

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Fuqiang CHEN et al.	Art Unit:	1636
Serial Nos.:	15/188,911; 15/188,924; & 15/456,204	Examiner:	Jennifer Ann DUNSTON
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For:	CRISPR-BASED GENOME MODIFICATION AND REGULATION		

July 19, 2019

URGENT PETITION TO THE DIRECTOR UNDER 37 C.F.R. §§ 1.181-1.183 AND TO THE CHIEF ADMINISTRATIVE PATENT JUDGE UNDER 37 C.F.R. §§ 41.3 & 41.103 TO DECLARE AN INTERFERENCE BETWEEN *THE REGENTS OF THE UNIVERSITY OF CALIFORNIA ET AL. V. SIGMA-ALDRICH* IN PARALLEL WITH RECENTLY DECLARED INTERFERENCE NO. 106,115 (*THE REGENTS OF THE UNIVERSITY OF CALIFORNIA ET AL. V. THE BROAD INSTITUTE INC. ET AL.*)

TO THE DIRECTOR AND THE CHIEF ADMINISTRATIVE PATENT JUDGE:

On Monday, June 24, 2019, the PTAB declared a patent interference directed to CRISPR-Cas9-based methods and compositions of matter in eukaryotic cells (e.g., human and animal cells). Int. No. 106,115 (*The Regents of The University of California et al. v. The Broad Institute Inc. et al.*) (individually, “UC” and “Broad Inst.”; together, “*UC v. Broad Inst.*”). Sigma-Aldrich’s pending patent applications (e.g., Serial Nos. 15/188,911, 15/456,204, and 15/188,924) are also directed to CRISPR-Cas9-based methods in eukaryotic cells. Of critical importance here, Sigma-Aldrich’s benefit applications **pre-date** the earliest possible benefit applications involved in the *UC v. Broad Inst.* interference with respect to their respective disclosures of CRISPR-Cas9 in eukaryotic cells. See *infra* Fig. 1. For the effective administration of justice, efficiencies of the USPTO and the parties, conservation of considerable valuable resources, and the public interest, Sigma-Aldrich respectfully requests that the PTAB declare a parallel interference between Sigma-Aldrich and UC.

Sigma-Aldrich recognizes, of course, that its pending applications’ claims have not yet been allowed, and thus declaring a patent interference now would – in ordinary

circumstances – be premature. However, the facts here are truly **extraordinary**, and Sigma-Aldrich feels compelled to apprise the Director and the CAPJ of the current situation and to briefly explain why the PTAB’s declaration of a parallel interference in this instance would be in the long-term best interests of everyone, including the USPTO, the parties, and the public. Indeed, the sole issue raised by this Petition has already been effectively decided by both the PTAB and the Federal Circuit, and those decisions completely support Sigma-Aldrich’s request here; namely, does UC’s disclosure of CRISPR-Cas9 in *in vitro* cell-free and nucleus-free test tube environments (hereinafter, “prokaryotic environment”) render obvious claims directed to CRISPR-Cas9 in eukaryotic cells? The controlling answer to this question is decidedly “no.” Sigma-Aldrich respectfully submits that the PTAB’s and the Federal Circuit’s “no” answer compels the grant of this Petition.

The following timeline – which shows the 2012 and early-2013 provisional applications of Sigma-Aldrich, UC, and Broad Inst. – is relevant to the issues presented herein:

