy ToolGen's lack of written description. Ex. 2008, ToolGen's P1, 5-9. "Proof of a reduction to practice, absent an adequate description in the specification of what is reduced to practice, does not serve to describe or identify the invention for purposes of the written description requirement." *Alonso*, 545 F.3d at 1021. As Dr. Bailey explains, codon optimization is not actually necessary to express a functional Cas9 protein in eukaryotic cells. Ex. 2015, Bailey Decl., ¶58; Ex. 2028, Hwang 2013; Ex. 2076, Nakayama 2013. The purported target DNA cleavage ToolGen reported in its examples could be from using a *non-codon-optimized* Cas9 nucleic acid expressing a functional Cas9 protein in the cells. *Id.*; MF42. So, even though ToolGen's P1 purports DNA cleavage using CRISPR-Cas9—an allegation CVC does not concede—P1 does not show cleavage occurred using a codon-

optimized Cas9 nucleic acid. Ex. 2015, Bailey Decl., ¶58. To prove that, consistent with ToolGen's statements to the Patent Office, its P1 would have needed to provide a comparison with the native *S. pyogenes* nucleic acid sequence *and* show that the Cas9 protein expressed from a codon-optimized nucleic acid had an enhanced expression compared to the native *S. pyogenes* nucleic acid—which it did not do. *Id*. Thus, ToolGen's P1 fails to satisfy written description for a codon-optimized Cas9 nucleic acid under ToolGen's view of unpredictability of codon optimization. *Id.*, ¶¶ 9, 38-67, 143.

"The public notice function of a patent and its prosecution history requires that a patentee be held to what he declares during the prosecution of his patent." *Springs Window,* 323 F.3d at 995. Here, the PTAB should hold ToolGen to its representations to the earlier PTAB panel, and assess its P1 for written description of a codon-optimized Cas9 nucleic acid in light of the alleged complexity and unpredictability that ToolGen repeatedly asserted is involved in expressing the Cas9 protein in eukaryotic cells. ToolGen having "assume[d] a certain position" before the Patent Office and "succeed[ed] in maintaining that position, [] may not [now], simply because [its] interests have changed, assume a contrary position . . . ." *Zedner*, 547 U.S. at 504.

Because ToolGen's P1 does not satisfy written description for a codon-optimized Cas9 nucleic acid and, thus, lacks a constructive reduction to practice in view of its representations to the Patent Office, the PTAB should deny ToolGen accorded benefit to its P1 filing date.

d. ToolGen's prosecution arguments do not bind CVC because CVC never argued that codon optimization is required for CRISPR-Cas9 to function in eukaryotic cells or that codon optimization is unpredictable.

Of course, CVC is not bound by ToolGen's prosecution statements. ToolGen's representations occurred in an *ex parte* setting where CVC was not involved. Importantly, unlike ToolGen, CVC has never taken a position that a codon-optimized Cas9 nucleic acid is required for CRISPR-Cas9 to function in eukaryotic cells. To the contrary, CVC has always maintained

that codon optimization may increase efficiency but is *not* necessary for CRISPR-Cas9 to function in eukaryotic cells. *See*, *e.g.*, Ex. 2444, Int. No. 106,115, CVC Motion 1 (for accorded benefit), 18:22-19:1, 20:18-20, 21:4-14; Ex. 2015, Bailey Decl., ¶58; Ex. 2028, Hwang 2013; Ex. 2076, Nakayama 2013. Thus, ToolGen's prosecution statements cannot apply to CVC. And, CVC need not rely on an embodiment that includes a codon-optimized Cas9 nucleic acid to show constructive reduction to practice of CVC's half of the count.

CVC has also never suggested that codon optimization is an essential element of its invention. The codon-optimization standard that ToolGen advanced during *ex parte* prosecution also does not apply to CVC. Unlike ToolGen, CVC has never argued unpredictability in codon optimization. To the contrary, CVC has repeatedly argued that by May 2012 codon optimization of nucleic acids was a routine technique such that skilled artisans would have expected to express a functional Cas9 protein from a codon-optimized nucleic acid in eukaryotic cells. Ex. 2444, Int. No. 106,115, CVC Motion 1 (for accorded benefit), 17:23-18:3, 20:18-20, 21:15-21. Accordingly, even if CVC were to rely on an embodiment that includes a codon-optimized Cas9 nucleic acid to show constructive reduction to practice, it is not bound by ToolGen's codon-optimization standard.

