Filed on behalf of Junior Party
THE REGENTS OF THE UNIVERSITY OF CALIFORNIA,
UNIVERSITY OF VIENNA, AND EMMANUELLE CHARPENTIER

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By: Eldora L. Ellison, Ph.D., Esq.
Eric K. Steffe, Esq.
David H. Holman, Ph.D., Esq.
Byron L. Pickard, Esq.
John Christopher Rozendaal, Esq.
Paul A. Ainsworth, Esq.
Michael E. Joffre, Ph.D., Esq.
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 New York Avenue, NW
Washington, D.C. 20005
Tel: (202) 371-2600
Fax: (202) 371-2540
eellison-PTAB@sternekessler.com
esteffe-PTAB@sternekessler.com
dholman-PTAB@sternekessler.com
bpickard-PTAB@sternekessler.com
jcrozendaal-PTAB@sternekessler.com
painsworth-PTAB@sternekessler.com
mjoffre-PTAB@sternekessler.com

By: Li-Hsien Rin-Laures, M.D., Esq.
RINLAURES LLC
321 N. Clark Street, 5th floor
Chicago, IL 60654
Tel. (773) 387-3200; Fax (773) 929-2391
lily@rinlauresip.com

Sandip H. Patel, Esq.
MARSHALL GERSTEIN & BORUN LLP
6300 Willis Tower, 233 South Wacker Drive
Chicago, IL 60606
Tel: (312) 474-6300; Fax: (312) 474-0448
spatel@marshallip.com

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.,

Senior Party
Application 14/685,510

Patent Interference No. 106,127 (DK)

CVC OPPOSITION TO TOOLGEN MISCELLANEOUS MOTION 1
(to exclude evidence)

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I. Statement of Precise Relief Requested

ToolGen moves to exclude substantial portions of all of CVC's expert witness testimony and all of CVC's fact witness testimony as inadmissible under the Federal Rules of Evidence and the PTAB's Standing Order. *See* Paper 862, ToolGen Misc. Motion 1, 1:1-4. CVC's evidence violates none of these authorities. The PTAB should therefore deny ToolGen's motion.

II. Argument

As the movant, ToolGen is required to demonstrate it is entitled to the relief requested—here, exclusion of evidence. *See* 37 C.F.R. § 41.121(a)(3) and (b); *see also* Standing Order, ¶s 121.3 and 155.2. ToolGen's motion fails. ToolGen ignores longstanding case law regarding the admissibility of witness testimony that contradicts its arguments, and misconstrues the Federal Rules of Evidence (FRE) and the PTAB's Standing Order (SO). As detailed below, each of ToolGen's arguments is factually baseless and contrary to law.

A. There Is No Basis to Exclude Dr. Bailey's Scientific Opinions Offered in the Context of a Legal Framework that ToolGen's Prosecution Requires

On page 1 lines 15-17, ToolGen moves to exclude paragraphs 38-66 of Dr. Bailey's first declaration (Ex. 2015) and paragraphs 28-39 and 40-86 of his second declaration (Ex. 2477) as violating FRE 702(b) and (d), which require expert opinions be based on sufficient facts and reliably apply relevant principles and methods to the facts. But the *sole* basis on which ToolGen contends that Dr. Bailey's opinions fail these requirements is that his opinions rely on assumptions. Specifically, his first declaration assumes that ToolGen is required to describe a codon-optimized Cas9 nucleic acid in order to show its entitlement to the benefit of ToolGen's P1 application. His second declaration assumes that ToolGen is required to describe an NLS-tagged and codon-optimized Cas9 nucleic acid to show constructive reduction to practice of an embodiment of ToolGen's half of the count based on the text in its P3 and PCT applications. The

response is that the requirements for what ToolGen's applications must describe—the relevant "principles" under FRE 702—are circumscribed by law. Dr. Bailey's assumption of these legal requirements, in framing the scope of his opinions, is therefore proper and also standard practice for scientific experts. *See* Fed. R. Evid. 702.

It is blackletter law that an expert may assume the truth of facts, data, or legal requirements in order to render an opinion. *See* Fed. R. Evid. 703, 705.1; *see also*, Fed. R. Civ. P. 26(b)(4)(C) (requiring discovery to "identify assumptions that the party's attorney provided and that the expert relied on in forming the opinions to be expressed."); *Huawei Techs. Co. Ltd., v. Verizon Comms. Inc.*, 2:20-cv-00030-JRG at *8 (E.D. Tex. Jul 2, 2021) (noting "it is permissible, where appropriate, for an expert to base his or her opinions on relevant assumptions") (citing *Robroy Indus. Tex. LLC v. Thomas & Betts Corp.*, Case No. 2:15-CV-512-WCB at *5 (E.D. Tex. Apr. 10, 2017) (Circuit Judge Bryson sitting by designation)); *Neagle v. Gusman*, No. 12-1910 R(2) (E.D. La. Feb. 10, 2016) (citing *Little v. Nat'l R.R. Passenger Corp.*, 1988 WL 145095 at *2 (D.C. Cir. 1988) for the proposition that an expert may assume a disputed fact as true so long as a factual predicate for the testimony exists).

