United States Court of Appeals for the Federal Circuit

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

v.

THE BROAD INSTITUTE, INC., MASSACHUSETTS INSTITUTE OF TECHNOLOGY, PRESIDENT AND FELLOWS OF HARVARD COLLEGE,
Cross-Appellants

2022-1594, 2022-1653

Appeals from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. 106,115.

Decided: May 12, 2025

JEFFREY A. LAMKEN, MoloLamken LLP, Washington, DC, argued for appellants. Also represented by LOIS AHN, KENNETH E. NOTTER, III; ELIZABETH KATHLEEN CLARKE, Chicago, IL, SARA MARGOLIS, New York, NY.

RAYMOND NIMROD, Quinn Emanuel Urquhart & Sullivan, LLP, New York, NY, argued for cross-appellants. Also represented by MATTHEW D. ROBSON; HUGH S. BALSAM,

STEVEN R. TRYBUS, Troutman Pepper Locke LLP, Chicago, IL.

Before REYNA, HUGHES, and CUNNINGHAM, *Circuit Judges*.

REYNA, *Circuit Judge*.

The Regents of the University of California, the University of Vienna, and Emmanuelle Charpentier (collectively "Regents") appeal from the Patent Trial and Appeal Board's determinations in a patent interference proceeding. The Broad Institute, Massachusetts Institute of Technology, and the President and Fellows of Harvard College (collectively "Broad") conditionally cross-appeal. After resolving preliminary motions, the Board issued a final decision concluding that Broad has priority over Regents with respect to a CRISPR-Cas9 system that contains a "single-guide" RNA that edits or cleaves DNA in eukaryotic cells. We affirm-in-part, vacate-in-part, and remand as to the main appeal and dismiss as to the cross-appeal.

BACKGROUND

This appeal involves an invention relating to the adaptation of "CRISPR"[1] systems to edit eukaryotic DNA. Appellant Br. 1; Cross-Appellant Br. 20. Scientists at Regents claim they invented this technology. Appellant Br. 1–2, 8–22. Scientists at Broad argue they are the true inventors. Cross-Appellant Br. 1–2, 14–22. As such, this

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[1] CRISPR ("clustered regularly interspaced short palindromic repeats") comprises a family of DNA loci. J.A. 3051 (U.S. Patent No. 8,697,359, at 15:58–61). A "CRISPR system" "refers collectively to transcripts and other elements involved in the expression of or directing the activity of CRISPR-associated ('Cas') genes[.]" *Id.* at 16:32–34.

dispute centers on one of the oldest doctrines in U.S. patent law, conception.

I.

A. Early Research

CRISPR systems are immune defense systems in prokaryotic cells that naturally edit DNA.[2] One of the "simplest" types of CRISPR systems, a "Type II CRISPR system," uses an RNA sequence, "crRNA," to guide a protein to a particular DNA sequence as part of the process of editing the DNA. J.A. 64098.

Scientists sought to use the natural editing capabilities of CRISPR systems to edit DNA in eukaryotic cells. Broad's and Regents' scientists claim that, by 2011 or early 2012, they knew CRISPR Type II systems edit DNA using three components: mature tracrRNA, mature crRNA, and a protein called "Cas9." J.A. 74998–99; J.A. 5597–641 (Martin Jinek et al., *A Programmable Dual-RNA-Guided DNA Endonuclease in Adaptive Bacterial Immunity*, 337 SCIENCE 816 (2012)) ("Jinek 2012"). According to Regents, its scientists believed this biological triptych—called a "CRISPR-Cas9 complex" or "CRISPR-Cas9 system"—could be used to edit eukaryotic DNA without having to design a new protein for every new target DNA sequence, as was necessary when using prior gene-editing tools. Appellant Br. 4–5.

Regents' scientists claim that they further simplified CRISPR-based gene editing in 2012 by linking two RNA

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[2] Every living organism is one of two types: prokaryotic or eukaryotic. Prokaryotes are single-celled organisms lacking a nucleus, such as bacteria, while eukaryotes are more complex organisms, such as animals and plants, whose cells possess a nucleus. Appellant Br. 4; Cross-Appellant Br. 10.

sequences in the CRISPR-Cas9 system into a single-molecule "chimeric" RNA, called a "single-guide" RNA ("sgRNA"). J.A. 57592, 67247–48. They claim that they made a CRISPR-Cas9 system from a sgRNA they designed, called "chimera A," and Cas9. Jinek 2012; J.A. 67260–61. They claim to have used this system to successfully target and edit DNA in a cell-free *in vitro* environment. J.A. 67260–61, 67286–87. As Regents puts it, this system "simpl[ified]" gene editing by allowing the system to be "reprogrammed by changing the crRNA." Appellant Br. 7.

Starting in March 2012, Regents' scientists, directed by Charpentier, Jennifer Doudna, and Martin Jinek, planned experiments to show the single RNA CRISPR-Cas9 system could be used to edit eukaryotic DNA. On March 1, 2012, Jinek wrote a notebook entry and exchanged emails with Doudna in which they described the system and experiments using it in mammalian cells, to test if the system could successfully edit eukaryotic DNA. J.A. 69007–09; *see Regents of the Univ. of Cal. v. Broad Inst., Inc.*, No. 106,115, 2022 WL 1664028, at *16 (P.T.A.B. Feb. 28, 2022) ("*Final Decision*"). On April 11, 2012, Jinek emailed Doudna an invention disclosure form describing various techniques for editing eukaryotic DNA using one of two methods, "microinjection" or expression "vectors," in various types of eukaryotic cells. J.A. 65628–31, 65643–51. After these initial plans, Regents filed its first provisional patent application, "P1" (U.S. Patent App. No. 61/652,086), on May 25, 2012.

