

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AQUESTIVE THERAPEUTICS, INC.
Petitioner

v.

IONO PHARMA, LLC
Patent Owner

Case No. IPR2025-00874
U.S. Patent No. 11,021,437

PATENT OWNER'S DISCRETIONARY DENIAL BRIEF

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PATENT OWNER'S EXHIBIT LIST

Exhibit No.	DESCRIPTION
2001	2016-06-03 Email from Ramona McCudden to Hassan Almoazen re MonoSol Rx
2002	2016-10-15 Email from Hassan Almoazen to Ramona McCudden re Epinephrine
2003	2016-10-22 Email from Hassan Almoazen to Steve Wargacki re Email
2004	Excerpt of File History of Application No. 17/086,409
2005	Excerpt of File History of Application No. 15/724,234
2006	Excerpt of File History of Application No. 17/835,442
2007	Excerpt of File History of Application No. 18/413,556
2008	2022-08-25 Email from Daniel Scola to Hassan Almoazen re Follow-up on our Discussions
2009	2023-12-06 Letter from Hemant Gupta to Daniela Scola re Collaboration Discussions with Iono Pharma, LLC
2010	MonoSol Rx Changes Name to Aquestive Therapeutics and Expands CNS Product Portfolio
2011	2016-10-18 Email from Hassan Almoazen to Steve Wargacki re Epinephrine in fast dissolving film
2012	File History of U.S. 11,021,437
2013	File History of U.S. Provisional No. 62/331,996
2014	2018-11-05 Email from Abby Trotter to Hassan Almoazen re 2018 Life Science Tennessee Venture Forum Class
2015	Email from Gareth Sheridan to Hassan Almoazen re update
2016	Email from Amy Hopper to Hassan Almoazen re Delta I-Fund Semifinals Round 1
2017	2020-10-20 Email from Lili Jiang to China Focus re You have scheduled meetings at China Focus Virtual Partnering Conference
2018	A copy of the Almoazen Paper (Exhibit 1022) highlighted to show portions cited in Petitioner's claim mapping.
2019	Declaration of Hassan Almoazen, Ph.D. under 37 C.F.R. § 1.130
2020	Declaration of Hassan Almoazen, Ph.D.

I. INTRODUCTION

Pursuant to the Director's March 26, 2025, Memorandum Regarding Interim Processes for PTAB Workload Management (the "Memo")¹, IPR2025-00874, challenging the patentability of U.S. Patent No. 11,021,437 (hereinafter the "'437 Patent"), should be discretionarily denied for at least three reasons.

First, settled expectations between the Petitioner Aquestive Therapeutics, Inc. and Patent Owner Iono Pharma, LLC warrant discretionary denial. In 2016, Petitioner reached out to Dr. Hassan Almoazen—the sole owner and employee of Iono Pharma and is listed as the sole inventor of the '437 Patent—after Dr. Almoazen published a paper related to the technology now being claimed in the '437 Patent. Between 2016 and 2024, Dr. Almoazen repeatedly expressed his desire to form a partnership with the Petitioner to bring to life the claimed technology and offered licenses to Petitioner. In fact, Petitioner repeatedly tried to purchase outright the '437 Patent. Only after the parties' negotiations broke down in 2024, and Dr. Almoazen told Petitioner that his prior licensing offer was no longer available, did Petitioner change course and decide to challenge the patentability of the '437 Patent. Petitioner's early knowledge of the application that led to the '437 Patent and

¹ <https://www.uspto.gov/sites/default/files/documents/InterimProcesses-PTABWorkloadMgmt-20250326.pdf>

Petitioner's deliberate choice to forgo any early review of the patent favor discretionary denial. *See iRhythm Tech., Inc. v. Welch Allyn, Inc.*, IPR2025-00363, Paper 10, at 2–3 (June 6, 2025).

Second, the Petition's lack of compelling merits weighs in favor of discretionary denial. In order to meet the claimed compounds, Petitioner relies on two prior art references it calls "Truelove 1" (Grounds 1 and 3) and "Truelove 3" (Grounds 2 and 3). But Truelove 1 is a reference that was prominently featured during the prosecution of and incorporated by reference into the '437 Patent. Petitioner argues that a typographical error in Truelove 1 and the correction to that typographical error—both of which were already before the Office—would have been easily recognized by a POSITA but not by the Examiner during prosecution. In fact, Petitioner goes so far as to make an incorrect correction to the typographical error in Truelove 1 in an attempt to read on claim 1. But Petitioner's proposed correction is not supported by the record and making the proper correction (as supported by other portions of Truelove 1) would render Truelove 1 to fall outside the scope of claim 1. *See infra* Sections III.D and IV.A.2.i.a. And Truelove 3 is even worse. None of the compounds described in Truelove 3 (*i.e.*, isoproterenol derivatives) read on the claimed compounds (*i.e.*, epinephrine prodrugs).

The deficiencies do not stop there. The Petition relies on two references (*i.e.*, "Almoazen Paper" (EX1022) and "Schobel" (EX1021)) that do not even qualify as

prior art. *See infra* Section III.A.1-2. And this is fatal to the entire Petition because Petitioner relies on **only** those two non-prior art references for one limitation across **all** challenged claims and across **all** Grounds. Accordingly, the Petition's lack of compelling merits favors discretionary denial.

Third, 35 U.S.C. § 325(d) warrants discretionary denial because the Petition is based on arguments and art that the patent examiner previously considered without any material error. Petitioner attempts to manufacture an examiner error arguing that the primary reference it relies on (Truelove 1) contains a typographical error (*i.e.*, the difference between ketone and ester derivatives of epinephrine). But (1) Petitioner provides no explanation why a POSITA would have immediately recognized the error but not the Examiner and (2) the Examiner was already made aware of the typographical error and the '437 Patent already made the appropriate corrections that the Examiner fully considered. *See infra* Section IV.A. And the other references were similarly considered by the Examiner during prosecution and/or are cumulative over the references already considered. Because Petitioner's arguments fail under the framework established in *Advanced Bionics LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 (Feb. 13, 2020) and *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 (Dec. 15, 2017), institution should be denied under § 325(d).

In summary, Petitioner's nearly decade-old relationship with Dr. Almoazen and the claimed technology, in combination with fatally weak merits-based arguments that not only rehash the same art and argument that the patent examiner previously rejected but relies on references that are not even prior art, presents a textbook example for exercising discretion to better allocate the PTAB's' resources elsewhere. Iono Pharma therefore respectfully submits that the Director should exercise her discretion to deny institution under 35 U.S.C. § 314(a).

II. SETTLED EXPECTATIONS WARRANT DISCRETIONARY DENIAL

The Memo states that “the parties are permitted to address all relevant considerations” for discretionary denial, including “[s]ettled expectations of the parties.” Here, Petitioner's dealings with Patent Owner dating back to 2016 regarding the patented technology demonstrate settled expectations that warrant discretionary denial.

On January 6, 2016, Dr. Hassan Almoazen published a paper titled “Development of a fast dissolving film of epinephrine hydrochloride as a potential anaphylactic treatment for pediatrics.” EX1022 (herein, the “Almoazen Paper”). On June 3, 2016, Petitioner sent an unsolicited email to Dr. Almoazen in an effort to hire him, in part due to the work published in the Almoazen Paper. EX2001 at 8-9. EX2020, ¶¶ 16, 18.

In October 2016, Dr. Almoazen informed Petitioner of his forthcoming patent application on “epinephrine fast dissolving film” (which ultimately resulted in the ’437 Patent). EX2002 at 4; EX2011 at 1 (October 18, 2016 email from Dr. Almoazen to Petitioner explaining that he developed “a solution to increase the absorption of epinephrine from the oral cavity” and that a “provisional patent ... will [be] file[d] next week”). On November 13, 2016, Dr. Almoazen filed his patent application. EX1001 at Cover. But Petitioner did not want to discuss the application with Dr. Almoazen nor develop the technology with him, so Dr. Almoazen declined to meet with Petitioner. EX2002 at 1-2. EX2020, ¶¶ 20-25.

In June 2018, Dr. Almoazen provided Petitioner with a copy of the published “PCT [application] for Epinephrine prodrug” that matured into the ’437 Patent to determine whether Petitioner had any further interest developing the technology with Dr. Almoazen. EX2003 at 1. Dr. Almoazen received no response. EX2020, ¶ 26.

In October 2021, Dr. Almoazen learned that Petitioner had also filed an application that is similar to the ’437 Patent. EX2004 at 144-146. But because Petitioner failed to cite the ’437 Patent, Dr. Almoazen provided a copy of his ’437 Patent to the Patent Office using a third-party submission process. EX2004 at 144-146. EX2020, ¶ 27. And Petitioner remained continually aware of the ’437 Patent, repeatedly citing it in a number of its related applications in 2021, 2023, and 2024. *See*, EX2005 at 253; EX2006 at 239; EX2007 at 92.

Not only was Petitioner aware of the '437 Patent in August and September 2022, but it also attempted to purchase “all rights concerning US Patent 11,021,437 ... for a one-time lump sum payment up front.” EX2008 at 4-5. It was only after Patent Owner ultimately informed Petitioner on March 29, 2024, that the '437 Patent was neither available for purchase or license, *see* EX2008 at 3, that Petitioner suddenly decided to reverse course and “question the value of [Dr. Almoazen's] patent rights.” *See* EX2009 at 2-4. EX2020, ¶¶ 28-32. The instant IPR was filed over a year later on May 16, 2025.

Dr. Almoazen made substantial personal investments, even dipping into his personal pension funds over the last decade, in an effort to bring to life the claimed technology. EX2020, ¶¶ 7-15. And those substantial investments were made during the time span when Petitioner (1) tried to hire Dr. Almoazen after his paper on this topic had published, (2) was informed about Dr. Almoazen's patenting efforts, (3) tried to secure patents in nearly identical technology area, and (4) unsuccessfully attempted to purchase the rights to the '437 Patent from Dr. Almoazen.

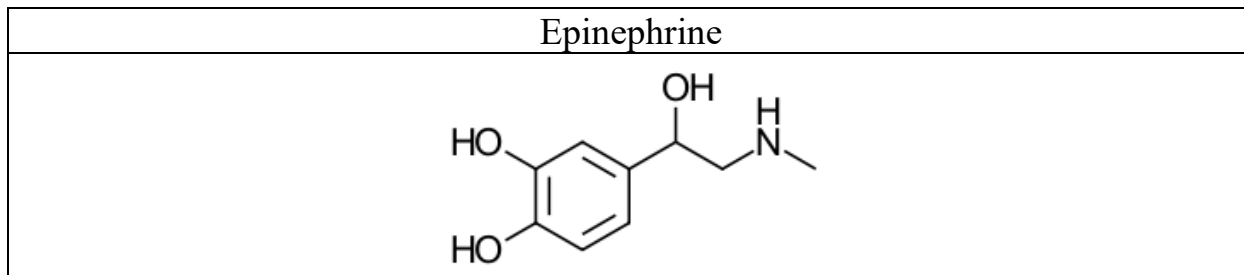
In sum, Petitioner's own actions through the course of the last decade demonstrate the extraordinary value of the '437 Patent. And Dr. Almoazen has rightfully developed a settled expectation that the '437 Patent's validity would not be challenged by the Petitioner—especially when Petitioner attempted numerous

times to acquire the rights to the '437 Patent itself. Accordingly, the Petition should be discretionarily denied.

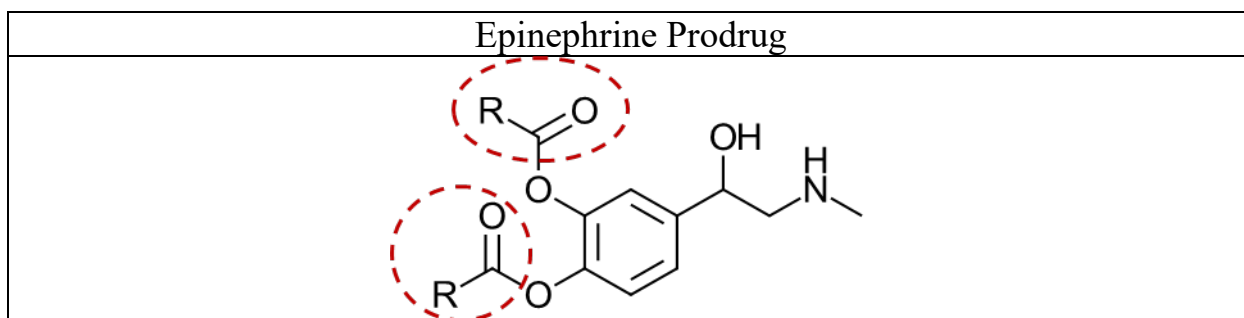
A. Factual Background

1. Dr. Almoazen Is The Founder of Iono Pharma, The Sole Inventor Of The '437 Patent, And Has Invested An Extraordinary Amount of Time, Money, And Resources Into Epinephrine Prodrugs Claimed In The '437 Patent

Dr. Almoazen began work on the technology that forms the basis of the '437 Patent—and this IPR—in 2012 while he was a professor and the Director of the Pharmaceutical Sciences Ph.D. Graduate Program and Dual Pharm.D./Ph.D. Program at the University of Tennessee Health Science Center. Dr. Almoazen founded Iono Pharma in October 2015 to develop various technologies directed towards pediatric drug delivery. Dr. Almoazen was particularly interested in pediatric treatments using fast dissolving films and tablets. He observed that treatments for severe allergies were pharmaceutically limited. At that time, epinephrine, as an example, was only available in an injectable formulation. EX2020, ¶¶ 7-9.



