

S. HRG. 119–92

REAUTHORIZATION OF THE OVER-THE-COUNTER MONOGRAPH DRUG USER FEE PROGRAM

HEARING OF THE COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS UNITED STATES SENATE ONE HUNDRED NINETEENTH CONGRESS FIRST SESSION ON EXAMINING THE REAUTHORIZATION OF THE OVER-THE-COUNTER MONOGRAPH DRUG USER FEE PROGRAM

JUNE 4, 2025

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REAUTHORIZATION OF THE OVER-THE-COUNTER MONOGRAPH DRUG USER FEE PROGRAM

Wednesday, June 4, 2025

U.S. SENATE,
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS,
Washington, DC.

The Committee met, pursuant to notice, at 10:01 a.m., in room 430, Dirksen Senate Office Building, Hon. Bill Cassidy, Chairman of the Committee, presiding.

Present: Senators Cassidy [presiding], Marshall, Tuberville, Hawley, Banks, Husted, Moody, Baldwin, Murphy, Kaine, Hassan, and Hickenlooper, Markey, Kim, Blunt Rochester, Alsobrooks.

OPENING STATEMENT OF SENATOR CASSIDY

The CHAIRMAN. The Senate—let’s try one more time. The Senate Committee on Health, Education, Labor, and Pensions will please come to order.

Over-the-counter drugs are part of the fabric of Americans maintaining their health, treating common ailments, including pain relief, allergies, and cold symptoms—I could use a little bit right now—at an affordable cost. They are available at every pharmacy and virtually every grocery store nationwide.

Being readily available to Americans, OTCs save Americans a lot of money. The drugs generate an estimated \$1.46 billion in annual sales from—in annual savings from fewer doctor’s visits and prescription drug purchases. For decades, OTCs were required to go through a cumbersome review before going onto the market. This process, known as a drug monograph, typically took years to finalize.

Many new OTC drugs were never fully approved. The review also made it more difficult for the FDA to update safety information on these drugs, sometimes delaying safety recommendations for several years.

As a result of these challenges, Congress created the bipartisan over-the-counter monograph drug user fee program, OMuFA, in 2020 to streamline FDA review of OTC drugs, making these drugs more quickly available to Americans while still ensuring safety. OMuFA is set to expire at the end of this Fiscal Year. As Congress looks to reauthorize, we must see how we can further improve the program to better serve Americans.

This is why today's hearing is so important. I highlight, today is the first time Congress will be hearing directly from the FDA about how they have implemented reforms to the OTC drug review and their plans to make more low-cost drugs directly available to Americans. I appreciate Dr. Corrigan-Curay coming before the Committee on behalf of the FDA.

While the FDA has made progress in improving the OTC review pathways since 2020, there is more to do. FDA has failed to ease regulatory hurdles that allow prescription drugs to be sold OTC. These delays make it harder for consumers to directly access low-cost treatments.

The agency continues to struggle with reviewing new sunscreens, despite the well-documented public health value of using sunscreen. FDA has not approved a new sunscreen filter since 1999.

In contrast, peer countries in Europe and Asia have many more high quality sunscreen products available to consumers. The FDA needs to do a better job with sunscreen. I look forward to discussing how Congress can improve OTC and the OTC review process. And with that, I recognize Senator Kaine for his opening statement.

OPENING STATEMENT OF SENATOR KAINE

Senator KAINE. Thank you, Chairman Cassidy, and thanks to my colleagues. Welcome, Dr. Corrigan-Curay. This is an important program because it is critically important for Americans to have access to safe and effective over-the-counter drugs.

Recognizing the importance of regulating drugs that can be used without a prescription and the challenges facing the FDA, Congress passed the Over-the-Counter Monograph User Fee Program in 2020 to support the work of the FDA and expand access to medications that are safe and that are also easy to access and use.

The magnitude of this is pretty big. U.S. consumers spent over \$40 billion on over-the-counter drugs in 2024. Eight in ten U.S. adults use over-the-counter products as a first response to a minor injury. Over-the-counter drugs can save Americans money, can save the healthcare system money.

Research has found that \$51.6 billion in drug cost savings occur when lower priced over-the-counter products are used instead of higher priced prescription drugs. So that is really important both for the public treasury and for consumers. While over-the-counter drugs can generate savings, they can also be misused, leading to 178,000 hospitalizations each year due to adverse drug events.

It is important that we get the balance right. Older adults represent one-third of over-the-counter drug users and over 65 percent of these adverse drug events. So proper oversight is important. That is why we are here today. I was happy to support the initial passage of this user fee program.

I am glad the Committee is back to marking up bipartisan legislation. Hope we will do more of it. I do want to just conclude by just putting on the table, we are obviously going to be grappling very soon with the reconciliation bill that deals pretty significantly with healthcare and with the FDA.

