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PERSPECTIVE

A "Bare Hope of A Result": The Second CRISPR Patent Appeal

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Abstract

On May 12, 2025, the US Court of Appeals for the Federal Circuit issued its second decision in the long-running CRISPR patent dispute between the Regents of the University of California and related institutions (CVC) and the Broad Institute. This Perspective recounts the principal dispute to date, reviews the Federal Circuit's recent opinion, and provides a critique of its analysis. In particular, this Perspective highlights how the decision is self-contradictory and in tension with patent law's conception doctrine—when an inventor has formed a "definite and permanent" idea of an invention in the mind or whether the invention was little more than a "bare hope" of a result. This Perspective briefly concludes with the implications of this recent decision and where the underlying dispute is likely headed.

Introduction

On May 12, 2025, the US Court of Appeals for the Federal Circuit issued a long-anticipated decision in the patent interference proceedings between Feng Zhang of the Broad Institute on one side and the Nobel Prize winners Jennifer Doudna and Emmanuelle Charpentier and their related institutions on the other (often referred to as the CVC team: C, for the University of California, Berkeley; V for the University of Vienna, Austria; and C for Charpentier herself).[1] The decision—the second appeal about who was the first to invent to single-guide CRISPR-Cas9 genome editing in eukaryotic cells—reversed a 2022 decision from the Patent Trial and Appeal Board (PTAB) in favor of the Broad Institute.[2] The Federal Circuit's decision now sends the proceedings back to the PTAB to reassess whether the CVC group indeed first "conceived"—a particular term of art in patent law—using CRISPR-Cas9 to edit eukaryotic genomes back on March 1, 2012, the date Martin Jínek famously documented the technique in his laboratory notebook.

While the Federal Circuit did not decide anything on the substance of the parties' dispute, the opinion has the potential to dramatically change the fortunes of the CVC group, which, a Nobel Prize notwithstanding, had long suffered losing hands in its contest with the Broad Institute. Yet, the decision is legally problematic in many respects; principally, it makes a mess of patent law's conception doctrine, which requires inventors to have a "definite and permanent" idea of their complete invention in contrast to a "bare hope" of a successful result. Whether the PTAB will dutifully apply the Federal Circuit's new understanding of conception, whether the Federal Circuit decision will be subject to a rehearing of the full court, or whether the decision will be taken up by the Supreme Court remains to be seen. As such, achieving outright victory—for any party—likely remains years away. Meanwhile, both sides' patents continue to slowly expire, the earliest of which will lapse into the public domain in 2033.[3]

This Perspective briefly reviews the current state of the patent litigation between the parties, examines and critiques this most recent decision form the Federal Circuit, and discusses the implications of these proceedings.

The CVC vs. Broad Institute Dispute, to Date

The patent dispute between the Broad Institute and CVC—previously reviewed in this journal[4–6]—stems from a set of competing patent applications filed by the Broad Institute and CVC back in 2012, before US patent law transitioned from a first-to-invent to a first-to-file system. In brief, the Broad Institute's earliest patent application was granted before CVC's, even though CVC had filed its original application first. Under patent law's first-to-invent

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rules, this meant that the Broad Institute's patents "interfered" with the issuance of CVC's patent applications. To demonstrate that its researchers were the first inventors—and to claim the economic landscape for lucrative licensing deals in human therapies and agriculture—CVC petitioned the US Patent and Trademark Office to declare an interference proceeding, which it did, on January 11, 2016.[7]

On February 15, 2017—after more than a year of heated litigation between the two sides—the PTAB issued its first substantive decision in the case.[8] There, the PTAB determined that the Broad Institute's patents did not, in fact, interfere with CVC's patent applications because the Broad Institute's specific claims regarding eukaryotic editing were "patentably distinct," i.e., consisted of different inventions, from those claimed in CVC's patent applications. This meant that the Broad Institute could command lucrative licenses for eukaryotic genome editing. It also painted a narrative that while Doudna and Charpentier invented sgRNA CRISPR-Cas9 genome editing for *prokaryotic* cells, Zhang was the true inventor for *eukaryotic* ones.

CVC subsequently appealed to the Federal Circuit, which issued a decision on September 10, 2018,[9] vigorously affirming the PTAB's decision that eukaryotic versus prokaryotic editing was patentably distinct. The court concluded that, at least back in March 2012, CVC did not have a "reasonable expectation of success" that CRISPR-Cas9 genome editing would work in eukaryotic cells. To the contrary, it found that "the success in applying similar prokaryotic systems in eukaryotes was unpredictable and had relied on tailoring particular conditions to the technology."[9] At the time, the decision appeared to be an almost unmitigated loss for CVC, which faced the likelihood of being forced to narrow its patent applications to prokaryotic applications back at the Patent Office.

But litigation, like science, is sometimes touched by serendipity. Back at the Patent Office, and in front of a new patent examiner, CVC's earliest beleaguered patent application was granted in full—without any limits on whether it was directed to pro- or eukaryotes.[3] (The real reasons for this are not entirely clear.) Thus, CVC was now the owner of a patent claiming CRISPR-Cas9 genome editing in all cell types—including those that the Federal Circuit had, only months earlier, concluded CVC's inventors lacked a "reasonable expectation of success" over when the patent application was filed.

