U.S. FOOD & DRUG ADMINISTRATION

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To: CDER Drug Shortage File

Subject: Resolution of Tirzepatide Injection Product Shortage and Supply Status

Tirzepatide injection products were first added to FDA's drug shortage list on December 15, 2022. The Agency determined that the shortage was resolved and removed tirzepatide injection products from FDA's drug shortage list on October 2, 2024.[1] FDA has now reevaluated that decision.[2] For the reasons below, FDA has determined upon reevaluation that the tirzepatide injection product shortage is resolved.

FDA is instructed to "maintain an up-to-date list of drugs that are determined by [FDA] to be in shortage in the United States,"[3] and 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."[4] Eli Lilly and Company ("Lilly"), the manufacturer of the relevant tirzepatide injection drug products, has provided FDA with detailed information and data regarding its production and inventory of these drug products at various points in time, including stock reports that show quantities supplied and demanded, and inventory held in stock, for all strengths of these drug products; 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. (See Section II.A.). We conclude that the information and data Lilly has provided to FDA demonstrate that Lilly's supply is currently meeting or exceeding demand for these drug products, and that Lilly has developed reserves that it now holds in its finished product inventory, plus significant units of semi-finished product, and has scheduled substantial additional production over the coming months, such that supply will meet or exceed projected demand.

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[1] https://dps.fda.gov/drugshortages/resolved/tirzepatide-injection.

[2] On October 7, 2024, FDA was sued in the U.S. District Court for the Northern District of Texas by the Outsourcing Facilities Association and North American Custom Laboratories, LLC d/b/a Farmakeio Custom Compounding regarding removal of tirzepatide injection from FDA's drug shortages list. On October 11, 2024, upon FDA's motion, a court order remanded the decision to the Agency for reevaluation. *See Outsourcing Facilities Ass'n v. FDA*, No. 4:24-cv-953, ECF Nos. 27, 28 (N.D. Tex. .

[3] Section 506E(a) of the FD&C Act.

[4] Section 506C h 2) of the FD&C Act; 21 CFR 314.81(b 3)(iii f).

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FDA has also considered potentially relevant information regarding the shortage determination from patients, healthcare providers, and others, including compounders, along with data from other sources that we independently identified. (See Section II.B.). After carefully evaluating this information, we find that it has important limitations. We conclude that this information does not undermine or outweigh the evidence demonstrating that Lilly's supply is currently meeting or exceeding demand and that, based on our best judgment, it will meet or exceed projected demand.

For example, FDA received reports that some patients and pharmacists are not able to obtain the approved drugs, and that a substantial amount of tirzepatide compounding is occurring. The information provided in Lilly's submissions demonstrate that the company is currently meeting or exceeding demand for Mounjaro and Zepbound. That is not inconsistent with some, and even many, individuals having had some trouble getting prescriptions for the affected drugs filled over the course of the shortage, and some individuals may still be currently encountering such challenges, even though Lilly's supply is now meeting or exceeding demand nationally. In our assessment, intermittent challenges of this kind are 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, including wholesale distributors and retailers. We recognize that significant compounding of tirzepatide injection products is occurring, and that some number of patients currently receiving those products can be expected to seek Lilly's approved products at a future point when compounding is curtailed. However, the additional information provided by patients, healthcare providers, and others, including compounders does not demonstrate that Lilly will be unable to meet projected demand, especially when weighed against the Lilly-provided data.

For all of these reasons and as explained further below, we determine that the shortage is resolved. Our determination is based on our conclusions that supply meets or exceeds current demand, and that, based on our best judgment looking at the available information with its limitations, supply will also meet or exceed projected demand.

FDA will continue to monitor supply and demand for these products, and whether any tirzepatide injection products should be included on the drug shortage list in the future, as appropriate.[5]

This memo also explains that, in addition to the representations FDA made regarding enforcement in October 2024 in connection with litigation,[6] FDA does not intend to take action against compounders for violations of the Federal Food, Drug, and Cosmetic Act (FD&C Act) arising from conditions that depend on tirzepatide injection products' inclusion on the FDA drug shortage list (see section 506E of the FD&C Act) [i.e., section 503A(b)(1)(D) (compounded drugs that are essentially a copy of a commercially available drug product) or sections

[5] Notwithstanding resolution of the shortage, FDA understands that patients and prescribers may still see intermittent localized supply disruptions as the products move through the supply chain from the manufacturer to wholesale distributors and pharmacies.

[6] *See* Defendants' Unopposed Motion for Voluntary Remand and Stay, *Outsourcing Facilities Ass'n v. FDA*, No. 4:24-cv-953, ECF No. 27, at 3. *See also* Letter from Gail Bormel, Office Director, CDER Office of Compounding Quality and Compliance, to Scott Brunner, Chief Executive Officer, Alliance for Pharmacy Compounding (APC) (Oct. 17, 2024), available at https://www.fda.gov/media/182948/download?attachment.

503B(a)(2)(A) (bulk drug substances used in compounding) and (a)(5) (compounded drugs that are essentially a copy of an FDA-approved drug product)] for the following time periods from the date of this memorandum:

- For state-licensed pharmacists or physicians compounding under section 503A of the FD&C Act, 60 calendar days from the date of this memorandum, until February 18, 2025; and
- For outsourcing facilities under section 503B of the FD&C Act, 90 calendar days from the date of this memorandum, until March 19, 2025.

I. Background

FDA maintains an up-to-date list of drugs that are determined by the Agency to be in shortage in the United States.[7] FDA's drug shortage list is publicly available on the Agency's website.[8] FDA's drug shortage list includes the names and National Drug Code (NDC) numbers for such drugs; the name of each applicant for such drugs, the reason for the shortage as determined by FDA, and the estimated duration of the shortage.[9]

In this context, a drug shortage means "a period of time when the demand or projected demand for the drug within the United States exceeds the supply of the drug."[10] As such, in determining whether a drug is in shortage for purposes of the FD&C Act, 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.[11] The Agency acknowledges that even when a shortage is considered resolved, patients and prescribers may still see intermittent localized supply disruptions as products move through the supply chain from the manufacturer and distributors to local pharmacies.

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[7] See section 506E(a of the FD&C Act (21 U.S.C. 356e) and 21 CFR 314.81(b 3) iii)(*d*)(*1*). Manufacturers of certain prescription drug products must notify FDA of a permanent discontinuance in the manufacture of the drug product, or an interruption in manufacturing of the drug product that is likely to lead to a meaningful disruption in supply of that drug in the United States, and the reasons for such discontinuance or interruption. For the same drugs, manufacturers are also required to report a permanent discontinuance in the manufacture of an active pharmaceutical ingredient of the drug or an interruption in the manufacture of an active pharmaceutical ingredient likely to lead to a meaningful disruption in supply of the manufacturer's drug, and the reasons for the discontinuance or interruption. See section 506C of the FD&C Act and 21 CFR 314.81(b) 3 iii).

[8] https://dps.fda.gov/drugshortages. See section 506E c) of the FD&C Act and 21 CFR 314.81(b) 3)(iii)(*d*)(*1*).

[9] See section 506E(b of the FD&C Act and 21 CFR 314.81(b)(3) iii)(*d*)(*1*). FDA cannot disclose trade secret or commercial or financial information that is considered confidential or privileged. See sections 506C(d) and 506E(c 2) of the FD&C Act and 21 CFR 314.81(b)(3)(iii)(*d*)(*2*). Additionally, FDA may choose not to make drug shortage information publicly available if FDA determines that disclosure of such information would adversely affect the public health (such as by increasing the possibility of hoarding or other disruption of the availability of drug products to patients). See section 506E c)(3 of the FD&C Act and 21 CFR 314.81(b)(3)(iii *d*)(*2*).

[10] Section 506C h 2) (21 U.S.C. 356c of the FD&C Act; see also 21 CFR 314.81(b)(3)(iii)(*f*).

[11] See FDA Strategic Plan for Preventing and Mitigating Drug Shortages (October 2013), available at https://www.fda.gov/media/86907/download. See also CDER's manual of policies and procedures on drug shortage management (MAPP 4190.1 Rev. 4), available at https://www.fda.gov/media/72447/download; and FDA's draft guidance for industry, *Notifying FDA of a Discontinuance or Interruption in Manufacturing of Finished Products or Active Pharmaceutical Ingredients Under Section 506C of the FD&C Act* (February 2024), available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/notifying-fda-discontinuance-or-interruption-manufacturing-finished-products-or-active. This draft guidance, when finalized, will represent FDA's current thinking on this topic.

FDA receives input regarding drug shortages from numerous stakeholders, including manufacturers, patients, healthcare providers, and others, including compounders.[12] In particular, manufacturers are required to notify FDA about discontinuances and manufacturing interruptions pertaining to certain drugs pursuant to statutory and regulatory requirements,[13] and they may voluntarily provide additional information as relevant about quality issues, increases in demand, recalls, or other events (e.g., relevant supply and demand conditions).

