UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF TEXAS
FORT WORTH DIVISION

OUTSOURCING FACILITIES ASSOCIATION and NORTH AMERICAN CUSTOM LABORATORIES, LLC d/b/a FARMAKEIO CUSTOM COMPOUNDING, Plaintiffs, v. UNITED STATES FOOD AND DRUG ADMINISTRATION et al., Defendants, and ELI LILLY AND COMPANY, Intervenor-Defendant.	CASE NO. 4:24-cv-953-P

ELI LILLY AND COMPANY'S MEMORANDUM OF LAW
IN OPPOSITION TO THE MOTION FOR PRELIMINARY INJUNCTION

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

Cases

Statutes

Other Authorities

INTRODUCTION

Over the course of nearly a decade, Eli Lilly and Company ("Lilly") conducted more than 37 pre-clinical and clinical trials and invested billions of dollars to secure approval from the Food and Drug Administration ("FDA") for Mounjaro® and Zepbound®, two groundbreaking medicines consisting of a macromolecule Lilly discovered called tirzepatide. Both medicines meet critical patient needs—Mounjaro® treats type 2 diabetes, and Zepbound® treats chronic weight management and sleep apnea in certain adults. As a result, both faced unprecedented demand for periods after they became commercially available. When FDA placed both medicines on its "drug shortage" list, a cast of so-called "compounders" began mass-manufacturing and mass-marketing their own untested, unapproved versions of them. FDA has cautioned that these knockoffs are "risky for patients" because they "do not undergo FDA's review for safety, effectiveness, and quality before they are marketed." The American Diabetes Association likewise recommends against using them "due to uncertainty about their content and resulting concerns about safety, quality, and effectiveness." Compounders nevertheless persisted, invoking FDA's shortage designation as their excuse. But fortunately, the shortage is over. Owing to its historic $23 billion manufacturing investment, Lilly has been able to meet demand for Mounjaro® and Zepbound® since at least August 2024 and will be able to do so going forward. FDA accordingly determined that any shortage of both medicines ended in October 2024.

Predictably, compounders were not happy to lose their excuse to sell (and profit from) their "risky" knockoff drugs, so a trade group called Outsourcing Facilities Association ("OFA") and a pharmacy called FarmaKeio Custom Compounding ("FarmaKeio") (collectively, "Plaintiffs") sued almost immediately. FDA promptly volunteered to reconsider its decision, and to consider any evidence Plaintiffs (and anyone else) wanted to provide regarding whether a shortage persists. But after reviewing "detailed information and data" from Lilly about supply and demand across

all of 2024, FDA concluded once again on December 19, 2024, that "Lilly's supply is currently meeting or exceeding demand for [tirzepatide] drug products." FDA Decision Memo ("DM") 1. In reaching that conclusion, FDA exhaustively "considered potentially relevant information ... from patients, healthcare providers, and others, including compounders," but it determined that their unscientific and anecdotal evidence did "not undermine or outweigh the evidence demonstrating that Lilly's supply is currently meeting or exceeding demand." *Id.* at 2.

Plaintiffs now attack FDA's decision once again, raising both substantive and procedural complaints, but their arguments are meritless. FDA thoroughly considered all the submissions it received and explained at length what it found probative (or not) and why. And the evidence is so one-sided that it would have been arbitrary and capricious to conclude that a shortage persists. FDA did not commit any procedural foot-faults either, but Plaintiffs could not complain even if it did, as they had ample opportunity to persuade FDA that there is a shortage. They just failed to do so—because the facts simply do not support that claim.

Nor can Plaintiffs satisfy any of the other preliminary-injunction factors. Neither Plaintiff has shown a risk of irreparable harm, and the equities weigh strongly against letting compounders continue to sell their knockoff drugs beyond the 60- and 90-day grace periods FDA has already given them. Congress consciously crafted a statutory regime in which compounding is a measure of last resort—and rightly so, as compounded drugs can be dangerous. They are not meaningfully regulated, they are often substandard, and they have far too often caused serious harm. Those concerns are front and center here, as FDA not only has repeatedly sent warning letters and forced recalls stemming from sterility and other serious problems with compounded tirzepatide, but also found serious safety and sterility problems when it inspected FarmaKeio.

For these reasons and those discussed below, the Court should deny Plaintiffs' motion.

BACKGROUND

I. Regulatory Framework

A. To protect patients, Congress has mandated that all prescription drugs must be approved and closely regulated by FDA.

Prescription medicines require FDA approval, *see* 21 U.S.C. § 355(a), which is famously hard to earn. More than 90% of drug candidates ultimately fail.[1] "On average, it takes 10–15 years and costs $2.6 billion to develop one new medicine."[2] Each drug must be evaluated through three increasingly complex phases of studies, typically culminating in double-blind, multi-center, placebo-controlled clinical trials. The sponsor must detail every ingredient and component in its application to FDA. *Id.* § 355(b)(1)(A)(i)–(viii). FDA conducts inspections to ensure compliance with current good manufacturing practice (cGMP), *id.* § 351(a)(2)(B), reviews the drug's labeling to ensure appropriate disclosure of side effects, warnings and contraindications, *id.* § 352(f)(1)–(2), and monitors advertising and promotion to ensure it is not misleading, *id.* §§ 321(n), 352(a)(1), 352(n). FDA also requires manufacturers to track and trace each finished product, *id.* § 360eee-1, to promptly report all adverse events, *id.* § 355(k), and to conduct further post-approval studies, *id.* § 355(o). Simply put, FDA oversight is "the gold standard for safety and effectiveness." Medicine Equity and Drug Safety Act, Pub. L. 106-387, § 745(b)(5), 114 Stat. 1549A-36 (2000).

Because obtaining FDA approval is so hard, Congress has incentivized costly investment in breakthrough medicines by granting statutory exclusivities (distinct from intellectual property rights) that allow innovators to be, for a time, the only lawful source of that medicine. Relevant here, new chemical entity ("NCE") exclusivity is earned whenever FDA approves a new medicine for the first time. 21 U.S.C. § 355(c)(3)(E)(ii), (j)(5)(F)(ii).