Whether a court or other tribunal ultimately adopts the legal and factual predicate underlying the expert opinion has no bearing on whether the expert's opinion was adequately supported and admissible for the purpose for which it is offered. *See, e.g.*, *Apple, Inc. v. Samsung Elecs. Co.*, 2013 WL 5955666, at *4 (N.D. Cal. Nov. 6, 2013). Even if it did, the contention that an expert's "assumptions are unfounded go to the weight, not the admissibility, of the testimony." *Amorgianos v. Nat'l R.R. Passenger Corp.*, 303 F.3d 256, 266 (2d Cir. 2002) (quoting *Daubert v. Merrel Dow Pharms. Inc.*, 509 U.S. 579, 593-94 (1993); *Payton v. Abbott Labs*, 780 F.2d 147, 156 (1st Cir. 1985) (same); *Pipitone v. Biomatrix, Inc.*, 288 F.3d 239, 250 (5th Cir. 2002) ("[T]he fact-finder is entitled to hear [an expert's] testimony and decide whether

it should accept or reject that testimony after considering all factors that weigh on credibility, including whether the predicate facts on which [the expert] relied are accurate.").

The relevant legal principles (or assumptions) provided to Dr. Bailey are based on CVC's legal argument that ToolGen, in defending its accorded benefit, is estopped from relying on an embodiment in its P1 lacking a codon-optimized Cas9 nucleic acid or an NLS-tagged and codon-optimized Cas9. Why? Because ToolGen argued to the Patent Office that codon-optimization and nuclear-localization sequences were critical to patentability of ToolGen's interfering claims, one of which is ToolGen's half of Count 1. *See* Paper 364, CVC Motion 2, 3-10. Although it was known in the art that codon optimization and NLSs are *not* required for CRISPR-Cas9 to function in eukaryotes, ToolGen only secured allowance of its involved claims by arguing that that these features are essential. Allowing ToolGen to prove either half of Count 1 using an embodiment that does not include codon optimization or an NLS would—contrary to law—unfairly permit ToolGen to first benefit from taking express material positions during prosecution, and now benefit from disavowing those positions during this Interference. *Id.,* 7-9.

To support CVC's position that ToolGen cannot show entitlement to its P1, P3, or PCT applications in view of its prosecution statements, CVC presented the declaration of Dr. Bailey. For purposes of rendering his opinions that ToolGen's applications fail to show written description of a codon-optimized Cas9 nucleic acid or an NLS-tagged and codon-optimized Cas9, Dr. Bailey properly assumed that such limitations were required. ToolGen argues it should not be required to support such an embodiment. *See* Paper 862, ToolGen Misc. Motion 1, 3:2-6 (presenting ToolGen's argument). But that legal argument is inapposite to whether Dr. Bailey's opinions are based on sufficient facts or reliable methodology. ToolGen's argument contests only the *legal predicate* of Dr. Bailey's opinion—not the reliability of his opinion. ToolGen's

substantive legal dispute is not an appropriate challenge to raise in a motion to exclude. *Amorgianos*, 303 F.3d at 266; *Payton*, 780 F.2d at 156; *Pipitone*, 288 F.3d at 250.

B. There Is No Basis to Exclude the Declarations of Drs. Sontheimer, Barrangou, Doudna, Sternberg, and Carroll, Which Factually Recall Events Each Personally Observed

On page 3 lines 20-24, ToolGen argues that the declarations of Drs. Sontheimer, Barrangou, Doudna, Sternberg, and Carroll (Exs. 2019, 2021, 2023, 2221, and 2348 respectively) exceed the limits of lay witness testimony under FRE 701(c) and are less reliable than their earlier unsworn statements. The response is that these witnesses are all scientists providing their personal recollections of historical events and understandings that they personally held during the relevant timeframe based on their first-hand knowledge of those events. Such testimony is admissible under FRE 602.

Even a cursory review of these declarations shows their testimony is factual and corroborated by contemporaneous documentary evidence that ToolGen does not move to exclude. Contrary to ToolGen's mischaracterizations, they are not offering expert opinions of record evidence about which they lack personal knowledge. ToolGen misconstrues FRE 701(c) to prohibit scientists or inventors from being fact witnesses, *per se*. Of course, that is not the law.

Consistent with FRE 701, scientists may—and regularly do—testify as fact witnesses about events that the scientist observed and other information about which the scientist has personal knowledge. Fed. R. Evid. 701; *see also*, Fed. R. Evid. 602 (allowing fact witnesses to testify to any facts within their personal knowledge); And consistent with these evidentiary rules, courts admit this testimony. *See, e.g., Sitrick v. Dreamworks, LLC*, 516 F.3d 993 (Fed. Cir. 2008) (affirming the admissibility of highly technical inventor testimony as a fact witness based on personal knowledge without being designated as an expert); *Supernus Pharm., Inc. v. TWi Pharm., Inc.*, No. 15-369 (RMB/JS), 2017 WL 4182809, at *20 n.12 (D.N.J. Sept. 21, 2017)

(finding that a witness "properly testified as to matters which, while technical and specialized, are squarely within his particularized firsthand knowledge and experience as a pharmaceutical scientist"); *Braun Corp. v. Maxon Lift Corp.*, 282 F.Supp.2d 931, 934 (N.D. Ind. 2003) (admitting inventor opinion testimony about the structure and function of the patented wheelchair lift because it was based on his personal perception), *aff'd,* 97 F. App'x 335 (Fed. Cir. 2004).

