

Filed on behalf of Senior Party ToolGen, Inc.

Paper No. ____

Anthony M. Insogna
Timothy J. Heverin
S. Christian Platt
JONES DAY
250 Vesey Street
New York, NY 10281
Tel: (212) 326-3939
Fax: (212) 755-7306
aminsogna@jonesday.com
tjheverin@jonesday.com
cplatt@jonesday.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

**THE BROAD INSTITUTE, INC., MASSACHUSETTS INSTITUTE OF
TECHNOLOGY, AND PRESIDENT AND FELLOWS OF
HARVARD COLLEGE,**

Junior Party,

Patents 8,697,359; 8,771,945; 8,795,965; 8,865,406; 8,871,445; 8,889,356;
8,889,418; 8,895,308; 8,906,616; 8,932,814; 8,945,839; 8,993,233; 8,999,641; and
9,840,713; and Applications 14/704,551 and 15/330,876,

v.

TOOLGEN, INC.

Senior Party.

Application 14/685,510

Patent Interference No. 106,126 (DK)

**TOOLGEN REPLY IN SUPPORT OF MISCELLANEOUS MOTION 1
(to exclude inadmissible evidence)**

TABLE OF CONTENTS

	Page
I. ARGUMENT	1
A. Broad’s Proffer Exhibits Are Devoid Of Authenticating Information	1
B. Broad Misunderstands Its Use of Hearsay	2
C. Broad and Dr. Seeger Impermissibly Rely On Post-Filing Exhibits	3
D. Dr. Seeger Serves As A Mere Conduit For Hearsay	4
II. CONCLUSION.....	5
APPENDIX 1: LIST OF EXHIBITS CITED	A1-1
APPENDIX 2: STATEMENT OF MATERIAL FACTS.....	A2-1

TABLE OF AUTHORITIES

	Page
CASES	
<i>Brookhill-Wilk I, LLC. v. Intuitive Surgical, Inc.</i> , 334 F.3d 1294 (Fed. Cir. 2003).....	3
<i>Knoll Pharm. Co. v. Teva Pharm. USA, Inc.</i> , 367 F.3d 1381 (Fed. Cir. 2004).....	4
<i>Rozbicki v. Chiang</i> , Interference. 105,898, Paper 154 (P.T.A.B. June 26, 2013).....	3
<i>Trustees of Bos. Univ. v. Everlight Elecs. Co.</i> , 141 F. Supp. 3d 147 (D. Mass. 2015).....	4
<i>Wi-Lan Inc., v. Sharp Electronics Corp.</i> , 992 F.3d 1366 (Fed. Cir. 2021).....	4
OTHER AUTHORITIES	
Fed. R. Evid. 703	4
Standing Order ¶122.4.2.1	2

1 Broad’s Opposition 1 (“Opp.”) vacillates between inadequately defending the admissibility
2 of its challenged exhibits and, because the challenged exhibits are not admissible, arguing that they
3 need not be. In doing so, Broad also argues the sufficiency of its proffer, which is not the subject
4 of ToolGen’s motion.

5 **I. ARGUMENT**

6 **A. Broad’s Proffer Exhibits Are Devoid Of Authenticating Information**

7 Broad’s opposition to ToolGen’s motion to exclude Exhibits 2526, 2530, 2533, 2535, 2536,
8 2563, 2565, 2566, 2581, 2582 and 2922 (the “proffer exhibits”) is confused and partially
9 misplaced.¹ Broad argues that the proffer exhibits are admissible (Opp. at 4:19–6:7), *and* that they
10 need not be admissible (Opp. at 3:13–21; 6:14–15), *and* that they are a sufficient proffer (Opp. at
11 3:24–4:8, 6:16–17). The response is that whether these proffer exhibits need be admissible as part
12 of a proffer is not at issue. The Board may consider inadmissible evidence as part of a proffer, but
13 Broad must show sufficiency of its proffer in its substantive Motion 1, not here. Instead, the
14 question is whether these exhibits need be admissible *when used as evidence*. Broad argues that
15 as a policy matter, proffer exhibits should not be subjected to a “mini-trial” on priority with
16 evidentiary rules. Opp. at 4:9–18. But Broad may not offer evidence into the record under the
17 guise of a proffer, thereby bypassing the evidentiary rules. And to be clear, Broad’s Opposition
18 argues for the admissibility of each challenged exhibit, including each exhibit in Broad’s proffer.
19 Opp. at 3–7.