The examiner's decision triggered a second interference, the subject of the most recent appeal. And, following even more heated litigation between the parties, the PTAB concluded that CVC would not be entitled to use its earliest "proofs" that it conceived of the invention first. This included the now famous March 1, 2012, notebook page from Jínek detailing all of the common elements of CRISPR-Cas9 editing in a generic cell system.[2] CVC offered that it should be entitled to this date as its date of conception—when the inventors had a "definite and permanent idea" of their invention in mind.

Jínek's lab notebook, according to the PTAB, was followed by a series of failed experiments and dispiriting e-mail exchanges among CVC's collaborators that—in the PTAB's telling—cast doubt on whether the CVC inventors' recognition of their invention was "definite and permanent" enough for patent law's purposes. These included off-handed statements that the experiments were "disappointing," had "a problem," and that there was "no good news" about the results.[2] Instead, according to the tribunal, the inventors' engaged in a "prolonged period of extensive research, experiment, and modification" that "reflect(ed) uncertainty that so undermines the specificity of the inventor's idea that it (was) not yet a definite and permanent reflection of the complete invention as it [would] be used in practice."[2] Without the March 1, 2012, conception date, the interference was then poised to turn on which party first successfully edited eukaryotic genomes, a position that strongly favored the Broad Institute.

CVC then appealed to the Federal Circuit for a second time, arguing its case on May 7, 2024.

The Second Appeal

The Federal Circuit issued its decision on May 12, 2025, more than a year after it heard oral arguments. While the opinion also discussed several other issues surrounding the interference, the opinion primarily focused on the question of conception—whether the CVC team had a "definite and permanent" idea of CRISPR-Cas9 genome-editing in eukaryotes by March 2012. On this, the Federal Circuit concluded the PTAB had "legally erred by conflating the distinct legal standards for conception and reduction to practice,"[1] remanding the decision back to the PTAB to reconsider the evidence.

The Federal Circuit's opinion separated the act of invention into three sequential steps: conception, reasonable diligence in achieving the invention, and finally, reduction to practice. This formulation means that one cannot "conceive" of an invention that does not ultimately work; thinking up fantastical machines that defy the laws of thermodynamics, for example, is not conception. This is true no matter how fervently one *believes* their invention will eventually operate. As a result, the Federal Circuit faulted the PTAB's opinion for "requiring (CVC) scientists to know their invention would work to prove conception"[1]

by overly focusing on the scientists' statements of doubt following a series of negative results. The PTAB should have, in the Federal Circuit's analysis, focused on whether the CVC scientists needed to modify the basic principles laid out in Jínek's lab notebook. The PTAB's attention toward the scientists' "statements of uncertainty, without considering whether those statements led to modifications in their experiments"[1] was incorrect.

The Federal Circuit also chastised the PTAB for discounting the work of other scientists who were able to edit eukaryotic genomes once the principles of CRISPR-Cas9 editing were known. For the court, this concerned whether Jínek's account of CRISPR-Cas9 genome editing was "definite and permanent" *enough* or merely a "bare hope" of a result "never before achieved."[1] Anyone who has worked with finicky equipment or sensitive enzymes can attest to how fine this line can be. But, in patent law, the line separates invention from "a research plan (that) requires extensive research before the inventor can have reasonable expectation that the limitations will actually be met."[1] The court analogized this to whether CVC's invention was merely the biological "result" of its experiments—and, therefore, more like a mere "hope" of success—versus the "function" of its technique—supposedly, more like a true invention.

With these instructions, the Federal Circuit sent the matter back to the PTAB to determine whether "(1) (CVC) was 'the first to conceive of the invention and that it exercised reasonable diligence in later reducing that invention to practice' . . . or (2) it had 'prior conception of the claimed subject matter and communication of the conception to the adverse claimant,'" a not-so-subtle dig at the Broad Institute's position.

Whither Conception?

Afforded more than a year of contemplation, one would think the Federal Circuit's recent opinion would be a model of judicial craft. But the opinion has little to commend it. It is internally contradictory, almost hopelessly so. It makes the same errors, in parts, that it complains the PTAB of having made, namely, grossly confusing conception with reduction to practice. And it seems to violate precedent—the prior 2018 decision in the CRISPR-Cas9 patent dispute.

First, it is hard to reconcile the decision's acknowledgement that CRISPR-Cas9—at least back in 2012—was "complex" and "highly unpredictable" with other statements in the opinion that eukaryotic genome editing could be achieved with nothing more than "routine skill." That may be so; it is what makes CRISPR such an attractive tool for researchers. But that is a miracle of biology, not evidence of researchers' expectations back in 2012. And it is those expectations—not biological fortuity—that go toward the conception inquiry.