Dr. Almoazen observed this complete lack of FDA-approved alternative treatments and he sought to fill that gap. He began researching scientific approaches to modify the physical and chemical properties of epinephrine. Dr. Almoazen determined that *prodrugs* of epinephrine could be formulated into fast dissolving films to treat severe allergies. Epinephrine *prodrugs* are different from epinephrine in that “the two hydroxyl (phenolic) groups in positions 3 and 4 on the benzene ring [are treated with] acid moieties to form an ester bond with different alkyl chains.” EX1001, Abstract.



Ultimately, Dr. Almoazen discovered that certain epinephrine *prodrugs* with certain desirable set of properties, which are claimed in the '437 Patent, can be formulated into fast dissolving films, which are now reflected in the claims of the '437 Patent. EX2020, ¶¶ 9, 17.

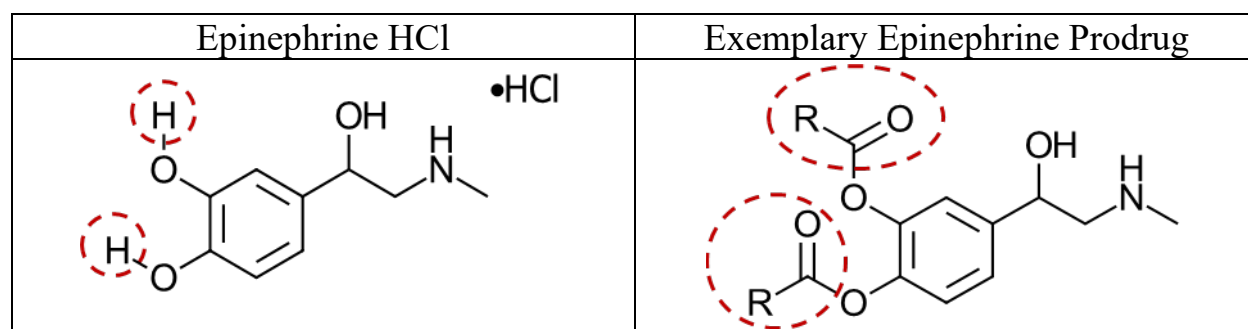
Dr. Almoazen made significant personal sacrifices to try to bring his invention to life. Dr. Almoazen paid tens of thousands of dollars for the prosecution of the '437 Patent from his own personal pension fund. Dr. Almoazen even began investing his pension into other avenues to develop his invention—such as by pursuing business relationships and licensing agreements with larger entities, including the Petitioner. To date, Dr. Almoazen has invested five figures from his pension fund—a large sum of money for a university professor—in an effort to protect and commercialize his novel idea. EX2020, ¶¶ 10-15.

2. Petitioner Sought To Acquire The Subject Matter Claimed In The '437 Patent Since At Least 2016

Dr. Almoazen's interactions with Petitioner began before any patent application directed to the '437 Patent was filed. In January 2016, Dr. Almoazen published the Almoazen Paper in the Pharmaceutical Development and Technology journal titled "*Development of a fast dissolving film of **epinephrine hydrochloride** as a potential anaphylactic treatment for pediatrics.*" EX1022. The Almoazen Paper discloses "potential proof for using [fast dissolving films] as a replacement therapy of epinephrine injections for pediatrics." *Id.* at 1. But Dr. Almoazen, however, identified a massive shortcoming with developing a sublingual treatment using just the **epinephrine hydrochloride (HCl)** discussed in the Almoazen Paper: **epinephrine HCl** alone demonstrates poor tissue permeability properties, and it

cannot be absorbed into the human body through any biological membranes, including buccal membrane or sublingual mucosa. EX2020, ¶¶ 16-17.

Recognizing that shortcoming, Dr. Almoazen began investigating *epinephrine prodrug* compounds that have different physical and chemical properties. Epinephrine *HCl* and one exemplary epinephrine *prodrug* claimed in the '437 Patent are shown below to highlight the molecules' structural differences.



These efforts ultimately led to the claims of the '437 Patent. Compare EX1001 at Tables 3-5 and Figures 8-9 with EX1022 at Tables 1-3 and Figures 1-2. EX2020, ¶ 17.

Returning back to 2016, just five months after the Almoazen Paper published, Ms. Ramona McCudden, a Human Resources representative at MonoSol Rx (hereinafter “Aquestive” or “Petitioner”)², sent an unsolicited email to Dr. Almoazen regarding “openings for Entry Level Formulation Scientists,” in part due to Dr.

² MonoSol Rx changed its name to Aquestive Therapeutics on November 30, 2017.

See EX2010.

Almoazen's work in the Almoazen Paper. EX2001 at 8. After Dr. Almoazen expressed interest in the position, Dr. Stephen Wargacki, then Petitioner's Chief Science Officer, asked if Dr. Almoazen would travel to New Jersey and present on "Pathways and Barriers on Transmucosal Permeation." *Id.* at 5. Dr. Almoazen, however, asked to defer the interview process and Petitioner instead requested to interview Dr. Almoazen's graduate students. *Id.* at 4. EX2020, ¶¶ 18-19.

In October 2016, Dr. Almoazen expressed interest in resuming discussions with Petitioner, *id.* at 3-4, and inquired if Petitioner "has an interest in the development of the epinephrine fast dissolving film," EX2002 at 4. Dr. Almoazen further informed Petitioner that he was in the process of preparing to file a provisional patent claiming that technology. EX2002 at 4. EX2020, ¶ 20. Dr. Almoazen ultimately filed that provisional application a month later on November 13, 2016, from which the '437 Patent claims priority. EX1001 at 1.

On October 17, 2016, Ms. McCudden informed Dr. Almoazen that he would need "to sign a confidentiality agreement" to discuss the forthcoming patent application with Dr. Wargacki. EX2002 at 3. The next day, Dr. Almoazen also emailed Dr. Wargacki stating that he "believe[s] [he] h[as] a solution to increase the absorption of epinephrine from the oral cavity" and that he "disclosed this solution in a provisional patent." EX2011 at 1. EX2020, ¶¶ 21-22.

On October 20, 2016, Dr. Almoazen agreed to sign the confidentiality agreement, but Petitioner changed course. Just a day later, Dr. Wargacki told Dr. Almoazen that “we do NOT want you to disclose ANY confidential information to us during your visit” but that Petitioner would “revisit [Dr. Almoazen’s] provisional” if he was “working directly for [Petitioner].” EX2002 at 2 (emphasis in original). Dr. Almoazen then canceled his upcoming interview with Petitioner because he sought to “negotiate partnership and employment agreements” rather than “abandon [his] research ideas.” *Id.* EX2020, ¶ 23.

On October 22, 2016, Dr. Wargacki responded that “do [sic] to the position of this particular molecule in our pipeline, we do not want to comprise our position and IP by discussing potential art with you” and that he hoped Dr. Almoazen could “understand this from [sic] business perspective.” *Id.* at 1. He further requested that Dr. Almoazen “reconsider with the perspective that this is about employment to be part of a team that drives the companies [sic] vision to reality” and that Dr. Almoazen’s “[e]xisting and pending IP would be a subject for discussion upon advancement in the hiring process.” *Id.* EX2020, ¶ 24.

Dr. Almoazen responded that same day—October 22, 2016—that he was not interested in working for Petitioner unless it agreed to discuss his forthcoming provisional application during the hiring process under a confidentiality agreement. *Id.* He further explained that he is “an entrepreneur and [he] founded Iono Pharma

LLC to advance the epinephrine project in addition to other projects [he] developed at the [University of Tennessee³] and [he was] looking for a pharma company like [Aquestive] to partner with [him] to advance [his] company.” *Id.* Dr. Almoazen did not hear from Petitioner. EX2020, ¶ 25.

Two years later, on June 9, 2018, after the PCT application that eventually matured into the '437 Patent had published, Dr. Almoazen informed Dr. Wargacki that it published, provided a hyperlink to the published PCT application, and again asked if Petitioner was interested in partnering with him to develop the technology behind the claimed epinephrine prodrugs. EX2003 at 1. Again, Petitioner never responded. EX2020, ¶ 26.

3. Petitioner Continued To Monitor The '437 Patent After It Issued

The '437 Patent is a national stage application of the PCT application that was provided to Petitioner on June 9, 2018. EX1001 at Cover. The '437 Patent issued on June 1, 2021. *Id.* Just four months later, on October 19, 2021, Dr. Almoazen was surprised to learn that Petitioner had been pursuing a patent application that closely resembles the '437 Patent. After having confirmed that the '437 Patent was not cited

³ University of Tennessee relinquished all rights to the intellectual property to Dr. Almoazen.

in Petitioner's application, Dr. Almoazen made a third-party submission of the '437 Patent under 37 CFR § 1.290 against Petitioner's patent application. EX2004 at 144-146. EX2020, ¶ 27.

After Dr. Almoazen's third-party submission, Petitioner began citing the '437 Patent in a number of its own patent applications over the next few years. *See, e.g.*, EX2005 at 253; EX2006 at 239; EX2007 at 92. Indeed, Petitioner's patent application 18/413,556 titled "Enhanced Delivery Epinephrine And Prodrug Compositions" received a final rejection on August 23, 2024, in light of the PCT application that matured into the '437 Patent. EX2007 at 234-235.

4. Petitioner Failed To Purchase The Rights To The '437 Patent

By August 2022, likely having recognized the importance of the '437 Patent, Petitioner sought to purchase it. On August 23, 2022, Dr. Almoazen received a phone call from Mr. Daniel A. Scola of Hoffman and Baron, LLP on behalf of Petitioner. Mr. Scola indicated that Petitioner wanted to purchase the '437 Patent and, threatened that if Dr. Almoazen did not sell it, Petitioner would "destroy it." Two days later, on August 25, 2022, Mr. Scola sent a follow-up email stating his "strong preference ... to find a suitable arrangement for [Petitioner] to obtain rights to your patent, rather than challenge it and ultimately destroy it." EX2008 at 4-5. Mr. Scola further stated that "[Petitioner] is prepared to cover the cost of your

obtaining the patent plus an increment of profit” in exchange for “all rights concerning” the ’437 Patent. *Id.* EX2020, ¶¶ 28-29.

On September 7, 2022, Dr. Almoazen declined Petitioner’s offer to purchase the ’437 Patent but indicated that he would “be interested in a licensing agreement.” Mr. Scola indicated that Petitioner would consider a licensing deal but ultimately failed to respond. EX2009 at 4. EX2020, ¶ 30.

A year later, on December 6, 2023, Iono Pharma’s lawyers reached out to Petitioner to “reopen the dialog” of a partnership between Dr. Almoazen and Petitioner. EX2009 at 1. Again, Petitioner failed to respond. Then, after months of continued silence from Petitioner, on March 29, 2024, Iono Pharma’s lawyers informed Petitioner that the “prior license offer communicated in Dr. Almoazen’s email to you on September 7, 2022, is no longer available as Iono Pharma, LLC and Dr. Almoazen are keeping options open with other interested parties.” *Id.* at 2-3. EX2020, ¶ 31.

Shortly thereafter, on April 9, 2024, Petitioner informed Dr. Almoazen that “[Petitioner] originally proposed a purchase of the ’437 Patent, as there may have been some future use, but, upon further inspection, the inherent infirmities in its content and prosecution are troublesome.” EX2009 at 4. Dr. Almoazen and Iono Pharma did not hear from Petitioner again until Petitioner filed its Petition a year later, on May 16, 2025. EX2020, ¶¶ 31-32.