¹ Broad misstates that only five proffer exhibits are challenged (Opp. at 5:3) but ToolGen challenges all eleven (Mot. at 2:21–22).

1 Broad offers a single authentication theory for the proffer exhibits: that Dr. Seeger “was
2 easily able to understand and opine on what these exhibits showed.” Opp. at 6:2–3 (citing Ex. 2454
3 at ¶¶184–99).² But Dr. Seeger’s declaration does not even cite or describe ten of the eleven
4 challenged exhibits, let alone demonstrate that he “easily” understood what they were. F19. Nor
5 does Dr. Seeger provide any information relevant to authentication, such as personal knowledge
6 of when the exhibits were created and by whom. And for the exhibit he does discuss, Dr. Seeger
7 makes only a conclusory statement not relevant to authentication. Ex. 2454, ¶190 (stating Exhibit
8 2526 “shows that Dr. Zhang had completed a vector design with the separate tracrRNA component
9 in his engineered system, to express the three components, Cas9, crRNA, and tracrRNA”).

10 **B. Broad Misunderstands Its Use of Hearsay**

11 Broad also sweepingly asserts that hearsay Exhibits 2704, 2705, 2708, 2710, 2716, 2734,
12 2751, 2770, 2771, 2772, 2773, 2775, 2777, 2780, 2781, 2782, 2784, 2793, 2829, 2830, 2842 and
13 2845 are also part of Broad’s proffer and need not be admissible. Opp. 6:10–17. The response is
14 that (1) again, to the extent that Broad claims they are admissible *as evidence*, and Broad does
15 defend them as such, they are inadmissible hearsay and (2) ToolGen also moved to exclude a
16 subset of the hearsay Exhibits—Nos. 2704, 2705, and 2793—which Broad used in its Motion 3,
17 which contained no proffer. *See* Mot. 3:3–12.

18 Substantively, Broad argues that the hearsay exhibits are not hearsay because they are
19 offered as proof of what they say, not for the truth of the matter asserted. Opp. at 6:18–22. The

² In violation of SO ¶122.4.2.1, Broad’s Opposition does not identify a single material fact, yet relies on such facts for its arguments. The Board should give no weight to any fact upon which Broad relies, such as Dr. Seeger’s alleged ability to understand what exhibits showed.

1 response is that they are being offered exactly for the truth of their contents. Belying its position,
2 Broad offers the *content* of challenged hearsay exhibits as *material facts* in Broad Motion 1. *See,*
3 *e.g.*, Paper 72, MF 11 (stating as a fact that Zhang “engineered and tested dual-molecule RNA
4 CRISPR systems in eukaryotic cells,” citing challenged Exs. 2751, 2770, 2771, 2772, 2773, 2775,
5 2777, 2780, 2781, 2782, 2784, 2829 and 2842 in support); MF 9 (characterizing the experiments
6 underlying a grant application, citing challenged Ex. 2716); MF 4 (alleging Broad’s earliest work
7 in CRISPR-Cas9 systems date to 2011, citing challenged Exs. 2708, 2716, and 2734); F20. Broad
8 offers the exhibits to prove the activities described therein, which is black-letter hearsay, as
9 Broad’s own authority confirms. *See Rozbicki v. Chiang*, Interference 105,898, Paper 154 at 25
10 (P.T.A.B. June 26, 2013) (“[T]he ‘truth’ of whether the disclosed events occurred and produced
11 the described results are necessarily hearsay.”).