Regents' scientists then planned two specific experiments. First, leading up to May 28, 2012, Jinek wrote notebook entries describing a plan to test the system's ability to edit eukaryotic DNA, using expression vector techniques with human cells. J.A. 69071–77, 67284–85 (Jinek testifying that he "started" these notebook entries "before May 28, 2012"). Second, on June 28, 2012, Charpentier and Krzysztof Chylinski, another Regents scientist, exchanged emails with two scientists from another laboratory, Florian Raible and Kristin Tessmar, describing a

second plan to test the system using microinjection techniques in "two well-established fish systems": zebrafish and medaka fish. J.A. 66308, 66311–13.

B. Testing the System

1. Tests by Other Scientists

Around the time Regents' scientists drew up their plans, Regents' scientists made public announcements in June 2012, describing the single RNA CRISPR-Cas9 system in a conference presentation at the University of California, Berkeley ("2012 Berkeley Conference Presentation") and an article in *Science*. J.A. 65907, 65915, 65929–34 (Krzysztof Chylinski & Martin Jinek, "A programmable dual RNA-guided DNA endonuclease in a Type II CRISPR system," Presentation at the University of California, Berkeley, June 2012); Jinek 2012.

Over the remainder of 2012, scientists from laboratories outside of Regents, including scientists at Broad, attempted to use the system to edit DNA in eukaryotic cells. Of these laboratories outside Regents, five reported success from July to December 2012, using expression vector or microinjection techniques. J.A. 53203–06, 15794–807, 79043–44, 47104–27, 75072–95, 75935–58, 76553–56. Regents claims these other scientists learned of the single RNA CRISPR-Cas9 system from Regents' scientists' June 2012 presentation or article. Appellant Br. 15–18.

One of these other laboratories was run by Feng Zhang, a scientist at Broad. Learning of the CRISPR-Cas9 system on June 26, 2012, Zhang immediately planned tests using the system to edit eukaryotic DNA.[3] J.A. 75005–07. His

[3] According to Regents, Zhang learned of the single RNA CRISPR-Cas9 system from another scientist, Luciano Marraffini. Appellant Br. 15. Regents notes Marraffini

plans described use of Regents' scientists' sgRNA, chimera A, with another Cas9 system of his own design, as well as expression vector techniques he asserts to have already developed. J.A. 74999, 75002, 75024–66. Zhang claims that, on July 20, 2012, he directed the implementation of his plan on mouse cells. J.A. 75066–72; *see also* J.A. 75920–35. He further claims that he soon recognized that the July 20, 2012 test showed that his Cas9 system successfully edited the mouse DNA. J.A. 75073–91; *see also* J.A. 75935–58. Zhang claims he then directed repetition of the experiment and subsequently recognized successful editing by July 31, 2012. J.A. 75073–91. On October 5, 2012, Zhang submitted these results to *Science*, which published them on January 3, 2013. J.A. 77018–53, 75012–16.

2. Tests by Regents' Scientists

During the time Zhang and others conducted their experiments, Regents' scientists performed tests which, according to Regents' scientists, implemented their two specific plans, as described above. From July through September 2012, Regents' scientists conducted microinjection tests in fish embryos, purportedly based on the June 28, 2012 emails between Charpentier, Chylinski, Raible, and Tessmar. Concurrently, from July through October 2012, Regents' scientists conducted expression vector tests in

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was a peer reviewer on Regents' scientists' manuscript in *Science* and emailed a diagram and description of chimera A to Zhang on June 26, 2012, stating the CRISPR-Cas9 system "would be an important tool for genome editing in eukaryotes specifically." Appellant Br. 15–16 (citing J.A. 77492 and quoting J.A. 80012 (68:13–21)). Broad and Zhang claim Marraffini learned of the single RNA CRISPR-Cas9 system from the 2012 Berkeley Conference Presentation, not the peer review process. Cross-Appellant Br. 17; J.A. 75052–53.

human cells, purportedly based on the notebook entries that Jinek had written before May 28, 2012.

a. Microinjection Tests in Fish Embryos

Regents' scientists began their microinjection experiments before they began their expression vector experiments. According to Chylinski, Raible and Tessmar were to perform the microinjection tests in zebrafish and medaka fish, respectively.[4] J.A. 67210. Raible claims that he conducted the first microinjection test in zebrafish on July 19, 2012, and that this test did not yield the eyeless mutation expected from editing. *Final Decision*, 2022 WL 1664028, at *7 (citation omitted). Raible further claims that he performed a second set of tests on August 8, 2012, and that one of these tests yielded "one of roughly 30 embryos" with the "characteristic eyeless morphological phenotype expected" from successful editing. J.A. 67122–23. According to Raible and Chylinski, the two met to discuss the results the next day, August 9, 2012. J.A. 67122–23, 67214–15. The same day, Chylinski emailed Charpentier to report "[p]otentially good news about fish" and to indicate that additional changes to the tests "might work but we shouldn't be overexcited now." *Final Decision*, 2022 WL 1664028, at *8 (citation and quotations omitted); *see* J.A. 67214–15.

On August 31, 2012, Chylinski emailed Charpentier and another colleague with slides reporting further details of the results from Raible's August 8, 2012 test. J.A. 68372–73; *see* J.A. 67215. One slide, entitled "[f]ish experiment results," reported a "[s]mall amount of putative mutants (1 in 30-50) seen in some of the experiments." J.A. 68381. These mutants included "'[l]ess green' embryos

[4] Tessmar's tests in medaka fish are briefly referenced in the decision below and not well documented in the Joint Appendix. Accordingly, we do not discuss them here.

for Medaka" and "no eyes or misdeveloped eyes for Zebrafish." *Id*. However, the slide stated that these mutants "might be unspecific," i.e., not due to editing. *Id*.; *see Final Decision*, 2022 WL 1664028, at *9. The slide concluded by noting that "[e]xperiments are still being repeated." J.A. 68381.