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[1] BIO, *Clinical Development Success Rates and Contributing Factors*, at 3 (Feb. 2021), https://tinyurl.com/bp5mb3xy.

[2] PhRMA, *Research and Development Policy Framework* (Sept. 2024), https://tinyurl.com/5eecdtm9.

B. To protect patients, Congress has strictly limited compounding.

"Compounding" means mixing ingredients together to create a medication. While compounding was common in the colonial era, it faded in the nineteenth century as pharmaceutical companies (including Lilly, founded in Indianapolis in 1876) began producing medicines at scale.[3] Today, the FDCA permits compounding in only narrow circumstances. Licensed pharmacists and physicians may compound a version of an FDA-approved product to address a patient-specific need. *See* 21 U.S.C. § 353a. For instance, patients unable to swallow might need "altered forms of medications for easier consumption." *Pros. & Patients for Customized Care v. Shalala*, 56 F.3d 592, 593 (5th Cir. 1995). But pharmacies may not "compound regularly or in inordinate amounts … any drug products that are essentially copies of a commercially available drug product"—in other words, they may not use this limited permission as an excuse to manufacture and sell knockoff drugs free from FDA oversight. *See* 21 U.S.C. § 353a(b)(1)(D).

Congress has also authorized some compounding when a drug is in shortage. The FDCA requires FDA to "maintain an up-to-date list of drugs that are determined … to be in shortage in the United States." *Id.* § 356e(a). A "shortage" is "a period of time when the demand or projected demand for the drug within the United States exceeds the supply of the drug." *Id.* § 356c(h)(2). When FDA places a drug on its shortage list, Section 503B permits entities known as "outsourcing facilities" to use "bulk drug substances" to perform what would otherwise be prohibited compounding of "essentially a copy of an approved drug." *Id.* § 353b(a)(2)(A)(ii), (d)(2)(A). But because compounding presents higher risks to consumers due to the lack of FDA approval and much more lax oversight, the FDCA permits this type of compounding only while the shortage

[3] *See, e.g.*, C. James Watson et al., *Pharmaceutical Compounding: a History, Regulatory Overview, and Systematic Review of Compounding Errors*, 17(2) J. MED. TOXICOLOGY 197, 199 (2020), https://tinyurl.com/2zffwuj7 (less than 1% of all U.S. prescriptions in 1970 "required some sort of in-pharmacy compounding").

persists. And Section 503B authorizes *only* registered outsourcing facilities—*not* Section 503A pharmacies—to compound drugs that are on the shortage list. That is a conscious choice on Congress's part, owing to the fact that outsourcing facilities, while still much less regulated than manufacturers of FDA-approved drugs, must at least register with FDA, report each drug they make, and comply with cGMP. *Id.* §§ 351(a)(2)(B), 353b(a)(1), (b)(1), (b)(2).

The tight restrictions Congress has placed on compounding are the product of a lesson it has learned (repeatedly) over time: There is an enormous incentive for entities to try to sell drugs *without* submitting to FDA oversight, which would mean, *inter alia*, skipping clinical trials and FDA approval, forgoing compliance with cGMP, and not even reporting patient adverse events. Time and again, entities that call themselves "pharmacies" have made and sold unapproved knockoff drugs "under the guise of compounding," working "an end-run around the new drug approval, adulteration, and misbranding provisions of the FDCA." *Med. Ctr. Pharmacy v. Mukasey*, 536 F.3d 383, 390 (5th Cir. 2008). And time and again, Congress has tried to stop them.

Congress first did so in the 1962 Amendments to the FDCA, which "were enacted in response to the rash of birth defects discovered in babies whose mothers had taken" an unapproved drug called thalidomide. *Abigail All. for Better Access v. von Eschenbach*, 495 F.3d 695, 725 (D.C. Cir. 2007). At that point, there were "hundreds of large and small (human and veterinary) compounders" in the United States "compounding the very same (or very similar) drugs" as those made by legitimate drug manufacturers.[4] Concerned that "drugs should not be on the market [in the United States] unless [FDA] knows who is making them, and where they are being made,"[5] Congress decreed that pharmacies may compound without FDA oversight <u>only</u> "in the regular

[4] *Drug Industry Act of 1962*, Hearings before the Committee on Interstate and Foreign Commerce, House of Representatives, 87th Cong., 475–76 (June to Aug. 1962).

[5] S. Rep. 87-1744, 13 (July 19, 1962).

course of their business of dispensing or selling drugs or devices at retail." 21 U.S.C. §§ 360(g)(1); 374(a)(2)(A). If pharmacies engage in compounding at scale—or for any other purpose—then they must register with FDA as drug manufacturers. *Id.* § 360(g)(1). If they fail to register, then *every* drug they make is misbranded, *id.* § 352(o), and selling their drugs is a crime, *id.* §§ 331(a), 333(a).

Nevertheless, unlawful compounding persisted and surged in the late 1980s, inevitably leading to patient harm. For example, in 1990, four patients died after contracting bacterial infections from a compounded cardioplegia solution, and two patients lost an eye and 10 more were hospitalized after contracting bacterial infections from compounded eye drops.[6] Congress responded in 1997 by enacting section 503A with its even stricter constraints on pharmacy compounding. But the 1997 statute was never implemented owing in part to legal challenges by compounders, *see Thompson v. W. States Med. Ctr.*, 535 U.S. 357 (2002), so pharmacy manufacturing disguised as compounding continued to proliferate—and cause harm. Between 2004 and 2006, 80 patients around the country were infected with bacteria from compounded heparin. And in 2007, three patients were killed by compounded colchicine injections, and eight patients in North Carolina were infected with bacteria (and one killed) by compounded fentanyl.[7]

Catastrophe finally struck when an entity called the New England Compounding Center ("NECC") shipped 17,000 knockoffs of Depo-Medrol® injection contaminated with fungal meningitis to 23 states, leaving scores dead and hundreds sickened. *See United States v. Cadden*, 965 F.3d 1, 8 (1st Cir. 2020). Congress responded once again, amending section 503A to address the legal issue that had stymied its implementation, and adding section 503B addressing

[6] Institute for Safe Medication Practices, *Sterile Compounding Tragedy is a Symptom of a Broken System on Many Levels* (Oct. 18, 2012), https://tinyurl.com/34d7c6cs

[7] Pew Charitable Trusts, *U.S. Illnesses and Deaths Associated With Compounded or Repackaged Medications, 2001–19* (Mar. 2020), https://tinyurl.com/4rswtudf

compounding by outsourcing facilities. *See* Pub. L. No. 113-54, § 106, 127 Stat. 587, 598 (2013). Even so, unlawful manufacturing under the guise of lawful compounding has continued—as has harm to patients. For instance, in 2013, 15 patients were infected with bacteria from compounded calcium gluconate injections. In 2016, three children were hospitalized when they received compounded morphine injections that were 2500 percent superpotent. In 2017, 43 patients experienced vision loss, macular swelling, and/or retinal degeneration from compounded intravitreal injections.[8] And many more harmful incidents likely remain unknown—because pharmacies do not have to report them and outsourcing facilities often fail to do so.