Contrary to ToolGen's arguments, the five declarations ToolGen moves to exclude do not provide any opinions violating these authorities. Specifically, these declarations do not provide opinions based on evidence about which the witnesses lack personal knowledge. They are therefore not expert opinions. *Cf., e.g.*, *Freedom Wireless, Inc. v. Boston Commc'ns Grp., Inc.*, 369 F.Supp.2d 155, 157 (D. Mass. 2005) (explaining that "[a]pplying [] specialized knowledge" to form an opinion on a matter "several degrees removed from actual experience, is the classic type of expert testimony contemplated by [FRE] 702"). Indeed, their testimony provides factual accounts of historical events of which each witness has first-hand knowledge, and are not opinions at all.

Specifically, on page 4 lines 11-17 and 20, ToolGen accuses Dr. Sontheimer of providing expert opinion and "improper lay testimony" when he recounted his personal reaction (and the reactions of others that he personally observed) to Drs. Chylinski and Jinek's seminal June 2012 presentation at the CRISPR conference. The response is that the above legal authorities permit Dr. Sontheimer to testify, as a fact witness, about his recollection regarding historical events that he personally observed, as a scientist working in the CRISPR field and present at the CRISPR conference. Dr. Sontheimer's declaration testimony is explicitly based on his "personal knowledge of the facts." Ex. 2019, ¶1. Indeed, in view of its cross-examination, ToolGen could

not argue that Dr. Sontheimer lacks the personal knowledge to provide such testimony under the Fed. R. Evid. 602.

On page 5 lines 1-7, ToolGen argues that Dr. Barrangou's declaration is impermissible lay testimony because it relates, among other things, to the CRISPR field and the scientific community's reaction to Drs. Chylinski's and Jinek's June 2012 CRISPR conference presentation. But, again, just because a scientist has personal knowledge about a scientific conference presentation does not mean that his or her *factual* recollections about that presentation are automatically *expert* opinions. Here, Dr. Barrangou is not rendering abstract opinions on evidence about which he lacks personal knowledge. *Cf., e.g.*, *Freedom Wireless*, 369 F.Supp.2d at 157. Rather, he has provided a factual account of historical events that he observed as a member of the relevant scientific community in 2012. *Cf. Liquid Dynamics Corp. v. Vaughan Co.*, No. 01 C 6934, 2004 WL 2260626, at *2 (N.D. Ill. Oct. 1, 2004) ("With proper foundation evidencing personal knowledge, [lay witness] testimony regarding prior art systems is not clearly inadmissible for all purposes."). The above legal authorities permit Dr. Barrangou to testify, as a fact witness, about his recollection regarding historical events that he personally observed, as a scientist working in the CRISPR field and present at the CRISPR conference. Dr. Barrangou's declaration testimony is explicitly based on his "personal knowledge of the facts." Ex. 2021, ¶1. That is properly the subject of fact witness testimony, and in view of its cross-examination, ToolGen cannot contend that Dr. Barrangou lacks personal knowledge. Fed. R. Evid. 602.

On page 6 lines 2-8, ToolGen argues that Dr. Sternberg's declaration is impermissible lay testimony because he describes his understanding in 2012 that a biochemical system demonstrated to work *in vitro* would also work in a variety of cellular environments, with adjustments that in 2012 he considered routine in his field. The response is that Dr. Sternberg

provides no expert opinions about what a person of ordinary skill in the art would have known or expected. To the contrary, Dr. Sternberg's declaration testimony is explicitly based on his "personal knowledge of the facts." Ex. 2221, ¶2. The above legal authorities permit Dr. Sternberg to testify, as a fact witness, about his personal knowledge and understanding as a scientist working in the field in 2012. That is properly the subject of fact witness testimony, and in view of its cross-examination, ToolGen cannot contend that Dr. Sternberg lacks personal knowledge. Fed. R. Evid. 602.

On page 6 lines 13-19, ToolGen argues that Dr. Carroll's declaration is improper expert testimony because it relates to matters that require scientific, technical, or other specialized knowledge. The response is that Dr. Carroll merely provides a factual account of what he wrote in journal articles based on his personal knowledge and understanding at the relevant time. Dr. Carroll has "personal knowledge of the facts" (Ex. 2348, ¶2), and in view of its cross-examination, ToolGen does not contend that he lacks personal knowledge. Fed. R. Evid. 602. Furthermore, ToolGen has relied on mischaracterizations of unsworn statements attributed to Dr. Carroll to support its positions in this interference. ToolGen now moves to exclude from the record Dr. Carroll's *sworn testimony* rebutting those mischaracterizations. But there is no authority to exclude Dr. Carroll's factual account of his personal understandings and impressions as of a particular time period, including as it relates to unsworn statements that ToolGen has mischaracterized and taken out of context. If those unsworn statements are being considered in this proceeding, then so must Dr. Carroll's sworn factual testimony about them.