Raible claims these results "show[ed] successful cleavage [i.e., editing] in a eukaryote using only routine techniques." J.A. 67128. Accordingly, Raible claims that he attempted to prove the "efficiency of CRISPR-Cas9" for editing eukaryotic DNA by conducting at least two more tests before ending his experimentation on September 12, 2012. J.A. 67128; *Final Decision*, 2022 WL 1664028, at *13 (citation omitted).

b. Expression Vector Tests in Human Cells

While testing with microinjection in fish embryos, Regents' scientists began simultaneously testing with expression vectors in human cells. A graduate student claims that Doudna and Jinek directed him to conduct expression vector experiments in human cells, starting in early July 2012. J.A. 67467. On August 10, 2012, the student sent an email reporting the results of tests conducted on July 31 and August 9, 2012. J.A. 67385–86 (citation omitted). That day, Doudna replied, copying Jinek and stating that the results of the August 9, 2012 test presented "very exciting" evidence of successful DNA editing. J.A. 67387 (citation and quotations omitted). By August 13, 2012, Jinek replied, agreeing that the results were "really exciting." J.A. 67302 (citation and quotations omitted). Regents' scientists claim that Doudna and Jinek instructed the student to conduct further experiments with some modifications related to the guide RNA. J.A. 67302, 67387–88, 67499.

After further experiments, on August 16, 2012, the graduate student sent an email to Doudna and Jinek reporting that his most recent results contained no evidence of editing. J.A. 68467. Under the Regents' scientists'

direction, the student continued experimentation in August and September 2012, using another expression vector technique for some of these additional tests. J.A. 67488–99. In a September 14, 2012 email, the student again reported no evidence of editing. J.A. 68085. Doudna responded, instructing the student to "simply repeat[] the original experiment" with one modification, to ensure the promising results from August 9, 2012 were "reproducib[le]" before changing other "variables." J.A. 68081. Doudna also suggested an adjustment to the expression vector technique. *Id.*

In late September 2012, according to Regents' scientists, Doudna and Jinek asked another graduate student to take over the expression vector tests. J.A. 67315, 67520. Both students initially collaborated to replicate the August 9, 2012 experiment, but, in emails dated October 10, 2012, the students reported no evidence of editing. J.A. 67520, 69442, 69428. The next day, Doudna replied, characterizing the latest results as "disappointing" and questioning if there needed to be further changes to the expression vector techniques or the "assembly and localization" of the single RNA CRISPR-Cas9 system itself. J.A. 69428, 69439 (referring to "the design and expression of the guide RNA" and suggesting this "may be the culprit"). Doudna informed the students that she and Jinek would "be in touch soon about next steps." J.A. 69439. Later that same day, Jinek emailed Doudna, "suspect[ing] we have a problem" with the expression vector techniques or the "RNA design per se." J.A. 87705. Over email, Doudna and Jinek agreed "[i]t would be great to test some alternate designs of the guide RNA" and to "discuss further tomorrow." J.A. 87705, 67065.

According to Doudna, she and Jinek instructed the two graduate students to continue trying to replicate the August 9, 2012 test. J.A. 67396–97 (citations omitted). On October 19, 2012, Regents filed a second provisional application, "P2" (U.S. Patent App. No. 61/716,256). Doudna

claims that, on October 29, the second student reported evidence of successful editing, and, soon after, reported replication of this result. J.A. 67397–400 (citations omitted).

II.

Throughout their research efforts, Regents and Broad filed patent applications relating to CRISPR technology. Both Regents and Broad claimed in those applications to be the inventor of the CRISPR technology at issue here, and, as a result, the Patent Trial and Appeal Board ("Board") declared Interference No. 106,115 ("'115 interference"), which is the subject of this appeal.[5] The '115 interference covers Count 1, which recites claim 18 of U.S. Patent No. 8,697,359 or claim 156 of U.S. Patent Application No. 15/981,807. *Final Decision*, 2022 WL 1664028, at *4–5. Claim 18 of the '359 patent recites:

> 18. The CRISPR-Cas system of claim 15, wherein the guide RNAs comprise a guide sequence fused to a tracr sequence.

Id. at *4. Claim 15 of the '359 patent recites:

> 15. An engineered, programmable, non-naturally occurring Type II CRISPR-Cas system comprising a Cas9 protein and at least one guide RNA that targets and hybridizes to a target sequence of a DNA molecule in a eukaryotic cell, wherein the DNA molecule encodes and the eukaryotic cell expresses at least one gene product and the Cas9 protein cleaves the DNA molecules, whereby expression of the at least one gene product is altered; and,

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[5] This court previously affirmed the Board's termination of a separate interference proceeding that involved the same parties. *See Regents of the Univ. of Cal. v. Broad Inst., Inc.*, 903 F.3d 1286, 1289 (Fed. Cir. 2018).

> wherein the Cas9 protein and the guide RNA do not naturally occur together.

Id. at *4. Claim 156 of the '807 application recites:

> 156. A eukaryotic cell comprising a target DNA molecule and an engineered and/or non-naturally occurring Type II Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) —— CRISPR associated (Cas) (CRISPR-Cas) system comprising
>
> a) a Cas9 protein, or a nucleic acid comprising a nucleotide sequence encoding said Cas9 protein; and
>
> b) a single molecule DNA-targeting RNA, or a nucleic acid comprising a nucleotide sequence encoding said single molecule DNA-targeting RNA; wherein the single molecule DNA-targeting RNA comprises:
>
> i) a targeter-RNA that is capable of hybridizing with a target sequence in the target DNA molecule, and
>
> ii) an activator-RNA that is capable of hybridizing with the targeter-RNA to form a double-stranded RNA duplex of a protein-binding segment,
>
> wherein the activator-RNA and the targeter-RNA are covalently linked to one another with intervening nucleotides; and
>
> wherein the single molecule DNA-targeting RNA is capable of forming a complex with the Cas9 protein, thereby targeting the Cas9 protein to the target DNA molecule, whereby said system is capable of cleaving or editing the target DNA molecule or modulating transcription of at least one gene encoded by the target DNA molecule.

Id. at *4–5.