Just in the last hour, the CBO released a report indicating that the House reconciliation bill would deprive 16 million Americans of health insurance. That is the House passed bill. That tells us what the stakes are as we grapple with the reconciliation bill. And obviously, I know my colleagues and I are going to be fighting very hard to avoid that. But let's just focus on the FDA.

Since the Administration took office, 20,000 employees at the Department of Health and Human Services have been dismissed. And this includes over 3,500 FDA staff currently on administrative leave.

Many other staff have been forced out or are leaving because of the chaos at the agency, including the Center for Drug Evaluation and Research, which we are here to talk about today. I asked Secretary Kennedy, who was before us, about the effect of some of these cuts. In particular, some detailed questions about how many of these folks laid off were veterans. I await an answer and haven't received it yet.

The mission of the FDA, to ensure the safety and effectiveness of thousands of drugs and medical products, including in this program that we are focused on today, is so important. And the way to overhaul the agency is not to indiscriminately fire thousands of experts.

I hope we get some answers about how the decisions were made on these layoffs and what impact they could have on the ability of the FDA to successfully implement the programs that we are here to discuss today. With that, Mr. Chairman, I yield back.

The CHAIRMAN. Thank you. We are joined today by Dr. Jacqueline Corrigan-Curay, the Acting Director of the Center for Drug Evaluation and Research, or CEDR, at the U.S. Food and Drug Administration. In her role as Acting CEDR Director, Dr. Corrigan-Curay is responsible for ensuring that safe, effective, and high quality drugs are available to the public.

She brings a long career in medical research, including numerous positions at FDA, as well as the NIH. Dr. Corrigan-Curay holds degrees from Harvard Law School, the University of Maryland School of Medicine, and Harvard University. I look forward to hearing from her today and thank you for joining us. Is your microphone—?

STATEMENT OF JACQUELINE CORRIGAN-CURAY, ACTING DIRECTOR, CENTER FOR DRUG EVALUATION AND RESEARCH, UNITED STATES FOOD AND DRUG ADMINISTRATION, SILVER SPRING, MD

Dr. CORRIGAN-CURAY. Thank you. Can you hear me now? Good morning, Chairman Cassidy, Senator Kaine, and Members of the Committee, and thank you for the opportunity to speak with you today.

I want to talk about something that benefits nearly every American household, over-the-counter medications. These are the products that millions rely on every day, an antiseptic when your child has a scrape, antihistamines when the pollen counts rise—

The CHAIRMAN. Will you pull the microphone closer to you, please?

Dr. CORRIGAN-CURAY. Yes—and an antacid after a heavy meal. They are trusted, essential, and they must be safe, effective, and up to date. And that is where the OTC Monograph User Program, or OMUFA, comes in.

Prior to 2020, our ability to regulate OTC drugs hadn't been modernized in decades. It was slow, outdated, and inflexible. Reform was overdue. When Congress passed the OTC monograph reform as part of the *CARES Act*, it was a bipartisan success that brought real change. Critically, the user fees that Congress authorized, OMUFA, are what facilitated and supported OTC monograph reform and has set the program for success.

Now, with Congressional support and timely reauthorization, we have the opportunity to realize the full potential of the OTC monograph reform, ensuring a nimble regulatory process, fostering innovation to better serve patients and consumers, and enhancing transparency and accountability from the FDA and industry.

What have we accomplished so far? In just 5 years, OMUFA has helped FDA modernize the OTC drug review process, transforming it from a paper heavy rulemaking system to a responsive electronic one. We have delivered five guidance documents providing clarity to manufacturers and enhancing public health protections.

We have posted 33 final orders and 5 proposed administrative orders, providing transparency for manufacturers on what is expected to market a particular OTC drugs. And I want to highlight our most recent proposed order because we believe it will foster some exciting innovation for children and families. If finalized, this order would let companies create new, easier to take forms of OTC medications like chewable tablets, tablets that melt in your mouth, and thin films.

These would be for certain medications that currently only come as tablets or capsules and could help people who have trouble swallowing them. OMUFA has also helped hire 85 dedicated staff members, scientists, safety reviewers, and regulatory experts who help ensure the products on our shelves are safe and effective.

Importantly, it has opened the door to more innovative products like a new sunscreen ingredient through the administrative order process. If Congress does not authorize OMUFA this year, the momentum would come to a grinding halt. The impact would be immediate and damaging.

Engagement on development programs and activities to oversee the safety and quality of OTC monograph products would slow or stop as dozens of FDA staff with clinical quality and safety expertise would lose their positions. Critical progress on proposed and final orders from the FDA's monograph forecast would be shelved, and these include essential updates on labeling, drug facts, and ingredients, including for products intended for pregnant women and children.

No new agreements from the recent commitment letter could be implemented, including important steps like improving meeting management with sponsors, and more quickly assessing the quality

of facilities as companies bring new products to the U.S. And perhaps most concerning, we risk sliding backward, losing the transparency, predictability, and innovation that OMUFA was designed to create.