Tirzepatide is a glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist. Mounjaro and Zepbound are the only FDA-approved tirzepatide products. Mounjaro (tirzepatide) injection, for subcutaneous use, is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Mounjaro is approved as pre-filled single-dose pens in several strengths (2.5 mg/0.5 mL, 5 mg/0.5 mL, 7.5 mg/0.5 mL, 10 mg/0.5 mL, 12.5 mg/0.5 mL, and 15 mg/0.5 mL). The Mounjaro pen products were approved by FDA in May 2022 NDA 215866) and added to FDA's drug shortage list in December 2022 due to high demand. Mounjaro single-dose vial products in the same strengths were approved in a supplement to NDA 215866 in July 2023, but are not currently marketed in the United States and have not been on FDA's drug shortage list. Zepbound (tirzepatide) injection, for subcutaneous use, is indicated in combination with a reduced-calorie diet and increased physical activity to reduce excess body weight and maintain weight reduction long term in adults with obesity or adults with overweight in the presence of at least one weight-related comorbid condition. Zepbound is also approved as pre-filled single-dose pens and single-dose vials in the same strengths as Mounjaro (2.5 mg/0.5 mL, 5 mg/0.5 mL, 7.5 mg/0.5 mL, 10 mg/0.5 mL, 12.5 mg/0.5 mL, and 15 mg/0.5 mL). The Zepbound pen products were approved by FDA in November 2023 NDA 217806) and added to FDA's drug shortage list in April 2024 due to high demand. The Zepbound single-dose vial products were approved in a supplement to NDA 217806 in March 2024, but only the 2.5 mg and 5.0 mg strengths are currently being marketed in the United States. The Zepbound vial products have never been on the shortage list.[14]

II. Discussion

A. Manufacturer-provided information about availability

Since August 2, 2024, Lilly has stated that it is able to meet or exceed demand for all strengths of Mounjaro (tirzepatide) injection and Zepbound (tirzepatide) injection in the United States.[15] Since (b) (4), Lilly has been providing FDA with supply and demand data on its tirzepatide injection products to support its assertion that no strengths of Mounjaro or Zepbound

[12] FDA's website includes information about drug shortage notifications for industry and a public portal for patients, healthcare providers, and organizations to report new shortages, available at https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages.

[13] Section 506C h 2) of the FD&C Act; 21 CFR 314.81(b 3)(iii f).

[14] (b) (4)

[15] See (b) (4), (b) (6)

are in shortage (b) (4).[16] These data included stock reports, cumulative supply and demand reports, and distributor inventory reports. In addition, Lilly has responded to multiple FDA requests for information regarding these data. We have reviewed Lilly's submissions and find that they support the conclusion that supply is currently exceeding demand and will meet or exceed projected demand across all strengths of Mounjaro and Zepbound.

1. Lilly's Data Demonstrate that Its Supply is Currently Meeting Demand

Inventory Data. (b) (4), Lilly has been providing "stock reports," which contain data on its inventory and orders for its Mounjaro and Zepbound products, by dosage strength.[17] These data demonstrate that Lilly has been filling wholesale orders as they are received while generally maintaining product in inventory net of open orders (i.e., allocating sufficient product to fulfill all existing orders before counting any product on hand as excess inventory). See Table 1 below for net inventory balances for each Mounjaro and Zepbound single-dose pens, by strength. (b) (4)

[16] (b) (4), (b) (6) Lilly first provided these data for tirzepatide generally, and later disaggregated the data between Mounjaro and Zepbound.

[17] (b) (4)

[18] Id.

(b) (4), Lilly had all strengths of Mounjaro and Zepbound in stock, net of open orders.[19]

Importantly, Lilly stated that it does not — and has not — limited the ability of any wholesaler to place orders for any quantities of Mounjaro or Zepbound.[20] (b) (4) Lilly states that (b) (4) [21] Lilly explained that (b) (4) [22]

Lilly's stock reports also provided FDA with information about the amount of "semi-finished units" (i.e., products that have already completed sterile manufacturing and are awaiting labeling and packaging) in its supply over time. Lilly explained that (b) (4)

Lilly has stated that it has a reserve supply (i.e., finished goods inventory in its warehouse) that supports maintaining (b) (4) depending on dose level demand, net of open orders.[24]

We find that the stock reports demonstrate that Lilly has been filling wholesale orders as they are received while maintaining product in inventory net of open orders. Significant units of semi-finished product also provide assurance that Lilly will continue to be able to fill orders as they are received. Therefore, these reports support our conclusion that supply is meeting or exceeding demand for these drugs.

[19] (b) (4)
[20] Id. at 7.
[21] Id.
[22] Id.
[23] Id. at 3.
[24] (b) (4)

Table 1. Net Inventory Balance and Doses of Semi-finished Syringe Product, by Dosage Strength (in thousands)[25]

	Product	Net Inventory Balance at Lilly, finished product (thousands of doses)*	Units of TZP Semi-finished Syringe Product at Lilly (thousands of doses)*
		(b) (4)	
2.5 mg	MJO		
	ZEP		
5 mg	MJO		
	ZEP		
7.5 mg	MJO		
	ZEP		
10 mg	MJO		
	ZEP		
12.5 mg	MJO		
	ZEP		
15 mg	MJO		
	ZEP		
TOTAL			

***** Lilly inventory reflects domestic inventory only and does not include (b) (4)

****** (b) (4)

Cumulative Supply and Demand Data. In addition to the stock reports, Lilly provided historic data on monthly cumulative supply and demand of the single-dose pens, by strength, of Mounjaro and Zepbound, since January 2024. The supply figures represent (b) (4) These data demonstrate that the company's supply has met or exceeded demand throughout 2024, with increasing amount of additional supply over the course of the year. In total, the company reported that it has supplied more than (b) (4) of tirzepatide injections since the beginning of 2024, significantly exceeding overall demand of around (b) (4).[28] Furthermore, cumulative supply for Mounjaro and Zepbound, in all strengths, has exceeded demand in this period. See Table 2 below for Lilly-reported demand and supply of Mounjaro, (b) (4), by strength. See Table 3 below for Lilly-reported demand and supply of

[25] (b) (4)

[26] (b) (4)

[27] Id. at 6.

[28] (b) (4)

Zepbound, (b) (4), by strength. Although Lilly did not provide cumulative supply and demand data broken down by product (b) (4) in its most recent submission (b) (4), we received aggregated data (b) (4) which shows the same trend – cumulative supply is continuing to outpace demand. See Table 4 below for Lilly-reported demand and supply of tirzepatide single-dose pens (b) (4) by strength. Therefore, the cumulative demand and supply data further support our conclusion that supply is meeting or exceeding demand for these drugs.

Table 2. Lilly-reported cumulative demand and cumulative supply of Mounjaro single-dose pens (thousands of doses)[29]

Cum. demand	(b) (4)
2.5	
5	
7.5	
10	
12.5	
15	
Total	
Cum. supply	
2.5	
5	
7.5	
10	
12.5	
15	
Total	
Net (cum. supply – cum. demand)	
2.5	
5	
7.5	
10	
12.5	
15	
Total	

[29] Id.

Table 3. Lilly-reported cumulative demand and cumulative supply of Zepbound single-dose pens (thousands of doses)[30]

Cum. demand	(b) (4)
2.5	
5	
7.5	
10	
12.5	
15	
Total	
Cum. supply	
2.5	
5	
7.5	
10	
12.5	
15	
Total	
Net (cum. supply – cum. demand)	
2.5	
5	
7.5	
10	
12.5	
15	
Total	

[30] Id. The table provides data only for pre-filled Zepbound pens and does not include vials.

Table 4. Lilly-reported cumulative demand and cumulative supply of tirzepatide single-dose pens (b) (4) (thousands of doses)[31]

Cum. demand	(b) (4)
2.5	
5	
7.5	
10	
12.5	
15	
Total	
Cum. supply	
2.5	
5	
7.5	
10	
12.5	
15	
Total	
Net (cum. supply – cum. demand)	
2.5	
5	
7.5	
10	
12.5	
15	
Total	

Lastly, we note that since August 2024, Lilly has also been selling vial forms of Zepbound (2.5mg and 5.0mg) directly to patients with prescriptions through "LillyDirect." Additionally, in December 2024, Lilly reportedly reached an agreement to market Zepbound vials through the telehealth platform Ro.[32] These vial products have never been listed as being in shortage, and Lilly has reported that, since marketing, their cumulative supply has exceeded cumulative demand. For example, Lilly reported that, (b) (4)

[31] (b) (4)

[32] Elaine Chen and Katie Palmer, "Eli Lilly strikes Zepbound deal with Ro, amid questions about future of compounded GLP-1s," STAT+ Pharma, Dec. 11, 2024, available at https://www.statnews.com/2024/12/11/eli-lilly-zepbound-ro-health-agreement-weight-loss/.

[33] (b) (4)

[34] Id.

1. Significant Inventory is Present Elsewhere in the Distribution Channel

In addition to the net inventory and semi-finished product held by Lilly discussed above, there is additional product in the distribution channel, i.e., the part of the supply chain between Lilly and individual patients, including wholesale distributors and retail pharmacies. Lilly explained that

(b) (4)

[redacted]

[35] (b) (4)

[36] Id. at 5.