On page 5 lines 14-18, ToolGen argues that Dr. Doudna's declaration is impermissible as lay testimony because it is based on her specialized knowledge and experience. The response is that Dr. Doudna is an inventor of CVC's CRISPR-Cas9 system. What she (and her co-inventors) knew or understood, and when, is a disputed matter of fact in this proceeding. Inventors may—

and often do—testify about their understanding of how their invention works, as well as when an invention was conceived and reduced to practice without being treated as experts. *Voice Techs. Grp., Inc. v. VMC Sys., Inc.*, 164 F.3d 605, 615 (Fed. Cir. 1999) ("An inventor is a competent witness to explain the invention and what was intended to be conveyed by the specification and covered by the claims. The testimony of the inventor may also provide background information, including explanation of the problems that existed at the time the invention was made and the inventor's solution to these problems."). An inventor's factual recollections about the nature and timing of events based on personal knowledge are proper, even though they may in some cases involve sophisticated scientific understanding. *See id.* It is entirely proper for an inventor to provide technical explanation or context for a factual account of events based on personal knowledge. *Id.* Here, Dr. Doudna has "personal knowledge of the facts" (Ex. 2023, ¶3), and in view of its cross-examination, ToolGen does not contend that she lacks personal knowledge concerning what is described in her declaration. Fed. R. Evid. 602.

Lastly, there is no factual or legal support for ToolGen's bald assertion (3:20-23) that these five declarants' earlier unsworn statements "are more reliable" than their sworn testimony. ToolGen deposed these witnesses, but failed to elicit cross-examination testimony that undermines their direct testimony and ToolGen offered no counterevidence. There is no basis, therefore, for the PTAB to exclude these witnesses' sworn testimony.

C. There Is No Basis to Exclude Dr. Doyon's Testimony

On page 7 lines 4-8,ToolGen argues that Dr. Doyon's testimony should be excluded because it relies on: (1) material published after the filing date of the relevant application(s), (2) inadmissible exhibits (i.e., exhibits addressed above), and (3) material that ToolGen alleges he did not review. The responses are, respectively, (1) an expert may rely on material published after the filing date(s) of the relevant application(s), for example, to explain what a person

having ordinary skill in the art would have known or expected at the time of filing, (2) the exhibits on which Dr. Doyon relies are not inadmissible, as discussed above, and (3) ToolGen misconstrues Dr. Doyon's cross-examination testimony regarding the materials he reviewed and relied upon.

First, ToolGen's argument that Dr. Doyon's discussion of articles published after the filing date of CVC's applications lacks merit. ToolGen merely provides a naked string cite of exhibits purportedly published after the relevant filing date, with no substantive analysis of what these exhibits are, what they disclose, or the purpose for which Dr. Doyon cites them. *See* Paper 862, ToolGen Misc. Motion 1, 7:21-9:13. Dr. Doyon relies on these exhibits not for their substantive teachings as prior art, but for what they evidence about the state of the art and the understandings of the skilled artisan *at the time of filing*. The Federal Circuit long ago established that reliance on such later-published articles is proper for this purpose. *Plant Genetic Sys., N.V. v. DeKalb Genetics Corp.*, 315 F.3d 1335, 1344 (Fed. Cir. 2003) ("This court has approved use of later publications as evidence of the state of art existing on the filing date of an application."); *Thomas & Betts Corp. v. Litton Sys. Inc.*, 720 F.2d 1572, 1581 (Fed. Cir. 1983) (same). ToolGen's comprehension of the law—that any document with a publication date after the filing date is *per se* inadmissible—is inconsistent with these precedents.

Second, ToolGen argues that Dr. Doyon's citation of the five fact-witness declarations (addressed above) is improper because those declarations are "impermissible because they are irrelevant or improper lay testimony." Paper 862, ToolGen Misc. Motion 1, 9:22-10:2. As discussed above, these declarations are not impermissible and are admissible. Regardless, there is nothing improper with Dr. Doyon's consideration of facts reported in these declarations. And, as the remainder of his detailed and comprehensive expert declaration makes clear, his opinions are based on his *own* analysis of the extensive record evidence in this case. His opinions do not

automatically become unreliable just because he also read and considered consistent, supportive factual testimony set out in five declarations. ToolGen, who bears the burden here, cites no authority to the contrary.

ToolGen also argues that various emails cited in Dr. Doyon's declaration are hearsay and also irrelevant because they do not speak to what a skilled person would have known or what P1 discloses. Paper 862, ToolGen Misc. Motion 1, 10:11-19. The emails are not hearsay because they are not offered for the truth of the matter asserted, but as objective proof that the CVC inventors corresponded via email during the relevant timeframe to communicate their understanding of the subject matter disclosed in P1 and the state of the art at the time. Even if these emails were being used for a hearsay purpose, they would fall under multiple hearsay exceptions, at least because they are (1) business records (correspondence kept in the ordinary course of business, Ex. 2023, ¶51), and (2) contemporaneous recordings of present-sense impressions. *See* Fed. R. Evid. 803. Finally, even if the emails were hearsay without any exception, there would be nothing unreliable or inadmissible about Dr. Doyon's use or consideration of them. Experts are generally permitted to rely on hearsay. Fed. R. Evid. 703.

Additionally, the emails are relevant. While the accorded benefit inquiry is limited to the four corners of the provisional application, the PTAB has previously considered extrinsic evidence regarding the CVC inventors' subjective understandings, as probative of possession in the context of deciding CVC's accorded benefit. *See* Decision on Motions 37 C.F.R. § 41.125(a), *The Regents of the Univ. of Calif. v. The Broad Inst., Inc.,* Patent Interference No. 106,115, Paper 877, (September 10, 2020). To the extent the PTAB considers evidence of the CVC inventors' statements probative of possession, then these emails demonstrate that, even before the filing date of P1, the CVC inventors understood and expected that their invention would work in eukaryotes. Dr. Doyon considers these emails among the *totality* of the record in that regard, and

not the limited record that CVC's opponents demand. And independent of these emails, Dr. Doyon provides a complete analysis supporting his own conclusion that disclosure within the four corners of P1 fully satisfies the written description and enablement inquiries underlying a determination to accord benefit.