Without reauthorization, the system that was finally fixed begins to break again. The recently negotiated agreement for the next 5 years of OMUFA includes smart, achievable goals, increasing opportunities for industry and FDA to interact to foster innovation, improving the transparency of the user fee program, investing in product quality and safety, and continuing to publish the annual guidance forecast that give industry and public health stakeholders a clear roadmap for the future. These aren't just words. They are commitment to the public.

A commitment to keep this progress going. Every delay in regulation or review affects real people. Without OMUFA, innovations are stalled, safety improvements are delayed, and consumers may unknowingly continue to use products that haven't been adequately reviewed under modern science. This isn't about red tape, it is about real lives, real trust, and the medications that Americans buy off the shelf every day.

In closing, Congress made a smart investment in 2020 when it created OMUFA. That investment is paying off, but we can't stop now. Reauthorizing OMUFA means continued modernization, supporting innovation, and most importantly, keeping American families safe. Thank you, and I look forward to your questions.

[The prepared statement of Dr. Corrigan-Curay follows.]

PREPARED STATEMENT OF JACQUELINE CORRIGAN-CURAY

Introduction

Chairman Cassidy, Ranking Member Sanders, and Members of the Committee, thank you for the opportunity to testify today on the reauthorization of the Over-the-Counter Monograph Drug User Fee Program, commonly referred to as OMUFA.

Over-the-Counter (OTC) drugs have long provided an effective, low-cost way for Americans to take care of everyday health needs without having to visit a doctor and obtain a prescription, saving American consumers time, effort, and money. Non-prescription drugs, including those for allergies, pain, fever, and various other ailments are widely available through online and retail outlets, providing safe and effective healthcare options to American consumers nationwide. One powerful example of the impact of nonprescription drugs are the approvals of naloxone nasal spray, which is used to reverse opioid overdoses. Availability of this medication without a prescription allows this life-saving medication to be sold directly to American consumers in drug stores, convenience stores, grocery stores, gas stations, and online. Although regulated under an approved application rather than the OTC monograph system, this example demonstrates how critical nonprescription products can be to individuals' lives and public health.

The work of this Committee, leading to enactment of OTC monograph reform and OMUFA in 2020 laid critical groundwork, establishing a long overdue, transformational framework for modernizing the regulation of many over-the-counter drugs. Now, with Congressional support and timely reauthorization of OMUFA, we have the opportunity to realize the full potential of the OTC monograph reform program—ensuring a more nimble regulatory process, fostering innovation to better serve patients and consumers, and enhancing transparency and accountability from FDA and industry.

History of Regulating OTC Drugs

More than 100,000 OTC drug products are marketed in the United States under what is known as the OTC monograph system. A monograph is essentially a rule book or a recipe book that establishes conditions under which an OTC drug in a

given therapeutic category (e.g., antacids, pain or cold medicines) is generally recognized as safe and effective (GRASE) for its intended use. Monograph conditions may include acceptable ingredients, doses, formulations, labeling, and testing. Products that meet the conditions outlined in a monograph¹ may be marketed without FDA premarket approval, in contrast to other drugs that must be approved before being marketed.

The OTC monograph process was established over 50 years ago and was largely envisioned as a “once and done” system. The science supporting these products was already considered established and innovation in this space was believed to be unlikely, which we now know is not true. The system utilized a three-phase multistep public rulemaking process to establish or change OTC monographs, significantly limiting the pace of innovation in these critical products. In particular, the time required for these process steps resulted in delays in finalizing monographs, challenges in responding quickly to urgent safety issues, and difficulty keeping pace with evolving science and a changing market.

Monograph Reform and User Fees

In March 2020, the *Coronavirus Aid, Relief, and Economic Security (CARES) Act*, Public Law No. 116–136, added section 505G to the Federal Food, Drug, and Cosmetic (*FD&C Act*). Section 505G reformed and modernized the framework for the regulation of OTC monograph drugs. These reforms, supported by OMUFA user fees, replaced rulemaking for monograph purposes with a more streamlined, efficient process—using Administrative Orders—that can be initiated by either FDA or industry (i.e., any person or group of persons marketing, manufacturing, processing, or developing a drug) to add, remove, or change a monograph. Under section 505G, industry can request that FDA issue an administrative order by submitting an OTC monograph order request (OMOR) to FDA. Section 505G also authorized establishment of new procedures under which FDA may meet with sponsor(s) or requestor(s) in advance of submission, and FDA has issued guidance regarding the process for those meetings. If FDA accepts the OMOR for filing, FDA will then review the OMOR and develop and issue a proposed order. FDA can also initiate the process by developing and issuing a proposed order; in both instances, there is an opportunity for public review and comment before a final order. FDA can also initiate an expedited process for developing and issuing an administrative order when a drug poses an imminent hazard to public health or a change in the labeling of a drug is expected to mitigate a significant risk of a serious adverse event associated with use of the drug.