[37] Id. at 7. (b) (4)

[redacted]

Id.

[38] Id. at 4.

Table 5. Lilly Reported Volume of Mounjaro and Zepbound Pre-Filled Pens Shipped to Wholesalers and Average Wholesaler Daily Inventory (in units, with each unit containing 4 doses)[39]

(b) (4)	Volume Shipped (Units)	Avg. Daily Inventory (Units)
Mounjaro		
2.5	(b) (4)	
5		
7.5		
10		
12.5		
15		
Total		
Zepbound		
2.5		
5		
7.5		
10		
12.5		
15		
Total		
Total Mounjaro + Zepbound		

Adequate supply at the wholesaler level is further supported by the fact that, (b) (4)

further indicate that nationwide supply for its products is exceeding demand.

[39] Id. at 5. The table provides data only for pre-filled Mounjaro and Zepbound pens and does not include vials.
[40] (b) (4)
[41] (b) (4)
[42] (b) (4)
[43] Id.

In sum, data relating to wholesaler inventory support our conclusion that supply is meeting or exceeding demand for these drugs.[44]

2. Supply is Forecasted to Exceed Projected Demand

As explained above, the FD&C Act defines a drug shortage as "a period of time when the demand or projected demand for the drug within the United States exceeds the supply of the drug."[45] As such, we must also consider whether supply will meet or exceed projected demand for these drugs. In its (b) (4), Lilly represented that it is "positioned to supply more than projected demand and without any large-scale nationwide disruptions."[46] Lilly went on to state that it is "now able to supply (b) (4) per month," and "[i]n just the first two months of Q4 2024, Lilly has already supplied (b) (4) of Mounjaro and Zepbound and expects to supply (b) (4) by the end of the quarter."[47]

Lilly explained that (b) (4)

[redacted]

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[44] (b) (4)

[redacted]

[45] Section 506C h 2) of the FD&C Act; see also 21 CFR 314.81(b) 3) iii)(*f*).

[46] (b) (4)

[47] Id.

[48] (b) (4)

[49] Id. at 7.

[50] Id. at 10.

[51] Id. at 7.

[52] Id.

[53] (b) (4)

[redacted]

With respect to compounding, Lilly explained that [redacted] For purposes of this analysis, we believe that approach was reasonable in light of the lack of reliable data from compounders, and the uncertainties in predicting future patient and prescriber behavior, for the reasons explained below (see section II.B.2 below). While we acknowledge the possibility that growth in demand for Lilly's products may exceed its current demand projections as a result of compounding being curtailed in the future, the information available to us does not support a conclusion that such growth in demand will exceed Lilly's supply.

Lilly explained that, based on its forecast, it [redacted] We

[redacted]

[54] [redacted]

[55] Id.

[56] [redacted]

[57] [redacted]

agree that Lilly has reasonably assessed projected supply and demand, (b) (4) gives us further confidence in the accuracy of Lilly's predictions of future demand. Based on this information, we conclude that based on our best judgment, supply will meet or exceed projected demand.

Table 6. Lilly-reported projected cumulative demand and cumulative supply of tirzepatide single-dose pens, (b) (4) (thousands of doses)[58]

Cum. demand	(b) (4)
2.5	
5	
7.5	
10	
12.5	
15	
Total	
Cum. supply	
2.5	
5	
7.5	
10	
12.5	
15	
Total	
Net (cum. supply – cum. demand)	
2.5	
5	
7.5	
10	
12.5	
15	
Total	

Lastly, we also note that with respect to the Zepbound vial products that have not been listed as being in shortage, Lilly has reported that (b) (4)

Taken as a whole, the data and information submitted by Lilly support our conclusion that supply is currently meeting or exceeding demand and, based on our best judgment looking at the available information with its limitations, will meet or exceed projected demand across all strengths of Mounjaro and Zepbound.[60]

58 (b) (4)
59 (b) (4)
60 (b) (4)

B. Other information about availability

FDA also has received and considered other information potentially related to supply and demand for tirzepatide injection products in the United States. This information can be generally categorized as (1) information from sources other than Lilly bearing on *current* supply and demand, (2) information about compounded drug products bearing on *projected* demand, and (3) other information. After careful consideration, this information does not alter our conclusions that supply is meeting or exceeding demand and, based on our best judgment looking at the available information with its limitations, will meet or exceed projected demand, and thus that the shortage is resolved.

1. Information from Sources Other Than Lilly Regarding Current Supply and Demand

FDA received submissions from multiple sources other than Lilly, including telehealth companies, pharmacy compounders, associations representing pharmacy compounders and outsourcing facilities, and individuals. Some stakeholders characterized their submissions as providing "evidence of extremely high demand for Tirzepatide, scarcity in various regions and at the national level, and delays in filling prescriptions" and "information demonstrating that supply continued to lag behind demand, even at stark levels."[61] The submitted information generally falls into the following categories, each of which is discussed in turn below.

- Information collected from individual customers reporting "inability of patients to obtain Mounjaro and Zepbound;"[62]
- Information regarding the ability of retail pharmacies to obtain Mounjaro and Zepbound from wholesalers;
- Articles reported in the press and published on industry websites;[63]
- Individual comments on FDA's general compounding docket, FDA-2015-N-0030; and
- Reports of "voluminous Tirzepatide compounding meeting high demand."[64]

i. Information collected from individual patients reporting "inability of patients to obtain Mounjaro and Zepbound."

FDA received multiple submissions stating that individual patients are unable to access Mounjaro or Zepbound, which the submitters urge FDA to consider as evidence that a shortage persists. FDA considered this information, and concludes that it does not undermine or outweigh the information submitted by Lilly, described above, which demonstrates that supply of

[61] Complaint, *Outsourcing Facilities Ass'n v. FDA*, No. 4:24-cv-00953-P (E.D. Tex. filed Oct. 7, 2024), Dkt. 1, at 9, ¶ 29. *See also id*. at 17, ¶ 69 (characterizing evidence as showing "continued inability of supply to keep pace with demand").
[62] Id.
[63] Id.
[64] Plaintiffs' Memorandum of Law in Support of a Temporary Restraining Order and Preliminary Injunction, *Outsourcing Facilities Ass'n*, No. 4:24-cv-00953-P, Dkt. 8, at 17 (Oct. 8, 2024); *id*. Dkt. 9 (Appendix in Support of Plaintiffs' Mot.).

Mounjaro and Zepbound is currently meeting demand. Below we discuss two examples of such submissions in detail.

As one example, Hims & Hers Health, Inc. submitted multiple reports to FDA that it characterized as demonstrating that "the shortage persists."[65] These reports include data regarding the number of people that have reported to Hims & Hers "an inability to access name brand GLP-1s," including Mounjaro and Zepbound, reported weekly and cumulatively.[66] Plaintiffs in *Outsourcing Facilities Ass'n v. FDA* characterized these reports as "survey data . . . show[ing] increasing numbers of patients unable to obtain branded GLP-1 agonist products, including specifically branded Tirzepatide products."[67] These reports appear to be generated by collecting data through the Hims & Hers website, using an internet form that anyone can complete.[68] The company describes the data it is collecting as "helping Hims & Hers keep the FDA updated on GLP-1 shortages across the country . . . This tracker allows people to share their experiences and keep the FDA updated with the latest supply information."[69] Hims & Hers further states that the tracker can be used by "[a]nyone who has had trouble getting access to a GLP-1 medication in the past," and that the way to "report a weight loss drug shortage to the FDA" is to "[s]hare your current state of residence, the GLP-1 medication, and the dosage you've had trouble accessing in the past."[70] No further limitations (such as by date, restricting reporting to recent access challenges) or instructions (such as defining "trouble accessing" a drug) are provided for those filling out the form, nor does the form collect any details regarding their location or experiences.[71]

As another example, the Outsourcing Facilities Association (OFA) submitted "time-stamped reports of drug shortages for FDA-approved tirzepatide that the OFA has received from patients."[72] The submitted list included, for around 100 entries, a date and time (presumably the date and time of the communication from the patient to OFA), patient zip code, and a yes/no answer to the question "Have you attempted to have a prescription filled at more than one pharmacy?" most but not all of which are answered "Yes" .[73] It is not clear how this

[65] Dec. 2, 2024 email from Andrew Van Ostrand, Vice President, Policy & Regulatory Affairs, Hims & Hers Health, Inc. to Valerie Jensen and Gail Bormel, FDA, "updated Hims & Hers Health, Inc. GLP-1 access/shortage data – the shortage persists," with attachments.
[66] *Id.* at attachment 1 and 2. See also Dec. 16, 2024 email from Andrew Van Ostrand to Valerie Jensen and Gail Bormel, "Hims & Hers Health, Inc. GLP-1 shortage data - as of 12/14/24," with attachment.
[67] Joint Status Report, *Outsourcing Facilities Ass'n v. FDA*, No. 4:24-cv-00953-P, Dkt. 30, at 1-2 (N.D. Tex., Nov. 21, 2024).
[68] See https://investors.hims.com/news/news-details/2024/Americans-Continue-to-Struggle-to-Access-Branded-GLP-1s-as-Shortages-Continue/default.aspx (describing "tracker").
[69] https://www.hims.com/weight-loss/supply-tracker (internet form 1) ("Frequently asked questions"); and https://www.forhers.com/weight-loss/supply-tracker (internet form 2) ("Frequently asked questions").
[70] Id.
[71] Id.
[72] Oct. 23, 2024 email from Marc Wagner, counsel for OFA, to Valerie Jensen and CDER DRUG SHORTAGES, FDA, "Patient reported shortages of FDA-approved tirzepatide," with attachments.
[73] Id. at attachment 1.

information was collected, and, like the information submitted by Hims & Hers, it does not include details of the reported individual experiences.