Second, and relatedly, that same line of reasoning itself conflates conception with reduction to practice—precisely the error the Federal Circuit faulted the PTAB for having made. Conception, in patent law, has always focused on what was going on in an inventor's mind—the act of human imagining.[10] Reduction to practice, meanwhile, is about what was done. Conception is about the brain; reduction to practice is about the hands. Thus, whether an invention *was* achieved with routine skill or whether modifications *were* ultimately needed—things the Federal Circuit faulted the PTAB for not paying enough attention to—tells us nothing about what was going on in the minds of the CVC team. And whether *other* scientists could achieve eukaryotic genome-editing similarly does not inform us about what, exactly, was going on in Jínek's head the day he detailed the workings of CRISPR-Cas9 in ink.

Even then, the success or failure of other scientist is asymmetrically informative about conception. If an inventor thinks that an invention will work and others dutifully achieve it, there is good reason to think an act of patentable conception occurred. If an inventor doubts an invention will work—and others in the field do, too—there is similarly good reason to think that, at the time, an act of invention had yet to occur. But if an inventor harbors doubts about an invention that others actually get to work, that tells us little about an inventor's state of mind—namely, whether the inventor "recognized and appreciated" the invention as such. Indeed, there is a long line of cases going back at least 80 years—none of which the Federal Circuit touches—rejecting earlier conception dates where there was success by others but no "recognition and appreciation of the invention" by the inventor.[11] This is not to say that the CVC team did not appreciate the significance of their invention—they surely did. Rather, only that the PTAB was correct to discount what other scientists were *doing* as evidence of what the CVC team was *thinking*.

This reasoning also obscures the object of conception—that is, what a putative inventor is supposed to have a definite and permanent idea *of*. The opinion, in recounting a previous case, *Hitzeman v. Rutter*[12]—the one that articulated the "bare hope" standard—tried to distinguish it by separating inventions that turned on biological "results" versus those that claimed biological "functions." But this distinction is exactly as untenable as it sounds. Is CRISPR-Cas9 genome editing a patently impermissible "result" of Cas9 paired with a guide RNA or a patentable "function" of the RNA-enzyme complex? The standard is hopelessly confusing, complete nonsense that will do nothing to guide the Patent Office or future inventors.

Lastly, the opinion also contradicts the court's previous one about CRISPR. The first CRISPR opinion concluded that eukaryotic genome editing was separately patentable over prokaryotic genome editing because the CVC inventors had no reasonable expectation of success of getting the invention to work in eukaryotes back in 2012. But this more recent opinion tasks the PTAB's *conception* analysis—again, what was going on in the CVC inventors' heads—with whether the scientists were able to eventually get the technique to work with routine materials and methods. It seems contradictory here too to say both that CVC had no reasonable expectation of success in editing eukaryotic cells but did have a definite and permanent idea of editing such cells with routine materials and methods. If there is daylight between those two conclusions, it is a fine sliver indeed.

Going Forward

The next few months will tell us whether the case is, in fact, headed back to the PTAB or instead subject to a rehearing by the full Federal Circuit or an unlikely stop at the Supreme Court. For a variety of reasons, that latter venue seemed impossibly remote when this dispute began. But conception is so fundamental to patent law that there is now at least a glimmer of a possibility the High Court will be interested.

Or not. Now that the US patent system has moved from a "first to invent" to a "first to file" regime, it is true that conception matters much less today than it did back in 2012. Were the foundational CRISPR patent applications filed a year later, both CVC's and the Broad's patent applications would likely have been issued by now, with their boundaries trimmed in any future litigation. But conception still remains important because of recent difficulties in assessing patents on AI-assisted inventions. The Patent Office has struggled with when and whether humans engage in patentable conception when AI is involved. At the moment, the Patent Office has struck an uneasy compromise by importing some of its analysis of that question from those concerning co-inventorship—a tacit acknowledgment that an AI could be involved in some of the mental activity of conception.[13] Thus, the patent dispute over the groundbreaking technology of the 2010s may affect the patentability determinations of the groundbreaking technology of the 2020s.

Closer to home, whether the Federal Circuit's decision will affect the current CRISPR-Cas9 license landscape is unclear. While it is difficult to quantify from public information, it appears that the lion's share of licenses for human therapeutics has been licensed from the Broad Institute, while licenses for agricultural uses were more mixed between Broad and CVC.[14] That said, there are some signs of cooperation between Broad and CVC, even during the litigation. DuPont Pioneer was able to secure a large set of cross-licenses from both the Broad and CVC and their respective surrogate companies to further agricultural development; the company now works with both sides on technology development.[14] And the Broad Institute eventually granted a license to CRISPR Therapeutics—a biotech company affiliated with CVC—after the company won FDA approval of Casgevy, the first CRISPR-based, commercial human therapy.[15] These developments suggest that, conception or not, there may be a deal to be made when the price is right.

Lawyers are fond of saying, "Bad facts make bad law"—namely, that confusing or one-sided litigation campaigns allow courts to be less than careful in their legal analyses. And while the facts are not "bad" in the usual sense, the intricacies of the case are a reminder of its opera of personalities and the complexities of its proceedings. The Federal Circuit's opinion, though, does not do that history—nor patent law's standard of conception—justice.

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