II. Factual Background

Tirzepatide is a complex macromolecule that targets two hormone receptors. Over the course of nearly a decade, Lilly completed ***thirty-seven*** pre-clinical studies and clinical trials of tirzepatide, resulting in two path-breaking FDA-approved medicines: Mounjaro®, first approved in 2022 to treat adults with type-2 diabetes; and Zepbound®, first approved in 2023 to help adults with chronic weight management and then approved in 2024 to treat moderate to severe obstructive sleep apnea in adults with obesity. Because tirzepatide is a new chemical entity, both Mounjaro® and Zepbound® are protected by NCE exclusivity through May 2027.

Mounjaro® and Zepbound® each come in six distinct dosage strengths, with patients typically starting at the lowest strength (2.5mg) and titrating up to higher strengths (of 5mg and up to 15mg) over time as needed, as directed by their doctor. And each medicine has been commercially available ever since its launch. *See, e.g.*, DM 7, 13 (finding that [redacted]). But for a time, Lilly experienced excess demand for both medicines, reflecting their immense value to patients and healthcare providers.

[8] *Id.*

Although it was not required to do so, Lilly informed FDA that it projected excess demand first for Mounjaro® and then later for Zepbound®; in response, FDA placed Mounjaro® on the shortage list in December 2022 and Zepbound® on the list in April 2024.

Lilly took swift action to address the high demand. It invested even more heavily in expanding its manufacturing capacity—$23 billion since 2020, the most significant manufacturing commitment in its nearly 150-year history. To increase patient access and affordability and further increase supply, in August 2024 Lilly also launched certain doses of Zepbound®, which was originally sold only in auto-injectors, in single-use vials. These unprecedented investments led FDA to confirm in August 2024 that "[a]ll doses of Mounjaro and Zepbound [were] available."[9] And on October 2, 2024, FDA determined that the shortage was over because Lilly "can meet the present and projected national demand."[10]

Five days later, Plaintiffs—a pharmacy and a trade association for outsourcing facilities—filed this lawsuit challenging that decision. FDA asked the Court to stay the litigation so FDA could "reevaluate" its decision. ECF Nos. 27, 28. FDA then let all interested parties submit additional information, which both Lilly and Plaintiffs (as well as many others) did. After considering that wealth of information, FDA issued a 12-page declaratory order and a 32-page supporting memorandum on December 19, 2024, confirming that Lilly's medicines are not in shortage. Because they wish to continue selling knockoffs of Lilly's medicines, Plaintiffs seek a preliminary injunction to put them both back on the shortage list.

[9] Ned Pagliarulo, *Zepbound, Mounjaro back in supply as Lilly resolves shortage*, BIOPHARMA DIVE (Aug. 5, 2024), https://tinyurl.com/4zkucwph.

[10] FDA, *FDA clarifies policies for compounders as national GLP-1 supply begins to stabilize* (Oct. 2, 2024), https://tinyurl.com/54aekvuh.

ARGUMENT

A preliminary injunction is an "extraordinary equitable remedy that is never awarded as of right" and requires the movant to "make a clear showing that he is likely to succeed on the merits, that he is likely to suffer irreparable harm in the absence of preliminary relief, that the balance of equities tips in his favor, and that an injunction is in the public interest." *Starbucks Corp. v. McKinney*, 602 U.S. 339, 345–46 (2024) (cleaned up). Plaintiffs fall well short of making any—let alone all—of those showings. Their claims are doomed on the merits, they have shown no risk of irreparable injury, and the equities strongly cut against allowing compounders to continue selling unapproved, untested, and often unsafe knockoffs of Lilly's FDA-approved medicines.

I. Plaintiffs have not shown a likelihood of success on any claim.

The preliminary-injunction analysis typically begins—and often ends—with "arguably the most important factor: likelihood of success on the merits." *Netflix, Inc. v. Babin*, 88 F.4th 1080, 1099 (5th Cir. 2023). A "substantial" likelihood of success is necessary—but not sufficient. *Planned Parenthood Ass'n of Hidalgo Cnty. Tex., Inc. v. Suehs*, 692 F.3d 343, 348 (5th Cir. 2012). Plaintiffs challenge FDA's decision on two grounds: (1) it is arbitrary and capricious and (2) FDA failed to use notice-and-comment procedures. Neither argument withstands scrutiny.

A. Plaintiffs cannot show that FDA's decision was arbitrary and capricious.

"The arbitrary or capricious standard requires that agency action be reasonable and reasonably explained." *Texas v. Biden*, 589 F. Supp. 3d 595, 618 (N.D. Tex. 2022). FDA's 32-page Decision Memorandum (DM) is plainly both. FDA thoroughly examined all the submissions before it, explained in detail which it found persuasive (or not) and why, and reached the only reasonable conclusion the record could sustain: Lilly's medicines are no longer in shortage. Plaintiffs' efforts to find fault with FDA's decision range from ineffective nitpicking to unfounded accusations. Their arbitrary-and-capricious claims are therefore exceedingly unlikely to succeed.