This information does not undermine or outweigh the information provided by Lilly, discussed in section II.A above, with respect to availability of its products. As discussed in greater detail above, the information and data provided in Lilly's submissions demonstrate that the company is currently meeting or exceeding demand for Mounjaro and Zepbound. That is not inconsistent with some, and even many, individuals having had some trouble getting prescriptions for the affected drugs filled over the course of the shortage, and some individuals may still be currently encountering such challenges, even though Lilly's supply is now meeting or exceeding demand nationally. In our assessment, continuing challenges of this kind are 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, including wholesale distributors and retailers. Lilly explained that "[e]ven when a medication is available, patients may not always be able to immediately fill their prescription at a particular pharmacy. That is especially true for refrigerated products and products with multiple dose strengths, due to factors like ordering practices and incentives, cold chain logistical considerations, and retailer capacity constraints. Patients may experience variability at a particular pharmacy location regardless of whether a drug is in shortage."[74] The company further explained that "not every pharmacy has sufficient refrigerator space to store sufficient stock of 12 doses across two brands of approved tirzepatide. (b) (4) and that (b) (4) [75] Also see the discussion in section II.B.1.ii below (regarding wholesaler operations issues that do not necessarily indicate nationwide shortage). In sum, the fact that some pharmacies do not have ample stock of these tirzepatide products on hand at certain points in time does not undermine Lilly's data supporting a conclusion that supply is meeting or exceeding demand.

Further, to the extent that individual challenges in filling prescriptions may bear on factors relevant to the required statutory analysis of supply and demand, the information FDA has received from these stakeholders is inadequate because of the limitations described above. The submitted information does not include details of the reported experiences, and accordingly is not interpretable as to what kind of challenges the individuals actually experienced. For example, one individual might be reporting a pharmacy telling the individual that the prescribed drug was not in stock. On the other hand, another individual might be reporting an inability to get a prescription from a doctor based on the doctor's medical judgment, or an inability to get insurance coverage for a prescribed drug based on the insurance company's policies, and neither situation is relevant to the questions of supply and demand that the statute tasks FDA with analyzing to determine whether a drug shortage exists,[76] but both are better understood as preventing individuals from becoming part of the demand for the drug. Further, the Hims & Hers

74 (b) (4)

75 (b) (4)

76 The statute defines "drug shortage" as "a period of time when the demand or projected demand for the drug within the United States exceeds the supply of the drug." Section 506C(h)(2) (21 U.S.C. 356c) of the FD&C Act; see also 21 CFR 314.81 b)(3)(iii)(*f*).

internet form used to collect data (an approach that may have been used by some or all of the other data collectors, as well) significantly limits its probative value. Individuals completing the form might not be representative of the U.S. patient population and the data is subject to bias. Because there appears to be no limit on who can fill out the Hims & Hers internet form, it is possible, and perhaps even likely given the context (*see* section II.B.1.iv below, discussing comments received as a product of an internet letter-writing campaign) that some individuals have completed it multiple times. Hims & Hers did not provide information to FDA regarding any controls they may have established to ensure the integrity of the data.[77] Nor did OFA regarding its similar data collection.[78]

Accordingly, these reports do not undermine or outweigh the comprehensive information provided by Lilly regarding supply and demand discussed in section II.A above. That evidence provides a detailed quantitative picture of the supply and demand situation both over time, and at the national level, and is therefore much more probative to the analysis FDA must conduct to determine the status of the shortage.

ii. Information regarding the ability of retail pharmacies to source Mounjaro and Zepbound from wholesalers

Hims & Hers also submitted to FDA certain screenshots that the company asserts demonstrate that "our affiliated pharmacies continue to struggle to source branded GLP-1s across our leading wholesale partners."[79] As relevant to tirzepatide, the most recent report contains a screenshot that appears to show a wholesaler's website listing Mounjaro 5 mg and 10 mg strengths as unavailable, as indicated by text that says "Notify me when this item is in stock."[80] While Hims & Hers indicates that the screenshot represents "Supplier data as of 12/02/2024," the screenshot itself is undated and does not include information about the length of time that the product is or was out of stock.[81] Earlier reports include a similarly limited selection of screenshots purporting to show wholesaler ordering websites with Mounjaro or Zepbound out of stock, such as the November 12, 2024 report, which includes one undated screenshot showing Zepbound 15 mg as "Notify me when this item is in stock," on a wholesaler website.[82]

Similarly, the Alliance for Pharmacy Compounding (APC) gathered similar screenshots on its website, https://a4pc.org/stillinshortage.[83] APC submitted an updated set of screenshots to FDA on December 17, 2024.[84] Like the Hims & Hers screenshots, many of the APC screenshots are

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[77] Dec. 2, 2024 email from Andrew Van Ostrand, Vice President, Policy & Regulatory Affairs, Hims & Hers Health, Inc. to Valerie Jensen and Gail Bormel, FDA, "updated Hims & Hers Health, Inc. GLP-1 access/shortage data – the shortage persists."
[78] Oct. 23, 2024 email from Marc Wagner, counsel for OFA, to Valerie Jensen and CDER DRUG SHORTAGES, FDA, "Patient reported shortages of FDA-approved tirzepatide," with attachments.
[79] Id. at attachment 1, page 4.
[80] Id.
[81] Id.
[82] Nov. 12, 2024 email from sfaltin@forhims.com to CDER DRUG SHORTAGES, "Hims & Hers Health, Week of Oct 6 2024, Weekly GLP-1 shortage data" with attachments, at attachment 1, page 4.
[83] The Outsourcing Facilities Association submitted an email to FDA directing the agency to the APC website, and attaching a screenshot. *See* Oct. 23, 2024 email from Marc Wagner, counsel for OFA, to Valerie Jensen and CDER DRUG SHORTAGES, FDA, "Patient reported shortages of FDA-approved tirzepatide," with attachments.
[84] December 17, 2024 letter from Tenille Davis to Robert Califf, Valerie Jensen, and Gail Bormel, with attachments.

undated.[85] Others, however, do contain date information, including "Updated as of," "Product issue(s) tracked since" and "Expected availability in DC [distribution center]."[86] Plaintiffs in *Outsourcing Facilities Ass'n v. FDA* characterized this evidence as showing that "[p]harmacy distributors continue to list branded Tirzepatide products as out-of-stock or available in only limited quantities."[87]

In addition, FDA received a letter dated October 2, 2024, from a law firm representing "numerous pharmacies," expressing concern that, at that time, they were "continu[ing] to experience significant difficulties in obtaining" tirzepatide.[88] The email stated that "none of the clients can purchase tirzepatide from either McKesson, Bergen, or Cardinal [wholesalers] as all of the local DCs [distribution centers] either have zero in stock or are allocating the pharmacies to 1-2 boxes per day."[89] The letter also stated that "one of our clients reported receiving over 400 prescriptions for tirzepatide but is restricted to purchasing only 2 boxes of drug product due to their wholesaler's purchasing policy."[90]

Similarly, on November 15, 2024, FarmaKeio submitted a comment to FDA's general compounding docket including similar screenshots.[91] The screenshots show multiple strengths of Mounjaro and Zepbound listed as "out of stock" and/or "restricted" in the number a retailer may purchase from wholesalers AmerisourceBergen and Anda on that date.[92]

Upon thorough review, none of this information undermines or outweighs the information provided by Lilly, discussed in section II.A above, with respect to availability of product to wholesalers and retailers. As discussed in greater detail above, Lilly's submission demonstrates that the company is currently meeting or exceeding wholesaler demand for Mounjaro and Zepbound, and the company confirmed that it is not limiting the amounts that wholesalers can order. Lilly provided detailed information to FDA regarding the supply chain dynamics that can result in particular pharmacies being temporarily unable to buy these products from a distributor.[93] Most notably, Lilly described (b) (4)

[85] Id. at attachment 2.
[86] Id.
[87] Joint Status Report*, Outsourcing Facilities Ass'n v. FDA*, No. 4:24-cv-00953-P, Dkt. 30, at 2 (N.D. Tex., Nov. 21, 2024).
[88] Oct. 2, 2024 email from Mark Boesen, Boesen & Snow Law, to Gail Bormel, FDA, "Tirzepatide Resolution," with attachment.
[89] Id.
[90] Id. at attachment.
[91] Nov. 15, 2024 Comment from FarmaKeio, Dkt. FDA-2015-N-0030. Tracking No. m3i-x61g-s9e4, with attachments.
[92] Id. at attachment. The submitted screenshots do not indicate the date; the comment's text and file names provide the only date information available.
[93] (b) (4)
[94] Id.