IV. CONCLUSION

ToolGen's admissions dictate that its P1 does not disclose an embodiment of the count. ToolGen argued during prosecution that a codon-optimized Cas9 nucleic acid is required for CRISPR-Cas9 to function in eukaryotic cells and that codon optimization is unpredictable. These arguments were crucial in ToolGen obtaining allowance of its involved claims over the prior art. But there is no embodiment of a codon-optimized Cas9 nucleic acid in ToolGen's P1 and no disclosure that would fill the gaps that ToolGen claimed would prevent a skilled artisan from

codon-optimizing a Cas9 nucleic acid. ToolGen is bound to the representations it made to the Patent Office and cannot argue in reply to this motion that its P1 described a functional embodiment of the count even though it lacked any disclosure of a codon-optimized Cas9 nucleic acid. For the foregoing reasons, CVC respectfully requests that the PTAB grant the motion to deny accorded benefit to ToolGen's P1.

Respectfully submitted,

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APPENDIX 1: LIST OF EXHIBITS

Exhibit No.	Description
2008	Prov. Appl. No. 61/717,324
2012	File History for U.S. Appl. No. 14/685,510
2015	Declaration of Scott Bailey, Ph.D.
2028	Hwang, W.Y., *et al*., "Efficient genome editing in zebrafish using a CRISPR-Cas system," *Nature Biotechnology*, 31(3):227-229, Supplementary Information (2013)
2073	Cai, Y., *et al*., "Optimizing the codon usage of synthetic gene with QPSO algorithm," *Journal of Theoretical Biology* 254:123–127 (2008)
2074	Puigbo, P., *et al*., "OPTIMIZER: a web server for optimizing the codon usage of DNA sequences," *Nucleic Acids Research* 35: W126–W131 (2007)
2075	Sandhu, K., *et al*., "GASCO: Genetic Algorithm Simulation for Codon Optimization," *In Silico Biology* 8: 187–192 (2008)
2076	Nakayama, T., *et al*., "Simple and efficient CRISPR/Cas9-mediated targeted mutagenesis in *Xenopus tropicalis*," *Genesis* 51(12): 835–843 (2013)
2077	Jorgensen, F.G., *et al*., "Comparative analysis of protein coding sequences from human, mouse and the domesticated pig," *BMC Biology* 3(2):1-15 (2005)
2078	Alff-Steinberger, C., "Codon Usage in Homo sapiens: Evidence for a Coding Pattern on the Non-Coding Strand and Evolutionary Implications of Dinucleotide Discrimination," *J. Theor. Biol.* 124:89-95 (1987)
2084	Hoover, D.M. and Lubkowski, J., "DNAWorks: an automated method for designing oligonucleotides for PCR-based gene synthesis," *Nucleic Acids Research* 30(10e43):1-7 (2002)
2085	Wu, G., *et al*., "The Synthetic Gene Designer: A flexible web platform to explore sequence manipulation for heterologous expression," *Protein Expression and Purification* 47: 441–445 (2006)
2086	Richardson, S., *et al*., "GeneDesign: Rapid, automated design of multikilobase synthetic genes," *Genome Research* 16:550–556 (2006)
2087	Fuglsang, A., "Codon optimizer: a freeware tool for codon optimization," *Protein Expression and Purification* 31:247–249 (2003)
2088	Gao, W., *et al*., "UpGene: Application of a Web-Based DNA Codon Optimization Algorithm," *Biotechnol. Prog.* 20:443−448 (2004)

Exhibit No.	Description
2089	Grote, A., *et al*., "JCat: a novel tool to adapt codon usage of a target gene to its potential expression host," *Nucleic Acids Research* 33:W526–W531 (2005)
2091	Harish, N., *et al*., "DyNAVacS: an integrative tool for optimized DNA vaccine design," *Nucleic Acids Research* 34:W264–W266 (2006)
2094	Jayaraj, S., *et al*., "GeMS: an advanced software package for designing synthetic genes," *Nucleic Acids Research* 33(9):3011–3016 (2005)
2444	CVC Substantive Motion 1 (for accorded benefit), *The Regents of the University of California v. The Broad Institute, Inc*., Patent Interference No. 106,115, Paper 212 (October 14, 2019)
2447	Streptococcus pyogenes SF370 chromosome, complete genome, available at https://www.ncbi.nlm.nih.gov/nuccore/NC_002737.1 (last visited May 19, 2021)
2448	Streptococcus pyogenes M1 GAS, complete sequence, available at https://www.ncbi.nlm.nih.gov/nuccore/NC_002737.2 (last visited May 18, 2021)
2449	Codon Usage Table Homo sapiens [gbpri]: 93487 CDS's (40662582 codons), available at https://www.kazusa.or.jp/codon/cgi-bin/showcodon.cgi?species=9606 (last visited May 19, 2021)

APPENDIX 2: STATEMENT OF MATERIAL FACTS

1. ToolGen's involved claims all require a Cas9 nucleic acid that "is codon-optimized for expression in mammalian cells." Paper 6.