B. Petitioner's Own Actions Developed A Settled Expectation That The Patentability Of The '437 Patent Would Not Be Challenged

At least the following three independent reasons demonstrate that settled expectation of quiet title developed over the course of the last decade—primarily through Petitioner's own actions (or inactions) dating back to 2016.

First, after Dr. Almoazen published the Almoazen Paper in January 2016, Petitioner reached out to Dr. Almoazen in an effort to hire him or his graduate students as an “entry level formulation scientist.” EX2001 at 4, 8. As part of that interview process, Petitioner learned of Dr. Almoazen's intent to pursue patent protection on October 15, 2016. EX2002 at 4. Dr. Almoazen again informed Petitioner on June 9, 2018, that the PCT application that ultimately became the '437 Patent had published. *See* EX2003 at 1. On October 19, 2021, Petitioner was again reminded of the '437 Patent when Dr. Almoazen utilized 37 CFR § 1.290 to submit the '437 Patent against Petitioner's then-pending patent application. EX2004 at 144-146. EX2020, ¶¶ 16-27. And Petitioner repeatedly cited the '437 Patent in several of its own patent applications over the next few years. *See*, EX2005 at 253; EX2006 at 239; EX2007 at 92. Such long-standing knowledge and awareness of Dr. Almoazen's patent filings alone demonstrate settled expectations that warrant discretionary denial. *See Nvidia Corp. v. Neural AI, LLC*, IPR2025-00606, Paper 16, 2-3 (July 14, 2025) (holding that “[a]lthough the patent originally issued in 2015,

the patent reissued in 2023 with different claims from the original patent... Petitioner and the original patent owner ... had a commercial relationship and, in 2017, [patent owner] sent Petitioner a presentation that included ... the original patent,” “Petitioner had actual notice of the challenged patents and Petitioner’s failure to seek early review of the patents favors denial.”).

Second, Petitioner’s delay in filing its IPR warrants discretionary denial. Despite being aware of the parent applications of the ’437 Patent for close to a decade, Petitioner failed to take advantage of any available means to challenge the patentability early. For example, during the four years while the ’437 Patent was undergoing examination at the Patent Office, Petitioner did not utilize the third-party submission process available under 37 CFR § 1.290 that Dr. Almoazen dutifully executed when Petitioner was prosecuting an application directed to similar technology. As another example, although now relying on a priority break argument purportedly based on a lack of written description support, Petitioner failed to use the post-grant review (PGR) challenge that was available as soon as the ’437 Patent issued in 2021. *See Nvidia*, IPR2025-00606, Paper 16 at 2-3 (“Petitioner had actual notice of the challenged patents and Petitioner’s failure to seek early review of the patents favors denial”); *see also LifeVac, LLC v. DCSTAR Inc.*, IPR2025-00454, Paper 11 at 2 (July 11, 2025) (“[P]etitions for post-grant review are favored because they must be filed no later than nine months from the grant of the patent (35 U.S.C.

§ 321(c)), are close in time to examination, and occur before expectations in the patent rights are strongly settled.”); *Therabody Inc. v. Datafeel Inc.*, PGR2025-00026, Paper 10 at 2 (July 17, 2025) (same).

Instead, Petitioner waited until 2025 to challenge the claims, despite numerous opportunities to raise the same art and arguments with the Patent Office that it now presents in its IPR petition. Such delay is especially unfair to solo inventors who have put their own personal finances—including Dr. Almoazen’s own pension—at stake for years trying to bring his patented technology to life. That prolonged inaction is yet another independent reason that supports discretionary denial. *See iRhythm*, IPR2025-00363, Paper 10 at 2-3 (explaining that “Petitioner’s awareness of Patent Owner’s applications and failure to seek early review of the patents favors denial.”). That same logic applies here: Petitioner’s early awareness, strategic delay, and failure to pursue an earlier available and more appropriate proceeding reflect gamesmanship, not diligence. Section 314(a) thus warrants denial.

Third, the fact that Petitioner attempted to purchase the rights to the ’437 Patent—albeit at below-fair-market-value—warrants discretionary denial. *See* EX2008 at 4-5. Dr. Almoazen was determined to develop the patented technology to see his claimed invention come to life. But Petitioner tried to develop the technology on its own by (1) attempting to hire Dr. Almoazen after his paper had

published; (2) turning down Dr. Almoazen's offer to enter into a partnership to develop the technology; and (3) ignoring Dr. Almoazen's offers to license the patent at fair-market-value. Moreover, Petitioner tried to independently and belatedly patent its own epinephrine prodrug compounds, only to have its application rejected by the Patent Office because the PCT application that matured into the '437 Patent served as prior art. EX2007 at 234-35. Thereafter, Petitioner threatened to "destroy" the patent if Dr. Almoazen refused to sell it. EX2008 at 4-5. But it was only after Dr. Almoazen stood firm and reiterated his intent to develop the technology—with other entities—that Petitioner decided to challenge the '437 Patent's patentability. EX2020, ¶¶ 28-32. This, too, demonstrates Dr. Almoazen's settled expectation that at least the Petitioner would not challenge the patentability of the claims that it attempted to acquire through several different avenues.

Accordingly, discretionary denial is warranted because Petitioner's interactions with Dr. Almoazen over the last decade demonstrates a settled expectation that Petitioner would not challenge the patentability of the '437 Patent.

III. THE PETITION LACKS COMPELLING MERITS

The Memo further clarifies that "the parties are permitted to address all relevant considerations" for discretionary denial, including "[t]he strength of the unpatentability challenge." The merits of each of Grounds 1-3 of the Petition are particularly weak and warrant discretionary denial.

A. Grounds 1-3: Petition Fails To Demonstrate That The Claimed Compounds Can Be “Formulated In A Unit Dosage Form As A Rapidly Dissolving Film”

The Table below summarizes the references the Petition relies on for limitation “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film.” But neither references are prior art nor are they directed to the compounds actually claimed in the challenged claims.

	“wherein the compound is formulated in a unit dosage form as a rapidly dissolving film”		
	Claim 1	Claim 2	Claim 3
Ground 1	Almoazen Paper (Pet. at 50)	Almoazen Paper (Pet. at 54)	Almoazen Paper (Pet. at 57)
Ground 2	Almoazen Paper (Pet. at 59)	Almoazen Paper (Pet. at 62)	Almoazen Paper (Pet. at 65)
Ground 3	Almoazen Paper Schobel (Pet. at 68)	Almoazen Paper Schobel (Pet. at 71)	Almoazen Paper (Pet. at 74)

1. The Almoazen Paper Is Not Prior Art And The Petition Fails To Articulate Any Objective Rationale Why The Almoazen Paper, Which Describes Epinephrine Hydrochloride, Suggests To A POSITA How And Why The Claimed Epinephrine Prodrugs Would Similarly Be Able To Form A “Fast Dissolving Film”

At the outset, the Almoazen Paper is not prior art. The portions of the Almoazen Paper's disclosures that the Petitioner relies on for the limitation “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film” are highlighted in EX2018. See Petition at 50, 54, 57, 59, 62, 65, 68, 71, 74, 89, 91, 94,

98, 102, and 103. These portions of the Almoazen Paper, however, were conceived solely by Dr. Almoazen himself and not the other listed authors. EX2019, ¶¶ 1-7. See EX2019, ¶¶ 5-6; see also *In re Katz*, 687 F.2d 450, 455-56 (C.C.P.A. 1982) (holding that “joint inventorship cannot be inferred in the face of sworn testimony” that the co-authors “were students working under the direction and supervision of the inventor”); *EmeraChem Holdings, LLC v. Volkswagen Group of Am.*, 859 F.3d 1341, 1347 (Fed. Cir. 2017) (agreeing with the rationale in *Katz* that “Mr. Katz’s explanation that his co-authors were students under his direction and supervision ... provides a clear alternative conclusion to the board’s inference that their names were on the article because they were coinventors.”)

Thus, because the Almoazen Paper published on January 6, 2016, within a year of the filing date of the earliest provisional application filed on November 13, 2016, and these portions were conceived of solely by Dr. Almoazen, the Almoazen Paper does not qualify as prior art under 35 U.S.C. § 102(b)(1)(A). Hence, each of Grounds 1 and 2 and claim 3 of Ground 3 fail because Petitioner relies solely on the Almoazen Paper in those instances for the limitation “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film.”

There is yet another independent reason why Petitioner’s reliance on the Almoazen Paper lacks compelling merits. Even if the Almoazen Paper were prior art—which it is not—the Almoazen Paper does not actually disclose any of the

claimed epinephrine *prodrug compounds*. The mere fact that some form of epinephrine may be formulated as a “rapidly dissolving film” does not necessarily mean a POSITA would have found that the *claimed epinephrine prodrugs* of claims 1-3 can also be formulated as a “rapidly dissolving film,” prior to the '437 Patent. And the Petition doesn't even attempt to provide such an explanation.

Specifically, the Almoazen Paper only discusses the formulation of a fast dissolving film that utilizes epinephrine hydrochloride (HCl)—not any one of the compounds claimed in claims 1-3. Epinephrine HCl's chemical structure is distinct from those claimed in claim 1-3. And such structural differences matter. For example, epinephrine HCl is not claimed in claims 1-3 because it does not possess the optimized set of properties, such as sufficient permeability rate (which in turn is influenced by log P value) that is required for the invention to properly function. *See* EX1001, 1:46-47 (stating that epinephrine has log P value of -0.68). Epinephrine HCl also does not have the claimed half-life values (*i.e.*, $t_{1/2}$ values), because the claimed half-life refers to “hydrolysis ... by plasma enzymes to *form epinephrine* when delivered.” EX1001, 5:43-47. Petitioner has not established any evidence demonstrating or even attempting to explain why a POSITA would have considered the *claimed epinephrine prodrugs* of claims 1-3 to be able to be formulated as a fast dissolving film, merely because **epinephrine HCl** was able to be formulated as fast dissolving film.

Accordingly, the Almoazen Paper is not prior art under § 102(b)(1)(A) and cannot supply the “rapidly dissolving film” limitation. Even if it was prior art, it concerns epinephrine HCl—not the claimed epinephrine prodrugs. Therefore, Grounds 1-3 that depend on the Almoazen Paper fail on the merits.

2. Schobel Is Not Prior Art And The Petition Fails To Articulate Objective Rationale Why The Claimed Epinephrine Prodrugs Would Similarly Be Able To Form The Claimed “Fast Dissolving Film”

Claims 1 and 2 of Ground 3 additionally rely on Schobel for the limitation “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film.” However, like the Almoazen Paper, Schobel also does not qualify as prior art to the '437 Patent. The Petition relies on Schobel's May 5, 2016 *provisional* filing date without having carried out the proper analysis to determine whether Schobel's “provisional ... to which the reference patent document claims a right of priority ... ‘describe[s] the subject matter’ relied upon in the reference patent as prior art.” *Penumbra, Inc. v. RapidPulse, Inc.*, IPR2021-01466, Paper 34 at 32 (March 10, 2023) (precedential).

Specifically, the Petitioner relies on Schobel for the disclosure of “films designed for administration of epinephrine and *salts and esters thereof*, i.e. epinephrine *prodrugs*, to human mucosa.” Pet. at 66 (citing EX1021, 15:62-65). But Schobel's provisional application discloses only epinephrine and epinephrine

bitartrate—not the *epinephrine prodrug* compounds recited in claims 1-3. *See generally* EX2014. In other words, Petitioner cannot establish that Schobel serves as prior art because the disclosure found in Schobel's *non-provisional* application is not found in Schobel's *provisional* application, rendering Schobel's non-provisional filing date of May 4, 2017, as the earliest possible prior art date. That date post-dates the '437 Patent's November 13, 2016, effective filing date.

Because Schobel is not prior art to the relied-upon subject matter, it cannot be considered in the § 103 analysis. Therefore, remaining claims 1 and 2 of Ground 3, which additionally relies on Schobel, lacks compelling merits.

B. Ground 2 Is Unclear As To Which References Petitioner Is Relying On And The Board Should Not Be Asked To “Play Archaeologist” With Petitioner’s Deficient Petition

Ground 2 allegedly relies solely on the combination of Truelove 3 with Ashraf and the Almoazen Paper.

2. Specific Statutory Grounds on Which the Challenge is Based (37 C.F.R. § 42.104(b)(2))			
Ground	References	Basis	Claims Challenged
1	Truelove 1 (EX1002), Ashraf (EX1003), Almoazen Paper (EX1022)	35 U.S.C. § 103	1-3
2	Truelove 3 (EX1008), Ashraf (EX1003), Almoazen Paper (EX1022)	35 U.S.C. § 103	1-3

Pet. at 4. But Petitioner confusingly incorporates by reference the teachings of Truelove 1 into Ground 2.