(b) (4)

As Lilly explained:

(b) (4)

In addition, Lilly provided additional explanation specific to the APC screenshots, (b) (4)

[7] Lilly also selected certain examples from the APC screenshots and (b) (4)

The limitations of the screenshot evidence, taken together and considered in light of Lilly's explanations, mean that the screenshots do not provide reliable evidence in assessing whether supply of Mounjaro and/or Zepbound is meeting demand. Accordingly, the screenshots do not undermine or outweigh the comprehensive information provided by Lilly regarding supply and demand – including supply in the wholesale portion of the distribution chain, discussed in section II.A above. Further, the pieces of evidence discussed in this section show at most only disconnected individual "snapshots" in time. The evidence provided by Lilly and analyzed above provides a much fuller picture of the supply and demand situation both over time, and at the national level. Lilly's evidence is therefore much more probative to the analysis FDA must conduct to determine the status of the shortage.

iii. Articles reported in the press and published on industry websites

FDA reviewed various articles and blog posts submitted by various groups, as well as other news coverage.[99] While these pieces discussed various aspects of the shortage situation, FDA did not find them to contain probative evidence relevant to the analysis FDA must conduct to determine whether a shortage has resolved. While some of these sources contained personal accounts of inability to get a particular product at a particular time, like the evidence discussed in sections

[95] Id.
[96] Id. at 9-10.
[97] Id. at 10-11.
[98] Id. at 10.
[99] *See*, *e.g.*, Appendix in Support of Plaintiff's Mot., *Outsourcing Facilities Ass'n*, No. 4:24-cv-00953-P, Dkt. 9 (Oct. 8, 2024) (identifying various articles, blog posts, and online discussions regarding availability of Mounjaro, Zepbound, and compounded tirzepatide).

II.B.1.i and ii above, those individual accounts do not undermine or outweigh the more specific, reliable, comprehensive, and current information that has been provided by Lilly demonstrating its ability to supply enough product to meet demand.

iv. Individual comments on Docket FDA-2015-N-0030

Thousands of individual comments discussing compounded GLP-1 drugs were recently submitted to FDA's compounding general docket, FDA-2015-N-0030.[100] Many of these comments are substantively identical. Each such commenter identifies themself as a patient "who has relied on compounded GLP-1 medications to effectively manage my health during the ongoing shortage of brand-name products from Eli Lilly and Novo Nordisk [the manufacturer of semaglutide]," and then includes a form letter asking FDA to "keep compounded GLP-1s available for patients."[101] The form letter does not specify whether the commenter uses tirzepatide, semaglutide, or both; nor does the form letter provide any specific evidence regarding inability to get a relevant product.[102] Like the evidence discussed in section II.B.1.i above, these comments do not provide reliable evidence that could be probative in assessing whether supply of Mounjaro or Zepbound is meeting demand on a nationwide scale, and they do not undermine or outweigh the more specific, reliable, comprehensive, and current information that has been provided by Lilly demonstrating its ability to supply enough product to meet demand.

v. Reports of "voluminous Tirzepatide compounding meeting high demand."

To the extent that stakeholders contend that the sales volume of compounded tirzepatide is *itself* evidence that the supply of Mounjaro or Zepbound is not currently keeping pace with demand for Mounjaro or Zepbound, FDA disagrees. The relevant demand here is the demand for the approved drug product,[103] and not the demand for a different drug, i.e., demand for a

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[100] For example, over three thousand posted comments are identical to docket no. FDA-2015-N-0030-8535, document ID FDA-2015-N-0030-8535.

[101] Id.

[102] Id.

[103] The FD&C Act requires FDA to maintain an up-to-date list of "drugs" in shortage, and defines a "drug shortage" as "a period of time when the demand or projected demand for the drug within the United States exceeds the supply of the drug." Sections 506E(a), 506C(h)(2), Section 506E(a). For this determination, when FDA applies the drug shortage definition to decide whether Lilly's tirzepatide injection products are in shortage, it cannot consider current demand for a compounded copy of these approved drugs part of the "demand" for the drug. The shortage definition requires FDA to determine whether demand or projected demand for a "drug" exceeds the supply of the "drug." If the compounded drug were considered the "drug" when FDA evaluates demand, then supply of the compounded drug would necessarily also be considered part of the "supply" of the drug under the statute– a nonsensical result that would upend the role of compounding during a shortage. It would mean, for example, that if outsourcing facilities began compounding a drug during the shortage of an approved drug, and the supply of the compounded drug combined with the supply of the approved drug were enough to meet demand, FDA would have to end the drug shortage – a decision that would end the outsourcing facility's ability continue compounding the drug and restart the shortage. (Under section 503B of the Act, outsourcing facilities may compound drugs that are identical or nearly identical to an approved drug while the approved drug is on FDA's drug shortage list; but must stop when the shortage ends.). Similarly, if section 503A compounding could end a shortage, that would call into question the ability of the section 503A compounders to continue "regularly" compounding drugs to address an ongoing shortage of an approved drug. *See* section 503A(b)(1)(D) (compounder may not compound drugs that are essentially a copy

compounded tirzepatide drug. Therefore, the information provided by Lilly relating to supply and demand for its Mounjaro and Zepbound products discussed above is the most relevant information to the 'current demand' aspect of the shortage determination. For example, Lilly's ability to fill orders from distributors most directly demonstrates that supply is currently meeting demand. With respect to compounded products, the submitted evidence does not demonstrate that patients seeking compounded tirzepatide are doing so *because* the approved products are in shortage. Patients may seek the compounded drug for many reasons, including differences in price or formulation, insurance coverage decisions, prescriber preferences, marketing efforts, and other reasons. Therefore, we consider the volume of compounding in itself to be of minimal relevance to the assessment of current demand. (By contrast, above in section II.B.1.i, we considered reports that consumers did, in fact, demand Lilly's approved products but were unable to obtain them.) We do, however, consider information the agency has received about the volume of compounding below, in section II.B.2., as part of our evaluation of *projected* demand for Lilly's pen products, which among other things considers the possible effect of the curtailing of compounding on demand for Lilly's products in the future.

2. Information about compounded drug products regarding projected demand

FDA's drug shortage decision focuses on whether the demand or projected demand for the FDA-approved tirzepatide injection products within the United States exceeds supply. However, FDA also considered the information it has received about the availability of, and demand for, compounded tirzepatide injection products insofar as that information may bear on projected demand for the FDA-approved products. FDA is aware that some patients and health care professionals have looked to unapproved, compounded tirzepatide injection products while the FDA-approved drug products were in shortage and while FDA has announced a period of intended enforcement discretion involving such compounded products.[104] We acknowledge reports of significant compounding, and that curtailing of such compounding is likely to have some effect on the demand for Lilly's products in the future. However, the agency does not have a sufficient, reliable basis to project the scope of this effect, and finds that, especially when weighed against the information provided by Lilly, it does not support a conclusion that as a result, projected demand will exceed Lilly's significant supply capacity.

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of a commercially available drug regularly or in inordinate amounts). Congress surely did not intend for this result. Therefore, it follows that, when evaluating "supply" and "demand" for Lilly's approved tirzepatide injection products previously on the drug shortage list, FDA must evaluate supply and demand for the approved drug, and not include demand and supply for compounded drugs that are essentially copies of those drugs.

[104] *See* Defendants' Unopposed Motion for Voluntary Remand and Stay, *Outsourcing Facilities Ass'n v. FDA*, No. 4:24-cv-953, ECF No. 27, at 3. *See also* Letter from Gail Bormel, Office Director, CDER Office of Compounding Quality and Compliance, to Scott Brunner, APC (Oct. 17, 2024), available at https://www.fda.gov/media/182948/download?attachment. Generally, when an FDA-approved drug product is on FDA's drug shortage list, some federal law restrictions do not apply, such as, in certain circumstances, restrictions on compounding drugs that are essentially copies of approved drugs. Although compounded drug products can serve an important patient need, they also pose a higher risk to patients than FDA-approved drug products. Compounded drug products are not FDA-approved, which means they are not reviewed by FDA for safety, effectiveness, or quality before they are marketed. Therefore, approved drug products should be used to treat patients whenever possible.

503B Compounding. FDA by law receives some drug production information from outsourcing facilities,[105] which are required to report semi-annually on the quantity of drugs they compounded.[106] The data reported for the first half of 2024, which is the most recent complete reporting period, indicate that limited quantities of tirzepatide injection products were being compounded relative to production levels for the approved drug.

Table 7. Outsourcing facility reports, first six months of 2024[107].