2. During prosecution, ToolGen narrowed the claims to require that a Cas9 "nucleic acid is codon-optimized for expression in mammalian cells" to distinguish the prior art and to overcome rejections under 35 U.S.C. §§ 102 and 103. Ex. 2012, 510 Appl. Pros. History, 6745-6749 (Resp., Mar. 3, 2017).

3. The examiner withdrew the anticipation rejection in view of ToolGen's claim amendment requiring that a Cas9 "nucleic acid is codon-optimized for expression in mammalian cells." *Id.*, 6783 (Office Action, Jun. 14, 2017).

4. ToolGen argued during prosecution that a skilled artisan "would ***not*** have reasonably expected that a Type II CRISPR/Cas9 system could successfully have been used . . . in eukaryotic (*e.g.*, mammalian) cells. The reasons . . . include . . . challenges presented by modification (*e.g.*, tagging and codon-optimization) of nucleic acids to be expressed in eukaryotic/mammalian cells." *Id.*, 6758 (Resp., Mar. 3, 2017) (emphasis in original) (internal citations omitted).

5. ToolGen argued during prosecution that a skilled artisan would not have reasonably expected the Cas9 protein expressed from a codon-optimized nucleic acid to be functional in "eukaryotic/mammalian cells" because a skilled artisan would have "(i) questioned whether Cas9 could properly fold when expressed in eukaryotic cells . . . ; (ii) recognized that modification of Cas9, *e.g.*, by tagging it with a NLS and/or optimizing its codon sequence, could have rendered [Cas9] inactive upon expression in a eukaryotic cell

. . . ; and (iii) understood the importance of native codon optimization to proper protein folding . . . .” *Id*., 6761-6762 (Resp., Mar. 3, 2017).

6. On appeal, ToolGen argued as follows: “Bacterial proteins may not fold properly in mammalian cells, and alteration of codons (which occurs as a result of codon optimization) can result in altered translation kinetics leading to misfolding. Since improperly folded proteins can lack activity, exhibit aberrant function or be degraded in cells, it would not have been predictable, whether a bacterial protein such as Cas9 and, in particular, codon-optimized Cas9 would fold in a mammalian cell in a way that would preserve its functionality.” *Id*., 6895-6896 (Appeal Br., June 13, 2018) (internal citations omitted).

7. On appeal, ToolGen argued as follows: “it was not known or reasonably expected in the art that a prokaryotic Type II CRISPR/Cas system with codon-optimized Cas9 would successfully function in mammalian cells.” *Id*., 6899 (Appeal Br., Jun. 13, 2018).

8. On appeal, ToolGen argued that “a POSA would have had no idea what the outcome may have been even if one were to apply codon optimization and NLS addition to CRISPR/Cas9.” *Id*., 8531 (Reply Br., Jan. 8, 2019).

9. During oral argument, ToolGen stated: “So, you have to introduce the nucleic acid [encoding Cas9] into the mammalian cell, and then in our case, we're explicitly claiming it has to have a nuclear localization signal, and it has to be codon optimized.” *Id*., 8604:1-3 (Oral Hr., Mar. 11, 2020).

10. During oral argument, ToolGen told the PTAB that in its claimed invention the “nucleic acid [that] has been engineered with . . . codon optimization” is the “main distinction” from the prior art. *Id.*, 8604:24-8605:25 (Oral Hr., Mar. 11, 2020).

11. During oral argument, ToolGen argued that codon optimization of Cas9 nucleic acid is "required in the science to get [CRISPR-Cas9] to work." *Id.*, 8606:5-11 (Oral Hr., Mar. 11, 2020).

12. Relying on ToolGen's representations and accepting its arguments, the PTAB reversed the examiner's obviousness rejection of ToolGen's involved claims. *Id*., 8638, 8642, 8643, 8645, 8646 (PTAB Decision, Jun. 22, 2020).

13. On remand, the examiner found ToolGen's claims to be in condition for allowance. *Id.*, 8651 (Office Comm., Oct. 23, 2020).

14. ToolGen's P1 does not provide a single codon-optimized Cas9 nucleic acid sequence. Ex. 2008, ToolGen's P1; Ex. 2015, Bailey Decl., ¶56.