Notably, the *CARES Act* also facilitated these reforms by amending the *FD&C Act* to authorize FDA to assess and collect user fees from industry to support the Agency’s OTC monograph drug activities. These activities involve evaluating OMORs, including reviewing safety and efficacy information for proposed new monograph active ingredients as part of GRASE determinations, developing and issuing proposed and final orders, conducting inspections of OTC monograph drug facilities, and monitoring OTC monograph drug safety, among other regulatory functions. This user fee program, commonly referred to as OMUFA, also supports modernizing IT systems, and recruiting and training skilled staff. Typically, accompanying authorization of such user fee programs is an agreement negotiated between FDA and industry, often referred to as a “goals document” or “commitment letter”, in which FDA agrees to adhere to performance goals in terms of conducting fee-supported activities, including specific timeframes to review and respond to certain industry submissions. FDA reports on its accomplishment of these goals annually in publicly available reports, which increases transparency and accountability for review work.

By improving the efficiency of FDA’s OTC regulatory process, consumers will have increased access to innovative, effective and safe OTC drug products.

¹ Products must meet the conditions outlined in a monograph, as established under section 505G of the *FD&C Act*, as well as other applicable requirements. Examples of other applicable requirements for OTC drugs include, but are not limited to, format and content requirements for OTC drug product labeling under 21 CFR 201.66, and conditions under 21 CFR 330.1, such as being manufactured in compliance with Current Good Manufacturing Practice (CGMP) regulations under 21 CFR 210 and 211, and using only safe and suitable inactive ingredients.

OMUFA I

Background

Under the OMUFA program, industry-paid fees help support FDA's regulatory activities related to OTC monograph drugs. However, in order for FDA to annually collect and spend authorized OMUFA user fees, the fees must be appropriated, and FDA must allocate for OTC monograph drug activities a minimum of \$12 million of appropriations (excluding user fees) multiplied by an adjustment factor. During each of the fiscal years under OMUFA I to date, FDA met both legal conditions.

Under OMUFA, FDA collects two types of fees: facility fees and OMOR fees. FDA calculates both fees in accordance with our statutory authority. OMOR fee rates for fiscal year 2021 were specified in statute, and are adjusted for inflation each year. Tier 1 OMORs represent significant changes to a monograph (e.g., new ingredients, indications, or therapeutic categories), while Tier 2 OMORs represent more minor changes to the monograph. Additionally, the statute mandates a process FDA follows to calculate the target total revenue from facility fees each year. FDA establishes facility fee rates with the goal of generating that target total facility fee revenue amount. Facility fees are assessed on qualifying persons who own an OTC monograph drug facility, including contract manufacturing organization facilities which pay a reduced fee. Over the course of OMUFA I, the target revenue for facility fees ramped up from \$23.3 million in fiscal year 2021 to \$36.5 million in fiscal year 2025. The total target revenue for OMUFA I was \$141.3 million over 5 years.

Building Infrastructure

Overall, FDA has been successful in implementing OTC monograph reform and meeting the goals set out in the first OMUFA user fee goals document, i.e., under OMUFA I. Notably, the *CARES Act* amendments established a new statutory framework for regulating OTC monograph drugs, under section 505G of the *FD&C Act*, and *concurrently* established authority in the *FD&C Act* for the OMUFA user fee program. Simultaneous enactment of both these programs created additional steps for implementation. In contrast, the statutory framework for new drug applications had been in place for decades before authority for the prescription drug user fee program was enacted and implemented. Therefore, during this first 5 years of the OMUFA user fee program, FDA has been focused on building an entirely new OTC monograph drug regulatory program from the ground up, which meant hiring and training staff, developing new procedures, and creating a system that could efficiently handle the review of OMORs and issuance of proposed and final monograph orders. OMUFA I supported hiring of 105 full-time equivalents, spread over the 5-year period, to supplement the 35 that were estimated to be working on monograph issues when the program was negotiated. At the end of fiscal year 2024, FDA had filled 85 of the 105 positions; however, three program staff have voluntarily left the FDA. Nine of the outstanding positions were agreed to be added during fiscal year 2025.

During the first 3 years following passage of the *CARES Act*, the majority of FDA's effective capacity with respect to OTC monograph drug activities was focused on developing the system to implement the statutory mandates for OTC monograph reform and OMUFA, including associated infrastructure development activities. In particular, significant resources were dedicated to the development of the first IT system to manage OTC monographs and the reformed OTC monograph process, allowing for more transparency and public access to OTC monographs and related administrative orders.