1. FDA reasonably credited Lilly's comprehensive, detailed data.

a. The central question before FDA was whether Lilly's drugs are in shortage—i.e., whether "the demand or projected demand for the drug within the United States exceeds the supply of the drug." 21 U.S.C. § 356c(h)(2). "FDA evaluates the supply and demand or projected demand of the drug on a nationwide level, across the entire market, not at the local level." DM 3. And Lilly provided FDA with a wealth of information that spoke directly to that comprehensive nationwide inquiry, supplying data "regarding its production and inventory of [Mounjaro® and Zepbound®] at various points in time, including stock reports that show quantities supplied and demanded, and inventory held in stock, for all strengths of [Mounjaro® and Zepbound®]; cumulative quantities supplied to and demanded by its customers in the year 2024; projected demand and supply in future months; and wholesaler inventory data, among other information." DM 1. As FDA's decision ably explains, each category of data Lilly provided strongly supports its finding that Lilly's supply of both Mounjaro® and Zepbound® exceeds nationwide demand.

For example, stock reports show that Lilly consistently has "fulfill[ed] all existing orders" from wholesalers "while generally maintaining … excess inventory." DM 5. Lilly [redacted]. DM 6, 10. [redacted] DM 5–6. [redacted] DM 5. [redacted], DM 12, FDA reasonably concluded that "these reports support [its] conclusion that supply is meeting or exceeding demand." DM 6.

Lilly also provided FDA with "historic data on monthly … supply and demand," enabling it

to [redacted] DM 7. [redacted] DM 10, tbl. 4. And that [redacted] DM 6. That data, which FDA [redacted], readily supports FDA's conclusion that Lilly's supply "significantly exceed[ed] overall demand" in 2024. DM 7–10, tbls. 2–4.

Lilly also [redacted]. DM 15. Lilly [redacted]. DM 13. And while Lilly [redacted]. DM 14. [redacted]. DM 14 & n.57. FDA thus fairly concluded that "Lilly has reasonably assessed projected supply and demand," that [redacted] "gives [FDA] further confidence in the accuracy of Lilly's predictions," and that those predictions showed that "supply will meet or exceed projected demand … [redacted] DM 15.

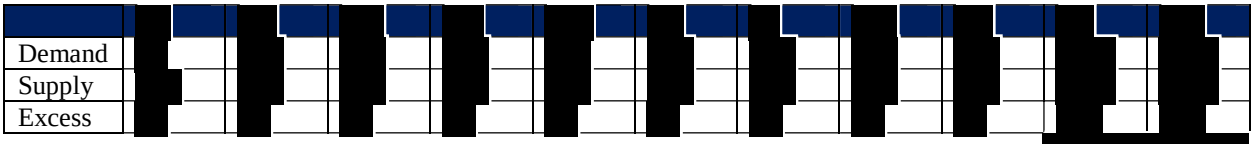
Lilly also provided data about inventory in the distribution channel, including wholesaler

inventory. FDA found that [redacted] DM 11; *see also* DM 12 & tbl. 5. Lilly also [redacted] DM 12. All of that likewise "indicate[s] that nationwide supply for [Lilly's] products is exceeding demand." *Id*. And [redacted] *see* DM 4–5, 15 n.60, [redacted]

b. Plaintiffs' efforts to find fault with that evidence, or FDA's analysis of it, are baseless. Plaintiffs try to analogize supply and demand of drugs to the cumulative record of a sports team, arguing that how a team performs in each month is not necessarily indicative of its overall record. Mem. 15. But that ignores that Lilly's supply does not reset to zero on the first of every month. Excess supply in one month carries over as supply the next month, as Lilly's medicines (which, unlike Plaintiffs', have been rigorously tested for stability) can be stored for up to 24 months with proper refrigeration. Given that dynamic, it would make no sense to look myopically at each month in isolation, or to consider only year-end totals, as neither would provide anywhere near as complete a picture of whether supply will *continue* to meet demand. And it would make particularly little sense to focus only on earlier months when Lilly's medicines were on the shortage list, as the question for FDA was whether they *remain* in shortage, not whether they ever were. It was therefore eminently reasonable for both Lilly and FDA to assess monthly supply and demand on a cumulative basis throughout 2024, focusing on the recent past, present, and future.

It was also eminently reasonable for FDA to find that this data supported its conclusion

that Lilly's medicines are no longer in shortage, as the data showed Lilly not only meeting demand but also growing its excess inventory:



DM at 7, 10. In fact, [redacted]. *Id.* at 10. [11]

FDA was not confused about any of this. *Contra* Mem. 15. Nor did it fail to make a "finding of demand under any consistently defined time period." Mem. 19. FDA consistently [redacted], DM 14 n.57, and that data consistently "demonstrate[d] … increasing amount of additional supply," DM 7, 10. If anyone is confused, it is Plaintiffs: They fault Lilly for not presenting "net inventory" data on a "cumulative" basis, Mem. 17, but net inventory *always* speaks cumulatively by showing the doses on a given day net of all sold doses and newly made doses. And Plaintiffs claim that [redacted], Mem. 18, only by ignoring net inventory: Lilly [redacted] DM 7, 10.[12]

In short, Lilly provided months of ongoing, real-time data showing that supply consistently exceeded demand and will continue to do so even under [redacted]. FDA's explanations for finding that data reliable are eminently reasonable.

[11] In addition to [redacted] *Id.*

[12] Plaintiffs also fault FDA for [redacted] Mem. 18; *see* DM 10, 15. But FDA [redacted] *Id.* at 14 (emphasis added). And, of course, [redacted]

2. FDA properly rejected Plaintiffs' unreliable submissions.

In stark contrast to Lilly's comprehensive hard data, Plaintiffs and their supporters offered a jumbled collection of form letters, unverified snapshots, and internet polls, almost all addressing supply and demand (if at all) in isolation, at the local level, and often for just a single dose, not all 12 that Lilly makes. After methodically considering all those submissions, FDA spent fully 13 of the 32 pages of its decision detailing why it did not find them useful, reliable, or probative. *See* DM 16–29. As it explained, all had "important limitations," and they did "not demonstrate that Lilly will be unable to meet projected demand, especially when weighed against the Lilly-provided data." *Id.* at 2. Once again, both FDA's analysis and its conclusions are eminently reasonable.