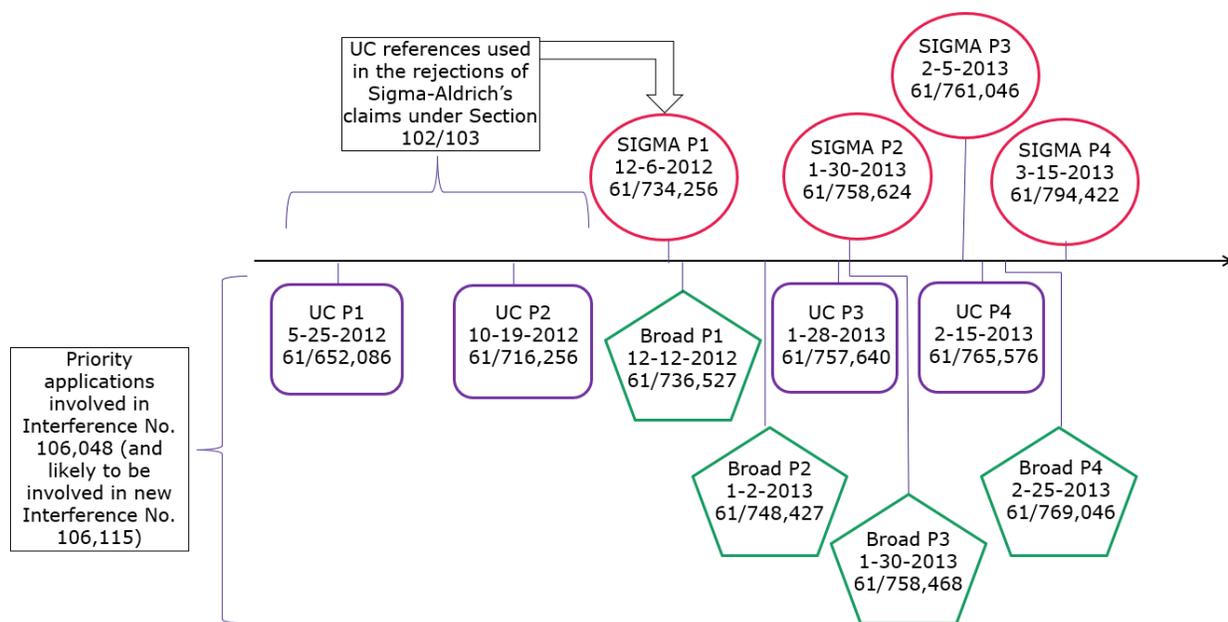


FIG. 1

I. BACKGROUND DISCUSSION: EUKARYOTIC IS NOT OBVIOUS OVER PROKARYOTIC

A. *Broad v. UC*: The PTAB And The Federal Circuit Both Decide That Eukaryotic Claims Are Patentable Over UC's Prokaryotic Applications

In a recent highly publicized interference, the PTAB found that UC's disclosure of CRISPR-Cas9 in a prokaryotic environment did not render obvious Broad Inst.'s claims to CRISPR-Cas9 in eukaryotic cells. *Broad Inst., Inc. v. Regents of the Univ. of Cal.*, Decision on Motions, Int'f No. 106,048 (DK), 2017 WL 657415, Paper 893 (PTAB Feb. 15, 2017). As the lengthy PTAB record reflects, the PTAB and the parties spent considerable time and resources litigating this pivotal and hotly contested issue. After weighing the parties' extensive arguments and voluminous evidence, the PTAB ultimately found that UC's disclosure of CRISPR-Cas9 in a prokaryotic environment did not render obvious Broad's claims to CRISPR-Cas9 in eukaryotic cells:

[T]he evidence shows that the invention of [CRISPR-Cas9] systems in eukaryotic cells would not have been obvious over the invention of CRISPR-Cas9 systems in any environment, ***including in prokaryotic cells or in vitro***, because one of ordinary skill in the art would not have reasonably expected a CRISPR-Cas9 system to be successful in a eukaryotic environment.

Broad Inst., Int'f No. 106,048, 2017 WL 657415, at *2, Paper 893 at 2 (emphasis added).

The preponderance of the evidence, including the contemporaneous statements of the [UC] inventors and others in the field, as well as the knowledge of ordinarily skilled artisans, demonstrates that ***one of ordinary skill would not have had a reasonable expectation of success that CRISPR-Cas9 could be used in a eukaryotic cell.***

Id. at *25, Paper 893 at 48-49 (emphasis added).