B. Ground 2: Truelove 3, Ashraf, Almoazen Paper [Claims 1-3]

The arguments in support of Ground 1 and the disclosures of Truelove 1, Ashraf, and the Almoazen Paper are incorporated herein. *Supra* pp.48-57.

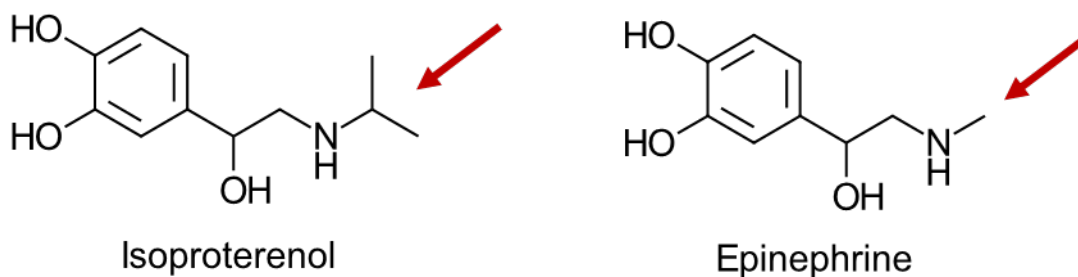
Petition at 57. It is entirely unclear whether Ground 2 relies on Truelove 1 or not.

In an IPR petition, the “Petitioner has the responsibility to make plain its challenges to the disputed claims.” *Nearmap US, Inc. v. Eagle View Techs.*, IPR2024-00716, Paper 9 at 13 (October 8, 2024). “It is not the Board’s responsibility to weave together Petitioners evidence into a cohesive case.” *Id.* Petitioner cannot ask the Board “to play archaeologist with the record.” *Parus Holdings, Inc. v. Google LLC*, 70 F.4th 1365, 1372 (Fed. Cir. 2023) . That alone guides in favor of discretionary denial.

1. If Petitioner Is Not Relying On Truelove 1 In Ground 2, None Of The References Relied Upon In Ground 2 (Truelove 3, Ashraf, And The Almoazen Paper) Read On The Claimed Compounds

Taking Petitioner’s proposed Ground 2 at face value (*i.e.*, relying only on the combination of Truelove 3, Ashraf, and the Almoazen Paper only (and not Truelove 1)), none of the references relied upon in Ground 2 read on the claimed compounds.

The specific compounds in Truelove 3⁴ are not even the epinephrine *prodrugs* recited in claims 1–3. As the Petition concedes, Truelove 3 describes diester isoproterenol derivatives—not epinephrine *prodrugs*. See Petition at 58 (“Truelove 3 also describes diester isoproterenol compounds...”). As shown below, isoproterenol and epinephrine are structurally distinct compounds:



Because Petition in Ground 2 provides no prior-art compound that meets the structural limitations of claim 1, there is no credible unpatentability case. “An obviousness determination generally requires a finding that ‘all claimed limitations are disclosed in the prior art.’” *Univ. of Strathclyde v. Clear-Vu Lighting LLC*, 17 F.4th 155, 160 (Fed. Cir. 2021) (quoting *PAR Pharm., Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1194 (Fed. Cir. 2014)).

⁴ The Petition does not rely on either Ashraf or the Almoazen Paper to meet the claimed compounds. See Petition at 79-83, 95-103.

Petitioner further offers no meaningful analysis or rationale to explain why the teachings regarding isoproterenol esters in Truelove 3 reasonably apply to the claimed epinephrine prodrugs—other than the mere fact that they are structurally similar. *See* Petition at 80. For example, other than its expert's conclusory statement, Petitioner offers no objective evidence showing that Truelove 3's isoproterenol compounds could be formulated in a unit dosage form for sublingual or buccal administration. *See, e.g.,* Pet. at 59. Similarly, Petitioner's assertion that a POSITA would expect epinephrine diesters to “have the same 1-6 minute half-life $t_{1/2}$ ” rests entirely on attorney and expert speculation. Pet. at 60. There is no objective evidence proffered by Petitioner to demonstrate that Truelove 3's isoproterenol derivatives would exhibit similar properties as the claimed epinephrine prodrugs other than mere attorney arguments and its experts' say-so.

Without Truelove 1, Ground 2 identifies no prior-art compound that meets the claims' structural limitations and relies only on conclusory assertions to import properties from a different molecule (isoproterenol). Therefore, Ground 2 lacks compelling merits.

C. Ground 3's Seven-Way Combination Lacks Compelling Merits

Ground 3 adds three additional references from those relied on in Grounds 1 and 2, leading to a Ground that relies on a combination of *seven* separate references—Truelove 1, Truelove 3, Ashraf, Almoazen Paper, Fuchs, Schobel, and

Florence. What results is an incoherent, scattershot assemblage of previously presented, cumulative, and inapplicable disclosures. Indeed, despite the seven-way combination, the Petition spends less than 2 pages (and a claim chart) explaining how the seven differences references would have been combined by a POSITA with a reasonable expectation of success. *See* Petition at 83-85, 104-109. In an IPR petition, the petitioner “must include ... a detailed explanation of the significance of the evidence,” 37 C.F.R. § 42.22(a)(2), and “cannot be met simply by throwing mountains of evidence at the Board without explanation or identification of the relevant portions.” *Parus*, 70 F.4th at 1371. As the Federal Circuit held, a “brief must make all arguments accessible to the judges, rather than ask them to play archaeologist with the record.” *Id.* at 1372. Yet, Petitioner improperly asks the Board to do so here.

D. Ground 1, Claim 1: Truelove 1 Does Not Read On Any Of The Claimed Compounds of Claim 1 When Properly Read

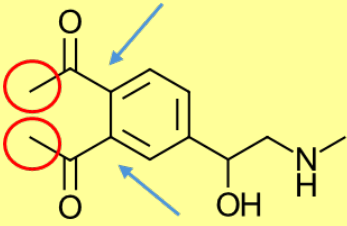
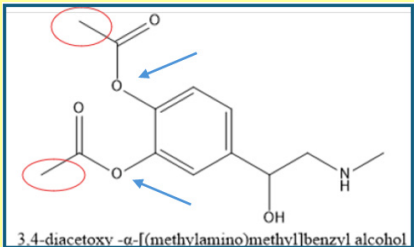
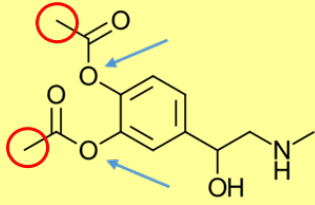
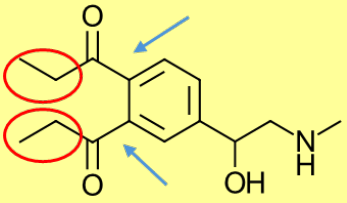
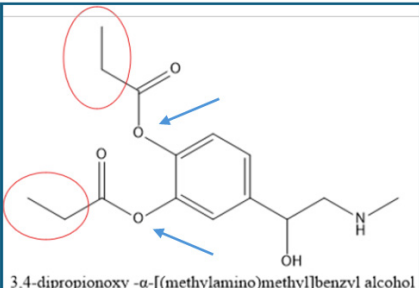
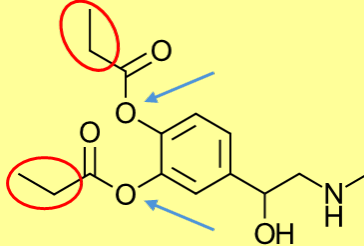
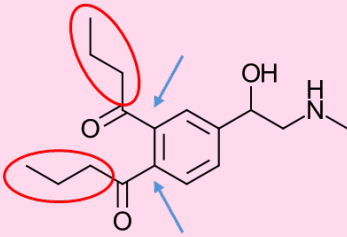
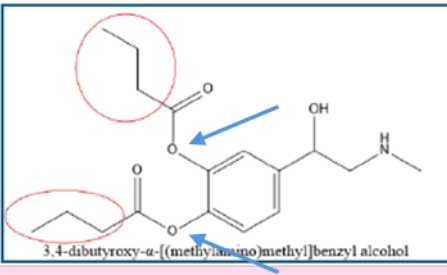
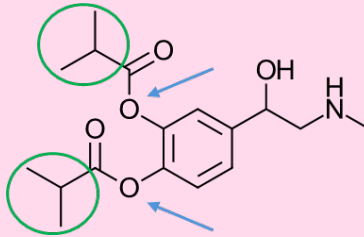
In Ground 1, the only reference Petitioner relies on to teach the claimed compound in claim 1 is Truelove 1. Pet. at 48-57. However, when Truelove 1 is properly read, it never teaches any compound of claim 1.

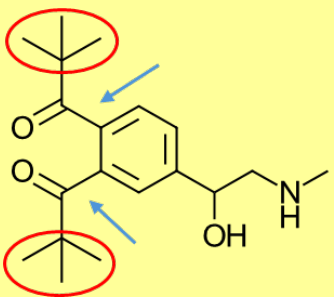
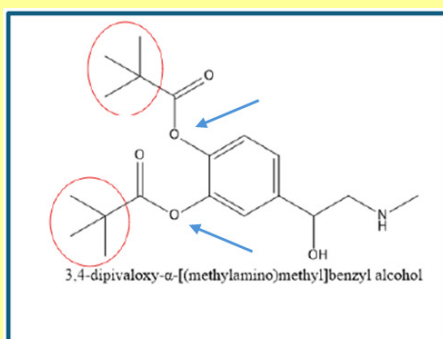
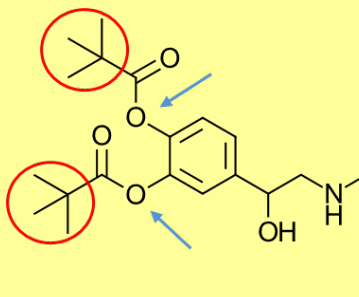
Both parties agree that Table 3 of Truelove 1 mis-labels epinephrine “esters” as “ketones” (*i.e.*, “yl-”) and that a POSITA would have recognized where the missing ester –O– (*i.e.*, “oxy-”) groups should be inserted. Pi et. at 26-34.

TABLE 3			
Compound	Rate of hydrolysis in $t_{1/2}$ seconds		
	Horse	Rabbit	Human
L-3,4-diacetyl- α -[(methylamino)-methyl] benzyl alcohol hydroperchlorate.....	20	45	180
L-3,4-dipropionyl- α -[(methylamino)methyl] benzyl alcohol hydroperchlorate.....	50	90	240
L-3,4-dibutyryl- α -[(methylamino)-methyl] benzyl alcohol hydroperchlorate.....	100	160	360
L-3,4-dipivalyl- α -[(methylamino)-methyl] benzyl alcohol hydroperchlorate.....	600	720	1,800

EX1002, Table 3.

The table below illustrates the original Truelove 1, Table 3 compound nomenclature and corresponding chemical structure on the left, Petitioner's Proposed Correction to the Table 3 compound nomenclature and the corresponding chemical structure in the middle, and Patent Owner's/Proper Correction to the Table 3 compound nomenclature and the corresponding chemical structure on the right. Both parties agree that a POSITA would read the first, second, and fourth compounds in Table 3 above and in the table below (highlighted in yellow) as **diacetoxy-**, **dipropionoxy-**, and **dipivaloxy-**epinephrine, respectively. Pet. at 36-38. Namely, the parties agree that only the portions in **blue** in the table below should be corrected to form **esters**. The only dispute concerns the third entry in Table 3 above and the table below (highlighted in pink).