Each party filed preliminary motions before the Board, three of which are relevant to this appeal: two from Broad and one from Regents. Before ruling on the parties' preliminary motions, the Board addressed a claim construction dispute about the claim term "guide RNA." This term appears in most of Broad's claims and is relevant to both of Broad's motions. Broad argued that the term "guide RNA" is "generic," meaning it is not limited to a single- or dual-molecule RNA configuration. J.A. 33. The Board disagreed and determined that the broadest reasonable interpretation of the claim term "'guide RNA' encompasses only a single-molecule RNA configuration." *Id.* The Board subsequently addressed each of the parties' motions in turn.

First, Broad moved to change the interference count from Count 1, which covers CRISPR-Cas9 systems that use sgRNA, to Broad's proposed "generic" Count 2, which covers both single- and dual-molecule RNA configurations. J.A. 33–35. The Board determined Broad's proposed Count 2 included several additional, unexplained changes beyond the expansion from sgRNA to single- and dual-molecule RNA configurations. J.A. 35. For example, while Count 1 is directed to a system or a eukaryotic cell, Broad's proposed Count 2 is directed to a method. J.A. 35. The Board deemed Broad's lack of explanation for the additional changes a major defect and denied Broad's motion "on this basis alone." J.A. 35.

Second, Broad alternatively argued that if the Board denied its prior motion to change the count, the Board should remove certain claims from the interference proceeding. J.A. 41–42. Broad premised its alternative motion on the assumption that if the Board denied its prior motion, the Board must have determined that claims to eukaryotic CRISPR-Cas9 systems containing sgRNA are separately patentable from claims to single- and dual-molecule RNA configurations. The Board disagreed with Broad's assumption that the Board made a determination

about separately patentable inventions and clarified that it did not reach such a determination. J.A. 43. The Board asserted that it had denied Broad's prior motion because Broad failed to explain the reasons for its proposed changes to the count. *Id*. The Board determined that Broad's mistaken assumption led Broad to fail to make a persuasive argument showing that the claims it sought to remove from the interference proceeding did not correspond to Count 1. *Id*. (citing 37 C.F.R. § 41.207(b)(2)); J.A. 47–53. On this basis, the Board denied Broad's alternative motion.

Third, Regents moved to be accorded the benefit of the May 2012 filing date of its P1 application for purposes of determining priority.[6] J.A. 80. In the alternative, Regents argued that it should be accorded the benefit of the October 2012 filing date of its P2 application, or the January 2013 filing date of its third provisional patent application, "P3" (U.S. Patent App. No. 61/757,640). J.A. 105. The Board determined that neither P1 nor P2 were a constructive reduction to practice of Count 1 because neither satisfied the written description requirement of 35 U.S.C. § 112. J.A. 104–05. The Board determined that P3 was a constructive reduction to practice of Count 1 because P3 sufficiently described and enabled an embodiment of Count 1. J.A. 106–07. Accordingly, the Board denied Regents' motion with respect to P1 and P2 but granted it with respect to P3. J.A. 107.

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[6] In an interference proceeding, a party may be accorded the benefit of the filing date of its patent application if that application is a constructive reduction to practice of at least one embodiment within the count of the interference. *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1362 (Fed. Cir. 2006). A constructive reduction to practice must be a described and enabled (pursuant to 35 U.S.C. § 112) anticipation of the subject matter of the count. 37 C.F.R. § 41.201.

As a result of the Board's resolution of the parties' preliminary motions, the Board designated Regents as the junior party and Broad as the senior party for purposes of the priority phase of the interference proceeding. J.A. 109. The interference proceeding continued under Count 1.

The Board determined Broad is entitled to priority over Regents with respect to Count 1. *Final Decision*, 2022 WL 1664028, at *1. The Board decided Broad reduced to practice by October 5, 2012, when Zhang submitted the manuscript to *Science*.[7] *Id*. at *33. The Board rejected Regents' earliest asserted date of reduction to practice of August 9, 2012, which was based on emails about Raible's second microinjection test.[8] *Id*. at *13–14. It further rejected Regents' earliest asserted date of conception on March 1, 2012, and later asserted dates through June 28, 2012, which were based on various disclosures: notebook entries, emails, and reports surrounding Regents' microinjection and expression vector tests. *Id*. at *24–26. Lastly, the Board rejected Regents' assertion that Broad "derived the system recited in Count 1 entirely from" Regents. *Id*. at *34–37.

Regents appeals the Board's decisions on conception and written description. Broad conditionally cross-appeals the Board's decision on claim construction. We have jurisdiction under pre-America Invents Act 28 U.S.C. § 1295(a)(4)(A). Technical Corrections—Leahy–

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[7] The Board did not evaluate Broad's asserted dates of actual reduction to practice or conception in July and August 2012, since it rejected earlier dates Regents asserted for conception and actual reduction to practice. *Id*. at *26.

[8] The Board did not decide Regents' other asserted dates of actual reduction to practice, since they postdated October 5, 2012, the date by which the Board determined Broad established actual reduction to practice. *Id*. at *14.

Smith America Invents Act, Pub. L. No. 112-274, 126 Stat. 2456, 2458 (2013).

STANDARD OF REVIEW

We set aside agency decisions if they are "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law, and we set aside factual findings that are unsupported by substantial evidence." *Falkner*, 448 F.3d at 1363 (citations omitted). Substantial evidence is "such relevant evidence as a reasonable mind might accept as adequate to support a conclusion." *Consol. Edison Co. v. NLRB*, 305 U.S. 197, 229 (1938). We review questions of law de novo. *Falkner*, 448 F.3d at 1363.

"Conception and inventorship are ultimately questions of law that we review *de novo*[.]" *In re VerHoef*, 888 F.3d 1362, 1365 (Fed. Cir. 2018), *as amended* (May 7, 2018). Conception and inventorship are premised on underlying fact findings that we review for substantial evidence. *Id*. Written description is a question of fact that we review for substantial evidence. *Falkner*, 448 F.3d at 1363.