By Year 3, FDA's OTC monograph-related resources grew to the point where some OMUFA performance goals began for meetings with industry as agreed to in the OMUFA I goals document. In Years 4 and 5, FDA has been implementing the agreed upon timelines and progressive performance goals for reviewing OMOR submissions, meeting management, guidance development, and other activities.

Specifically, FDA issued five draft and one final guidance related to OTC monograph drugs, including in fulfillment of statutory requirements. These guidances serve as "how to" guides for navigating the new system established by Congress, and were written while the system was being operationalized. FDA has been working diligently to finalize the remaining draft guidances in a timely manner. In accordance with the OMUFA I goals document, FDA has also posted an annual monograph forecast outlining FDA's intended monograph activities over the next 3 years. This level of planning helps provide predictability for industry while fostering FDA accountability for progress. All of these activities laid the groundwork for realizing the full benefit of OTC monograph reform in the coming years.

Taking Action

In addition to building the extensive infrastructure needed to implement monograph reform, in years 4 and 5, FDA has begun to meaningfully use the modernized OTC regulatory process supported by OMUFA I. As required by statute, FDA has posted 33 final administrative orders that were deemed established by section 505G upon its enactment under the *CARES Act*.

Additionally, in June 2024, FDA issued a proposed order (the first discretionary proposed order initiated by the Agency) to address a safety issue related to OTC monograph drug products containing acetaminophen. If finalized, this proposed order would require drug companies to add a warning to the labeling of these products to alert American consumers that the use of acetaminophen may cause severe skin reactions. Although FDA alerted the public to this safety concern in 2013 via a drug safety communication, the complex rulemaking process applicable to OTC monograph drugs at that time limited the Agency's ability to rapidly modify the relevant monograph to require this warning to align labeling with nonprescription acetaminophen drug products with approved applications.

Also in 2024, FDA issued a proposed order to amend the relevant OTC monograph to remove oral phenylephrine as an active ingredient for temporary relief of nasal congestion because it is not effective for this use. This proposed order also reassesses the risks and benefits of this cough/cold active ingredient in children under 6 years of age. Before making the decision to issue the proposed order, FDA held an Advisory Committee meeting to discuss the GRASE status of oral phenylephrine as a nasal decongestant. Based on review of the current data and a unanimous recommendation from the Advisory Committee, FDA published the proposed order to inform the public and garner comments. If, after considering comments on the proposed order, FDA concludes that oral phenylephrine is not effective as a nasal decongestant, FDA would issue a final order amending the applicable OTC monograph to remove this ingredient as an oral nasal decongestant.²

FDA also published a proposed order on sunscreens, proposing new monograph conditions under which nonprescription sunscreen drug products would be determined to be generally recognized as safe and effective (GRASE) under the *FD&C Act*. Notably, in September 2024, FDA received the first OMOR submitted by industry, requesting to add a new ingredient to the sunscreen monograph, potentially increasing choice for American consumers. FDA is actively reviewing that submission according to the timelines established in the user fee goals document, and has a current goal date of late February 2026.

Overall, these accomplishments during the first 5 years of the OMUFA program demonstrate that OMUFA I fee resources not only helped make the OTC monograph system more efficient, but supported the development of the infrastructure needed for continued success.

OMUFA II Reauthorization

Reauthorization of OMUFA is instrumental to build upon the successes of OMUFA I to create a transparent, modernized regulatory system for safe and effective OTC monograph drugs.

OMUFA resources are key to supporting the safety of the OTC drug products consumers use every day. For example, in 2023, there was a worldwide safety alert regarding over-the-counter medicines, primarily children's cold medicines, contaminated with diethylene glycol (DEG) and ethylene glycol, the main ingredient in antifreeze, resulting in more than 300 deaths in children in multiple countries. Because of quick work by FDA to issue guidance for testing, request for records from manufacturers, and issue import alerts for affected products, American consumers were spared this tragedy. FDA continues to conduct quality surveillance for this contaminant—with multiple import alerts issued so far this year for toothpaste products potentially contaminated with DEG. Although a disaster prevented often goes unnoticed, having a robust system for ensuring drug safety, efficacy, and quality is why American consumers can confidently choose OTC drugs in the United States. The resources and commitments related to improved quality surveillance and transparency included in the OMUFA II proposal are needed to help ensure this consumer confidence is both maintained and enhanced.

Similarly, without the resources from OMUFA, FDA will not have sufficient capacity to help ensure the safety and efficacy of OTC monograph products. If

² <https://www.fda.gov/drugs/drug-safety-and-availability/fda-clarifies-results-recent-advisory-committee-meeting-oral-phenylephrine>.

OMUFA were not reauthorized, some of the actions FDA has planned could take a decade or longer to implement. These are actions that impact our most vulnerable Americans—including pregnant women and children. For example, FDA will be working to address:

- pediatric weight-based dosing for acetaminophen,
- pregnancy labeling for non-steroidal anti-inflammatory drugs,
- risks associated for codeine-containing cough medicine in adults and children,
- the safety and efficacy of oral anesthetics containing benzocaine, including for infants,
- greater availability of child-friendly options of certain oral medications for children.