For example, Plaintiffs and a compounder called Hims & Hers Health ("Hims") submitted putative surveys (really just webforms on its own websites) purportedly addressing supply issues. DM 16–17. These "surveys" had no reliability controls to avoid fabricated or even automated submissions, did not detail what challenge the respondent faced (*e.g.*, if a doctor refused to prescribe a drug), and did not address how long it persisted (*e.g.*, if a prescription was filled the next day). DM 17, 19. Nevertheless, FDA considered them. It just concluded that—at most—they showed only that individuals occasionally had "trouble getting prescriptions" filled, which is "most likely explained not by a continuing national shortage of supply, but by the practical dynamics of the portion of the supply chain between Lilly and the individual customers." DM 18. For example, a distributor may delay stocking a particular pharmacy "due to factors like ordering practices and incentives, cold chain logistical considerations, and retailer capacity constraints." DM 18.

Plaintiffs, Hims, and a compounder advocacy group also submitted screenshots—many undated—purporting to show that certain pharmacies could not order a particular dose at a particular time from one or another "Big Three" wholesaler. DM 19–20. A lawyer for "numerous pharmacies" similarly claimed that those pharmacies "'experienc[ed] significant difficulties in

obtaining' tirzepatide." *Id.* at 20. But those submissions did "not include information about the length of time that the product [was] ... out of stock," leaving it entirely possible that the pharmacy filled the order the very next day. *Id* at 19. Even so, FDA considered them. It just found them [redacted] but rather confirmed through more comprehensive data that [redacted]—the opposite of a nationwide shortage. *Id.* at 20–21. FDA likewise found that anecdotal news or blog accounts did not undermine or outweigh the hard data that Lilly submitted. *Id.* at 21–22, 28.[13]

FDA also explained why the production data supplied by 503B outsourcing facilities and 503A pharmacies did not support finding a shortage. "[F]or the first half of 2024"—[redacted]—503B pharmacies reported manufacturing only [redacted] doses compared to Lilly's [redacted] doses. *Id.* at 10, 24. OFA claimed its members (503Bs) produced [redacted] in "September 2024," but Lilly supplied more than [redacted] doses that month. *Id.* at 10, 25. And, while an advocacy group claimed that four 503A pharmacies filled [redacted] prescriptions in a single month (appx. [redacted] doses), the total reported volume compounded paled in comparison to the [redacted] doses Lilly maintained as ***excess inventory*** between September and November 2024. *Id.* at 10, 26. Indeed, the best Plaintiffs could muster was a news article claiming that compounded tirzepatide and compounded semaglutide—a different drug made by a different manufacturer—*collectively* served "up to 2 million Americans," which [redacted]. *Id.*

[13] Plaintiffs claim that the most "probative evidence" of a shortage is availability of a drug "from the 'Big Three' wholesalers," Mem. 19, and they cite a November 1, 2024 earnings call transcript for one wholesaler, Cardinal Health, claiming "supply that does not meet ... demand" for "GLP-1s" based on inventory was observed "over the last several quarters." App. 87. But this extra-record evidence is not probative at all. The speaker was commenting on its inventory of *all* GLP-1s, not tirzepatide specifically, and Lilly's main competitor in this space *is* still on FDA's shortage list. Moreover, the speaker was referring to the quarters leading ***up to*** October 2024.

In short, FDA found that Plaintiffs' proffered evidence suffered from a common defect: *All* the screenshots, surveys, and comments revealed supposed unavailability only at a single, isolated point in time, omitting the nature of the purported "difficulty" in obtaining Mounjaro® or Zepbound® and any context showing how long it persisted. At very best, that evidence suggested that a patient was unable to get medicine on a particular day at a particular location, which is manifestly insufficient to show that demand exceeded supply nationwide. Lilly's data, by contrast, provided aggregate, nationwide data over time, which enabled FDA to assess trends, cumulative effect, and how long any intermittent backorder or temporary disruption lasted. *See, e.g.*, DM 5–7, 11, 12, 14.

Ultimately, Plaintiffs' real complaint is not that FDA failed to consider their submissions but that FDA did not find them particularly relevant or persuasive. Indeed, they accuse FDA of having "indulge[d]" Lilly at every turn while evincing "hyper-skepticism of all contrary evidence." Mem. 19. In reality, FDA held all submissions to the same standard. For instance, it [redacted] DM 13 n.44. FDA also [redacted]. *See* DM 13–14 n. 53.

Perhaps recognizing they cannot win the evidentiary battle, Plaintiffs try to lower the bar, claiming that a medication is in shortage any time some "patients cannot get" it, at some place in the United States (however isolated), at any given moment (however temporary). Mem. 20. But Congress defined a "drug shortage" as "when the demand or projected demand for the drug *within*

the United States exceeds the supply." 21 U.S.C. § 356c(h)(2) (emphasis added)); *see also id.* § 356e(a) (requiring Secretary to list drugs determined "to be in shortage in the United States"). Congress similarly required manufacturers to report problems that are "likely to lead to a meaningful disruption in the supply of that drug in the United States." *Id.* § 356c(a)(2). And the statute defines "meaningful disruption" as "more than negligible" and "affect[ing] the ability of the manufacturer to fill orders or meet expected demand," while excluding routine maintenance or insignificant interruptions if "the manufacturer expects to resume operations in a short period of time." *Id.* § 356c(h)(3). All of that is why FDA correctly "evaluates the supply and demand or projected demand of the drug on a nationwide level, across the entire market, not at the local level." DM 3. And Plaintiffs' proffered "evidence" does not remotely suggest any nationwide shortage.

As a last-ditch effort, Plaintiffs complain that their submissions "should have prompted the agency to investigate" more. Mem. 22. But an agency has no obligation "to conduct or commission [its] own empirical or statistical studies." *FCC v. Prometheus Radio Project*, 592 U.S. 414, 427 (2021). Plaintiffs had their chance to give FDA relevant information. FDA just (understandably) did not find what they came up with compelling, especially contrasted with the "detailed quantitative picture of the supply and demand situation both over time, and at the national level," Lilly supplied. DM 19. There is nothing arbitrary and capricious about that.