12 **C. Broad and Dr. Seeger Impermissibly Rely On Post-Filing Exhibits**

13 Broad next argues that the challenged post-filing Exhibits are admissible in part because
14 they are relevant to the meaning of claim terms at the relevant time and as evidence of state of the
15 art/secondary considerations of non-obviousness. Opp. 7:11–9:3, 9:20–24. The response is that
16 the post-filing exhibits provide no insight into how a skilled artisan would understand claim terms
17 *at the relevant filing date*. And Broad does not offer evidence to the contrary. For example, Broad
18 and Dr. Seeger rely on Exhibit 2217 to assert that “guide RNA” is a general term encompassing
19 both single-and dual-molecule guide RNAs. Ex. 2454, ¶168. That the authors of Ex. 2217 used
20 the term “guide RNA” in 2014 is not probative of an artisan’s understanding years earlier. In
21 *Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1299 (Fed. Cir. 2003), the Federal
22 Circuit did not consider references published years after the patent’s filing because they were
23 “dated well after” the patent was filed or issued and therefore “are not contemporaneous with the

1 patent, [and] do not reflect the meanings that would have been attributed to the words in dispute
2 by persons of ordinary skill in the art as of the grant of the” patent.

3 Further, post-filing publications not related to the claimed invention are not relevant to
4 secondary considerations of the same. For example, unlike *Knoll* (Opp. at 7:11–8:2), Ex. 2654,
5 which Dr. Seeger admits concerns only “Cas12a nucleases” (Ex. 2454 at ¶256), *does not actually*
6 *relate to Cas9* and is therefore irrelevant to Broad’s proposed count which recites SaCas9 or
7 chimeric RNA. *See, e.g., Knoll Pharm. Co. v. Teva Pharm. USA, Inc.*, 367 F.3d 1381, 1385 (Fed.
8 Cir. 2004) (discussing that evidence developed after the patent grant is not excluded because it
9 pertains to the “full range of *an invention*” (emphasis added)); F21.

10 **D. Dr. Seeger Serves As A Mere Conduit For Hearsay**

11 Finally, Broad argues that FRE 703 allows for expert witnesses to rely on hearsay Exhibits
12 2704, 2705, 2708, 2750 and 2793 “[i]f experts in the particular field would reasonably rely on
13 those kinds of facts or data in forming an opinion.” Fed. R. Evid. 703; Opp. 10:15–17. While this
14 general principal is correct, the response is that FRE 703 does not permit an expert or party to
15 evade hearsay rules by simply incorporating inadmissible out-of-court statements into the record
16 via the expert’s testimony. *See Wi-Lan Inc., v. Sharp Electronics Corp.*, 992 F.3d 1366, 1375
17 (Fed. Cir. 2021) (affirming the district court’s exclusion of expert testimony based on an
18 inadmissible exhibit because the proponent had “not made a showing that source code experts
19 reasonably rely on unauthenticated source code printouts”); *Trustees of Bos. Univ. v. Everlight*
20 *Elects. Co.*, 141 F. Supp. 3d 147, 149 (D. Mass. 2015). Dr. Seeger does exactly this. For instance,
21 in ¶266 of his declaration, Dr. Seeger merely quotes sentences from hearsay Exhibits 2704 and
22 2705 (emails with Dr. Doudna). F22. Similarly, in ¶192 of his declaration, Dr. Seeger does
23 nothing but summarize the contents of hearsay Exhibit 2708 (an unauthenticated email from Dr.

1 Zhang with the first page dated August 2011 and remaining pages dated December 2020). *See*
2 *also* Ex. 2454, ¶199 (summarizing Ex. 2750); F23.

3 **II. CONCLUSION**

4 The Board should grant ToolGen's Miscellaneous Motion 1.

5 Respectfully submitted,

6 Dated: October 15, 2021

/Timothy J. Heverin/

7 Timothy J. Heverin

8 Reg. No. 77,386

9 JONES DAY

10 Counsel for Senior Party ToolGen, Inc.

APPENDIX 1: LIST OF EXHIBITS CITED

Ex. No.	Description
2201	Cong et al., Multiplex Genome Engineering Using CRISPR/Cas Systems, 339(6121) Science 819–823 (2013) with Supplemental Material.
2217	Sternberg et al., DNA interrogation by the CRISPR RNA-guided endonuclease Cas9, 507 Nature 62–67 (2014)
2226	Ran et al., In vivo genome editing using Staphylococcus aureus Cas9, 520 Nature 186–191 (2015).
2231	Fonfara et al., Phylogeny of Cas9 determines functional exchangeability of dual-RNA and Cas9 among orthologous type II CRISPR-Cas systems, 42 Nucleic Acids Res. 2577–2590 (2013) and Supplementary Materials.
2232	Chylinski et al., The tracrRNA and Cas9 families of type II CRISPR-Cas immunity systems, 10 RNA Biology 726–737 (2013).
2454	Declaration of Christoph Seeger, executed May 28, 2021
2526	Sequence Streptococcus thermophilus LMD9 CRISPR1 region
2530	Gel image of the surveyor assay for the NTF3 72 hour time point
2533	March 1, 2012 Evernote Record
2535	Image 293F_AAV1GFP_a.pdf
2536	Image 293F_AAV1GFP_b.pdf
2563	Gel image
2565	Picture of Drawing on Whiteboard
2566	Gel Image