Truelove 1 Table 3	Petitioner's Proposed Correction	Patent Owner's/Proper Correction
L-3,4-diacetyl-α- [(methylamino)- methyl]benzyl alcohol 	3,4-diacetoxy-α- [(methylamino)- methyl]benzyl alcohol  Pet. at 36	3,4-diacetoxy-α- [(methylamino)- methyl]benzyl alcohol 
L-3,4-dipropionyl-α- [(methylamino)- methyl]benzyl alcohol 	3,4-dipropionoxy-α- [(methylamino)- methyl]benzyl alcohol  Pet. at 37	3,4-dipropionoxy-α- [(methylamino)- methyl]benzyl alcohol 
L-3,4-dibutyryl-α- [(methylamino)- methyl]benzyl alcohol 	3,4-dibutyroxy-α- [(methylamino)- methyl]benzyl alcohol  Pet. at 38	3,4-diisobutyroxy-α- [(methylamino)- methyl]benzyl alcohol 

Truelove 1 Table 3	Petitioner's Proposed Correction	Patent Owner's/Proper Correction
L-3,4-dipivalyl-α- [(methylamino)- methyl]benzyl alcohol 	3,4-dipivaloxy-α- [(methylamino)- methyl]benzyl alcohol  Pet. at 38	3,4-dipivaloxy-α- [(methylamino)- methyl]benzyl alcohol 

Examining the compound highlighted in pink, Petitioner rewrites L-3,4-**dibutyryl**- α -[(methylamino)-methyl]benzyl alcohol as 3,4-**dibutyroxy**- α -[(methylamino)-methyl]benzyl alcohol, citing only the unsupported statements from its two experts. *See* Pet. at 33 (citing “Rautio (EX1050), ¶¶146-151, 170-178; Meanwell (EX1051), ¶¶59-60, 76, 80-81, 84, 90”).

But the intrinsic record shows that both the **red** and the **blue** portions require correction in Truelove 1 because it is clear that Truelove 1 meant the “**iso-**” “**oxy**” form, *i.e.*, 3,4-**diisobutyroxy**- α -[(methylamino)-methyl]benzyl alcohol. This compound is first introduced at col. 8, lines 22-32 of Truelove 1, along with the names of the other three yellow highlighted compounds in the same order:

acylated and other acylated compounds as a control. The observed results indicated no mydriasis for L-3,4-dihydroxy - α - [(methylamino)methyl]benzyl alcohol bitartrate, no mydriasis for L-3,4-diacetyl- α -[(methylamino)methyl]benzyl alcohol hydroperchlorate, marginal mydriasis for L - 3,4-dipropionyl- α -[(methylamino)methyl]benzyl alcohol hydroperchlorate, marginal mydriasis for L-3,4-diisobutyryl- α -[(methylamino)methyl]benzyl alcohol hydroperchlorate, and extensive mydriasis for L-3,4-dipivalyl- α -[(methylamino)methyl]benzyl alcohol hydroperchlorate.

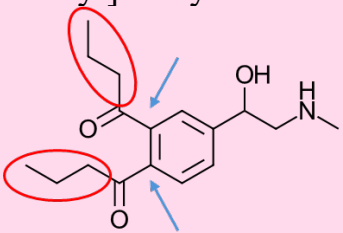
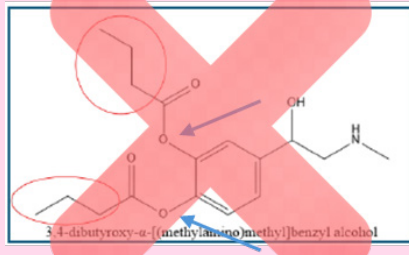
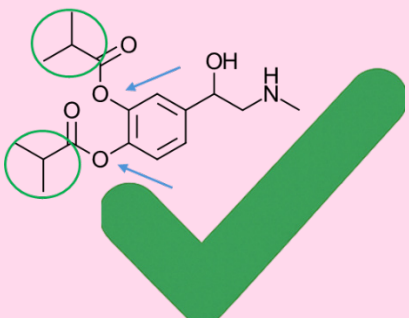
EX1002, 8:22-32. Truelove 1 identifies the particular compound as L-3,4-diisobutyryl- α -[(methylamino)-methyl]benzyl alcohol. The identical “iso-” name appears in Table 1 (EX1002, 8:50-63) and Table 2 (EX1002, 9:3-14), again along with the names of the other three yellow highlighted compounds in the same order:

TABLE 1	
Compound:	Delay before onset of seizure in minutes
Control	1-2
L - 3,4 - dihydroxy- α -[(methylamino)methyl]benzyl alcohol bitartrate	5.5
L - 3,4 - diacetyl - α -[(methylamino)methyl]benzyl alcohol hydroperchlorate	4
L - 3,4 - dipropionyl- α -[(methylamino)methyl]benzyl alcohol hydroperchlorate	5
L - 3,4-diisobutyryl- α -[(methylamino)methyl]benzyl alcohol hydroperchlorate	5
L - 3,4 - dipivalyl- α -[(methylamino)methyl]benzyl alcohol hydroperchlorate	8-10

TABLE 2		
Compound	Hydrolysis, $t_{1/2}$	Oxidation, days
L-3,4-dihydroxy- α -[(methylamino)methyl]benzyl alcohol bitartrate		15
L-3,4-diacetyl- α -[(methylamino)methyl]benzyl alcohol hydroperchlorate	30	20
L-3,4-dipropionyl- α -[(methylamino)methyl]benzyl alcohol hydroperchlorate	34	35
L-3,4-diisobutyryl- α -[(methylamino)methyl]benzyl alcohol hydroperchlorate	50	35
L-3,4-dipivalyl- α -[(methylamino)methyl]benzyl alcohol hydroperchlorate	700	300

Only in Table 3, which lists the “rate of hydrolysis in $t_{1/2}$ seconds” for the four compounds that Truelove 1 had been discussing in Example 1 of Truelove 1, does the “*iso*—” drop out. This is an obvious second typo that a POSITA would have been able to correct.

Thus, the pink highlighted compound 3 in Table 3 contains *two* typographical errors, not just one. Correcting both—consistent with how the compound was described in other parts of Truelove 1—yields an L-3,4-diisobutyroxy- α -[(methylamino)-methyl]benzyl alcohol— which does not match *any* structure recited in claim 1.

Truelove 1 Table 3	Petitioner's Proposed Correction	Patent Owner's/Proper Correction
L-3,4- dibutyryl -α-[(methylamino)-methyl]benzyl alcohol 	L-3,4- dibutyroxy -α-[(methylamino)-methyl]benzyl alcohol 	L-3,4- diisobutyroxy -α-[(methylamino)-methyl]benzyl alcohol 

The reason why Petitioner is proposing this “single” typographical error of L-3,4-**dibutyroxy**-α-[(methylamino)-methyl]benzyl alcohol instead of the proper “double” typographical error of L-3,4-**diisobutyroxy**-α-[(methylamino)-methyl]benzyl alcohol is self-evident. It is only with the “single” typographical error correction that Truelove 1 reads on claim 1, where the claimed “R” is “—CH₂CH₂CH₃.” If Truelove 1 is properly read to correct the “double” typographical error, Truelove 1 does not read on *any* of the claimed compounds of claim 1.

Because the Petition identifies no prior-art compound meeting every structural limitation of claim 1, Ground 1 fails on the merits. *See Univ. of Strathclyde*, 17 F.4th at 160 (quoting *PAR Pharm.*, 773 F.3d at 1194).

IV. 35 U.S.C. § 325(d) WARRANTS DISCRETIONARY DENIAL AS THE PETITION FAILS TO PRESENT MATERIALLY DISTINCT ART OR ARGUMENTS.

The Board uses a two-pronged test to determine whether it will deny institution under 35 U.S.C. § 325(d): (1) whether the same or substantially the same art or arguments were previously presented to the Office; and (2) if so, whether the Office erred in a manner material to patentability. *See Advanced Bionics*, IPR2019-01469, Paper 6 at 7 (precedential); *see also Becton, Dickinson*, IPR2017-01586, Paper 8 at 17-18 (precedential).

The Petition should be discretionarily denied under 35 U.S.C. § 325(d) because the Petition relies on art and arguments that were previously presented to and considered by the Office without error. As summarized below, the Petition presents three separate Grounds as reproduced below. Pet. at 4.

Ground	References	Basis	Claims Challenged
1	Truelove 1 (EX1002), Ashraf (EX1003), Almoazen Paper (EX1022)	35 U.S.C. § 103	1-3
2	Truelove 3 (EX1008), Ashraf (EX1003), Almoazen Paper (EX1022)	35 U.S.C. § 103	1-3
3	Truelove 1 (EX1002), Truelove 3 (EX1008), Ashraf (EX1003), Almoazen Paper (EX1022), Fuchs (EX1004), Schobel (EX1021), Florence (EX1015)	35 U.S.C. § 103	1-3

Among the three primary references that Petitioner relies on in Grounds 1 and 3 (*i.e.*, Truelove 1⁵, Ashraf, and Almoazen Paper), Truelove 1 and Ashraf were already considered during prosecution of the '437 Patent. *See* Sections IV.A.1 and IV.A.3. The fourth and sixth references (*i.e.*, the Almoazen Paper and Schobel) do not qualify as prior art. *See* Sections III.A.1 and III.A.2. Petitioner also relies on three additional references—Truelove 3, Fuchs, and Florence—that (i) were either previously considered and/or (iii) are cumulative of references already considered. And the Petitioner identifies no material error in any of Examiner's analysis that

⁵ Patent Owner is assuming that Truelove 1 is not part of Ground 2, but Petitioner may be relying on Truelove 1 in Ground 2 as well. *See* Section III.B.

warrant another consideration of these previously considered and/or cumulative references.

Accordingly, under *Advanced Bionics* and *Becton, Dickinson* factors (a)–(f), institution should be denied under § 325(d).

A. Ground 1 Is Based On Art And Arguments That Were Previously Considered By The Patent Office Without Error—Or Art That Is Not Even Prior Art

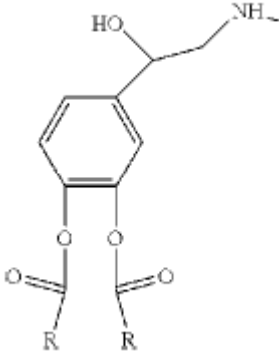
1. Truelove 1 Was Cited, Discussed, And Previously Considered For The Same Limitations The Petition Now Relies On

As shown below, Grounds 1 and 3 explicitly rely on Truelove 1⁶ as the primary prior art reference for just about all of the limitations of the challenged claims. Moreover, the Petition incorporates “[t]he arguments in support of Ground 1 and the disclosures of Truelove 1” into Ground 2 as well.⁷ Pet. at 57.

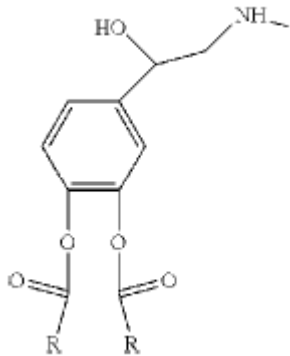
⁶ Truelove 1 (EX1002) lists Anwar Hussain and James E. Truelove as named inventors. EX1002, Cover. The '437 Patent, in both the specification and during prosecution, referred to Truelove 1 as “Hussain et. al.” It is unclear why Petitioner chose to utilize “Truelove 1” in referring to the same reference in the instant IPR petition.

⁷ In this regard, Grounds 2 and 3 may be duplicative of one another.

More specifically, the Petition primarily relies on Truelove 1 for the following limitations of the challenged claims:

Claims	Preamble/Limitation
1	“A compound formulated as a pharmaceutical composition in a unit dosage form configured for sublingual or buccal administration”  “of a Formula: wherein R is selected from the group consisting of: ... -CH₂CH₂CH₃, ... or a pharmaceutically acceptable salt thereof” “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film”⁸ “and has a half-life $t_{1/2}$ range from 1-6 minutes.”

⁸ For this limitation colored in purple in claims 1-3, while Petitioner's claim charts at pages 86-109 purport to rely on Truelove 1 for this limitation, the Petition's more detailed description section at pages 47-85 does not appear to rely on Truelove 1. Patent Owner includes this limitation out of abundance of caution.

2	• “A compound of a Formula  wherein R is selected from the group consisting of: CH₃, CH₂CH₃ and CH(CH₃)₂” • “wherein the compound is formulated in a unit dosage form as a sublingual or buccal administration and” • “wherein the compound formulated in a unit dosage form as a rapidly dissolving film”⁴ • “and has a half-life t_{1/2} range from 1-6 minutes.”
3	• “The compound of claim 2,” • “wherein the compound is selected from the group consisting of: 4-(1-hydroxy-2-(methylamino)ethyl)-1,2-phenylene diacetate, 4-(1-hydroxy-2(methylamino)ethyl)-1,2-phenylene bis(2-methylpropanoate), 4-(1-hydroxy-2-(methylamino)ethyl)-1,2-phenylene dipropionate; and” • “a pharmaceutically acceptable carrier or a pharmaceutically acceptable excipient” • “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film.”⁴

See, e.g., Petition at 86-109; *see also id.*, 48-74, 79, 83-85. In other words, the Petition relies on Truelove 1 for just about all of the limitations, except for one (“wherein said compound has a Log P value in the range of about 0.5-6.0”) or possibly two (“wherein the compound is formulated in a unit dosage form as a rapidly dissolving film”) limitations.⁹

Truelove 1 was not only cited and acknowledged as having been considered by the Examiner during prosecution (EX2012, at 268)¹⁰, it was also incorporated by reference into the '437 Patent and extensively discussed and considered by the Examiner during prosecution for exactly the same limitations that the Petition relies on—namely the (1) specific compounds; (2) unit dosage form as a sublingual or buccal administration; and (3) half-life. EX2012, 357-360.