Establishment	Active Ingredients Info	Package Description	Packages Produced
Mark Cuban Cost Plus Manufacturing and Compounding LLC (118916218)	2.5 mg/0.5 mL	2 mL in 1 VIAL, MULTI-DOSE	(b) (4)
PQ Pharmacy LLC (117479731)	10 mg/1 mL	1 mL in 1 VIAL, MULTI-DOSE	(b) (4)
Mark Cuban Cost Plus Manufacturing and Compounding LLC (118916218)	15 mg/0.5 mL	2 mL in 1 VIAL, MULTI-DOSE	(b) (4)
PQ Pharmacy LLC (117479731)	20 mg/1 mL	1 mL in 1 VIAL, MULTI-DOSE	(b) (4)
Olympia Pharmacy (017674368)	25 mg/1 mL	3 mL in 1 VIAL	(b) (4)

While we do not know how these products were prescribed, assuming that patients were expected to take 0.5mL in each dose, as with the approved drug, the reported production would represent (b) (4) doses over six months, or an average of (b) (4) doses per month. More recently, one outsourcing facility has stated that it compounded approximately (b) (4) mL of tirzepatide in September 2024,[108] which would represent (b) (4) doses if we assume, again, that there is 0.5mL per dose,[109] and OFA has represented that "OFA members have produced hundreds of thousands of doses of compounded tirzepatide in September 2024."[110] Even assuming that all of these doses have been supplied to the market and, upon the curtailing of compounding, would translate to demand for Lilly's products, this would represent a very small amount relative to Lilly's production and inventory. (b) (4), Lilly reported that it

[105] Section 503B of the FD&C Act (21 U.S.C. 353b) describes the conditions that must be satisfied for human drug products compounded in an outsourcing facility to be exempt from certain sections of the FD&C Act. Bulk drug substances used to compound a drug that is not on FDA's drug shortage list must be on a list of bulk drug substances established by the Secretary for which there is a clinical need (the 503B Bulks List). *See* section 503B(a)(2)(A) of the FD&C Act. Outsourcing facilities may not compound a drug that is essentially a copy of one or more FDA approved drugs, and under the applicable statutory definition, a drug compounded by an outsourcing facility is essentially a copy of an approved drug unless the approved drug is on FDA's drug shortage list at the time the compounded drug is compounded, distributed, and dispensed. *See* sections 503B(a)(5) and (d)(2) of the FD&C Act.

[106] Outsourcing facilities register with FDA (see section 503B(b)(1) of the FD&C Act) and report semi-annually on the drug products they compound (see section 503B(b)(2) of the FD&C Act).

[107] The Outsourcing Facility Product Report database is available at https://dps.fda.gov/outsourcingfacility. The number of packages produced is available in each facility's product reports.

[108] Declaration of Dan DeNeui, at 3 (App. 3) ¶ 15, *Outsourcing Facilities Ass'n v. FDA* (N.D. Tex. Oct. 8, 2024) (No. 4:24-cv-953) ECF No. 9.

[109] Based on the information FarmaKeio provided, this may represent fewer doses. FarmaKeio noted that tirzepatide injection products are dosed weekly (approximately 4 times a month) and that the varied weekly dosing of tirzepatide supplied approximately (b) (4) patients, *see id.*, which suggests a figure under (b) (4) doses.

[110] Declaration of Lee Rosebush, at 9 (App. 13) ¶ 39, *Outsourcing Facilities Ass'n v. FDA* (N.D. Tex. October 8, 2024) (No. 4:24-cv-953) ECF No. 9.

is able to supply (b) (4) per month, and its most recent stock report shows that its current autoinjector inventory contains (b) (4) and (b) (4) [111]

503A Compounding. State-licensed pharmacies compounding drugs under section 503A are primarily regulated by the states, and generally do not register with FDA or report to FDA the quantity or characteristics of the drugs they compound. FDA has been contacted by compounding trade associations and other companies involved in the marketing of compounded tirzepatide products, who have made multiple submissions contending that a substantial volume of compounding has been occurring in 503A facilities. While we acknowledge that compounding is occurring in section 503A facilities, most of these submissions have serious limitations. For example, OFA has directed FDA to news articles from June 2024 which reported that large compounding pharmacies may be "provisioning up to 2 million American patients with regular doses of semaglutide… or tirzepatide."[112] However, the articles do not provide support for this estimate[113] or provide enough detail for meaningful evaluation. For example, the articles do not separately estimate quantities for semaglutide and tirzepatide compounding, even though semaglutide compounding apparently represents a substantial part of the GLP-1 drug compounding,[114] and they do not present information about different strengths. The trade

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[111] (b) (4)

[112] Arthur Allen, "Why Millions Are Trying Alternatives to Big Pharma's Weight Loss Drugs." July 20, 2024, *CBS News Health Watch*. Plaintiffs' Exhibit 6, *Outsourcing Facilities Ass'n v. FDA* (N.D. Tex. October 8, 2024) (No. 4:24-cv-953) ECF No. 9. This story was republished by *KFF Health News* under the same title on July 23, 2024, Plaintiffs' Exhibit 7, *Outsourcing Facilities Ass'n v. FDA* (N.D. Tex. October 8, 2024) (No. 4:24-cv-953) ECF No. 9; and a similar story appeared as: Arthur Allen, Copycat weight-loss drugs are major players with consumers," *Washington Post*, July 31, 2024, Plaintiffs' Exhibit 8, *Outsourcing Facilities Ass'n v. FDA* (N.D. Tex. October 8, 2024 No. 4:24-cv-953) ECF No. 9. *See also* Patrick Wingrove and Bhanvi Satija, "Americans hungry for weight-loss drugs grapple with supply and insurance hurdles," Reuters, Nov. 4, 2024 (Reporting an analyst's estimate that "based on his conversations with compounding experts, as many as 2 million people in the U.S. could be taking compounded versions of the weight-loss drugs," but also stating that pharmacies were selling more compounded semaglutide than tirzepatide, and that "[a]nalysts have struggled to estimate the size of the compounded market for weight-loss drugs because their sale is not tracked in traditional channels. They are not covered by healthcare insurance plans and the pharmacies that make them do not have to report everything to the FDA."), available at https://www.reuters.com/business/healthcare-pharmaceuticals/americans-hungry-weight-loss-drugs-grapple-with-supply-insurance-hurdles-2024-11-04/.

[113] The reporter for the stories OFA cited said the estimate was based on interviews with "industry officials." Plaintiffs' Exhibit 6, at 2 (App. 51), *Outsourcing Facilities Ass'n v. FDA* (N.D. Tex. October 8, 2024 No. 4:24-cv-953) ECF No. 9. One of these officials, the CEO of a compounding firm, frankly acknowledged that "no one … is tracking sales in the industry", and that his estimate of the market share for compounded GLP-1 products was "a "wild ballpark figure." *Id.* at 4 (App. 53).

[114] Available information does not allow FDA to make a reliable estimate of market share for compounded semaglutide and tirzepatide products, although there are many indications that compounded semaglutide has a substantial share of this market. As noted, *see* footnote 112, the Wingrove and Satija article reports that online pharmacies like Noom and Hims & Hers "are selling versions of Wegovy [semaglutide] *and to a lesser extent*, Zepbound…". (Emphasis added.) This is consistent with more recent reports indicating that Hims & Hers does not market a compounded tirzepatide product, and that another online marketer of weight loss drugs, Ro, has stopped selling compounded tirzepatide products, and agreed to begin selling Lilly's approved Zepbound vial products. *See* Sneha S.K., "Lilly to offer single-dose vials of weight-loss drug on telehealth platform Ro," Reuters, Dec. 11, 2024, available at https://www.reuters.com/business/healthcare-pharmaceuticals/telehealth-firm-ro-provide-single-dose-vials-lillys-zepbound-obesity-patients-2024-12-11; Elaine Chen and Katie Palmer, "Eli Lilly strikes Zepbound deal with Ro, amid questions about future of compounded GLP-1s," STAT+ Pharma, Dec. 11, 2024, available at https://www.statnews.com/2024/12/11/eli-lilly-zepbound-ro-health-agreement-weight-loss/.

associations and industry also submitted complaints they have collected from people reporting they have had difficulty accessing compounded drugs; the many difficulties of relying on such reports to ascertain the volume of compounding have been described above in section II.B.1.i.

On December 17, 2024, the Association for Pharmacy Compounding (APC) submitted a letter stating that its analysis of dispensing data from forty compounding pharmacies indicates that they had "collectively dispensed 125,000 compounded tirzepatide prescriptions over the past month….", and that these forty pharmacies represent "a fraction of compounders preparing these medications."[115] We acknowledge that a substantial volume of compounding of tirzepatide injection products is currently ongoing. However, if we assume for purposes of this decision that the quantities reported by APC are accurate, and add them to the quantities reported by OFA, the total amount remains small relative to Lilly's production and inventory. We acknowledge APC's statement that additional compounding is occurring beyond what it has identified. However, APC has not provided information that would help inform a different estimate.