DISCUSSION

I. Conception

Conception is defined as "the formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is hereafter to be applied in practice." *Burroughs Wellcome Co. v. Barr Lab'ys, Inc.*, 40 F.3d 1223, 1228 (Fed. Cir. 1994). "Conception is complete only when the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation." *Id*.

A.

The Board determined that Regents did not prove conception of the invention prior to Broad's actual reduction to practice on October 5, 2012, because Regents' scientists did

not know their CRISPR-Cas9 system would produce the effects on genes in a eukaryotic cell recited in Count 1. *Final Decision*, 2022 WL 1664028, at *14–26, *33–37. Regents argues the Board legally erred by requiring Regents' scientists to know that their invention would work. Appellant Br. 30–44. We hold that the Board legally erred by conflating the distinct legal standards for conception and reduction to practice.

There are three stages to the inventive process: (1) conception, (2) reasonable diligence, and (3) reduction to practice. *Mahurkar v. C.R. Bard, Inc.*, 79 F.3d 1572, 1577 (Fed. Cir. 1996). At the conception stage, it is well-established that "an inventor need not know that his invention will work for conception to be complete." *Burroughs*, 40 F.3d at 1228. Knowledge that the invention will work, "necessarily, can rest only on an actual reduction to practice." *Applegate v. Scherer*, 332 F.2d 571, 573 (CCPA 1964); *see also Univ. of Pittsburgh of Commonwealth Sys. of Higher Educ. v. Hedrick*, 573 F.3d 1290, 1299 (Fed. Cir. 2009) ("Proof that the invention works to a scientific certainty is reduction to practice."). The Board therefore legally erred by requiring Regents' scientists to know their invention would work to prove conception.

B.

The Board relied almost exclusively on Regents' scientists' statements expressing uncertainty about whether the experiments had succeeded and suggesting modifications to their CRISPR-Cas9 system to conclude that they did not have a "definite and permanent idea." *Final Decision*, 2022 WL 1664028, at *22–26 (citing *Burroughs*, 40 F.3d at 1229–30). Regents argues that the Board legally erred by focusing on those statements without considering whether Regents' scientists actually and substantively modified the system. Appellant Br. 30–44. We agree.

Burroughs distinguished between "factual uncertainty . . . that bears on the problem of conception" and

"general uncertainty surrounding experimental sciences." 40 F.3d at 1229. Factual uncertainty is when "the subsequent course of experimentation, especially experimental failures, reveals uncertainty that so undermines the specificity of the inventor's idea that it is not yet a definite and permanent reflection of the complete invention as it will be used in practice." *Id.* "[W]hat matters for conception is whether the inventors had a definite and permanent idea of the operative inventions," as evidenced in *Burroughs* by the fact that "no prolonged period of extensive research, experiment, and modification followed the alleged conception." *Id.* at 1230. The Board therefore legally erred by focusing on Regents' scientists' statements of uncertainty, without considering whether those statements led to modifications in their experiments that substantively changed their original idea, when determining whether they had a "definite and permanent idea." *See id.*

C.

Regents argues the Board erred by failing to consider whether scientists at Regents or elsewhere were able to successfully experiment on Regents' scientists' idea using only "routine skill" or "routine techniques." Appellant Br. 35–41. Instead, Regents argues, the Board improperly "focused solely on [Regents'] purported struggles in reducing its invention to practice" and related statements of doubt, taking a "singular focus on inventor success." *Id.* at 35, 37–40.

The key question here is "whether [Regents' scientists] had formed the idea of [the invention's] use for [its intended] purpose in sufficiently final form that only the exercise of *ordinary skill* remained to reduce it to practice" "without extensive research or experimentation." *Burroughs*, 40 F.3d at 1228, 1231 (emphasis added). Third-party evidence of experimental difficulties is relevant to this inquiry. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1207 (Fed. Cir. 1991) (in determining there was no

conception, noting that "several companies, as well as Amgen and GI, were unsuccessful"). So, too, is third-party evidence of experimental success using routine skill or methods. *Brand v. Thomas*, 96 F.2d 301, 303 (CCPA 1938).

Also relevant is whether an *alleged inventor* contemplated the use of routine skill or methods at an asserted conception date, or used such routine skill or methods during subsequent, successful experimentation conducted by the alleged inventor. In *Burroughs*, we credited alleged inventors' "normal course of clinical trials that mark the path of any drug to the marketplace" to "confirm[]" that "only the exercise of ordinary skill remained to reduce [the invention] to practice." 40 F.3d at 1229–31. *Burroughs* cited *MacMillan v. Moffett*, which determined that the success of "standard" tests contemplated by an alleged inventor at an asserted date indicated that he had "thought specifically about" the use of "available" methods to produce the claimed invention. 432 F.2d 1237, 1238–39 (CCPA 1970); *see also Lazo v. Tso*, 480 F.2d 908, 910–11 (CCPA 1973) (crediting an alleged inventor's "master plan" at an asserted date, which he then used to obtain "encouraging results" with a "basic concept of testing").

The Board erred in its analysis by failing to consider routine methods or skill, and, instead, focusing almost entirely on Regents' scientists' statements about perceived experimental difficulties and doubts about success. First, the Board legally erred by expressly refusing to consider whether a person of ordinary skill in the art could have reduced the invention to practice. The Board decided it was insufficient that Regents' disclosures only described "the mechanics of a CRISPR-Cas9 system" and determined that it was not enough for Regents' scientists to have "conceived of the *mechanics* of" the system; they must have had an "*operative* invention." *Final Decision*, 2022 WL 1664028, at *26 (emphases added).