ToolGen also argues that Dr. Jinek's lab notebook (Ex. 2232) should be excluded under FRE 901 as allegedly lacking authentication. Paper 862, ToolGen Misc. Motion 1, 10:22-11:2. The argument lacks merit. Dr. Sternberg's declaration more than adequately authenticates this exhibit as a true and correct copy of the notebook pages that Dr. Sternberg remembers personally witnessing on March 1, 2012. Ex. 2221, ¶¶4-7.

Third, ToolGen argues that Dr. Doyon relies on material he allegedly did not review, namely a supplementary Figure corresponding to a Jinek 2013 paper and the lab notebooks underlying the data in that paper or CVC's P3. Paper 862, ToolGen Misc. Motion 1, 11:5-13. The response is that Dr. Doyon did *not* admit that he did failed to review any relevant information. He simply did not recall the specific data presented in that supplementary figure. Ex. 1604, 23:8-10. He then answered extensive questions about the data, explaining why they were not necessary to his opinions, but nonetheless further supported his analysis that the CVC inventors successfully used their sgRNA CRISPR-Cas9 system in human cells. *Id.*, 24:13-32:11. Similarly, whether he reviewed certain lab notebooks does not undermine his reliance on the data reproduced in Jinek 2013 and P3. Indeed, that publicly available information (rather than unpublished laboratory notebooks) is the most probative evidence of what a POSA would have understood and expected in view of P3. Whether Dr. Doyon's opinions could have considered *additional* information bears only on the weight, and not admissibility, of his opinion.

D. There Is No Basis to Exclude Dr. Zamore's Testimony

On page 11 line 23 through page 12 line 3, ToolGen argues that Dr. Zamore's opinions are improper because he cites some articles that were published after the filing date of CVC P1. The response is that, as discussed above, there is nothing per se inadmissible about articles that were published after the relevant filing date. Such articles can still be probative of what a skilled person would have understood at the time of filing. *Plant Genetic*, 315 F.3d at 1344 ("[the Federal Circuit] has approved use of later publications as evidence of the state of art existing on the filing date of an application."); *Thomas*, 720 F.2d at 1581. Dr. Zamore cited those articles for that proper purpose.

ToolGen then incredibly argues that the PTAB should exclude CVC's briefing that cites Drs. Doyon and Zamore's expert testimony. Paper 862, ToolGen Misc. Motion 1, 12:6-16. ToolGen's naked string cite of pages in CVC's briefing, with no analysis of how the briefing uses the purportedly improper testimony or which of ToolGen's diverse arguments apply to which portions of CVC's briefing cannot satisfy ToolGen's burden of articulating precise relief requested and proving entitlement to that relief. *See* Standing Order ¶ 121.3. As discussed above, each of ToolGen's arguments lack merit.

E. Dr. Marraffini's '115 Deposition transcript is admissible

On page 12 lines 18-24, ToolGen argues that Dr. Marraffini's deposition transcript (from the '115 interference) is hearsay, offered improperly without cross-examination. The response is that the deposition transcript is admissible under various hearsay exceptions and the opponent of Dr. Marraffini's testimony had a full opportunity to depose him. Fed. R. Evid. 801(d), 803(b). Additionally, ToolGen did not ask CVC or the PTAB to depose Dr. Marraffini. Having never asked for a deposition of Dr. Marraffini, ToolGen has no basis to complain about the transcript, as an evidentiary matter or otherwise.

As an initial matter, transcripts prepared by court reporters of depositions given under oath are admissible for their truth in future unrelated proceedings. *See* Fed. R. Evid. 804(b)(1), (3); Fed. R. Civ. P. 32(a)(8) ("[a] deposition lawfully taken and, if required, filed in any federal – or state – court action may be used in a later action involving the same subject matter between the same parties, or their representatives or successors in interest, to the same extent as if taken in the later action."); *Cf. Hub v. Sun Valley Co.*, 682 F.2d 776, 778 (9th Cir. 1982) (noting that admitting deposition testimony from a prior proceeding may increase efficiency at trial without jeopardizing accurate fact finding).

Courts have admitted deposition testimony from prior proceedings even between *different* parties where the adverse party in the former proceeding had a similar motivation to cross-examine the witness as the adverse party in the latter. *See, e.g.*, *Dykes v. Raymark Indus., Inc.*, 801 F.2d 810, 816 (6th Cir. 1986) (deeming an unrelated party a "predecessor in interest" where "it appears that in the former suit a party having a like motive to cross-examine about the same matters as the present party would have, was accorded an adequate opportunity for such examination."); *see also United States v. DiNapoli*, 8 F.3d 909, 912-13 (2d Cir. 1993); *Hendrix v. Raybestos-Manhattan, Inc.*, 776 F.2d 1492, 1506 (11th Cir. 1985). In the '115 interference, Broad had a similar—if not even greater and more expansive—motivation to cross-examine Dr. Marraffini as ToolGen has in this interference. ToolGen's motion does not allege that Broad's appearance for the Dr. Marraffini deposition in the '115 interference was inadequate to serve ToolGen's interests here.