Process to Development OMUFA II Recommendations

Many stakeholders including consumer groups, medical societies, pharmacy associations, academics, and regulated industry recognize OMUFA's critical role in establishing and maintaining an efficient and transparent OTC monograph system. To ensure the OMUFA II reauthorization recommendations reflect shared priorities, FDA held two public meetings and gathered additional feedback via a public docket. In addition, we held 25 extensive negotiation sessions with industry stakeholders.³

Because OMUFA I was authorized from fiscal years 2021–2025, this was the first negotiation with industry to develop reauthorization recommendations, for fiscal years 2026–2030. Throughout the negotiation, FDA and industry remained aligned on the common goal of advancing public health while maintaining scientific standards and promoting innovation. Given the relative newness of the OTC monograph reform program, recommendations for OMUFA II focus on ensuring stable funding for the program, enhanced transparency of the OMOR process, and enhanced regulatory efficiency and predictability.

With Congress' support and a timely OMUFA reauthorization, we are excited to begin realizing the full potential of OMUFA—to meaningfully advance our efforts to help American families have access to safe and effective drugs regulated through the OTC monograph system, including by reviewing OMORs and developing and issuing proposed and final administrative orders, facilitating innovation and up-to-date safety information about these important products. The commitments FDA can achieve with timely reauthorization thematically fall into the following categories, discussed below:

- Funding Stability
- Monograph Drug Product Quality Enhancement
- Financial efficiency and transparency
- Information transparency
- Meetings with industry and notice of Advisory Committee meetings
- Education for industry
- Updating testing methods in monographs

The reauthorization proposals for OMUFA that are described below were submitted to Congress in January, under the previous Administration. The Trump administration looks forward to working with Congress toward reauthorization of the important OMUFA program to build upon the successes of OMUFA I and facilitate a transparent, modernized regulatory system for safe and effective OTC monograph drugs.

Funding Stability

OMUFA II recommendations reflect the goal of ensuring stable funding for the program, including avoiding large fee increases. Under OMUFA, FDA sets annual facility fees to generate the total facility fee revenues for each fiscal year established by section 744M(b) of the *FD&C Act*. The yearly base revenue amount is the starting point for setting annual facility fee rates. The OMUFA II proposal resets the starting base revenue under the statute for OMUFA II to include the additional direct cost adjustment of \$3 million from the final year of OMUFA I, which is approximately 8 percent of the total revenue in fiscal year 2025. This adjustment helps en-

³ <https://www.fda.gov/industry/fda-user-fee-programs/omufa-reauthorization-fiscal-years-2026-2030>.

sure that the OTC monograph drug program is adequately resourced to meet increasing demands. The proposed base revenue for fiscal year 2026 will be approximately \$36.5 million, and the additional proposed funding will increase fee revenue by 12 percent over the course of the 5-year authorization period, in addition to inflationary increases. Overall, total target revenue for OMUFA II is proposed to be an estimated \$206.8 million, including estimated inflation. These increases will continue to support increased efficiency of the OTC program in FDA, creating value for the American consumer.

The OMUFA II reauthorization recommendations support an addition of 11 new full-time equivalents (FTEs), added over the first 3 years of the reauthorization period. These new hires will support the growing responsibilities and commitments associated with conducting FDA's OTC monograph drug activities, and will bring total OMUFA funded FTEs to 116. In addition to personnel, the proposal supports a modest allocation for contract expenses tied to the proposed new OMUFA II commitments.

Monograph Drug Product Quality Enhancement

The OMUFA II recommendations include commitments to enhance monograph product quality surveillance and transparency. The commitment letter agreement includes a new commitment from FDA to more quickly vet new registrants to confirm whether they should be included in CDER's catalog of OTC monograph drugs and establishments. Today, when a new facility registers with FDA and lists the drugs that they make for the U.S. market, FDA commonly needs to correspond with the registrant to obtain further information to confirm, for example, that the registrant is making a drug and not a cosmetic, or that a foreign registrant is actively shipping to the U.S. The proposed OMUFA II funding will provide additional resources to enable FDA to more quickly gain accurate information from registrants about the drugs they are producing as well to request and review information about the registrant's compliance with applicable current good manufacturing practice (CGMP) requirements to inform FDA's risk-based manufacturing facility inspections.

Additionally, FDA agreed to hold a workshop aimed at helping industry stakeholders enhance quality and ensure compliance with CGMP requirements. FDA also committed to updating the risk-based inspection site selection model, which is used to prioritize surveillance inspections, and the associated Manual of Policies and Procedures (MAPP), to include risk factors specific to OTC monograph drugs. For example, given an initial observed association between failure to pay OMUFA fees and violative surveillance inspection outcomes, FDA will evaluate the failure to pay OMUFA fees as an important risk factor to be included. These commitments from both FDA and industry to enhance product quality will help ensure American consumers continue to have access to safe and effective OTC drugs.