The Board relied on *Hitzeman v. Rutter* for the conclusion that "[w]e do not base our decision on a lack of reasonable expectation of success by [Regents' scientists as persons 'of at least ordinary skill'] that the system would be capable of editing DNA in a eukaryotic cell," and that "we are not persuaded by either party's evidence of what those [skilled] in the art expected at the time." *Id.* at *24–26 (citing 243 F.3d 1345, 1358–59 (Fed. Cir. 2001)). In *Hitzeman*, we found that a "bare hope" of a result "never before . . . achieved" is not sufficient to establish conception. 243 F.3d at 1357. We arrived at this conclusion because "Hitzeman chose to claim the invention by reciting the particular result of an intracellular process," for which there was no method known by skilled artisans or contemplated by Hitzeman that would achieve that result. *Id.* at 1356–57 ("[I]t appears that Hitzeman remained unclear for at least two years after reducing his invention to practice as to how the particles are formed in yeast."). We concluded that

> the critical deficiency is that Hitzeman specifically claimed the result of a biological process (i.e., the expression by yeast of the S-protein, followed by the assembly of the S-protein into particles) with no more than a hope, or wish, that yeast would perform this assembly process that had never before been achieved in yeast.

Id. Thus, we held that "complete conception has not occurred" if "a research plan requires extensive research before the inventor *can* have a reasonable expectation that the limitations of the count will actually be met." *Id.* at 1357 (emphasis added). To determine whether an alleged inventor "can" reasonably expect reduction to practice, the court considered the reasonable expectation of *a person of ordinary skill in the art*. *Id.* We focused on whether "[o]ne skilled in the art at the time" of asserted conception would "have been able to reasonably predict" that experimentation would produce the claimed result.

Id. (citation and quotations omitted) (also considering whether experimentation would be "reasonably predictable").

Unlike in *Hitzeman*, the claim limitations at issue do not describe *the result* of using the single RNA CRISPR-Cas9 system in a eukaryotic cell, but rather "a single RNA CRISPR-Cas9 system that *functions* in eukaryotic cells." *Final Decision*, 2022 WL 1664028, at *2 (emphasis added). The Board erred by refusing to consider whether a person of ordinary skill could have achieved the *function* of editing eukaryotic DNA. *See id*. at *24–26. The appropriate analysis should turn on whether Regents' scientists "had formed the idea of their use for that purpose in sufficiently final form that only the *exercise of ordinary skill* remained to reduce it to practice"—more than a "general hope," but less than knowing with certainty that the invention would work. *Burroughs*, 40 F.3d at 1230–31 (emphasis added).

Second, the Board legally erred in failing to consider evidence of purported experimental success by others presented on the record. *See Amgen*, 927 F.2d at 1206–07. For example, the Board acknowledged Regents' argument that, despite difficulties, "in the end only routine materials and techniques, as described by" Regents' scientists, "were required for a sgRNA CRISPR-Cas9 that can edit DNA in eukaryotic cells." *Final Decision*, 2022 WL 1664028, at *25. Elsewhere, the Board rejected Regents' "attempts to shift our focus to the activities of other, competing inventors, rather than the activities of its own inventors." *Id*. at *34. It was legal error for the Board to categorically disregard evidence of purported experimental success by others.

Third, the Board legally erred by failing to consider whether Regents' scientists described routine methods or skill in their disclosures at asserted conception dates, and whether they used routine methods or skill in subsequent, purportedly successful experiments. *See Burroughs*, 40 F.3d at 1229–31; *MacMillan*, 432 F.2d at 1238–39. The

Board determined that Regents did not "directly address" Broad's argument that Regents' scientists' emails during the experiments in human cells showed that Regents' scientists "had to redesign their components and strategy beyond what would have been routine techniques for one of ordinary skill in the art." *Final Decision*, 2022 WL 1664028, at *21–22. Later, the Board addressed Regents' argument that Regents' scientists "had the materials" (i.e., the single RNA CRISPR Cas9 system and routine techniques for eukaryotic DNA editing) that were eventually used to achieve "one unrecognized positive result" in the zebrafish experiments on August 8, 2012, and to achieve alleged actual reduction to practice in the human cell experiments by October 31, 2012. *Id*. at *24. The Board determined that Regents' scientists "engaged in a 'prolonged period of extensive research, experiment, and modification' following the alleged conception on 1 March 2012," during which Regents' scientists encountered "several failures with zebrafish embryos and several months of failed experiments and doubt with human cells." *Id*. (quoting *Burroughs*, 40 F.3d at 1230). The Board went on to conclude that, "[g]iven that the scientists performing these experiments were of at least ordinary skill," these perceived failures and doubts showed that Regents' scientists' "idea" was "not yet a definite and permanent reflection of the complete invention *as it [would] be used in practice*." *Id*. (quoting *Burroughs*, 40 F.3d at 1229) (quotations omitted) (emphasis added). While the Board mentioned Regents' argument that only routine techniques were necessary to achieve reduction to practice, the Board did not actually consider whether, despite subsequent, perceived difficulties and doubts, Regents' scientists described routine methods or skill at the asserted conception dates and used those methods or that skill to achieve purported successes during subsequent experimentation. This constitutes legal error.

In its analysis, the Board assumed that an alleged inventor's experimental difficulties must indicate that a

skilled artisan could not have carried out the invention without undue experimentation. *Final Decision*, 2022 WL 1664028, at *24 (citing *Burroughs*, 40 F.3d at 1230). The Board determined that conception in this case was not complete due to extensive experimentation, despite acknowledging Regents' argument that Regents' scientists had "described" "routine materials and techniques" and then used them to successfully "edit DNA in eukaryotic cells." *Final Decision*, 2022 WL 1664028, at *24, *25. However, we have held that "the existence of research or experimentation does not necessarily indicate, by itself, that complete conception did not exist," and that there must be a "nexus between the research or experimentation and the subject for which patent protection is sought." *Sewall v. Walters*, 21 F.3d 411, 415 n.3 (Fed. Cir. 1994) (citing *Bac v. Loomis,* 252 F.2d 571, 577 (CCPA 1958)). In *Rey–Bellet v. Engelhardt*, our predecessor court determined that there was conception, partly due to an absence of "extensive research," but mainly because a disclosure offered as corroboration required only "routine skill." 493 F.2d 1380, 1387 (CCPA 1974). There, the Board failed to consider that "the extent of testing or other research done after the mental formulation of an invention is not a reliable indicator that ['perplexing intricate difficulties'] . . . have been encountered" that show a skilled artisan could not have reduced the invention to practice. *Id*. (citing *Alpert v. Slatin*, 305 F.2d 891, 894 (CCPA 1962)). In this case, the Board erred in determining that Regents' scientists' experimentation was extensive or undue, without asking whether Regents' scientists described the use of routine methods or skill at asserted conception dates, or later used routine methods or skill to successfully edit eukaryotic DNA.