ToolGen wrongly speculates that "CVC did not and could not offer Dr. Marraffini for cross-examination in this interference because it had to subpoena Dr. Marraffini for his '115 testimony." Paper 862, ToolGen Misc. Motion 1, 12:24-13:2. To the extent ToolGen had any independent right to depose Dr. Marraffini, ToolGen has waived that right. ToolGen never

requested, or even mentioned, such a deposition to CVC. Nor did ToolGen undertake any effort to ask the PTAB for authorization to depose Dr. Marraffini. The fact that Dr. Marraffini was successfully subpoenaed in the past belies ToolGen's speculation that he *could not* have been produced to testify here.

Even if ToolGen were right that Dr. Marraffini—a non-party witness—is not available for cross-examination in this proceeding, that would only provide yet another basis on which his prior deposition is admissible. Fed. R. Evid. 804(b)(1); *Cf.* Fed. R. Civ. P. 32(a)(4) (providing that if the deponent is a non-party and is unavailable, then his deposition may be admitted at trial).

III. Conclusion

ToolGen's Miscellaneous Motion 1 does not demonstrate ToolGen is entitled to any of the relief requested. The motion lacks factual support and/or legal authorities supporting the requested relief. The PTAB should therefore deny the motion.

Respectfully submitted,

By /Eldora L. Ellison/
Eldora L. Ellison, Ph.D., Esq.
Lead Attorney for UC and UV
Registration No. 39,967
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 New York Avenue, NW
Washington, D.C. 20005

By /Li-Hsien Rin-Laures/
Li-Hsien Rin-Laures, M.D., Esq.
Lead Attorney for EC
Registration No. 33,547
RINLAURES LLC
321 N. Clark Street, 5th floor
Chicago, IL 60654

Date: October 8, 2021

Date: October 8, 2021

APPENDIX A: EXHIBIT LIST

Exhibit No.	Description
1500	Deposition Transcript of Erik Sontheimer, Ph.D., The Regents of the University of California v. ToolGen, Inc., Interference No. 106,127, June 15, 2021.
1510	Deposition Transcript of Samuel H. Sternberg, Ph.D., The Regents of the University of California v. ToolGen, Inc., Interference No. 106,127, June 16, 2021.
1550	Deposition Transcript of Scott Bailey, Ph.D., The Regents of the University of California v. ToolGen, Inc., Interference No. 106, 127, June 25, 2021.
1560	Deposition Transcript of Yannick Doyon, Ph.D., The Regents of the University of California v. ToolGen, Inc., Interference No. 106, 127, July 2, 2021.
1570	Deposition Transcript of Jennifer Doudna, Ph.D., The Regents of the University of California v. ToolGen, Inc., Interference No. 106,127, July 8, 2021.
1603	Second Deposition Transcript of Dr. Scott Bailey, The Regents of the University of California v. ToolGen, Inc., Interference No. 106,127, August 10, 2021
1604	Second Deposition Transcript of Dr. Yannick Doyon The Regents of the University of California v. ToolGen, Inc., Interference No. 106,127, August 12, 2021
2013	Declaration of Yannick Doyon, Ph.D.
2015	Declaration of Scott Bailey, Ph.D.
2017	Declaration of Phillip Zamore, Ph.D.
2019	Declaration of Erik Sontheimer, Ph.D.
2021	Declaration of Rodolphe Barrangou, Ph.D.
2023	Declaration of Jennifer Doudna, Ph.D.
2156	Shen, B., *et al*., "Generation of gene-modified mice via Cas9/RNA-mediated gene targeting," *Cell Research* 23:720-723, Supplementary Information (2013)
2221	Declaration of Samuel Sternberg, Ph.D.
2232	Martin Jinek, Ph.D., laboratory notebook excerpt
2250	Email from Jennifer Doudna to Martin Jinek, dated April 14, 2012, with attachments, 33 pages
2294	Email from Aaron Cheng to Jennifer Doudna, Jamie Cate and D. Rubin, dated April 16, 2012, 1 page
2295	Email from Aaron Cheng to Jennifer Doudna, dated April 17, 2012, 1 page
2296	Email from Martin Jinek to Aaron Cheng, dated April 25, 2012, 3 pages
2297	Email from Martin Jinek to himself, dated May 18, 2012, with attachments – gfp pics, 7 pages
2303	Email from Emmanuelle Charpentier to Claudia Lupp, Angela Eggleston and Jennifer Doudna, dated May 28, 2012, 2 pages

Exhibit No.	Description
2304	Email from Guy Riddihough to Jennifer Doudna and Emmanualla Charpentier, dated May 29, 2012, 2 pages
2313	Email from Florian Raible to Krzysztof Chylinski, dated June 28, 2012, 3 pages
2348	Declaration of Dana Carroll, Ph.D.
2384	Bokhove, M., *et al*., "A structured interdomain linker directs self-polymerization of human uromodulin," *PNAS* 113(6): 1552–1557 (2016)
2455	Deposition transcript of Luciano Marraffini, Ph.D., *The Regents of the University of California v. The Broad Institute, Inc*., Patent Interference No.106,115 (March 11, 2021)
2476	Third Declaration of Yannick Doyon, Ph.D.
2477	Second Declaration of Scott Bailey, Ph.D.