Ex. No.	Description
2581	Gel Image
2582	Le Cong Electronic Notebook
2654	Liu, R.M., Liang, L.L., Freed, E. et al. Synthetic chimeric nucleases function for efficient genome editing. Nat Commun 10, 5524 (2019). https://doi.org/10.1038/s41467-019-13500-y
2683	Ma, D., et al. Engineer chimeric Cas9 to expand PAM recognition based on evolutionary information. Nat Commun 10, 560 (2019), https://doi.org/10.1038/s41467-019-08395-8 (Ma 2019)
2704	Email from Martin Jinek to Jennifer Doudna, dated May 8, 2012, 1 page
2705	Email from Aaron Cheng to Jennifer Doudna, dated September 14, 2012, 4 pages
2708	Email from Feng Zhang to Mike Shao, dated August 7, 2011, with 11 page attachment, 12 pages total
2710	Email from Feng Zhang to Shuailiang Lin, dated October 24, 2011, 1 page
2716	Email from Feng Zhang to Kiran Musunuru, David Altshuler, Chad Cowan, and Jennifer Hyne, dated January 7, 2012, with 32 page attachment, 33 pages total
2734	Email from order_confirmation@lifetech.com to Feng Zhang, dated March 5, 2012, with 4 page attachment, 5 pages total
2750	Email from Luciano Marraffini to Feng Zhang, dated June 26, 2012, 3 pages
2751	Email from Feng Zhang to Le Cong, dated June 27, 2012, 1 page
2770	Email from Feng Zhang to Le Cong and Grace Gao, dated July 17, 2012, with 167 page attachment, 168 pages total
2771	Email from Le Cong to Feng Zhang, dated July 20, 2012, 1 page

Ex. No.	Description
2772	Email from Feng Zhang to Le Cong, dated July 20, 2012, with 2 page attachment, 3 pages total
2773	Email from Le Cong to Feng Zhang, dated July 21, 2012, 1 pages
2775	Email from Le Cong to Feng Zhang, dated July 22, 2012, 2 pages
2777	Email from Feng Zhang to Le Cong, dated July 23, 2012, 1 page
2780	Email from Le Cong to Feng Zhang, dated July 29, 2012, 4 pages
2781	Email from dnaseq@genewiz.com to Le Cong, dated July 30, 2012, 3 pages
2782	Email from dnaseq@genewiz.com to Le Cong, dated July 30, 2012, 3 pages
2784	Email from Feng Zhang to Le Cong, dated July 31, 2012, with 1 page attachment, 3 pages total
2793	Email from Le Cong to Feng Zhang, Shuailiang Lin, David Cox, and Michael Yim, dated August 29, 2012, with 20 page attachment, 21 pages total
2829	Email from Le Cong to David Cox, dated July 25, 2012, 2 pages
2830	Email from Le Cong to Feng Zhang, dated July 31, 2012, 2 pages
2842	Email from Grace Gao to Le Cong and Feng Zhang, dated July 25, 2012, 2 pages total
2845	Email from Shuailiang Lin to Neville Sanjana, dated October 26, 2011, 1 page
2922	Gel Image 2012-07-20 22hr 21 min.scn

APPENDIX 2: STATEMENT OF MATERIAL FACTS

Senior Party ToolGen's Material Facts 1–18 and Junior Party's Answers

1
2
3 1. ToolGen raised proper and timely objections to the evidence against which it moves. *See*
4 Ex. 1113 (ToolGen's Objections to Junior Party Evidence); 37 C.F.R. § 41.155(b)(1).