Financial Efficiency and Transparency

The OMUFA II recommendations address industry concerns about financial transparency and management through several key initiatives. The proposed statutory amendments aim to enhance financial efficiency by aligning the annual OMUFA facility fee due date with the October 1 fiscal year-start due date for annual fees under other drug user fee programs, helping streamline the assessment and collection process for both FDA and industry. This common-sense reform benefits both the Agency and industry (who may pay other annual drug user fees), enhancing efficiency and predictability.

Additionally, to improve unpaid fee recovery and transparency, OMUFA II commitments will increase visibility of facilities that have not paid fees, including breakdowns of foreign and domestic firms in arrears. This will promote accountability in the industry and help level the playing field for American manufacturers. FDA will also use information obtained from records requests to focus recovery efforts on outstanding OMUFA user fee delinquencies. Additionally, the proposed OMUFA II amendments to statutory fee setting introduce a new contingent adjustment to annual target revenue, allowing for a one-time upward adjustment if the number of fee-liable OMUFA facilities increases over a specified level. If necessary, this would help ensure that FDA can accommodate the additional work required to oversee a growing number of facilities, both foreign and domestic, without compromising quality or efficiency. These financial enhancements demonstrate FDA's commitment to responsible fiscal management while maintaining robust oversight.

Information Transparency

FDA commitments under OMFUFA II would take significant strides in terms of information transparency, including through agreeing to post information on FDA's Web site about monograph-related exclusivity, updating and maintaining monograph-related Web site links, and ensuring Web site accessibility of historic monograph-related materials and regulatory information. These measures address industry demands for clear, more consistent information about the OTC monograph process, including FDA's review of OMORs and development and issuance of proposed and final orders addressing safe and effective conditions of use for OTC monograph drugs. In particular, the information regarding monograph-related exclusivity will ensure uniform access to such information for all OTC manufacturers and stakeholders. FDA will post a page on its Web site addressing monograph-related exclusivity afforded by final administrative orders, including a table of relevant monograph change(s), requestor(s), the final order date, and relevant listing updates for drugs subject to the final order.

FDA will also report annually on its Web site aggregate information about records requests issued to OTC monograph drug manufacturers under section 704(a)(4) of the *FD&C Act*. This reporting provides industry with more transparency regarding the information FDA is requesting related to compliance with CGMP requirements and how often the information provided leads to FDA action. Reporting will begin in fiscal year 2027 if the aggregate number of requests issued exceeds 20; otherwise, reporting will begin in fiscal year 2028. Similarly, FDA will enhance the Agency's warning letter Web page to improve its search capability for warning letters issued to OTC monograph drug manufacturers. Both of these actions will not only improve transparency, but also will contribute to efforts aimed at ensuring product quality and safety—key pillars of the OTC monograph reform program supported by OMFUFA.

Meeting and Advisory Committee Refinement

OMFUFA II commitments significantly enhance the utility of FDA-industry meetings, including by providing for advance notice of certain Advisory Committee meetings, which directly addresses industry's requests for more productive and transparent communication with FDA. OMFUFA II commitments also include a new follow-up opportunity which allows OMOR requestors to confirm or clarify with FDA something in meeting minutes or written response, similar to a PDUFA VII enhancement. It also includes the potential for extended meeting options for complex topics, allowing more meaningful engagement for sponsors. Similarly, OMFUFA II will facilitate the ability of requestors to seek feedback on protocol synopses, improving both regulatory efficiency and predictability.

Regarding Advisory Committee meetings specifically, FDA has agreed to provide at least 100 business days' advance notice for a specific subset of OTC monograph-related Advisory Committee meetings. FDA recognizes that this advance notice can help provide stakeholders time to coordinate and prepare for meaningful Advisory Committee discussion. This commitment will not apply to situations where the Advisory Committee is planning to discuss an emerging safety issue or if existing policy on advanced notice for certain Advisory Committee meetings applies.

Education for Industry

The OMFUFA II proposal also demonstrates FDA's commitment to transparency and predictability through ongoing education and outreach efforts for industry to facilitate innovation and safe and effective OTC monograph drug products for Americans. In addition to the CGMP webinar mentioned above, FDA has agreed to host a webinar on OMOR submission through the Next Gen Portal, as well as a crowd sourced session on OMOR submissions and GRASE determinations. Finally, FDA has committed to introducing draft guidance on filing eligibility for OMORs proposing new monograph active ingredients and another on the handling of confidential information submitted to the Agency in connection with proceedings on an OTC monograph order. Taken together, the recommendations for OMFUFA II demonstrate a significant commitment to addressing the priorities of the public, the regulated industry, FDA, and public health.