Moreover, it is not clear how many patients currently using a compounded tirzepatide injection product will choose to switch to Lilly's approved pen products when compounding is curtailed. That is, it is not reasonable to project that demand for compounded products will appear in the future one-for-one as demand for Lilly's approved autoinjector pen products. *First*, OFA and APC, among others, have indicated on many occasions that unapproved, compounded products are less expensive than Lilly's approved pen products.[116] Future demand is likely to be affected by the prices consumers face, and it is difficult to predict how many patients purchasing compounded tirzepatide injection at current price points will switch to the approved Lilly autoinjector pen products at future price points, or to competitor products at their price points. We note, for example, that Lilly has begun direct marketing of Zepbound 2.5mg and 5mg vials (which have not been in shortage), at prices that are substantially lower than its autoinjector product, and recently reached agreement with a large telehealth organization (which previously distributed compounded tirzepatide drugs) to sell Lilly's vial product. (b) (4)

In addition, because the approved semaglutide products received approval earlier than tirzepatide, they have had more time to build recognition and acceptance. For Q3 2024, Novo Nordisk reported sales of Wegovy and Ozempic roughly double those of Lilly's Zepbound and Mounjaro. *See* "Lilly reports Q3 2024 financial results highlighted by strong volume-driven revenue growth from New Products," dated Oct. 30, 2024, available at https://investor.lilly.com/news-releases/news-release-details/lilly-reports-q3-2024-financial-results-highlighted-strong; Novo Nordisk "Financial report for the period 1 January 2024 to 30 September 2024," available at https://ml-eu.globenewswire.com/Resource/Download/11f24e9a-5374-4abf-afc1-a31bc257a98a. The above data and information do not allow for an estimate of market share for compounded tirzpetide and semaglutide, but do illustrate why aggregated estimates of *GLP-1* compounding should not be considered estimates of *tirzepatide* compounding.

[115] Tenille Davis to Robert Califf et al, Dec. 17, 2024, at 1.

[116] E.g., Jensen to Thakur et al., Sept. 9, 2024; DeNeui Declaration, paragraph 10 ("compounding pharmacies have provided doses of Tirzepatide at substantially lower costs, such as one-half or even one-quarter the cost of brand-name alternatives"); Declaration of Lee Rosebush, submitted in *Outsourcing Facilities Ass'n v. FDA*, No. 4:24-cv-953, ECF Nos. 27, 28 (N.D. Tex.), paragraph 13 ("Patients report that they will continue using compounded versions of Tirzepatide for as long as possible because the cost is substantially lower"). While FDA recognizes the importance of prices to patients and the hardships that can be caused by higher prices, the drug shortage and compounding authorities in the FD&C Act require FDA to consider the supply of and demand for the approved drug in shortage.

(b) (4).[117] *Second*, we have received reports asserting that compounded products are in some cases promoted for uses that differ from the labeled indications of the approved drugs, such as for use for weight loss for patients who are not obese.[118] FDA has not made a finding that tirzepatide products are safe and effective for such uses, and if tirzepatide for these uses is not covered by insurance, consumers currently taking a compounded drug for such uses may decide not to purchase the approved drug when compounding of tirzepatide is curtailed. *Third*, an unknown quantity of compounded tirzepatide products have differences in formulation from the approved drug.[119] We do not know, and have no basis to reliably forecast, how many patients currently receiving these compounded drugs will choose to take up the approved drug. *Fourth,* it cannot be known at this time how regulatory decisions may affect the supply of other GLP-1 agonists when compounding is curtailed, or what marketing decisions other manufacturers may make to the curtailment of compounding. For all of these reasons, there remains considerable uncertainty about how future demand may increase due to patients who currently use compounded tirzepatide products switching to Lilly's approved pen products when compounding is curtailed.

Balanced against these uncertainties about projected demand, as described in section II.A. above, Lilly's supply of its pen products is currently meeting or exceeding demand, and Lilly credibly represents that it is able to manufacture (b) (4) of its tirzepatide injection products each month. Lilly also has substantial inventories of its approved pen products and vials and a larger volume of semi-filled syringes that can be packaged and relabeled quickly, and has demonstrated the ability to monitor supply and demand to rebalance production as needed. The company specifically projects that it will be able to continue meeting demand over the coming months, as it has been doing over the past few months.

Taking the available information together, while we recognize that significant compounding of tirzepatide injection products is occurring, and that some patients currently receiving those products can be expected to seek Lilly's approved products at a future point when compounding is curtailed, based on our best judgment and looking at the available information with its limitations, we conclude that Lilly's supply will meet or exceed projected demand.

Lilly has agreed to submit supply and demand information to the FDA every two weeks, and the agency will closely monitor supply and demand over the coming months. FDA will also continue to expedite review of applications that Lilly submits, if any, if we determine they could help prevent a future shortage, for example, by increasing Lilly's capacity to supply its tirzepatide

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117 (b) (4)

118 (b) (4), (b) (6)

[119] For example, while APC recently reported a quantity of "tirzepatide prescriptions" that were dispensed, it did not provide more information about the products that were compounded. Davis to Califf et al, Dec. 17, 2024, at 1, Similarly, OFA reported a quantity of "compounded tirzepatide" made by its members, without detail. See Declaration of Lee Rosebush, at 9 App. 13) ¶ 39, Outsourcing Facilities Ass'n v. FDA (N.D. Tex. October 8, 2024) (No. 4:24-cv-953 ECF No. 9. These do not indicate whether the compounded products have changes from the approved drug. We have received information that some compounders are preparing tirzepatide drug products in oral and sublingual dosage forms, or have been modifying the product formulation, e.g., by adding vitamin B12 or glycine. See (b) (4), (b) (6) *See also* FDA Warning Letter to Veronvy, December 10, 2024 (regarding "Elily Veronvy" and "Elily Veronvy 40+" drops), available at https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/veronvy-694688-12102024.

injection products.[120] If in the future, nationwide demand exceeds supply (whether because of a higher than anticipated volume of patients seeking Lilly's products after compounding is curtailed or otherwise), FDA will return tirzepatide injection products to the drug shortage list.

In addition, the enforcement discretion period we describe below should provide an additional period for an orderly transition of patients currently taking compounded tirzepatide to seek and receive prescriptions for the approved product, which we expect to avoid unnecessary disruption to patient treatment and to help facilitate an orderly transition.

3. Other information

In some cases, FDA may consider IQVIA National Sales Perspectives data when evaluating supply and demand of a drug. IQVIA data is available from a private company that reports information, for covered entities, on the sales volume of prescription drug products moving from distributors and manufacturers into various outlets within the retail and non-retail markets.[121] These data can provide a signal about supply conditions in some cases. For example, if a drug that has established a consistent baseline of sales goes into shortage, the return of sales to the previously established baseline may suggest that supply has recovered. However, the tirzepatide injection products we consider here did not have a stable baseline, because the shortage was due to increased demand, so there is no baseline to compare. More generally, these sales data have important limitations for making the drug shortage determination. For example, IQVIA only covers part of the market, and even if there are changes in sales levels, these may not reflect changes in supply available from the manufacturer. We do ascertain through review of the data that sales are increasing, consistent with Lilly's reports.

Furthermore, although FDA does not commonly review data on prescription dispensing, reversals, and rejections when analyzing whether a drug is in shortage, in October we did review such data from a third party, Symphony Health's Metys database, to consider whether it might be useful with respect to tirzepatide injection products. We concluded that these data have very limited utility. They only provide information for about half of outpatient prescriptions, and with respect to those prescriptions, ambiguous information about supply and demand.[122] These data are not inconsistent with our conclusions about supply and demand as they have been trending consistently to the IQVIA sales data and Lilly's reports.

FDA also received a comment recommending that we consider tirzepatide injection products to be in shortage because on November 26, 2024, HHS issued a proposed regulation that, if

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120 (b) (4)

121 IQVIA, Available IQVIA Data, https://www.iqvia.com/insights/the-iqvia-institute/available-iqvia-data.

122 For example, while the data provide information about prescription reversals (where a prescription presented to a pharmacy is not picked up and is therefore closed out), the data did not reveal the reason – for example, whether the patient abandoned the prescription due to the co-pay, or had the prescription filled at another pharmacy that offered a lower price or more convenient location, or because the patient decided not to take the drug. And, to the extent the prescription was not picked up due to supply at a pharmacy, whether that was due to factors unrelated to supply in the United States – e.g., business decisions made by distributors or retailers about how much product to stock - rather than nationwide supply conditions. See Memo from Grace Chai, Jing Xu, Sonal Goyal, Corrine Woods, through Gerald Dal Pan, to CDER, October 23, 2024, "Injectable Semaglutide and Tirzepatide Prescription Transaction Data."

finalized in current form, would expand Medicare Part D and Medicaid coverage for GLP-1 products.[123] However, the rule was proposed for contract year 2026.[124] It is not clear how the market for GLP-1 or related drugs will change before then, or what supply conditions will be if the rule takes effect for contract year 2026. Additionally, this is a proposed rule in an early stage of development; the period for public comment is open through January 27, 2025. It is not yet clear whether the proposal will be finalized in current form, or if it will be modified or withdrawn. Accordingly, we do not consider the proposed rule to be a basis for considering tirzepatide injection products currently in shortage and will monitor the rulemaking and related developments.