5 **Broad Response: Denied**

6 2. Broad relies on numerous unauthenticated exhibits that are inadmissible for failure to meet
7 the requirements of FRE 901. *See* Mot. 1, 7:11–10:6 (citing Exs. 2526, 2530, 2533, 2535, 2536,
8 2563, 2565, 2566, 2581, 2582, 2922).

9 **Broad Response: Denied**

10 3. Broad has not offered any evidence that Exhibits 2526, 2530, 2533, 2535, 2536, 2563,
11 2565, 2566, 2581, 2582, and 2922, which Broad contends are their “best proofs” (lab notes,
12 images, and notebook entries), are what Broad claims them to be.

13 **Broad Response: Denied**

14 4. Exhibit 2526 purports to show a genetic map and sequence of a CRISPR system in a
15 bacterium, and it includes a “Dec. 2, 2020” printed date. *See* Ex. 2526.

16 **Broad Response: Denied**

17 5. Exhibit 2530 contains only a single annotated red arrow in the middle of the exhibit. There
18 are no dates, labels, or other identifying marks (*e.g.*, molecular ladder or identity of samples in
19 each experimental lane) that typically would be present in such an image of a gel electrophoresis
20 meant to prove the contents of the underlying experiment. *See* Ex. 2530.

21 **Broad Response: Denied**

22 6. Exhibits 2535, 2536, and 2563, alleged by Broad to show successful single and dual-
23 molecule systems, Mot. 1, Paper 72, 9:6–10:6, are unannotated images without identifying

1 features. *See* Exs. 2535, 2536, and 2563.

2 **Broad Response: Denied**

3 7. Broad does not offer any sponsoring witness who has personal knowledge of Exhibits
4 2526, 2530, 2533, 2535, 2536, 2563, 2565, 2566, 2581, 2582, and 2922 to verify their authenticity.
5 Dr. Seeger does not profess to have any knowledge of the aforementioned exhibits.

6 **Broad Response: Denied**

7 8. Broad cites various emails between Broad inventors, colleagues, and third parties, each of
8 which are inadmissible hearsay. *See* Mot. 1, 7:11–9:13 (citing Exs. 2708, 2710, 2716, 2734, 2751,
9 2770, 2771, 2772, 2773, 2775, 2777, 2780, 2781, 2782, 2784, 2829, 2830, 2842, 2845); *see also*
10 Mot. 3, Paper 73, 17:10–13, 18:7–15 (citing Exs. 2704, 2705, 2793).

11 **Broad Response: Denied**

12 9. Each of the above-identified emails (Exs. 2704, 2705, 2708, 2710, 2716, 2734, 2751, 2770,
13 2771, 2772, 2773, 2775, 2777, 2780, 2781, 2782, 2784, 2793, 2829, 2830, 2842, 2845) consists of
14 out-of-court statements, which Broad offers to prove that Broad’s experiments allegedly show
15 successful reduction to practice of Broad’s Proposed Count 2.

16 **Broad Response: Denied**

17 10. Broad has not demonstrated that any exception to the hearsay rules apply to Exhibits 2704,
18 2705, 2708, 2710, 2716, 2734, 2751, 2770, 2771, 2772, 2773, 2775, 2777, 2780, 2781, 2782, 2784,
19 2793, 2829, 2830, 2842, and 2845.

20 **Broad Response: Denied**

21 11. Broad and Dr. Seeger rely on Exhibit 2217, which was published after December 12, 2012,
22 as allegedly pertaining to the definition of guide RNA. Ex. 2454, ¶¶166–168 (Ex. 2217 (published
23 2014)).

1 **Broad Response: Denied**

2 12. Broad and Dr. Seeger rely on post-December 12, 2012 Exhibits 2201, 2226, 2231, 2232,
3 2654 and 2683 for the proposition that SaCas9 and chimeric Cas9 are distinct inventions, Mot. 3,
4 10:20–21, 14:14–19, in an effort to support Dr. Seeger’s opinions regarding the designation of
5 claims to the present or proposed counts: Ex. 2454, ¶¶233–34, 237, 240 (citing Ex. 2226 (published
6 2015)); ¶¶238, 242–43 (Ex. 2201 (published 2013)), (Ex. 2231 (published 2013)), (Ex. 2232
7 (published 2013)); ¶¶255–57 (Ex. 2683 (published 2019)), (Ex. 2654 (published 2019)).