In sum, the Board erred by failing to consider routine methods or skill, focusing almost entirely on Regents' scientists' perceived experimental difficulties and related statements of doubt. We thus vacate the Board's decision on conception and remand for the Board to decide on

conception under the proper application of the legal framework.[9] On remand, the later party to reduce to practice will have the opportunity to show, under a conception date established by the correct standard, either (1) it was "the first to conceive of the invention and that it exercised reasonable diligence in later reducing that invention to practice," *Cooper v. Goldfarb*, 154 F.3d 1321, 1327 (Fed. Cir. 1998), or (2) it had "prior conception of the claimed subject matter and communication of the conception to the adverse claimant." *Price v. Symsek*, 988 F.2d 1187, 1190 (Fed. Cir. 1993).

II. Written Description

We turn next to Regents' challenge to the Board's written description determination. In resolving Regents' preliminary motion, the Board determined that Regents' P1 and P2 applications lacked written description support for Count 1, which covers a single RNA CRISPR-Cas9 system that functions in eukaryotic cells. Regents argues the Board applied the wrong legal standard for written description by requiring the P1 application to "convince" a person of ordinary skill in the art that the invention will work in eukaryotes.[10] Appellant Br. 55–56, 60–66. Regents also

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[9] Regents also raises an Administrative Procedure Act ("APA") challenge to the Board's conception analysis. Appellant Br. 47–54. We need not resolve that challenge because we have determined that vacatur and remand are warranted as to the Board's conception analysis.

[10] Although Regents argues in passing that its P2 application also includes adequate written description support, Regents does not challenge the Board's written description determination for its P2 application on any separate grounds from its challenge to the Board's determination for its P1 application. Appellant Br. 57. We thus only address P1 for the remainder of this section. *See Trading*

separately argues that the Board's written description analysis violates the reasoned decision-making requirement of the APA. Appellant Br. 47, 54–55. We address each argument in turn.

Turning to Regents' first argument, Regents argues the Board applied the wrong legal standard for written description. Specifically, Regents argues the Board legally erred by rejecting P1's identification of the essential components of the CRISPR-Cas9 complex of Count 1, its explanation of why the complex works, and its explanation of how to use the complex in eukaryotes. Appellant Br. 56. Instead, according to Regents, the Board required the P1 application to "convince" a person of ordinary skill in the art that the invention will work in eukaryotes despite obstacles raised by Broad. Appellant Br. 55–56, 60–66. We disagree with Regents that the Board legally erred.

Section 112 of the Patent Act provides that a patent specification must contain a written description of the invention. 35 U.S.C. § 112(a). To satisfy the written description requirement, a patent's disclosure must "clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (alteration in original) (citations omitted). That is, the test for sufficiency is whether the disclosure "reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* (citations omitted). This test and its concept of possession requires us to determine how a person of ordinary skill in the art would understand the four corners of the specification. *Id.*

Techs. Int'l, Inc. v. IBG LLC, 921 F.3d 1378, 1385 (Fed. Cir. 2019) ("[A] conclusory assertion with no analysis is insufficient to preserve the issue for appeal." (citation omitted)).

Key to this appeal is the well-established principle that "the level of detail required to satisfy the written description requirement varies depending on the nature and scope of the claims and on *the complexity and predictability of the relevant technology*." *Id.* (emphasis added) (citation omitted). When the technology at issue is "complex" and "highly unpredictable," as is the case here, the level of detail required to satisfy the written description requirement may be greater.[11] *See, e.g.*, J.A. 91, 103; *Ariad*, 598 F.3d at 1351. Nonetheless, it is also well-established that working examples or an actual reduction to practice are not necessary to satisfy the written description requirement. *Ariad*, 598 F.3d at 1352.

Contrary to Regents' arguments, the Board did not require P1 to convince a person of ordinary skill in the art of the success of Regents' invention. The Board correctly analyzed whether a person of ordinary skill in the art would understand that Regents had possession of the claimed subject matter, given the Board's uncontested determination that the subject matter at issue is highly unpredictable and complex. *See* J.A. 103. The Board determined that at the time of filing in 2012, a person of ordinary skill in the art would have been aware of the complexities and the unpredictable nature of adapting prokaryotic systems to eukaryotic cells. J.A. 88–91. Given that the P1 applicants failed to disclose specific instructions or conditions necessary for CRISPR-Cas9 activity in a eukaryotic cell, or an indication that no specific instructions or conditions were necessary, the Board ruled that a person of ordinary skill in the art would not understand P1 to show or establish possession. J.A. 91. In so ruling, the Board properly tailored its analysis to the specific facts of this case, rather

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[11] Neither party challenges the Board's determinations about the complexity and predictability of the art on appeal.

than applying a one-size-fits-all approach. *Ariad*, 598 F.3d at 1351; *Capon v. Eshhar*, 418 F.3d 1349, 1357–58 (Fed. Cir. 2005). Each case must be decided in relation to the specific facts and circumstances presented, and that is what the Board did here.