15. ToolGen's P1 never mentions "codon optimization" at all. Ex. 2008, ToolGen's P1; Ex. 2015, Bailey Decl., ¶56.

16. ToolGen's P1 states that "[t]he Cas9-coding sequence (4,104 bp), derived from *Streptococcus pyogenes* strain M1 GAS (NC_002737.1), was reconstituted using the human codon usage table and synthesized using oligonucleotides." Ex. 2008, ToolGen's P1, 11; Ex. 2015, Bailey Decl., ¶56.

17. NC_002737.1 is the accession number for the nucleic acid sequence record of the complete genome of M1 GAS strain of *S. pyogenes* in the NCBI database, which at best includes the nucleotide range of the location of the Cas9 gene in the genome. Ex. 2015, Bailey Decl., ¶59; Ex. 2447; Ex. 2448.

18. ToolGen's P1 does not disclose a single human codon-usage table. Ex. 2008, ToolGen's P1; Ex. 2015, Bailey Decl., ¶60.

19. Without knowing the specific codon-usage table or the process or set of rules for selecting codons from the table, numerous sequences could be reconstituted from a codon-usage table. Ex. 2015, Bailey Decl., ¶¶60, 64.

20. In ToolGen's P1, there is no disclosure of what the sequence was or that the reconstituted sequence was in fact optimized vis-à-vis the wild-type *Streptococcus pyogenes* strain. Ex. 2008, ToolGen's P1; Ex. 2015, Bailey Decl., ¶57.

21. Multiple human codon-usage tables were known in the art by October 23, 2012. Ex. 2015; Bailey Decl., ¶¶41-46, 61; Ex. 2449, Kazusa 2007; Ex. 2077, Jorgensen 2005, Table 8; Ex. 2078, Alff-Steinberger 1987, Table 1.

22. Different human codon-usage tables known in the art by October 23, 2012 identified a different codon as the most frequent codon for certain amino acids. Ex. 2015, Bailey Decl., ¶¶41-46, 61; Ex. 2449, Kazusa 2007; Ex. 2077, Jorgensen 2005, Table 8; Ex. 2078, Alff-Steinberger 1987, Table 1.

23. ToolGen's P1 does not provide any human codon-usage information to reconstitute the Cas9 sequence. Ex. 2008, ToolGen's P1; Ex. 2015, Bailey Decl., ¶60.

24. ToolGen's P1 does not indicate which human codon-usage table should be used to reconstitute the Cas9 sequence. Ex. 2008, ToolGen's P1; Ex. 2015, Bailey Decl., ¶60.

25. The codon-usage frequencies for as many as 12 of the 20 possible amino acids differed from table to table. Ex. 2015, Bailey Decl., ¶¶39-46, 61.

26. If the most frequent codon for each amino acid were picked from multiple possible human codon-usage tables, ToolGen's P1 reconstituted myriad different Cas9 nucleic acids from the native *S. pyogenes* nucleic acid sequence. Ex. 2015, Bailey Decl., ¶¶39-46, 60-61, 63-65.

27. ToolGen's P1 does not identify a particular codon-optimization program. Ex. 2008, ToolGen's P1; Ex. 2015, Bailey Decl., ¶62.

28. Several human codon-optimization programs were known in the art by October 23, 2012. Ex. 2015, Bailey Decl., ¶¶47-49, 62; Ex. 2084; Ex. 2088; Ex. 2094; Ex. 2089; Ex. 2087; Ex. 2085; Ex. 2086; Ex. 2091; Ex. 2074; Ex. 2073.

29. The codon-optimization programs known by October 23, 2012 relied on codon-usage data from different tables. Ex. 2015, Bailey Decl., ¶¶47-49.

30. The codon-optimization programs known by October 23, 2012 applied different criteria to select codons to generate a codon-optimized nucleic acid sequence. Ex. 2015, Bailey Decl., ¶¶47-49, 62.

31. Different codon-optimization programs known in the art by October 23, 2012 would have generated myriad different codon-optimized Cas9 nucleic acid sequences from the native *S. pyogenes* Cas9 nucleic acid (NC_002737.1) disclosed in ToolGen's P1. Ex. 2015, Bailey Decl., ¶¶47-49, 62-64; Ex. 2008, ToolGen's P1.

32. ToolGen argued during prosecution that a codon-optimized Cas9 nucleic acid is required for CRISPR-Cas9 to function in eukaryotic cells. Ex. 2012, 510 Appl. Pros. History, 8606:5-11 (Oral Hr., Mar. 11, 2020).