Accordingly, the PTAB determined that Broad Inst., albeit the Junior Party, was nonetheless entitled to its involved patents because Broad Inst.'s CRISPR-Cas9 eukaryotic claims represented a novel and nonobvious (and thus patentable) contribution over UC's work, which included UC's earlier disclosure in UC's P1 and P2 provisional applications of CRISPR-Cas9 in a prokaryotic environment.

Not surprisingly, UC appealed the PTAB's decision to the Federal Circuit. *Regents of the Univ. of Cal. v. Broad Inst., Inc.*, 903 F.3d 1286 (Fed. Cir. 2018). The parties' appellant arguments and evidence on this pivotal "prokaryotic v. eukaryotic" issue were again extensive and voluminous. Ultimately, however, the Federal Circuit affirmed the PTAB, holding that the PTAB correctly determined (*i.e.*, substantial evidence supported the PTAB's decision) that UC's mere disclosure of CRISPR-Cas9 in a prokaryotic environment did not render obvious Broad Inst.'s claims to CRISPR-Cas9 in eukaryotic cells:

The [PTAB] determined there was no interference-in-fact because, **given the differences between eukaryotic and prokaryotic systems**, a person of ordinary skill in the art would not have had a reasonable expectation of success in applying the CRISPR-Cas9 system in eukaryotes.

* * *

The [PTAB] performed a thorough analysis of the factual evidence and considered a variety of statements by experts for both parties and the inventors, past failures and successes in the field, evidence of simultaneous invention, and the extent to which the art provided instructions for **applying the CRISPR-Cas9 technology in a new environment**. In light of this exhaustive analysis and on this record, we conclude that substantial evidence supports the [PTAB's] finding that there was not a reasonable expectation of success

UC v. Broad, 903 F.3d at 1290, 1296 (emphases added).

Accordingly, the controlling precedent compels a conclusion that UC's P1 and P2 provisional applications, disclosing a CRISPR-Cas9 system in a prokaryotic environment, neither anticipate nor render obvious Sigma-Aldrich's claims directed to a CRISPR-Cas9 system in eukaryotic cells.

B. *Sigma-Aldrich v. UC*: Examiner Repeatedly Insists That Sigma's Eukaryotic Claims Are Not Patentable Over UC's Prokaryotic Applications

Turning now to Sigma-Aldrich's pending applications, which claim the benefit of its December 6, 2012, priority application (SIGMA P1), Yogi Berra's oft-quoted "It's like déjà vu all over again" comes immediately to mind. The sole reason that the Examiner refuses to allow Sigma-Aldrich's pending claims is her continued insistence that UC's

disclosure in its P1 (May 25, 2012) and P2 (Oct. 19, 2012) provisional applications (see *supra* Fig. 1) of CRISPR-Cas9 in a prokaryotic environment renders obvious Sigma-Aldrich's CRISPR-Cas9 eukaryotic claims. There are no other outstanding rejections to Sigma-Aldrich's claims – the same previously litigated UC applications are the Examiner's only primary references for her Section 102/103 rejections. And there are no other substantive issues – the “prokaryotic v. eukaryotic” issue is the fundamental basis for the Section 102/103 rejections.

Indeed, Sigma-Aldrich's examination record here is even more extensive than the record in the now-concluded *Broad Inst. v. UC* interference and subsequent appeal. Sigma-Aldrich has not simply relied upon that existing third-party record, but has amplified upon it significantly, with multiple declarations from prominent experts explaining in even greater detail why (a) UC's disclosure of CRISPR-Cas9 in a prokaryotic environment does not render obvious Sigma-Aldrich's CRISPR-Cas9 eukaryotic claims, and (b) UC's provisional applications (UC P1 and UC P2) do not enable or adequately describe use of CRISPR-Cas9 in eukaryotic cells. Frustratingly, the Examiner – without providing any rebuttal evidence other than the same purported UC P1 and P2 provisional applications – simply responds again and again that she finds Sigma-Aldrich's evidence “unpersuasive.”