III. Status of compounding following this decision

In connection with the litigation noted above,[125] FDA stated that during the reevaluation and for a period after the Agency makes its decision, FDA does not intend to take action against compounders for violations of the FD&C Act arising from conditions that depend on tirzepatide injection products' inclusion on FDA's drug shortage list, i.e., section 503A(b)(1)(D) (compounded drugs that are essentially a copy of a commercially available drug product) or sections 503B(a)(2)(A) (bulk drug substances used in compounding) and (a)(5)) (compounded drugs that are essentially a copy of an FDA-approved drug product .

In addition to that representation, as explained further below, to avoid unnecessary disruption to patient treatment and to help facilitate an orderly transition, for the same violations described above, FDA does not intend to take action against a compounder that is not registered as an outsourcing facility for compounding, distributing, or dispensing tirzepatide injection products that are essentially a copy of a commercially available drug product[126] within 60 days of this decision. In addition, FDA does not intend to take action against an outsourcing facility for use of the bulk drug substance tirzepatide to compound, distribute, or dispense a drug product that appeared on FDA's drug shortage list,[127] or for compounding, distributing, or dispensing tirzepatide injection products that are essentially a copy of an FDA-approved drug product,[128] within 90 days of this decision.

Neither FDA's statements in the court case, the court's order, nor this decision prevents FDA from taking action for violations of any other statutory or regulatory requirements, such as to address findings that a product may be of substandard quality or otherwise unsafe.

The enforcement discretion described here is based on the following considerations.

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[123] Email from Lee Rosebush to Gail Bormel et al., Nov. 26, 2024.
[124] *See* 89 F.R. 237 (Dec. 10, 2024).
[125] *See* Defendants' Unopposed Motion for Voluntary Remand and Stay, *Outsourcing Facilities Ass'n v. FDA*, No. 4:24-cv-953, ECF No. 27, at 3. *See also* Letter from Gail Bormel, Office Director, CDER Office of Compounding Quality and Compliance, to Scott Brunner, APC (Oct. 17, 2024), available at https://www.fda.gov/media/182948/download?attachment.
[126] See section 503A(b)(1)(D) of the FD&C Act.
[127] See section 503B(a)(2)(A) of the FD&C Act.
[128] See section 503B(a)(5) of the FD&C Act.

First, as explained in FDA's guidance documents, "Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act" and "Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act," the FD&C Act generally limits the compounding of drugs that are essentially copies of commercially available and approved drugs, respectively.

Although compounded drug products can provide treatment options for patients during a drug shortage, compounded drugs have not undergone FDA premarket review for safety, effectiveness, and quality, and lack a premarket inspection and finding of manufacturing quality that is part of the drug approval process. Further, drug products that meet the conditions under section 503A are not subject to CGMP requirements and are subject to less robust production standards that provide less assurance of quality. Accordingly, the statute includes restrictions on compounding drugs that are essentially copies of commercially available drugs[129] and approved drug products that are not on FDA's drug shortage list. These restrictions help reduce the risk that compounders will prepare these unapproved drug products for patients whose medical needs could be met by an approved product. This helps to protect patients from unnecessary exposure to drugs that have not been shown to be safe and effective, and that offer fewer assurances of manufacturing quality.

The copies restrictions also protect the integrity of the new drug and abbreviated new drug (ANDA) approval processes by, for example, incentivizing sponsors to invest in and seek approval of innovative, life-saving medications - by limiting the ability of compounders to, after a drug is approved, compound "substitutes" that may be less expensive because they have not had to demonstrate safety and effectiveness or be labeled with adequate directions for use, and, for drugs compounded under section 503A, are not produced in accordance with CGMP requirements.[130]

For the above reasons, an indefinite or overly long period of enforcement discretion for continued compounding of drugs that may be essentially copies of an approved drug that is no longer in shortage would not be appropriate.

FDA has also considered public health concerns and reliance interests (as discussed further below), and the enforcement discretion described here takes those concerns into account. FDA considers that the 60/90-day period described here will allow patients a reasonable amount of time to transfer their prescriptions, as needed, to different pharmacies to obtain the FDA-approved drug. Patients who used compounded tirzepatide injection products during the shortage may otherwise face gaps in their ability to access treatment.[131] The additional time will

[129] For purposes of section 503A, FDA does not consider a drug on FDA's drug shortage list to be "commercially available."

[130] Less directly relevant in this case, involving copies of sterile injectable products, the copies restrictions also help protect FDA's drug monograph process by limiting the ability of compounders to produce drugs without having to comply with monograph standards or CGMP requirements that apply to such products.

[131] See October 3, 2024, letter from Scott Brunner, APC, to OCQC (docket no. FDA-2015-N-0030, document ID FDA-2015-N-0030-8519), stating that a 60-day transition period "would allow for a smoother transition, giving pharmacies time to contact prescribers for updated prescriptions and to navigate insurance prior authorization processes" and "would prevent abrupt discontinuations in patient care that will undoubtedly result from the sudden

allow local pharmacies to adjust their stocking and ordering patterns to adjust to new patterns of patient demand, which should help to minimize local disruptions.[132]

FDA also recognizes that compounded versions of drugs on FDA's drug shortage list can provide an important treatment option to patients during the shortage, and that compounders who prepare such drugs may be holding finished, compounded products, or inputs to compounded drugs, when a shortage resolves and the approved drug is taken off FDA's drug shortage list. For example, the compounder may have compounded drugs that are essentially copies of the approved drug and be waiting for the results of sterility tests before releasing them. FDA is required by statute to maintain an "up-to-date list" of drugs in shortage, 21 U.S.C. § 356e(a), and does not give advance notice of its decisions to move drugs on and off the list. In recognition of this fact, FDA's guidance for outsourcing facilities has previously described a brief period of enforcement discretion at the end of a drug shortage to account for such materials to be sold off.[133]

The above considerations are particularly relevant to the tirzepatide injection products shortage. We note that the shortage was ongoing for some time,[134] and compounders and other stakeholders report that a significant amount of compounding has been occurring. Additionally, FDA's re-evaluation of the shortage decision in the context of litigation may have caused some uncertainty about whether or when compounded copies would leave the market, slowing market transition. A period of enforcement discretion should help facilitate an orderly transition, as the adjustments described above take place. Although the 60/90-day period described here is longer than the period previously described in FDA's guidance documents, we conclude that it is justified in light of the considerations described here, including the information FDA has reviewed in connection with the tirzepatide injection products shortage. That this period is relatively brief also mitigates concerns about potential effects on patients, the integrity of the drug approval process, and any reliance interests of the approved drug manufacturer. While the approved drug manufacturer may have an interest in FDA providing only the more limited enforcement discretion stated in the Agency's existing guidances, FDA has considered any such

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unavailability of compounded copies"; and October 7, 2024, letter from Scott Brunner, APC, and Ronna Hauser, SVP, Policy and Pharmacy Affairs, National Community Pharmacists Association, to FDA, DSS, and OCQC (docket no. FDA-2015-N-0030, document ID FDA-2015-N-0030-8520), stating that during a 60-day transition period, "prescriptions can be authorized for the FDA-approved products, coverage determinations made by insurance companies, and the FDA-approved products can be obtained by pharmacies to fill the prescriptions."

[132] FDA recognizes that local and regional conditions can make it difficult for patients to get a drug through their local pharmacies, even if that drug is not in a nationwide shortage. FDA's authorities relating to drug shortages are limited to shortages that exist "in the United States," that is, at the national level. Section 506E(a) of the FD&C Act. Thus, FDA does not treat local or regional supply disruptions the same way as the Agency treats national shortages.

[133] FDA's guidance for outsourcing facilities provides a period of enforcement discretion of 60 days for orders received during a drug shortage. See 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 Jan. 2018 , at 8; Guidance for Industry: Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act (Jan. 2017), at 7. FDA's guidance document for section 503A compounders, Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act (January 2018 does not address FDA's enforcement policy for this provision at the end of a drug shortage. CDER is currently re-evaluating these policies pertaining to removal of compounded drugs from the market at the end of a shortage.

[134] Since December 15, 2022.

reliance interest and concludes that it is outweighed by the reasons discussed here that otherwise support this brief additional period of enforcement discretion.

The amount of time FDA intends to exercise enforcement discretion is longer for outsourcing facilities (90 days) than for those compounding under 503A (60 days) because:

- Drugs compounded in outsourcing facilities under section 503B provide more assurances of quality than drugs compounded under section 503A because they are made in facilities registered with FDA that are subject to FDA inspection and cGMP requirements.
- FDA understands that outsourcing facilities need to invest relatively more resources and time before they can produce product during a shortage because of these quality standards.

IV. Conclusion

For the reasons above, FDA determines that the shortage of tirzepatide injection products, which first began in December 2022, is resolved. FDA continues to monitor supply and demand for these products.