8 **Broad Response: Denied**

9 13. Dr. Seeger’s testimony relies upon several exhibits created or published months or even
10 years after the relevant filing dates of the patent applications in question. Ex. 2454, ¶¶166–168,
11 233, 234, 237–243, 255–57.

12 **Broad Response: Denied**

13 14. Dr. Seeger relies on numerous exhibits created or published after December 12, 2012. *See*
14 Ex. 2454, ¶¶166–168 (citing Ex. 2217), ¶¶233, 234, 237–243, 255–57 (citing Exs. 2201, 2226,
15 2231, 2232, 2654, 2683).

16 **Broad Response: Denied**

17 15. Dr. Seeger refers without citation to “patent applications filed in . . . 2013,” and “after
18 2012”— post-December 12, 2012—as also supporting his definition of guide RNA. Ex. 2454,
19 ¶¶167–68.

20 **Broad Response: Denied**

21 16. To opine that Dr. Zhang purportedly completed a vector design with tracrRNA, Dr. Seeger
22 relies on unauthenticated Exhibit 2526, which is devoid of any identifying features, has a
23 “Dec. 2, 2020” printed date, and is unsponsored by any witness with personal knowledge. *See*,

1 *e.g.*, Ex. 2454, ¶¶190, 191 (citing Ex. 2526).

2 **Broad Response: Denied**

3 17. Dr. Seeger relies on several emails between Broad inventors, colleagues, and third parties,
4 which are inadmissible hearsay under FRE 801 and 802. Ex. 2454, ¶¶192, 199, 266, 270 (citing
5 Exs. 2704, 2705, 2708, 2750, 2793).

6 **Broad Response: Denied**

7 18. Exhibits 2704, 2705, 2708, 2750, and 2793 are emails that consist of out-of-court
8 statements offered for the supposed truth of the matter asserted—Broad’s experiments allegedly
9 showing successful reduction to practice of dual-molecule CRISPR-Cas9 in a eukaryotic system
10 and that certain claims are separately patentable inventions.

11 **Broad Response: Denied**

Senior Party ToolGen’s Additional Material Facts 19–23

1
2 19. Dr. Seeger’s declaration only cites one out of eleven challenged proof exhibits. Ex.
3 2454, ¶190.

4 20. Broad offers the content of challenged hearsay exhibits as material facts in Broad
5 Motion 1. *See, e.g.*, Broad Motion 1, Paper 72, MF 11; MF 9; MF 4.

6 21. Exhibit 2654 does not relate to Cas9, which Dr. Seeger admits concerns only
7 “Cas12a nucleases.” Ex. 2454 at ¶256.

8 22. In ¶266 of his declaration, Dr. Seeger quotes sentences from hearsay Exhibits 2704
9 and 2705 (emails with Dr. Doudna). Ex. 2454, ¶266; Ex. 2704; Ex. 2705.

10 23. In ¶192 of his declaration, Dr. Seeger summarizes Exhibit 2708 and in ¶199 he
11 summarizes Ex. 2750. Ex. 2454, ¶192; Ex. 2454, ¶199.

CERTIFICATE OF SERVICE

I hereby certify that the foregoing **TOOLGEN REPLY IN SUPPORT OF MISCELLANEOUS MOTION 1** was filed via the Interference Web Portal on October 15, 2021 by 8:00 PM EDT, and thereby served on the attorneys of record for the Junior Party pursuant to ¶105.3 of the Standing Order. Pursuant to agreement of the parties, service copies are being sent by email by 11:00 pm ET to counsel for Junior Party as follows:

Steven Trybus
Steven.Trybus@lockelord.com

Ray Nimrod
raynimrod@quinnemanuel.com

Ian Ibarra
ianibarra@quinnemanuel.com

Matthew Robson
matthewrobson@quinnemanuel.com

Zach Summers
zachsummers@quinnemanuel.com

Interference106126@lockelord.com

/Timothy J. Heverin/
Timothy J. Heverin
Reg. No. 77,386
JONES DAY
Counsel for Senior Party ToolGen, Inc.