B. Plaintiffs cannot succeed on their notice-and-comment claim.

Plaintiffs spill substantial ink arguing that FDA should have engaged in notice-and-comment rulemaking. *See* Mem. 7–13. Yet they never address their hypocrisy. FDA did not engage in notice and comment when it put Lilly's medicines on the shortage list. By Plaintiffs' own telling, that is what enabled them to sell knockoff tirzepatide in the first place. But the APA "mandate[s] that agencies use the same procedures when they amend or repeal a rule as they used to issue the rule in the first instance." *Perez v. Mortg. Bankers Ass'n*, 575 U.S. 92, 101 (2015). So if Plaintiffs

are right, then FDA's listing decision was improper; if they are wrong, then FDA's delisting decision was proper. Either way, Plaintiffs should not be compounding copies of Lilly's medicines, which is reason enough to reject their notice-and-comment claim.

That said, this is not a close call on the merits. FDA's memorandum crunched numbers as an evidentiary matter; it did not make any policy judgments. That is not rulemaking. Plaintiffs rely heavily on *Safari Club Int'l v. Zinke*, 878 F.3d 316, 332 (D.C. Cir. 2017), in arguing to the contrary. *See* Mem. 10. But *Safari Club* derived "[t]he basic distinction between rulemaking and adjudication," 878 F.3d at 332, from the Supreme Court's decision in *United States v. Florida East Coast Railway Co.*, which distinguished "proceedings for the purpose of promulgating policy-type rules or standards" from "proceedings designed to adjudicate disputed facts in particular cases," 410 U.S. 224, 225 (1973). In *Safari Club*, the Fish and Wildlife Service made a prospective policy judgment about whether and when killing elephants enhances the species' survival, which "implemented and interpreted [a rule's] enhancement requirement" and thus bore "all of the qualities of a legislative rule." 878 F.3d at 333, 334. Here, by contrast, FDA's determination whether supply for two medicines is outstripped by demand bears none.

At any rate, even if notice and comment were required, Plaintiffs cannot show prejudice. While they are unwilling to concede that prejudice "matters," Mem. 12–13, it does: The APA mandates that "due account shall be taken of the rule of prejudicial error." 5 U.S.C. § 706; *accord Little Sisters of the Poor Saints Peter & Paul Home v. Pennsylvania*, 591 U.S. 657, 684 (2020); *United States v. Johnson*, 632 F.3d 912, 930 (5th Cir. 2011). The "touchstone" of that analysis "is 'whether it is clear that the lack of notice and comment did not prejudice the petitioner.'" *City of Arlington v. FCC*, 668 F.3d 229, 244 (5th Cir. 2012), *aff'd*, 569 U.S. 290 (2013). And the burden falls squarely on the plaintiff "to demonstrate prejudice from the error." *Id.* at 243. Plaintiffs cannot

make that showing, as they admit that they not only "were aware of FDA's consideration" but "were able to provide evidence." Mem. 12. Indeed, neither Plaintiff identifies a single thing it would have submitted had FDA treated the decision as a rule.

Nor could they, as FDA abided by virtually all the requirements of notice-and-comment rulemaking. *Cf. Little Sisters*, 591 U.S. at 683–84 (holding that agencies satisfy the APA when they provide all required elements, "[f]ormal labels aside"). Notice-and-comment rulemaking requires an agency to publish its proposed action in the Federal Register, identify the legal authority for it, describe the subjects or issues involved, provide an opportunity to submit views, concisely state its final reasoning, and leave 30 days before the rule takes effect. *Little Sisters*, 591 U.S. at 683–84, 685–86 (citing 5 U.S.C. § 553(b)). The only one of those things FDA did not do is publish notice in the Federal Register—and that is not even a hard-and-fast requirement. 5 U.S.C. § 553(b) (publication not required in cases involving "actual notice"). Again, Plaintiffs concede that they not only "were aware of FDA's consideration" but "were able to provide evidence." Mem. 12. "[F]air notice" requires nothing more. *Little Sisters*, 591 U.S. at 684.

Plaintiffs are left speculating that maybe someone *else* might have provided more evidence had more notice been provided. That claim is hard to take seriously when Plaintiffs undertook an extensive "internet letter-writing campaign," DM 19, to ensure that their supporters would come out in force. But more to the point, it is legally irrelevant, as Plaintiffs must show harm to the "*the petitioner*," not to some unidentified, other hypothetical commenter. *City of Arlington*, 668 F.3d at 243–44 (emphasis added); *see also Little Sisters*, 591 U.S. at 684. Plaintiffs' procedural claim thus fails several times over.

II. Plaintiffs have not shown likely irreparable harm.

Neither plaintiff has shown irreparable harm. OFA is a trade association that has failed to identify any injured member, and FarmaKeio is a 503A pharmacy, not a 503B outsourcing facility,

so its rights to compound do not turn in any way on whether tirzepatide is in shortage.

A. OFA has not sufficiently alleged any harm to its members.

To show even injury-in-fact, "plaintiff-organizations" like OFA must make a specific showing "that at least one *identified* member has suffered or would suffer harm." *Summers v. Earth Island Inst.*, 555 U.S. 488, 498 (2009) (emphasis added).[14] OFA has not done so. According to the complaint, OFA "is a trade association representing outsourcing facilities." Am. Compl. ¶ 5. But at no point does the complaint identify *any* member of the association, much less an OFA member who has been compounding tirzepatide and now must stop because the shortage is over. And OFA's declaration just refers vaguely to conferring with members, while never identifying actual members who will be harmed. That is a fatal deficiency. *See FW/PBS, Inc. v. Dallas*, 493 U.S. 215, 235 (1990) (affidavit insufficient where it "fail[ed] to identify the individuals" allegedly harmed).

B. FarmaKeio has no legal interest in this case.

FarmaKeio at least alleges that it compounds tirzepatide for mass distribution, and it claims that it could lawfully continue to do so if Lilly's tirzepatide drugs remained on the shortage list. *See* Am. Compl. ¶¶ 22, 60–61. But FarmaKeio says it is a 503A pharmacy, not a 503B outsourcing facility, *cf.* Mem. 21–22 (chastising FDA for "erroneously" referring to FarmaKeio "as an outsourcing facility"), and Section 503A does not give pharmacies any right to compound to address a shortage.