⁹ See *supra* note 8.

¹⁰ This alone satisfies the first prong of the *Advanced Bionics* framework, which asks whether the same or substantially the same art was previously presented to the Office. *See Ecto World, LLC v. RAI Strategic Holdings, Inc.*, IPR2024-01280, Paper 13 at 4 (May 19, 2025) (precedential as to § A) (“Challenging the claims using the same prior art that was previously presented on an IDS is sufficient to satisfy the first part of the *Advanced Bionics* framework.”).

2. Truelove 1: Petitioner Has Not Shown Any Examiner Error In The Office's Consideration Of Truelove 1

Petitioner contends that Examiner erred because Applicant selectively cited compound 7D—reporting a 30-minute half-life—while ignoring other Truelove 1 compounds (7A–7C) that are recited in the challenged claims and exhibit shorter half-lives. Pet. at 23-24. Petitioner argues that this misled the Examiner and prevented a proper evaluation of this reference. *Id.* Petitioner also points to a typographical error in Table 3 of Truelove 1, suggesting that the Examiner failed to recognize the correct chemical identities of the disclosed compounds. *Id.* at 9, 28–29.

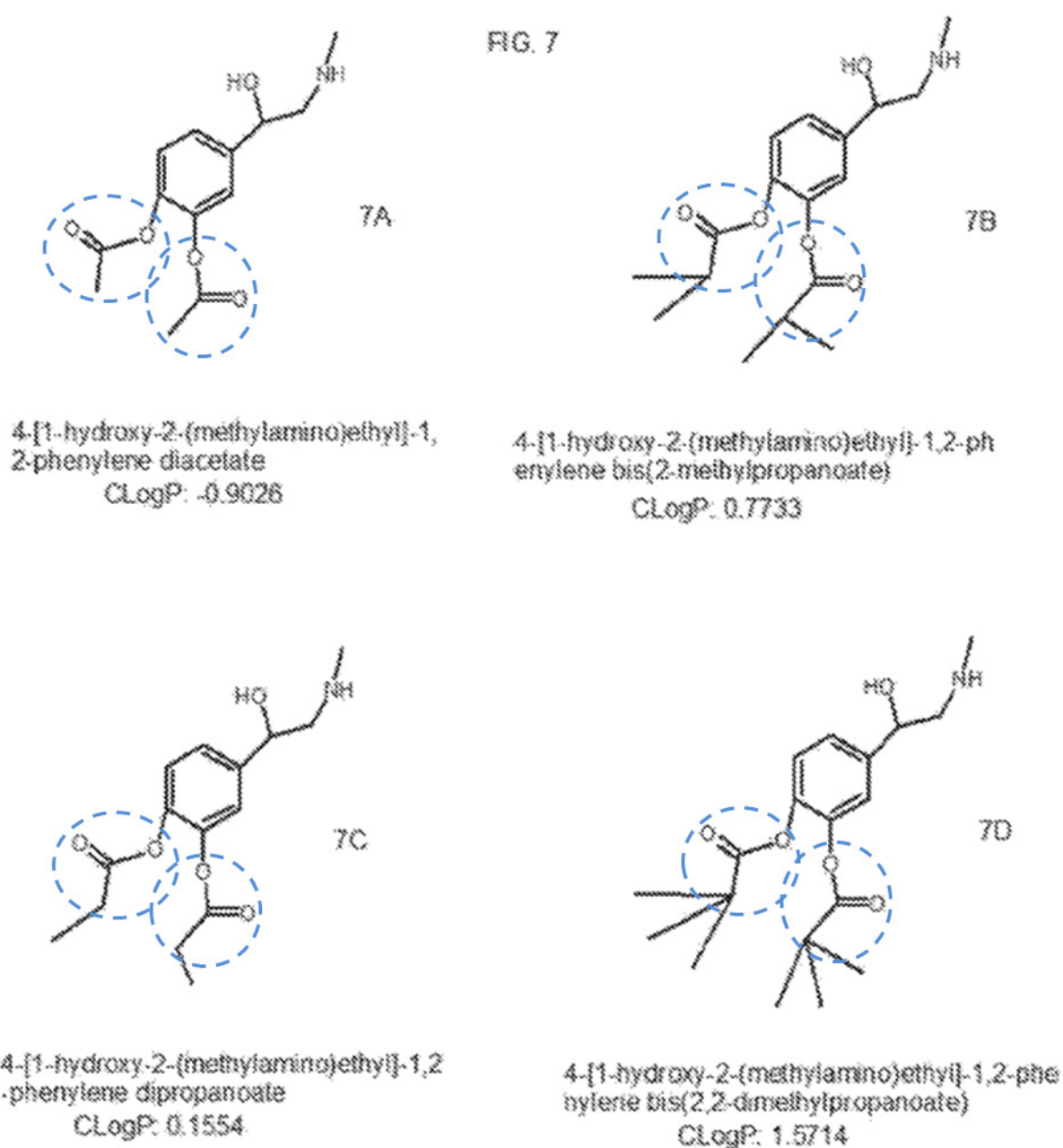
However, Petitioner mischaracterizes the record. Applicant clearly disclosed and discussed all **relevant compounds** from Truelove 1, including their **half-lives** and suitability for treating anaphylaxis through **buccal or sublingual administration**, and the Examiner fully considered this information without error. Accordingly, there was no error by the Examiner during prosecution that would justify institution under § 325(d).

i. Truelove 1's **Specific Compounds Were Disclosed To The Examiner And Fully Considered**

Petitioner argues that the Examiner erred by relying on an allegedly misleading characterization of Truelove 1. Specifically, Petitioner asserts that in an Office Action response, Applicant cited only Truelove 1's compound 7D—reporting

a 30-minute plasma half-life—while ignoring compounds 7A–7C, which exhibit shorter half-lives of 1–6 minutes and are recited in the challenged claims. Pet. at 23. According to Petitioner, this alleged “selective citation” led the Examiner to “simply accept[] and rel[y] on Almoazen’s misleading arguments regarding Truelove 1 as the basis for withdrawing the rejections.” *Id.*

This assertion is incorrect. Applicant did not obscure the existence of Truelove 1’s compounds 7A–7C. On the contrary, Applicant highlighted the compounds discussed in Truelove 1, not only in the specification of the ’437 Patent, but specifically during prosecution in response to the last Office Action before the Notice of Allowance was issued. See EX1001, 2:5-38 (“Anwar A. Hussain and James B. Truelove were granted patents related to the synthesis of novel esters of [(methylamino)methyl] benzyl alcohol which is epinephrine. (see structures 7A, 7B, 7C, 7D).”); EX2012, at 357 (“Anwar A. Hussain and James B. Truelove were granted patents related to the synthesis of novel esters of [(methylamino)methyl] benzyl alcohol which is epinephrine.”); EX1001, 6:42-57 (“Now referring to FIG. 7, the compounds of the invention as shown in U.S. Pat. Nos. 3,809,714 [Truelove 1] ... hereby incorporated by reference. Representative molecules include: 7A ... 7B ... 7C ... 7D”). These molecules 7A, 7B, 7C, and 7D were presented to the Office in Figure 7 of the ’437 Patent and reproduced below.



EX1001, Figure 7 (annotations added in blue showing the ester groups).

The Examiner fully considered these compounds and determined that the claims, *as a whole*, are patentable. See EX2012, 385 (“None of the prior art teaches in a single disclosure, nor fairly suggests in any combination, Applicants claimed

product of a compound of the claimed Formula, *formulated as a pharmaceutical composition in a unit dosage form configured for sublingual or buccal administration*. ... Applicant's disclosure includes embodiments built around the claimed Formula *and discloses the species embodiments and their LogP value.*").

Accordingly, the Examiner did not err during prosecution when evaluating what compounds were disclosed in Truelove 1 and discretionary denial is warranted.

a. The Typographical Error in Truelove 1's Table 3 Did Not Lead To Examiner Error

To the extent Petitioner argues the Examiner erred due to a typographical error in Table 3 of Truelove 1, that argument is both immaterial and unsupported.

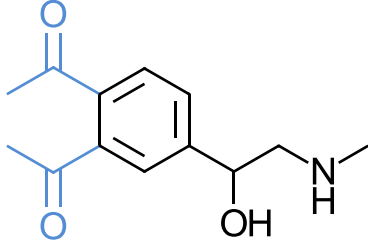
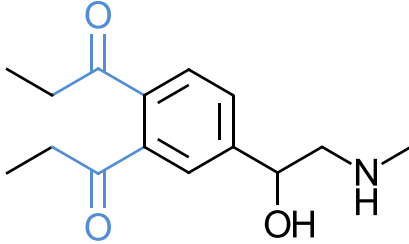
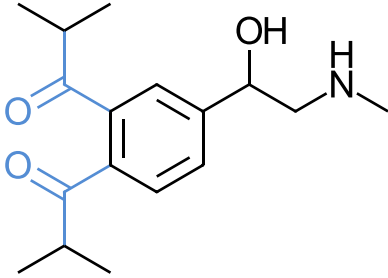
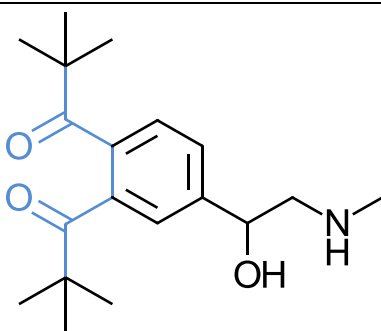
TABLE 3

Compound	Rate of hydrolysis in $t_{1/2}$ seconds		
	Horse	Rabbit	Human
L-3,4-diacetyl- α -[(methylamino)-methyl] benzyl alcohol hydroperchlorate.....	20	45	180
L-3,4-dipropionyl- α -[(methylamino)methyl] benzyl alcohol hydroperchlorate.....	50	90	240
L-3,4-dibutyryl- α -[(methylamino)-methyl] benzyl alcohol hydroperchlorate.....	100	160	360
L-3,4-dipivalyl- α -[(methylamino)-methyl] benzyl alcohol hydroperchlorate.....	600	720	1,800

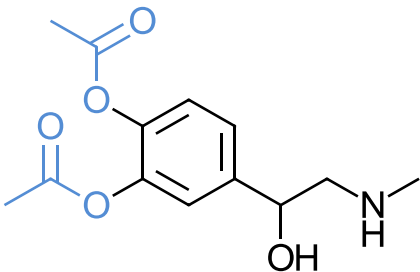
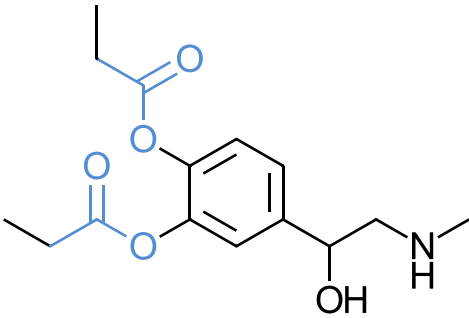
EX1002, Table 3.

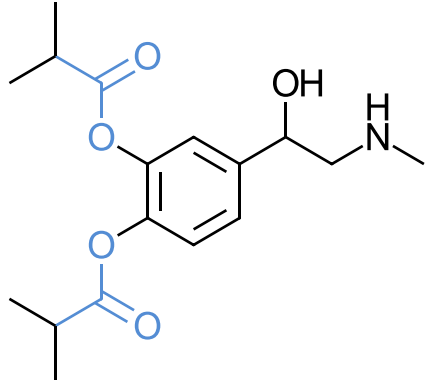
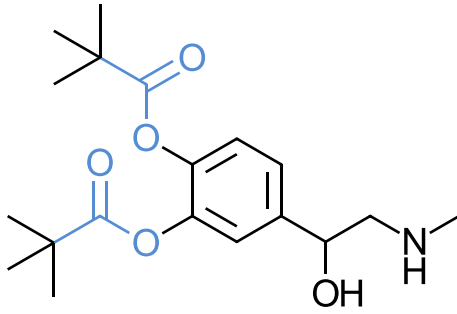
Petitioner relies on the first three compounds listed in Table 3 of Truelove 1. Pet. at 13. As Petitioner acknowledges, these compounds “were incorrectly identified *as ketone derivatives* of epinephrine,” when they are in fact diesters—a

mistake that the Petitioner acknowledges would have readily recognized and corrected by a ***POSITA***. Petition at 9, 28-29; *see also* Section III.D. The chemical structures of these ketone derivatives are shown below.