APPENDIX B: CVC'S RESPONSES TO TOOLGEN'S STATEMENT OF MATERIAL FACTS

1. Dr. Bailey opines that ToolGen is not entitled to the benefit of its P1, P3, and PCT applications because they do not adequately describe a codon-optimized Cas9 nucleic acid and a nuclear localization signal ("NLS"). Dr. Bailey so opines despite testifying that CVC's alternative of Count 1 does not require either element and that both were well-known by POSAs at the relevant time. Ex. 2015, ¶39, FN 1, 95-98, 134.

CVC Response: Admitted.

2. Dr. Bailey premises his testimony entirely upon instructions provided by CVC's lawyers that instructed Dr. Bailey to ignore Count 1 and the knowledge of those skilled in the art, and instead to assume that ToolGen must show written description of both codon optimization (Exs. 2015 and 2477) and an NLS (Ex. 2477) to meet the requirements of Count 1.

CVC Response: Denied.

3. Dr. Bailey testified that to analyze ToolGen's P3 and PCT, he was "asked by counsel to assume that in the context of Embodiment 3-1, ToolGen's P3 must describe an embodiment of an NLS-tagged, codon-optimized Cas9 mRNA for expression in mouse cells[.]" Ex. 2477, ¶42.

CVC Response: Admitted that Dr. Bailey testified that this is one assumption that he was asked to make for purposes of some opinions.

4. Dr. Bailey testified that for his analysis of ToolGen's P1 he was "asked to assess whether ToolGen's P1 as of October 23, 2012, adequately describes a Cas9 nucleic acid that is 'codon- optimized for expression.'" Ex. 2015, ¶38.

CVC Response: Admitted that Dr. Bailey testified that this is one assessment he was asked to make.

5. Dr. Bailey admitted twice that he did not consider the CVC alternative of Count 1, which does not require codon optimization or an NLS. Ex. 1550, 125:9-16; Ex. 1603, 23:8-13.

CVC Response: Denied.

6. Dr. Sontheimer, Ex. 2019, ¶2; Ex. 1500 (Sontheimer Tr.), 11:19-21, Dr. Barrangou, Ex. 2021, ¶2, Dr. Doudna, Ex. 2023, ¶3, 6-18; Ex. 1570 (Doudna Tr.), 20:7-9, Dr. Sternberg, Ex. 2221, ¶2; Ex. 1510 (Sternberg Tr.), 23:13-14, and Dr. Carroll, Ex. 2348, ¶2; Ex. 1520 (Carroll Tr.), 23;11-13, each admitted they did not offer expert testimony.

CVC Response: Admitted that Drs. Sontheimer, Barrangou, Doudna, Sternberg, and Carroll are testifying as fact witnesses according to their personal knowledge and are not rendering expert opinions in this proceeding.

7. Dr. Sontheimer testified that he "appreciated that after the Chylinski and Jinek presentation, scientists in the field would be able to quickly apply the CVC inventors' sgRNA CRISPR-Cas9 system . . . ." Ex. 2019, ¶¶21.

CVC Response: Admitted that the quotation is accurate and reflects Dr. Sontheimer's recollection of his personal views at the time.

8. Dr. Barrangou testified that "the CVC inventors' system, particularly the sgRNA CRISPR-Cas9 system, made CRISPR-Cas9-mediated genome editing in eukaryotes simpler and easier such that genome editing could be done in a fraction of the time and at a fraction of the cost as compared with zinc-finger nucleases (ZFNs) and TALENs." Ex. 2021, ¶16.

CVC Response: Admitted.

9. Dr. Doudna testified about the state of the CRISPR field and past efforts to develop successful gene editing systems. Ex. 2023, ¶15 ("[G]roup II introns and ribozymes had also been used to influence genetic expression in eukaryotic cells, with varying degrees of efficiency.").

CVC Response: Admitted.

10. Dr. Sternberg testified that "once the components of a system are identified in vitro, independent of a particular cellular environment, it is reasonable to expect the system to work in a range of cellular environments, assuming routine adjustments." Ex. 2221, ¶8.

CVC Response: Admitted.

11. Dr. Carroll contradicted his former statements, testifying that he "understood at the time of this article that well-known molecular biology techniques could be used to apply the CRISPR-Cas9 system described in Jinek *et al.* in a eukaryotic cell." Ex. 2348, ¶8.

CVC Response: Denied that Dr. Carroll contradicted his former statements. Admitted that Dr. Carroll explained and clarified his former statements, and that the quoted language is accurate.

12. Dr. Doyon's first declaration is from a POSA's perspective as of May 25, 2012, yet he cites to many exhibits created or published after that date. Ex. 2013 at ¶¶7, 8-12, 18-20, 54-69, 117-122, 131, 145, 151, 154, 173, 191, 193, 205-210, 214-19, 221, 233-39, 258-64, 302, 308-38.

CVC Response: Admitted that portions of Dr. Doyon's first declaration speak to a POSA's perspective as of May 25, 2012, otherwise denied.

13. Dr. Doyon's third declaration is from the perspective of a POSA as of January 28, 2013, yet he cites numerous materials published after that date. Ex. 2476 at ¶¶54, 65-69.