As explained, Congress added section 503B to allow *outsourcing facilities* to compound FDA-approved medicines during a shortage. *See supra* Background § I(B). But Congress did not grant comparable authorization for pharmacies under Section 503A—for good reason. While outsourcing facilities still fall far short of FDA-approved manufacturers, Congress at least holds

[14] There is an exception to name-names requirement if an association can show that *all* its members are affected by the challenged activity. *Summers*, 555 U.S. at 498–99. But OFA does not and cannot make any such claim here.

them to higher standards than pharmacies: They must register, report their drugs, follow cGMP, and report adverse events. Pharmacies are not required to do any of those things. And Congress was legislating in the wake of the NECC catastrophe, which raised severe safety concerns about pharmacy compounding.

FarmaKeio nevertheless claims that it may mass produce drugs that are on the shortage list, on the theory Section 503A *prohibits* pharmacies from manufacturing only "drug products that are essentially copies of a *commercially available* drug product," 21 U.S.C. § 353a(b)(1)(D) (emphasis added), and "commercially available" (according to FarmaKeio) means not in shortage. *See* Am. Compl. ¶ 22. FarmaKeio is wrong.[15] Congress defined "shortage" in its economic sense of demand exceeding supply, on a national scale. *See* 21 U.S.C. § 356c(h)(2). The phrase "commercially available," by contrast, simply means available to be bought and sold. *See, e.g.*, *N.B. Indus. v. Wells Fargo & Co.*, 465 F. App'x 640, 642 (9th Cir. 2012); *cf. W. States*, 535 U.S. at 361 (equating a "commercially available" drug with a "mass-produced product"). As the Supreme Court has explained, because "'available' resources are different from those *in hand*," something can be "available" even if someone does not have it. *Schweiker v. Gray Panthers*, 453 U.S. 34, 48 (1981). Indeed, many, if not most, medications that are in shortage are still bought and sold every day. Lilly's medicines are a case in point, as they have always been "available": Lilly shipped [redacted] doses of approved tirzepatide in 2024 alone. *See* DM 7, 13. To pretend that approved tirzepatide is not commercially available today would be absurd.

FarmaKeio's reading of the statute also ignores the rule that courts must "ascribe

[15] To the extent FDA shares that view, *see* FDA, Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act at 5 (2018), https://tinyurl.com/u95bzckb, its interpretation of Section 503A is entitled to no deference. Courts must adopt the "best" interpretation of a statute, applying traditional tools of statutory construction, not defer to agencies. *See Loper Bright Enters. v. Raimondo*, 603 U.S. 369, 400, 412–13 (2024).

significance" to Congress's decision to use explicitly different language in sections 503A and 503B. *See Babb v. Wilkie*, 589 U.S. 399, 412 (2020); *Russello v. United States*, 464 U.S. 16, 23 (1983)). That basic rule of construction holds even where "two statutes may be similar in language and objective." *N. Haven Bd. of Ed. v. Bell*, 456 U.S. 512, 530 (1982); *see United States v. Sullivan*, 332 U.S. 689, 699 (1948) ("The [FDCA] is long and complicated. … The differences are as important as the similarities, and cannot be ignored."). Courts must not adopt "an interpretation that violates the rule against ascribing to one word a meaning so broad that it assumes the same meaning as another statutory term." *Ysleta del Sur Pueblo v. Texas*, 596 U.S. 685, 698 (2022) (cleaned up). FarmaKeio's interpretation does exactly what *Ysleta* prohibits: It reads "commercially available" in Section 503A so broadly as to mean the same thing as a different statutory phrase ("appears on the shortage list") that Congress used *only* in Section 503B.

The Court should see FarmaKeio for what it is. FarmaKeio openly boasts that it is a large-scale drug manufacturer operating under the guise of Section 503A pharmacy compounding. By its own telling, it has been selling $1,750,000 to $2,000,000 worth of unapproved, untested tirzepatide every month, Mem. 23, and has produced 67 liters of tirzepatide (equivalent by volume to 134,000 vials of Mounjaro®) in just the fourth quarter of 2024. App. 2, ¶ 14. That manufacturing "so clearly transcend[s] the level of normal pharmacy operation as to leave no question" that FarmaKeio is an unregistered drug maker, *Cedars North*, 1978 U.S. Dist. LEXIS 15829 at *6—and an unsafe one, at that, *see infra* pp. 23–24.

III. The balance of the equities and the public interest cut against an injunction.

If any more were needed, the balance of the equities and the public interest cut strongly against letting compounders continue to sell knockoffs of Lilly's medicines. Of course, every day that compounders are allowed to violate Lilly's statutory exclusivity is irreparable harm to Lilly. *See Hi-Tech Pharmacal Co. v. FDA*, 587 F. Supp. 2d 1, 12 (D.D.C. 2008). But more importantly,

every day that compounders are allowed to sell their knockoff drugs puts patients at risk.

Lilly's medicines are fully regulated by FDA, and they have been exhaustively evaluated to ensure their safety and efficacy. Compounded drugs, by contrast, are not meaningfully regulated by FDA. They are not studied or approved by FDA. And when made by a 503A pharmacy, they are not listed with FDA, made in a facility registered with FDA, or required to be made in accordance with cGMP. Their labeling typically lacks "important information such as adequate directions to help ensure the drugs are used safely."[16] And they are not subject to the serialization or track-and-trace requirements that help protect U.S. patients from illegitimate or counterfeit products. In short, they "do not have the same safety, quality, and effectiveness assurances as approved drugs,"[17] which is why FDA routinely cautions patients and doctors to avoid compounded drugs when rigorously tested, safe and effective, approved medicines are available.[18]

FarmaKeio is a prime example. When FDA inspected FarmaKeio, it found that FarmaKeio "routinely uses non-pharmaceutical grade components for compounding drug products," used materials and supplies that "were not disinfected," and used non-sterilized equipment "in sterile drug production."[19] "[A]ctionable microbial contamination was found to be present," including a "visible pink residue" on the ceiling wall and exhaust vent.[20] FDA has warned "patients and health care professionals not to use products intended to be sterile" made by FarmaKeio.[21] That warning

[16] FDA, *Understanding the Risks of Compounded Drugs* (Dec. 18, 2024), https://tinyurl.com/ukyfr8j8.