Sigma-Aldrich has repeatedly emphasized to the Examiner the importance of the PTAB's decision in the *Broad Inst. v. UC* interference, and the Federal Circuit's published opinion affirming that PTAB decision. Indeed, Sigma-Aldrich conducted an in-person interview with the Examiner, her Supervisory Patent Examiner, two Interference Practice Specialists, and the Group Art Unit Director to explain why the Examiner's maintenance of the Section 102/103 rejections over the same UC applications directly contravenes the PTAB's and the Federal Circuit's controlling decisions. Unfortunately, those explanations have fallen on deaf ears, and the Examiner remains “unpersuaded” to this day. Indeed, in her most recent Office Action in Sigma-Aldrich's '911 application (dated July 18, 2019), the Examiner used the phrases “unpersuasive” or “not found persuasive” over 70 times, despite Sigma-Aldrich's presentation of even stronger evidence than that considered and relied upon by the PTAB in the completed *Broad Inst. v. UC* interference.

Moreover, in its most recent response to the Examiner's Office Action in the '911, '924, '204 applications, Sigma-Aldrich devoted over 30 pages of its response to an explanation and analysis of the pivotal importance and controlling precedent of the first *Broad Inst. v. UC* interference, including the Federal Circuit's appellate decision. See, e.g., '911 Application, Amendment and Response Under 37 C.F.R. 1.114, at 47-78 (April 29, 2019). In response, the Examiner simply dismissed Sigma-Aldrich's entire discussion in little more than a single paragraph, superficially stating that Sigma-Aldrich's arguments are "not found persuasive," and incorrectly concluding that the PTAB's and Federal Circuit's decisions "are not precedential in this case." See, e.g., '911 Application, Office Action, at 56 & 142 (July 18, 2019).

II. NEXT STEPS: A FAIR AND EFFICIENT PARALLEL INTERFERENCE NOW, OR AN UNFAIR AND DUPLICATIVE INTERFERENCE MUCH LATER

As noted above, Sigma-Aldrich fully appreciates that in the ordinary sequence of events, USPTO procedures would involve Sigma-Aldrich appealing the Examiner's Section 102/103 rejections to the PTAB, and perhaps thereafter to the Federal Circuit. Only then – after the PTAB (or the Federal Circuit) re-affirms that UC's disclosure of CRISPR-Cas9 in a prokaryotic environment does not render obvious CRISPR-Cas9 eukaryotic claims – would Sigma-Aldrich's applications be in condition for allowance, and hence a patent interference. There are a number of reasons, however, why such a protracted series of events would be directly contrary to the effective administration of justice, efficiencies of the USPTO and the parties, conservation of considerable valuable resources, and the public interest.

A. Administration Of Justice: A Level Playing Field For Sigma-Aldrich

First, the USPTO has made clear that it seeks fairness and a "level playing field" for all parties appearing before it. E.g., A. Iancu, *Statement Delivered Before the United States Senate Subcommittee on Intellectual Property Committee on the Judiciary* (March 13, 2019) ("The USPTO has made several significant improvements to AIA trial proceedings during the past year for enhanced transparency, fairness, certainty, and predictability."); A. Iancu, *Testimony During Confirmation Hearing Before the Senate Judiciary Committee* (Nov. 29, 2017) ("The playing field must be even for all."). In this

situation, the Agency is treating Sigma-Aldrich very differently and unfairly when compared to the Agency's treatment of Broad Inst. and UC.

For example, as discussed above with regard to the first *Broad Inst. v. UC* interference, the Agency (*viz.*, the PTAB) concluded that Broad Inst.'s CRISPR-Cas9 eukaryotic claims are patentable over UC's disclosures of CRISPR-Cas9 in a prokaryotic environment. The PTAB's conclusion, affirmed by the Federal Circuit, was based on a fundamental finding that, for CRISPR-Cas9, eukaryotic is not obvious over prokaryotic, as disclosed in UC's P1 and P2 provisional applications. In direct contrast, however, the Agency (*viz.*, the Examiner, the SPE, and the IPSs) have treated Sigma-Aldrich very differently, repeatedly rejecting Sigma-Aldrich's Cas9 eukaryotic claims as obvious over UC's P1 and P2 disclosures of CRISPR-Cas9 in a prokaryotic environment. See *supra* Part I.B.