Name	Structure (ketone group marked in blue)
3,4-diacetyl- α -(methylamino)-methyl benzyl alcohol	
3,4-dipropionyl- α -(methylamino)-methyl benzyl alcohol	
3,4-diisobutyryl- α -(methylamino)-methyl benzyl alcohol	
3,4-dipivaloyl- α -(methylamino)-methyl benzyl alcohol	

Petitioner further concedes that ketone derivatives of epinephrine cannot function as prodrugs, and that a **POSITA** would have understood Truelove 1 to disclose **diester** compounds, consistent with the rest of the reference. Pet. at 28. This admission undercuts any suggestion by the Petitioner that the **Examiner** misunderstood the nature of the compounds disclosed in Table 3. The corresponding **diester** structures are shown below.

Name	Structure (ester group marked in blue)
3,4-diacetyl oxy - α -(methylamino)-methyl benzyl alcohol	
3,4-dipropionyl oxy - α -(methylamino)-methyl benzyl alcohol	

3,4-diisobutyryl ~~oxy~~ - α -(methylamino)-methyl benzyl alcohol	
3,4-dipivaloyl ~~oxy~~ - α -(methylamino)-methyl benzyl alcohol	

The Petition offers no evidence that the Examiner relied on the erroneous naming in Table 3 in any way that affected the patentability analysis. The Examiner had access to the full context of Truelove 1, and the disclosure in the specification and Figure 7 of the '437 Patent—each of which clearly identifies the compounds as diesters. There is no indication that the Examiner misunderstood the reference or made any decision based on the mislabeling.

A typographical error that a POSITA would immediately recognize does not constitute material error under *Advanced Bionics*, particularly where the record confirms that the Examiner was fully informed and did not rely on the mistaken terminology. Petitioner fails to identify any new rationale, additional evidence, or

material distinction that would call into question the Office's treatment of Truelove 1.

ii. Petitioner Identifies No Material Error in the Examiner's Consideration of Truelove 1's Buccal Administration Disclosures

Although Truelove 1 includes a single, boilerplate sentence listing various potential dosage forms—including “buccal patches”—it provides no supporting data, formulation details, or analysis specific to buccal or sublingual administration. EX1002, 6:29-33. During prosecution, Applicant explained this to the Examiner stating that Truelove 1 “didn't evaluate the log P of these molecules nor did they evaluate the sublingual or buccal permeability or absorption.” EX2012, 357. Indeed, this is also identically stated in the specification. *See* EX1001, 2:16-18 (“[Truelove 1] didn't evaluate the log P of these molecules nor did they evaluate the sublingual or buccal permeability or absorption.”).

Applicant also explained that only a subset of epinephrine esters—some of which were disclosed in Truelove 1—were appropriate for buccal or sublingual administration to treat anaphylaxis. EX2012, 357-362. As part of that rationale, Applicant stated that “[we] learned from the Hussain-Truelove patent ... that higher carbon chain leads to higher hydrolysis half-life in plasma.” EX2012, 359. Consistent with that principle, Hussain and Truelove selected compound 7D—

having a **long** half-life of approximately 1800 seconds—for ocular applications, where such long half-life was desirable. EX2012, 357-359.

In contrast, claims 1-2 of the '437 Patent, for example, claim a pharmaceutical composition formulated for **sublingual or buccal administration** using epinephrine prodrugs with **short half-lives** ranging from **1-6 minutes**. Applicant explained that “[f]or a successful epinephrine prodrug to be used for anaphylaxis, the **half-life** should be **1-6 minutes**.” EX2012, 359. This rapid hydrolysis is essential for effective anaphylaxis treatment. The claimed compounds were selected with this property in mind.

The Examiner fully considered these arguments and explanations regarding Truelove 1's lack of disclosure and determined that the claims, as a whole, are patentable. *See* EX2012, 385 (“None of the prior art teaches in a single disclosure, nor fairly suggest in any combination, Applicants claimed product of a compound of the claimed Formula, formulated as a pharmaceutical composition in a unit dosage form configured for **sublingual or buccal administration**.”).

iii. Petitioner Fails To Show Material Error In The Examiner's Consideration of Truelove 1's **Half-Life Data**

Applicant also explicitly informed the Examiner—both during prosecution and in the specification—that Truelove 1 discusses half-life ($t_{1/2}$) values. For example, the specification discusses the various half-life values reported in Truelove

1. *See* EX1001, 2:5-32 (“Anwar A. Hussain and James B. Truelove were granted patents... [T]he second quality was the rate of hydrolysis expressed as $t_{1/2}$ in human plasma...”); 6:42-57 (“Now referring to FIG. 7, the compounds of the invention as shown in U.S. Pat. Nos. 3,809,714 [Truelove 1] ... Representative molecules include: 7A ... 7B ... 7C ... 7D ... If these molecules show fast permeability through the sublingual and buccal membranes and fast hydrolysis by the enzyme (half-life 1-6 minutes)...”).

These disclosures were not overlooked by the Examiner. In the Notice of Allowance, the Examiner acknowledged Applicant's explanation of the relevant half-life range. *See* EX2012, 385 (“Applicant has amended claims and persuasively argued the unexpected result of the claimed epinephrine prodrug genus having a rapid half-life ranging from 1 to 6 minutes. ... The instantly claimed genus is thus suitable for sublingual or buccal administration having a much shorter half-life. ... None of the prior art teaches in a single disclosure, nor fairly suggest in any combination, Applicants claimed product of a compound of the claimed Formula, formulated as a pharmaceutical composition in a unit dosage form configured for sublingual or buccal administration.”).

In summary, under *Advanced Bionics* and *Becton, Dickinson* factors (c), (e), and (f), there was no material error, and discretionary denial under § 325(d) is warranted.

3. **Ashraf Was Considered During Prosecution Without Error For The Same Log P Disclosure Cited In The Petition**

Ashraf was already considered during prosecution for the same log P disclosure that Petitioner now cites in the Petition. Specifically, Petition relies on Ashraf for Grounds 1 through 3 for the limitation—“wherein said compound has a log P value in the range of about 0.5 – 6.0.” *See* Pet. at 50, 59, 68. But as Petitioner concedes, the '437 Patent specification already acknowledged Ashraf and specifically cited it as the source for the claimed log P range. *See* EX1001, 5:6-12 (“The prodrugs of epinephrine preferably have a Log P value in the range of about 0.5-6.0, and more preferably between 1.0-5.0. This range was listed as a table of marketed sublingual tablets and films in Ashraf et. al “Considerations in developing sublingual tables—An overview”, Pharmaceutical Technology, 2014, 38(11).”); *see also* Pet. at 42-43.

But more importantly, Ashraf does not disclose any of the claimed epinephrine *prodrugs*—let alone their specific log P values. Ashraf is a general review paper about sublingual tablets, and does not address the structure, function, or pharmacokinetic properties of the epinephrine *prodrug* compounds recited in claims 1–3. Listing typical log P ranges for marketed sublingual products does not amount to a teaching that the claimed epinephrine *prodrugs* also fall within that range.

Petitioner also asserts that “Ashraf was not discussed or applied by the Examiner.” Pet. at 43. But Ashraf is expressly discussed in the specification of the ’437 Patent. EX1001, 5:6-12. Thus, Ashraf was presented to the Patent Office. *See* 37 C.F.R. § 1.104(a)(1) (“taking up an application for examination..., the examiner shall make a thorough study thereof...”); *see also Ind. Mills & Mfg., Inc. v. Dorel Indus. Inc.*, 458 F. Supp. 2d 890, 931 (S.D. Ind. 2006) (presuming consideration of references “clearly cited in the specification.”); *Polaroid Corp. v. Eastman Kodak Co.*, 641 F. Supp. 828, 833 (D. Mass. 1985), *aff’d*, 789 F.2d 1556 (Fed. Cir. 1986) (“[P]rior art described in the specifications is expected to be considered by the Examiner.”); *Gould v. Gen. Photonics Corp.*, 534 F. Supp. 399, 403 (N.D. Cal. 1982) (“To the extent that the Townes ’439 patent contains disclosure of an optically pumped maser, this subject matter was discussed as prior art in the specification of the patent-in-suit and therefore was considered by the Examiner as prior art in issuing the patent-in-suit...”).

In other words, Ashraf provides no teaching the Examiner did not already consider. Therefore, under *Advanced Bionics* and *Becton, Dickinson* factors (c), (e), and (f), Petitioner’s reliance on Ashraf—and particularly in combination with Truelove 1—fails to show any material error by the Office.

4. Almoazen Paper Is Not Prior Art To The ’437 Patent

The Petition relies on the Almoazen Paper for the following limitations:

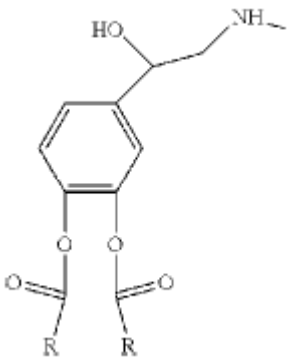
Claims	Preamble/Limitation
1	• “A compound formulated as a pharmaceutical composition in a unit dosage form configured for sublingual or buccal administration” • “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film”
2	• “wherein the compound is formulated in a unit dosage form as a sublingual or buccal administration and” • “wherein the compound formulated in a unit dosage form as a rapidly dissolving film”
3	• “a pharmaceutically acceptable carrier or a pharmaceutically acceptable excipient” • “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film.”

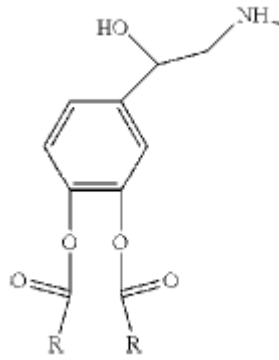
But as explained in Section III.A.1 above, the Almoazen Paper is not even *prior* art. Petitioner's reliance on Almoazen Paper is merely an attempt to create an appearance that at least one of the “art” being relied upon was never previously considered by the Patent Office. *See* Petition at 42 (arguing “Applicant never disclosed the Almoazen Paper to the Patent Office”). But because the Almoazen paper does not qualify as prior art, there was no reason for Applicant to disclose the Almoazen Paper to the Patent Office and Ground 1.

B. Grounds 2's Reliance on Truelove 3 Does Not Present a Materially Distinct Argument from the Examiner's Prior Consideration of Truelove 1

1. Truelove 3 Does Not Even Disclose The Claimed Epinephrine Prodrugs Of Claims 1-3

The Petition relies on Truelove 3 for just about the same limitations of the challenged claims as that of Truelove 1. These include the claimed **unit dosage form for sublingual or buccal administration**, **specific epinephrine prodrugs**, and a **half-life of 1–6 minutes** for specific epinephrine prodrugs recited in claims 1–3.

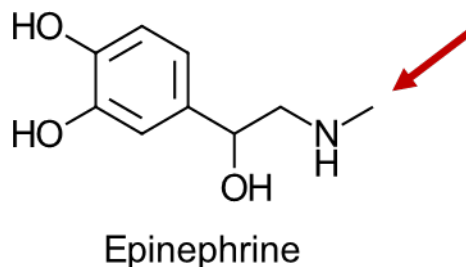
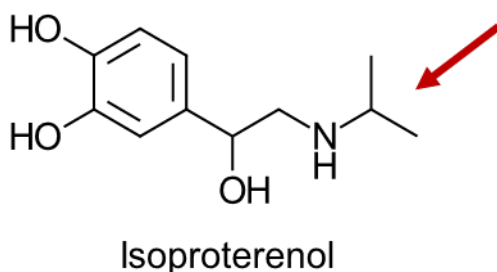
Claims	Preamble/Limitation
1	“A compound formulated as a pharmaceutical composition in a unit dosage form configured for sublingual or buccal administration”  “of a Formula: wherein R is selected from the group consisting of: ... -CH₂CH₂CH₃, ... or a pharmaceutically acceptable salt thereof”

	• “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film”¹¹ • “and has a half-life $t_{1/2}$ range from 1-6 minutes.”
2	 • “A compound of a Formula wherein R is selected from the group consisting of: CH₃, CH₂CH₃ and CH(CH₃)₂” • “wherein the compound is formulated in a unit dosage form as a sublingual or buccal administration and” • “wherein the compound formulated in a unit dosage form as a rapidly dissolving film” • “and has a half-life $t_{1/2}$ range from 1-6 minutes.”
3	• “The compound of claim 2,” • “wherein the compound is selected from the group consisting of: 4-(1-hydroxy-2-(methylamino)ethyl)-1,2-

¹¹ For this limitation colored in **purple** for claims 1-3, while Petitioner's claim charts at pages 104-109 purport to rely on Truelove 3 for this limitation, the Petition's more detailed description section at pages 83-85 does not appear to rely on Truelove 3. Patent Owner includes this limitation out of abundance of caution.

	phenylene diacetate, 4-(1-hydroxy-2(methylamino)ethyl)-1,2-phenylene bis(2-methylpropanoate), 4-(1-hydroxy-2-(methylamino)ethyl)-1,2-phenylene dipropionate; and” • “a pharmaceutically acceptable carrier or a pharmaceutically acceptable excipient” • “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film.”
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Under the first prong of *Advanced Bionics* framework, Truelove 3 presents “the same”—and in fact weaker—arguments than those already considered by the Office in connection with Truelove 1. As explained in Section III.B.1 above, the **specific compounds** in Truelove 3 are not even the *epinephrine* prodrugs recited in claims 1–3. Truelove 3 describes diester *isoproterenol* derivatives—not *epinephrine* prodrugs.