[17] FDA, *Compounding and the FDA: Questions and Answers* (June 29, 2022), https://tinyurl.com/2dypvs2y.

[18] *See, e.g., id.* ("Unnecessary use of compounded drugs unnecessarily exposes patients to potentially serious health risks."); FDA, *Guidance for Industry: Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act*, 3 (Jan. 2018), https://tinyurl.com/y4dhe3ee ("[C]ompounded drugs should only be distributed to health care facilities or dispensed to patients to fulfill the needs of patients whose medical needs cannot be met by an FDA-approved drug.");.

[19] FDA, *Form 483 Inspection Report* (Mar. 10, 2022) at 1–3, https://tinyurl.com/3a83cj4z.

[20] *Id.* at 2–3.

[21] FDA, *FDA warns patients and health care professionals not to use sterile products from FarmaKeio Superior*

led to a recall of at least seven lots of substandard injections.[22] FDA later issued a warning letter concluding that compounded drugs sold by FarmaKeio "put patients at risk."[23] That warning letter appears to remain open and unresolved.

Although compounding by 503B outsourcing facilities is at least better regulated than compounding by 503A pharmacies, drugs made by outsourcing facilities still present significantly more risk to patients than FDA-approved medicines. They are not studied or approved by FDA before they are sold. FDA does not inspect outsourcing facilities before they may begin production. And on the relatively infrequent occasions when FDA has inspected outsourcing facilities after they commenced compounding, inspectors have often found serious deficiencies—including with compounding tirzepatide. For instance, following a failed inspection in August 2024, an outsourcing facility was forced to recall *3,258 vials* from three different lots of compounded tirzepatide due to a "[l]ack of [a]ssurance of [s]terility."[24]

And that is just one of many problems FDA has found with compounded tirzepatide. In May 2023, FDA oversaw a nationwide recall of subpotent tirzepatide made by a compounder in Houston,[25] and a second, nationwide recall of mislabeled tirzepatide made by the same Houston compounder in May 2024.[26] In November 2024, FDA issued an urgent warning that a compounder in California had sold supposedly sterile injections containing a visible black particulate.[27] In

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Custom Compounding (Mar. 30, 2022), https://tinyurl.com/3fb2mj3u.

[22] FDA, *Enforcement Report, Event ID: 89954* (Apr. 5, 2022), https://tinyurl.com/43267pc2.

[23] FDA, *Warning Letter FarmaKeio Superior Custom Compounding* (Nov. 18, 2022), https://tinyurl.com/4hvwwfyn.

[24] FDA, *Enforcement Report, Event ID: 95190* (Sept. 11, 2024), https://tinyurl.com/2bxpn5kj; *see also* FDA, *Warning Letter to ProRx, LLC* (Dec. 20, 2024), https://tinyurl.com/2wctva8x.

[25] FDA, *Enforcement Report, Event ID: 92329* (May 11, 2023), https://tinyurl.com/2s4hmxmz.

[26] FDA, *Enforcement Report, Event ID: 94550* (Apr. 20, 2024), https://tinyurl.com/4r9rsbpe.

[27] FDA, *FDA warns patients and health care professionals not to use compounded drugs from Fullerton Wellness* (Nov. 1, 2024), https://tinyurl.com/y7spnt3r.

December 2024, FDA determined that a compounder in Pennsylvania had been selling adulterated and misbranded tirzepatide.[28] All of that led FDA to issue a general warning that compounded tirzepatide is "risky for patients."[29] And those known incidents likely only scratch the surface since pharmacies do not have to report adverse incidents with their compounded drugs and outsourcing facilities often fail to do so. Unsurprisingly, others have expressed concerns with compounded tirzepatide too. In December 2024, the American Diabetes Association concluded that "[n]on-FDA-approved compounded incretin products are not recommended for use due to uncertainty about their content and resulting concerns about safety, quality, and effectiveness."[30] The National Consumers League has warned against them too,[31] as have foreign governments.[32]

In short, the safety risks here are real, and FDA reasonably found that there is no longer anything that justifies subjecting patients to them. Plaintiffs identify no basis to disturb that finding and perpetuate the dangers posed by compounded tirzepatide.

CONCLUSION

For all these reasons, the Court should deny Plaintiffs' Motion.

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[28] FDA, *Warning Letter to ProRx, LLC* (Dec. 20, 2024), https://tinyurl.com/2wctva8x.

[29] FDA, *FDA's Concerns with Unapproved GLP-1 Drugs Used for Weight Loss* (Dec. 18, 2024), https://tinyurl.com/5x847mut.

[30] Joshua Neumiller et al., *Compounded GLP-1 and Dual GIP/GLP-1 Receptor Agonists: A Statement from the American Diabetes Assoc.* 48 Diabetes Care 177 (Feb. 2025), https://tinyurl.com/ycxj9frm ("Non-FDA-approved compounded incretin products are not recommended for use due to uncertainty about their content and resulting concerns about safety, quality, and effectiveness.").

[31] Nat'l Consumers League, *NCL urges the public to heed warnings about unregulated versions of GLP-1 weight loss drugs* (Feb. 4, 2025), https://tinyurl.com/2vawuhx4.

[32] *See, e.g.*, Press Release, *Protecting Australians from unsafe compounding of replica weight loss products*, DEP'T OF HEALTH & AGED CARE (May 22, 2024), https://tinyurl.com/4h97py7b (Australian government banning development and sale of compounded anti-obesity products because of "increasing community concern" and "increasing reports of patients coming to harm from" compounded drugs promoted to aid weight loss); Press Release, *SAHPRA's Position On GLP1 And GIP-GLP1 Products That Are Compounded, Substandard And Falsified*, S. AFRICAN HEALTH PRODS. REGULATORY AUTH. (Nov. 8, 2024), https://tinyurl.com/mr2r6mkw (South African authorities warning that these compounded drugs "pose[] a public health and safety risk" due to "the unknown nature and safety of ingredients used in compounding").

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I certify that on February 18, 2025, I served the foregoing document electronically in accordance with the Federal Rules of Civil Procedure.

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