CVC Response: Admitted.

14. Dr. Doyon testified: "So a POSA . . . could not be aware of [a] publication published after May 25, 2012."). *See* Ex. 1560 (Doyon Tr.), 50:2-8.

CVC Response: Admitted.

15. Dr. Doyon's first declaration, Ex. 2013 at ¶¶8-12, cites to the irrelevant and impermissible lay opinions of CVC's five fact declarants (Exs. 2019, 2021, 2023, 2221, and 2348).

CVC Response: Admitted that Dr. Doyon's first declaration cites Exs. 2019, 2021, 2023, 2221, and 2348. Denied that CVC's five fact declarants are irrelevant or present impermissible lay opinions.

16. Dr. Doyon cites numerous emails between the CVC inventors and various colleagues that are irrelevant and hearsay. Ex. 2013, ¶¶321-336 (citing Exs. 2250, 2294-2297, 2303-2304, 2313).

CVC Response: Admitted that Dr. Doyon cites Exs. 2250, 2294-2297, 2303-2304, 2313. Denied that these emails are irrelevant or hearsay.

17. Dr. Doyon relies on Dr. Jinek's unauthenticated lab notebook, Ex. 2233, of which he does not have personal knowledge, and where CVC provided no sponsoring witness. Ex. 2013, ¶¶326-27, 331 and images reproduced therein.

CVC Response: Admitted that Dr. Doyon cites Ex. 2233, otherwise denied.

18. Dr. Doyon admitted he did not review a critical part of Jinek 2013. Ex. 1604, 23:4-10 (admitting he did not recall "the specific [sequencing] data [of mutated alleles in experimental HEK293T cells] that are presented in supplementary Figure 1 of Jinek 2013").

CVC Response: Denied.

19. Dr. Doyon did not review the experiments or the lab notebooks underlying Jinek 2013 or CVC P3 in preparing his third declaration. Ex. 1604, 41:6-43:22.

CVC Response: Denied.

20. Dr. Zamore's declaration is from the perspective of a POSA and "the general knowledge in the art as of May 25, 2012, the filing date of P1." Ex. 2017, ¶13. Yet, Dr. Zamore cites materials published after May 25, 2012: ¶23 (Ex. 2156 (2013)), ¶34 (Ex. 2384 (2016)).

CVC Response: Admitted that portions of Dr. Zamore's declaration relate to the perspective of POSA and that ¶ 13 contains the words "the general knowledge in the art as of May 25, 2012, the filing date of P1," otherwise denied.

21. CVC offers Ex. 2455 from the '115 Interference to prove the truth of the matters CVC asserts—Dr. Marraffini and the field's expectations for CRISPR-Cas9 in eukaryotes (notably after CVC P1). CVC did not and could not offer Dr. Marraffini for cross-examination in this interference, considering it had to subpoena Dr. Marraffini for his '115 testimony. *See* Order- Motion Regarding Subpoena, 106,115 Interference Paper 888.

CVC Response: Denied.

CVC'S STATEMENT OF MATERIAL FACTS

1. CVC argued that ToolGen, in defending its accorded benefit, should be estopped from relying on CVC's half of the count, due to express arguments ToolGen made to the Patent Office about the criticality of codon-optimization and nuclear-localization sequences to ToolGen's interfering claims, one of which is ToolGen's half of Count 1. *See* Paper 364,CVC Motion 2, 3-10.

2. Codon optimization and nuclear localization sequences are not required for CRISPR-Cas9 to function in eukaryotes.

3. For purposes of rendering his opinions that ToolGen's P1 and other filings fail to show written description of a codon-optimized Cas9 with nuclear localization sequence, Dr. Bailey logically assumed that such limitations were required.

4. Dr. Doyon is familiar with Dr. Jinek's notebook (Ex. 2233) and its authenticity from its use in the '115 Interference, where Dr. Jinek authenticated it and Dr. Doyon cited it in analyzing priority.

5. The Broad Institute was present for the subpoenaed deposition of Dr. Marraffini in the '115 Interference and had a full and fair opportunity to ask him questions.

6. ToolGen's motion does not allege that Broad's opportunity to depose Dr. Marraffini in the '115 interference inadequately served ToolGen's interests here.

7. ToolGen never asked the PTAB for authorization to depose Dr. Marraffini in this proceeding, nor did ToolGen ask CVC to produce him for a deposition.

CERTIFICATE OF SERVICE

I hereby certify that the foregoing **JUNIOR PARTY'S OPPOSITION TO TOOLGEN'S MISCELLANEOUS MOTION 1 (Motion to Exclude)** is being filed via the Interference Web Portal by 8:00 PM Eastern Time on October 8, 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:

Anthony M. Insogna
Timothy J. Heverin
Nikolaos C. George
S. Christian Platt
Roger C. Rich
JONES DAY
250 Vesey Street
New York, NY 10281-1047
aminsogna@jonesday.com
tjheverin@jonesday.com
ncgeorge@jonesday.com
cplatt@jonesday.com
rcrich@jonesday.com
ToolGenUC127@jonesday.com

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C

/Eldora L. Ellison/
Eldora L. Ellison, Ph.D., Esq.
Lead Attorney for UC and UV
Registration No. 39,967

Date: October 8, 2021

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 New York Avenue, NW
Washington, DC 20005-3934