Further, the Agency (*viz.*, the examining corps) has repeatedly determined that Broad Inst.'s CRISPR-Cas9 eukaryotic claims are patentable over UC's CRISPR-Cas9 prokaryotic P1 and P2 provisional applications, thus allowing Broad Inst.'s claims over those UC applications (with reference to Fig. 1 above):

Until the filing date of [UC's P3] on January 28, 2013, to which [UC's PCT Application] claims priority, it was not known whether such a system could function in eukaryotic cells. ***At the time [UC's] prior provisional applications were filed, to which [UC's PCT Application] also claims priority ([UC's P1, filed May 25, 2012, and UC's P2, filed October 19, 2012]), it was not known if the CRISPR-Cas9 system could function in eukaryotic cells.***

* * *

Thus, prior to the filing date of [Broad Inst.'s USSN 14/054,414] ***the priority applications for [UC's PCT Application] [i.e., UC's P1 and P2] did not fairly disclose or suggest a CRISPR-Cas9 system or a method of altering gene expression in eukaryotic cells using such a system.***

Notice of Allowance, Broad Inst.'s USSN 14/054,414 (now U.S. Pat. No. 8,697,359) (Feb. 20, 2014) (emphases added). The disparity in Sigma-Aldrich's treatment by the Agency could not be more glaring, and is punctuated by the fact that the Supervisory

Patent Examiner (“SPE”) on Sigma-Aldrich's applications is the **same SPE** who supervised the above-quoted allowance for Broad Inst.

Indeed, the USPTO has now granted Broad Inst. over a dozen issued patents. In direct contrast, the USPTO continues to reject Sigma-Aldrich’s CRISPR-Cas9 eukaryotic claims as **not** patentable over those **same** UC CRISPR-Cas9 prokaryotic provisional applications that the USPTO has repeatedly found have been successfully overcome by Broad Inst.’s eukaryotic claims. This blatant inconsistency – and thus the demonstrable unfairness to Sigma-Aldrich – could not be more palpable. Indeed, the USPTO’s continued maintenance of the Section 102/103 rejections against Sigma-Aldrich’s eukaryotic claims runs afoul of the Agency’s commitment to treat all parties coming before it with fairness and equity. Accordingly, Sigma-Aldrich feels compelled to raise this issue with the Director and CAPJ at this juncture, not only to Sigma-Aldrich’s benefit, but also to the Agency’s benefit. In today’s highly charged political environment, certainly the Director and CAPJ are sensitive to criticism leveled at the Agency regarding issues of fairness and equity, e.g., whether the USPTO provides “a level playing field.” Sigma-Aldrich therefore respectfully submits that it would be in the Agency’s best interest to eliminate the present unfair treatment of Sigma-Aldrich as soon as possible. The longer the inequity persists, the more “fodder” that Agency critics may have regarding the USPTO’s commitment to its stated and commendable goals of fairness and justice.

Finally, resolution of the issues in the anticipated motions presented in the new *UC v. Broad Inst.* interference may adversely impact Sigma-Aldrich’s pending patent applications, particularly if Sigma-Aldrich is not allowed to present its arguments and evidence on those anticipated contested issues while the PTAB is considering them. To deny Sigma-Aldrich the opportunity to participate in a parallel *Sigma-Aldrich v. UC* interference, thereby allowing Sigma-Aldrich a full and fair opportunity to present its own arguments and evidence, could effectively amount to a “justice delayed is justice denied” scenario.