We note that the Board inquired into whether P1 provided results of successful working examples. Yet the Board did not do so to determine whether P1 would convince a person of ordinary skill in the art that the invention would work. J.A. 103 (recognizing there is no "general requirement" to provide working examples or an expectation of success). Instead, the Board inquired about working examples as but one indication, in addition to others, of whether a person of ordinary skill in the art would understand P1 to establish possession despite the complex and unpredictable nature of the technology at hand. In doing so, the Board faithfully applied our precedent. *See Capon*, 418 F.3d at 1357–58; *see also LizardTech, Inc. v. Earth Res. Mapping, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005) (explaining that "only enough must be included to *convince* a person of skill in the art that the inventor *possessed* the invention" (emphasis added)). Both in form and in substance, the Board correctly assessed possession and thus did not commit legal error.

We turn next to Regents' APA challenge to the Board's written description analysis. Regents argues the Board's decision is arbitrary and capricious because in determining P1 lacks adequate written description support, the Board exclusively relied on doubts a person of ordinary skill in the art might have about using only one of the methods proposed by P1—expression vectors—to express the CRISPR-Cas9 system in eukaryotes. Appellant Br. 54. According to Regents, the Board never engaged with Regents' argument that P1's disclosure of microinjection, as an alternative method, would negate those doubts. *Id.* at 52. Regents says this is error because a person of ordinary skill in the

art would understand P1's disclosure of microinjection to establish possession. We disagree.

The APA requires agencies to follow a "logical and rational" process in reaching their decisions. *Allentown Mack Sales and Serv., Inc. v. NLRB*, 522 U.S. 359, 374 (1998). This requirement does not require an agency to "address every argument raised by a party or explain every possible reason supporting its conclusion." *Synopsys, Inc. v. Mentor Graphics Corp.*, 814 F.3d 1309, 1322 (Fed. Cir. 2016), *overruled on other grounds by Aqua Prods., Inc. v. Matal*, 872 F.3d 1290 (Fed. Cir. 2017) (en banc).

The Board's written description analysis satisfies the APA. The Board thoroughly considered both parties' arguments and the evidence supporting those arguments. J.A. 80–107. Many of the parties' arguments are not specific to expression vectors or microinjection. J.A. 82 (Broad arguing that "the unpredictable nature, well-known obstacles, and prior failures and difficulties in adapting prior art prokaryotic systems to eukaryotic cells" support that P1 lacks written description). And many of the Board's determinations stand independent of the specific method used, expression vectors or microinjection, to achieve the invention. J.A. 81 (Regents "does not direct us to a disclosure in P1 of results from a CRISPR-Cas system in any of these eukaryotic cells."). We see no indication that the Board limited its written description analysis to using expression vectors rather than microinjection, as Regents suggests. In the absence of any such indication, we cannot say that the Board's determinations are in fact limited to the use of expression vectors, nor can we say that the Board's decision is arbitrary or capricious. *See Regents of the Univ. of Minn. v. Gilead Scis., Inc.*, 61 F.4th 1350, 1358–59 (Fed. Cir. 2023).

III. Claim Construction

We turn to Broad's cross-appeal. The Board determined that the broadest reasonable interpretation of the

claim term "'guide RNA' encompasses only a single-molecule RNA configuration." J.A. 33. Broad argues that the Board's claim construction analysis is erroneous because the term "guide RNA" had a plain and ordinary meaning in the art at the time of filing, and Broad's patents do not define the term more narrowly. Cross-Appellant Br. 83–85. Regents argues Broad's cross-appeal is moot because the Board denied Broad's preliminary motions on independently sufficient grounds, unrelated to claim construction, that Broad does not challenge on appeal. Appellant Reply Br. 35, 43–48. Broad responds that the Board's claim construction necessarily impacted its decisions on Broad's preliminary motions. Cross-Appellant Reply Br. 26. We agree with Regents that Broad's cross-appeal is moot.

"The test for mootness is whether the relief sought, if granted, would make a difference to the legal interests of the parties." *Acceleration Bay LLC v. 2K Sports, Inc.*, 15 F.4th 1069, 1076 (Fed. Cir. 2021) (internal quotations and citations omitted). Thus, an issue is only moot when "it is impossible for a court to grant any effectual relief whatever." *Mission Prod. Holdings, Inc. v. Tempnology, LLC*, 587 U.S. 370, 376–77 (2019) (quoting *Chafin v. Chafin*, 568 U.S. 165, 172 (2013)).

Even if we agree with Broad that the Board's claim construction analysis was erroneous, we could not grant Broad any effectual relief. The Board's denial of Broad's preliminary motions would remain intact because both rulings were based on independently sufficient grounds for denial, irrespective of the Board's claim construction ruling. *Acceleration Bay*, 15 F.4th at 1076–77. For Broad's motion to change the count, the Board stated that it denied Broad's motion irrespective of claim construction. J.A. 35 (denying Broad's motion on the independent "basis alone" that Broad failed to explain all of its proposed changes to the count). For Broad's other, alternative motion, the Board determined Broad's *entire* motion was premised on the

incorrect assumption that the Board must have determined that claims to eukaryotic CRISPR-Cas9 systems containing sgRNA are a separately patentable invention from single- and dual-molecule RNA claims. J.A. 42–43. This assumption led Broad to fail to make any meaningful argument as to why *any* claims it sought to remove from the interference proceeding would not be anticipated or rendered obvious by Count 1, regardless of claim construction. J.A. 42–43, 51–53. Yet Broad chose to only appeal the Board's claim construction analysis. Because the relief sought would not have an impact on the legal interests of the parties, we must dismiss Broad's cross-appeal as moot.

CONCLUSION

For the above reasons, we affirm the Board's written description decision and dismiss Broad's cross-appeal as moot. We hold that the Board incorrectly applied the legal standard for conception. We vacate the Board's determination as to conception and remand for further proceedings. On remand, we instruct the Board to reconsider the issue of conception in a manner consistent with this opinion.

AFFIRMED-IN-PART, VACATED-IN-PART, AND REMANDED AS TO THE MAIN APPEAL DISMISSED AS TO THE CROSS-APPEAL

COSTS

No costs.