33. ToolGen argued during prosecution that a codon-optimized Cas9 nucleic acid is required for CRISPR-Cas9 to function in mammalian cells. *Id*., 8606:5-11 (Oral Hr., Mar. 11, 2020).

34. ToolGen argued during prosecution that a codon-optimization is unpredictable. *Id*., 6895-6896, 6899 (Appeal Br., Jun. 13, 2018); *see also id*., 8531 (Reply Br., Jan. 8, 2019); *see also id.*, 6758, 6761-6762, 6767 (Resp., Mar. 3, 2017).

35. ToolGen argued during prosecution that a codon-optimized nucleic acid is unlikely to express a functional Cas9 protein in eukaryotic cells due to alleged unpredictability in protein folding. *See, e.g., id*., 6895-6896 (Appeal Br., Jun. 13, 2018) *see also id.*, 6761-6762 (Resp., Mar. 3, 2017).

36. ToolGen argued during prosecution that a codon-optimized nucleic acid is unlikely to express a functional Cas9 protein in eukaryotic cells due to unpredictability in codon optimization. *Id*., 6895-6896, 6899 (Appeal Br., Jun. 13, 2018); *see also id*., 8531 (Reply Br., Jan. 8, 2019); *see also id.*, 6758, 6761-6762, 6767 (Resp., Mar. 3, 2017).

37. ToolGen argued during prosecution that a codon-optimized nucleic acid is unlikely to express a functional Cas9 protein in mammalian cells due to unpredictability in protein folding. *See, e.g., id*., 6895-6896 (Appeal Br., Jun. 13, 2018) *see also id.*, 6761-6762 (Resp., Mar. 3, 2017).

38. ToolGen argued during prosecution that a codon-optimized nucleic acid is unlikely to express a functional Cas9 protein in mammalian cells due to unpredictability in codon optimization. *Id*., 6895-6896, 6899 (Appeal Br., Jun. 13, 2018); *see also id*., 8531 (Reply Br., Jan. 8, 2019); *see also id.*, 6758, 6761-6762, 6767 (Resp., Mar. 3, 2017).

39. ToolGen's P1 does not disclose a single Cas9 nucleic acid sequence from among the myriad different Cas9 sequences that can be reconstituted using different codon usage tables or different codon optimization algorithms. Ex. 2015, Bailey Decl., ¶¶55-65; Ex. 2008, ToolGen's P1.

40. A skilled artisan reading its P1 would not have been able to know or predict which of the myriad Cas9 nucleic acid sequences reconstituted using human codon-usage tables

known by October 23, 2012 would express a functional Cas9 protein in eukaryotic cells. Ex. 2015, Bailey Decl., ¶¶60-61, 63-65; Ex. 2008, ToolGen's P1.

41. A skilled artisan reading its P1 would not have been able to know or predict which of the myriad Cas9 nucleic acid sequences reconstituted using human codon-optimization programs known by October 23, 2012 would express a functional Cas9 protein in eukaryotic cells. Ex. 2015, Bailey Decl., ¶¶62, 63-65; Ex. 2008, ToolGen's P1.

42. The purported target DNA cleavage reported in ToolGen's examples could be from using a non-codon-optimized Cas9 nucleic acid expressing a functional Cas9 protein in the cells. Ex. 2015, Bailey Decl., ¶58.

43. ToolGen argued during prosecution that codon-optimized Cas9 nucleic acid is required for patentability of its involved claims. Ex. 2012, 510 Appl. Pros. History, 8604:24-8605:25 (Oral Hr., Mar. 11, 2020).

44. ToolGen argued during prosecution that a codon-optimized Cas9 nucleic acid is required for CRISPR-Cas9 to function in its claimed invention. *Id*., 8606:5-11 (Oral Hr., Mar. 11, 2020).

45. ToolGen argued during prosecution that not all codon-optimized Cas9 nucleic acids would be functional. *Id*., 6895-6896, 6899 (Appeal Br., Jun. 13, 2018); *see also id*., 8531 (Reply Br., Jan. 8, 2019); *see also id.*, 6758, 6761-6762, 6767 (Resp., Mar. 3, 2017).

CERTIFICATE OF SERVICE

I hereby certify that the foregoing **CVC MOTION 2 (to deny ToolGen P1 benefit)** and the related exhibits were filed via the Interference Web Portal by 8:00 PM Eastern Time on May 20, 2021, pursuant to an agreement between the parties, and thereby served on the attorney of record for the Senior Party pursuant to ¶ 105.3 of the Standing Order. Pursuant to the agreement between the parties, the foregoing was also served via email by 11:00 PM Eastern Time on counsel for the Senior Party at:

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