Petitioner offers no meaningful analysis or rationale to explain why the teachings regarding *isoproterenol* in Truelove 3 reasonably apply to the claimed *epinephrine*

prodrugs, including formulation in a unit dosage form for sublingual or buccal administration and its half-life values.

Even if Petitioner's arguments were accepted—which Patent Owner does not concede—Truelove 3's half-life values are, at best, cumulative of those already disclosed in Truelove 1. As shown below, Truelove 1 reports similar half-life data for epinephrine prodrugs. Furthermore, as discussed in Section IV.A.1, Truelove 1 was explicitly cited in the '437 Patent specification and considered during prosecution. Petitioner's reliance on Truelove 3 for half-life values, to extent it has any relevance at all, fails to present a materially distinct argument and is cumulative of art the Examiner already considered.

TABLE 3

Compound	Rate of hydrolysis in $t_{1/2}$ seconds		
	Horse	Rabbit	Human
L-3,4-diacetyl- α -[(methylamino)-methyl] benzyl alcohol hydroperchlorate.....	20	45	180
L-3,4-dipropionyl- α -[(methylamino)methyl] benzyl alcohol hydroperchlorate.....	50	90	240
L-3,4-dibutyryl- α -[(methylamino)-methyl] benzyl alcohol hydroperchlorate.....	100	160	360
L-3,4-dipivalyl- α -[(methylamino)-methyl] benzyl alcohol hydroperchlorate.....	600	720	1,800

EX1002 (Truelove 1), Table 3.¹²

TABLE 3

Compound	Rate of Hydrolysis in $t_{1/2}$ Seconds		
	Horse	Rabbit	Hu- man
3,4-diacetoxy- α [(isopropylamino)-methyl]benzyl alcohol hydrochloride	20	45	180
3,4-dipropionyloxy- α [(isopropylamino)-methyl]benzyl alcohol hydrochloride	50	90	240
3,4-dibutyroxy- α [(isopropylamino)-methyl]benzyl alcohol hydrochloride	100	160	360
3,4-dipivaloxy- α [(isopropylamino)-methyl]benzyl alcohol hydrochloride	600	720	1800

EX1008, (Truelove 3), Table 3.

Hence, under the first prong of *Advanced Bionics* and *Becton, Dickinson* factors (a), (b), and (d), even substantively stronger arguments than those now being presented through Truelove 3 were considered by the Office during prosecution and discretionary denial is warranted.

¹² As discussed in Sections III.D and IV.A.2.i.a, Table 3 of Truelove 1 contains a number of typographical errors but the corrected information was already provided to the Examiner during prosecution.

C. Ground 3's Seven-Way Combination Merely Compiles Previously Considered, Cumulative, and Irrelevant Disclosures

Ground 3 adds three additional references, leading to a Ground that relies on a combination of seven separate references—Truelove 1, Truelove 3, Ashraf, Almoazen Paper, Fuchs, Schobel, and Florence. Truelove 1, Truelove 3, Ashraf, and Almoazen Paper were discussed in Sections IV.A and IV.B, and those arguments are equally applicable here.

The three additional references—Fuchs, Schobel, and Florence—do not alter the outcome regarding why discretionary denial is favored under *Advanced Bionics*.

1. Fuchs: The Same Art And Arguments Made In the Petition Were Already Presented To The Office.

Petition relies on Fuchs for the following limitations of the challenged claims:

Claims	Preamble/Limitation
1	• “A compound formulated as a pharmaceutical composition in a unit dosage form configured for sublingual or buccal administration” • “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film”¹³

¹³ For this limitation colored in **purple** for claim 1, while Petitioner's claim charts at pages 104-109 purport to rely on Fuchs for this limitation, the Petition's more detailed description section at pages 83-85 does not appear to rely on Fuchs. Patent Owner includes this limitation out of abundance of caution.

2	• “wherein the compound is formulated in a unit dosage form as a sublingual or buccal administration and” • “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film”
3	• “a pharmaceutically acceptable carrier or a pharmaceutically acceptable excipient” • “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film.”

Petition at 84, 104. In other words, the Petition relies on Fuchs for the limitations that it already relies on Truelove 1, Truelove 3, and Almoazen Paper for.

Petitioner fails to mention that Fuchs was already cited and acknowledged as having been considered by the Examiner during prosecution. EX2012, 268. Not only that, Fuchs was also explicitly discussed in the specification of the '437 Patent as disclosing mucosal film dosage forms, including for sublingual administration. *See* EX1001, 2:39-47; *see also* Petition at 66, 84 (relying on Fuchs for the same teachings as those already discussed in the '437 Patent's specification). Petitioner does not rely on Fuchs for any new or different teaching. There is no material error under § 325(d).

Therefore, under *Advanced Bionics* and *Becton, Dickinson* factors (c), (e), and (f), Petitioner's reliance on Fuchs fails to show any material error by the Office.

2. **Schobel Is Not Prior Art To The '437 Patent And Was Already In Front Of The Examiner**

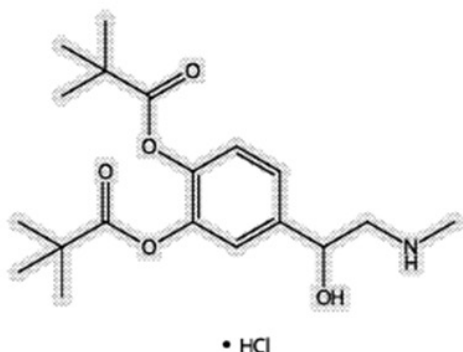
Petitioner relies on Schobel for the following limitations of the challenged claims:

Claims	Preamble/Limitation
1	• “A compound formulated as a pharmaceutical composition in a unit dosage form configured for sublingual or buccal administration” • “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film”
2	• “wherein the compound is formulated in a unit dosage form as a sublingual or buccal administration and” • “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film”
3	• “wherein the compound is formulated in a unit dosage form as a rapidly dissolving film”

In particular, Petitioner relies on Schobel for disclosure of “films designed for administration of epinephrine and salts and esters thereof, *i.e.* epinephrine prodrugs, to human mucosa.” Pet. at 66. But as explained above in Section III.A.2, Schobel is not prior art to any limitation related to epinephrine prodrugs because the relied-upon subject matter lacks written description support in the provisional, Schobel's effective prior art date is no earlier than the filing date of its non-provisional application, May 4, 2017. That date post-dates the '437 Patent's November 13, 2016

priority date. Accordingly, Schobel does not qualify as prior art under 35 U.S.C. § 102, and the Examiner had no legal obligation or basis to consider it for patentability purposes. Under § 325(d), there can be no material error in the Office's decision not to rely on a reference that could not legally bear on patentability. Institution should therefore be denied under § 325(d).

Furthermore, the Examiner did evaluate Schobel during prosecution. The Examiner conducted a structure-based search using the claimed diester compounds and retrieved the earlier printed publication version of Schobel (*i.e.*, U.S. Patent Application Publication No. 2017/0348251). *See* EX2012, 279, EX1021, Cover (listing Prior Publication Data). Despite having found and considered Schobel (and more specifically, the earlier printed publication of Schobel), the Examiner did not reject the claims—confirming that the reference was previously considered and without any error.



L5 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2020 ACS on STN

ACCESSION NUMBER: 2019:168236 CAPLUS Full-text

DOCUMENT NUMBER: 170:237067

TITLE: Enhanced delivery epinephrine and prodrug compositions

INVENTOR(S): Schobel, Alexander Mark; Varjan, Stephanie Marie; Wargacki, Stephen Paul

PATENT ASSIGNEE(S): Aquestive Therapeutics, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 59pp., Cont.-in-part of U.S. Ser. No. 791,249.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20190022023	A1	20190124	US 2018-16143821	20180927
US 20170348251	A1	20171207	US 2017-15587364	20170504
US 20180125977	A1	20180510	US 2017-15717859	20170927
US 20180104195	A1	20180419	US 2017-15791249	20171023
PRIORITY APPLN. INFO.:			US 2016-62331996	P 20160505
			US 2017-15587364	A2 20170504
			US 2017-15717859	A2 20170927
			US 2017-15791249	A2 20171023

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASFORMULTNS 2019:168236

AB Pharmaceutical compns. having enhanced active component permeation properties are described.

IT 52365-63-6, Dipivefrin

RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(enhanced delivery epinephrine and prodrug compns.)

RN 52365-63-6 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, 1,1'-[4-[1-hydroxy-2-(methylamino)ethyl]-1,2-phenylene] ester (CA INDEX NAME)

EX2012, 279.

To the extent Petitioner relies on Schobel only for disclosure of films for buccal administration of drugs, this disclosure is cumulative of Fuchs, as discussed

in Section IV.C.1. Specifically, Fuchs was explicitly discussed in the specification of the '437 Patent as disclosing mucosal film dosage forms, including for sublingual administration. *See* EX1001, 2:39-47.

Accordingly, there was no error by the Examiner during prosecution that would justify institution under § 325(d).

3. Florence: The Same Arguments Made In The Petition Were Already Presented To The Office

Petitioner cites Florence solely for the proposition that “the ideal log P values for buccal absorption typically falls within the range of 3.52 to 5.52.” Pet. at 68. But this teaching is cumulative of Ashraf, which, as discussed in Section IV.A.3, was explicitly discussed in the specification and relied on by Petitioner for the teaching of what log P values are suitable for sublingual tablets and films.

Moreover, Florence provides no disclosure or analysis of the log P values of the specific epinephrine prodrugs recited in the challenged claims. It does not mention the claimed compounds, suggest they fall within the cited log P range, or provide any compound-specific data whatsoever. As such, Florence is not only cumulative of Ashraf—it is not materially relevant to the patentability of the challenged claims.

Because Florence offers no new or materially distinct teaching, and merely reiterates general background already of record, it fails to satisfy the second prong

of *Advanced Bionics*. Under *Becton, Dickinson* factors (c), (e), and (f), Petitioner's reliance on Florence does not establish Examiner error, and institution should be denied under § 325(d).

* * *

Across all three Grounds, Petitioner relies on the same art and arguments the Office already considered and rejected during prosecution. None of the references—alone or in combination—presents a materially distinct teaching or calls into question the Examiner's reasoning. Because the Petition fails both prongs of the *Advanced Bionics* framework, institution should be denied under § 325(d).

V. CONCLUSION

For the reasons discussed above, Patent Owner respectfully requests that the Director exercises her discretion and denies institution of this *inter partes* review proceeding.

Patent Owner's Discretionary Denial Brief

Dated: August 18, 2025

Respectfully submitted,

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CERTIFICATION UNDER 37 C.F.R. § 42.24(d)

I hereby certify that this Patent Owner's Discretionary Denial Brief for *Inter Partes* Review of U.S. Patent No. 11,021,437 has, excluding the portions exempted under 37 C.F.R. § 42.24(a), 11,305 words as counted by the word-processing system used to prepare this document, in compliance with 37 C.F.R. § 42.24(d).

Dated: August 18, 2025

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), the undersigned certifies that on August 18, 2025, a complete copy of the foregoing Patent Owner's Discretionary Denial Brief and corresponding exhibits were served on counsel of record for the Petitioner by filing this document through P-TACTS and by sending this document via electronic mail to the following addresses:

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