B. Efficiencies Of The USPTO And The Parties: Two Parallel Interferences Consume Far Fewer Resources Of All Involved

Next, there is no doubt that a PTAB appeal, possibly followed by a Federal Circuit appeal, would consume considerable time and resources of all parties involved, including the patent examining corps (e.g., the Examiner, the SPE, the IPSs, etc.), the PTAB, Sigma-Aldrich, and possibly the Federal Circuit. Moreover, conducting yet a third entirely separate and unrelated interference in the distant future on the CRISPR-Cas9 eukaryotic invention would be grossly inefficient for the USPTO. As the record in the original *Broad Inst. v. UC* interference reflects, that first dispute consumed an inordinate amount of the PTAB's resources, not to mention the immense resources of the involved parties. Moreover, if that previous interference is any predictor – and legal observers opine that it is – the newly declared second *UC v. Broad Inst.* interference will be even more resource consumptive. E.g., P. Forbes, *Homo Hackensis*, Los Angeles Review of Books (July 3, 2019) (“Two rival groups, each with a patent to protect, are fighting it out in the courts, racking up huge legal bills, because when the therapies, modified crops, and ecological interventions arrive in volume, the payoff will be enormous.”); A. Houldsworth, *New Battle in CRISPR Patent War Adds to the Uncertainty Surrounding the Technology*, IAM (June 28, 2019) (“This is the latest development in the parties’ fiercely contested dispute over fundamental rights to the revolutionary technology, which is expected to have highly lucrative applications (especially in the fields of human therapeutics and agriculture).”). Sigma-Aldrich does not contend that a parallel *UC v. Sigma-Aldrich* third interference will require **no** additional resources. However, conducting the requested third interference in parallel with the new second interference would allow the PTAB to proceed with the inevitable *UC v. Sigma-Aldrich* dispute in the most efficient manner possible. At this early stage of the two cases, their schedules could be largely coordinated, and many of the particularly resource-consumptive activities could be conducted in parallel (e.g., teleconferences, cross-examinations, oral hearings, etc.). Further, all of the parties’ arguments and evidence could be presented to the PTAB now, in a coordinated manner, allowing the PTAB to consider the full disputed landscape before making any important decisions regarding this significant technology.

The timing of this Petition is not coincidental or happenstance. The PTAB's recent declaration of the second *UC v. Broad Inst.* interference (less than four weeks ago) motivated Sigma-Aldrich to raise this issue promptly with the Director and the CAPJ. Sigma-Aldrich appreciates that the *UC v. Broad Inst.* interference is already underway (albeit in its very early stage), and the parties' respective Motions Lists are due on July 30, 2019, in advance of the parties' currently scheduled conference call with the PTAB Panel on August 5, 2019. Any significant delay in declaring a parallel *UC v. Sigma-Aldrich* interference, where the case schedules would not be largely coordinated, could compromise the proposed efficiencies of conducting the two interferences in parallel. Accordingly, Sigma-Aldrich respectfully submits that this Petition is urgent, and that declaring a parallel *UC v. Sigma-Aldrich* interference now would provide the most streamlined and efficient mechanism for all parties involved.

C. Public Interest: Resolving Patent Rights Sooner Rather Than Later Greatly Benefits The Scientific And Investment Communities, Hence The Public

Finally, the Director and the CAPJ are undoubtedly aware that the CRISPR technology is nearly universally considered to be an important scientific development, being the focus of countless articles, stories, and discussions in both the scientific press and the popular media. Not surprisingly, the scientific community is keenly interested in the allocation of patent rights to the several competing entities, including primarily UC, Broad, and Sigma-Aldrich. *E.g.*, S. Begley, *Patent Office Reopens Major CRISPR Battle Between Broad Institute and Univ. of California*, STAT (June 25, 2019) ("The outcome could also affect who the science record books, to say nothing of the Nobel Prize committee, recognizes as the inventors of this revolutionary technology."). Moreover, given the commercial potential for the CRISPR technology, the investment community is also intensely interested in learning, as soon as possible, how the landscape of legal rights will ultimately "shake out." *Id.* ("The answer to [who invented CRISPR in eukaryotes] would reverberate well beyond the potentially billion-dollar market for CRISPR therapies."). Still further, companies and research institutions are in a constant state of confusion regarding which party or parties they need to take licenses from in order to practice the CRISPR-Cas9 eukaryotic technology. *E.g.*, U. Storz, *CRISPR Cas9 – Licensing the Unlicensable*, J. Biotech., Vol. 265, p. 86-92 (Jan. 10,

2018) (“[D]ue to legal battles and conflicting patent estates, third parties may find it difficult to decide where to acquire licenses.”). This ongoing uncertainty in the patent landscape provides a significant chilling effect on the funding of both research efforts and commercial endeavors. And of course, some scientific and marketplace potential actors may choose to sit on the sidelines and observe the ongoing IP battle until the smoke clears. All of this uncertainty and trepidation inures to the detriment of the public, who could potentially benefit greatly from the treatments and therapies that CRISPR-based gene-editing therapies promise.

Allowing Sigma-Aldrich’s patent applications to languish with an intransigent Examiner, when the only remaining issue (*i.e.*, prokaryotic v. eukaryotic) has already been decided by the PTAB and the Federal Circuit, provides a profound disservice to the public interest. As set forth above, Sigma-Aldrich respectfully submits that declaring a parallel *UC v. Sigma-Aldrich* interference now would strongly favor the public interest, allowing for far greater certainty in the patent landscape in the near future.

III. REGULATORY AUTHORITY FOR THIS PETITION AND PAYMENT OF THE REQUISITE PETITION FEES

Sigma-Aldrich brings this Petition to the Director pursuant to 37 C.F.R. §§ 1.181-1.183, and to the Chief Administrative Patent Judge pursuant to 37 C.F.R. §§ 41.3 & 41.103. Those regulatory provisions provide, in relevant part:

1.181 Petition to the Director.

(a) Petition may be taken to the Director:

* * *

(3) To invoke the supervisory authority of the Director in appropriate circumstances.

1.182 Questions not specifically provided for.

All situations not specifically provided for in the regulations of this part will be decided in accordance with the merits of each situation by or under the authority of the Director, subject to such other requirements as may be imposed, and such decision will be communicated to the interested parties in writing.

1.183 Suspension of rules.

In an extraordinary situation, when justice requires, any requirement of the regulations in this part which is not a requirement of the statutes may be suspended or waived by the Director or the Director's designee, sua sponte, or on petition of the interested party, subject to such other requirements as may be imposed.

41.3 Petitions.

(a) Deciding official. Petitions must be addressed to the Chief Administrative Patent Judge.

(b) Scope. This section covers petitions on matters pending before the Board (§§ 41.35, 41.64, 41.103, and 41.205)[.]

41.103 Jurisdiction over involved files.

The Board acquires jurisdiction over any involved file when the Board initiates a contested case.

In addition, the provisions of 37 C.F.R. §§ 1.181-1.183 state that “[a]ny petition seeking a decision under this section must be accompanied by the petition fee set forth in § 1.17(f),” and the provisions of 37 C.F.R. §§ 41.3 & 41.103 state that “[t]he fee set in § 41.20(a) must accompany any petition under this section.” Accordingly, submitted herewith are both of these petition fees under 37 C.F.R. § 1.17(f) and 37 C.F.R. § 41.20(a). Sigma-Aldrich believes that no additional fees are due with the filing of this Petition. The Commissioner, however, is hereby authorized to charge any fees, or credit any overpayment, to Deposit Account 50-5915.

IV. CONCLUSION

In light of the foregoing, Sigma-Aldrich respectfully requests that, with the Director's consult and at the Director's direction, the PTAB declare a parallel *UC v. Sigma-Aldrich* interference. The undersigned practitioners remain fully prepared to assist the PTAB in formalizing the declaration of that proposed interference in an expedited manner, including promptly filing a complete statement under 37 C.F.R. § 41.202.

Respectfully submitted,



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