Conclusion

OTC monograph reform, supported by OMFUFA I, has been transformative for OTC drug regulation and has created a faster, more transparent, and more predictable system that benefits American consumers. Through additional resources pro-

vided under OMUFA I, FDA built the necessary infrastructure for implementing OTC monograph reform, hired and trained staff, launched a modern IT system to facilitate efficiency, and issued important guidance for industry. In just a few years, we met OMUFA performance goals, issued five key guidances, and provided a forward-looking monograph forecast. We also posted 33 final administrative orders defining baseline monograph conditions for various therapeutic categories of OTC drugs, as established upon enactment of section 505G of the *FD&C Act*, and issued two FDA-initiated proposed orders to update the monograph conditions for safety and efficacy of certain OTC drugs. These achievements would have been impossible under the previous regulatory framework.

This progress cannot continue without OMUFA reauthorization. OMUFA II resources are critical to maintaining efficiency, ensuring safety, and fostering innovation in the OTC market. Without it, we risk losing the gains we have made and returning to slower responses to safety and fewer innovative choices for American consumers. I look forward to working with you to authorize OMUFA II and secure the future of a modern, responsive OTC monograph system.

The CHAIRMAN. Thank you, doctor. So, I have a question here, but it kind of goes against the flavor of your testimony. And your testimony was very positive about the positive things that OMUFA has done.

But my question is, it seems like the Rx to OTC switch, which is from prescription to non-prescription, that FDA has struggled to make that happen. So, is that a misperception of my part, or is there a—has it been more successful than I have understood?

Dr. CORRIGAN-CURAY. Thank you for that question. In the past few years, we have brought certain prescription drugs to over-the-counter, and that would include the Naloxone that became over-the-counter and was very critical, I believe, in helping us address the opioid crisis.

We have brought the—[technical problems]—contraceptive over-the-counter as well, and we have bought some of the nasal allergy sprays over-the-counter. And as you also may be aware, we have a rule that should be finalized, and that would be to bring additional medications over-the-counter with a condition of use.

To have a new way of bringing medications over-the-counter and we hope that would greatly expand.

The CHAIRMAN. Explain the condition of use.

Dr. CORRIGAN-CURAY. Yes. So, under this rule, if we determine that you could not bring a drug over-the-counter with just the drug facts label, because with that label alone, a person could not appropriately self-select for that drug and use it, then a company could propose an additional condition.

It might be a mobile app or something with some questions. And then if we can show that with use of that additional condition or those questions before they access the product, they can access it safely, that would open the door to products that we currently do not have over-the-counter.

The CHAIRMAN. Now, can you give an example of that, or is it—?

Dr. CORRIGAN-CURAY. They are still in development. There are things in development, but we could think potentially about drugs that might be more for chronic conditions where we could select a population for which that drug was safe to take over-the-counter.

The CHAIRMAN. Now, let me go back to, you listed some that have become over-the-counter, but you listed like five or six. And there is a heck of a lot of drugs out there that could be over-the-counter.

Is it that you are just giving me a sample, that there is—you are giving me sample, for example, five or six drugs I am going to mention, or is it, no, that is the universe of those that have been approved? Because, let me ask you that.

Dr. CORRIGAN-CURAY. Thank you. In the recent timeframe, those were the ones I highlighted. We certainly work hard to look for opportunities to bring drugs over-the-counter that patients can safely self-select and use. And then, as I said, I think our—

The CHAIRMAN. No, let me understand the process. Don't mean to interrupt, but I have limited time.

Dr. CORRIGAN-CURAY. No, please. Sorry.

The CHAIRMAN. Does the drug company have to apply, or can you—for example, Benadryl, I think, used to be like a prescription drug. And so—and Claritin used to be a prescription drugs.

Dr. CORRIGAN-CURAY. Right.

The CHAIRMAN. But really, you could have looked at those and said, this doesn't have to be a prescription drug, I mean, this could be over-the-counter. So do the drug companies have to apply, or can the agency say, this drug can safely be given OTC?

Dr. CORRIGAN-CURAY. Thank you for that question. It does—the application does need to come in. However, in the case of Naloxone, if I recall, we put out an FR notice saying that we were open to working to bring Naloxone over-the-counter.

I think we have opportunities to signal where we think there might be opportunity. We also do speak to companies, and we can suggest that we might be open to a development program. It does require a development program to show that they—

The CHAIRMAN. And what do you mean by development program?

Dr. CORRIGAN-CURAY. Yes. So a company would need to show that consumers can self-select appropriately and use it with the information that is on the drug facts label.

The CHAIRMAN. Now, let's go back to something like Tagamet, which again at one point was a prescription drug, or Prozac, which was a prescriptions drug. You could have looked at that initial—I am saying you, rhetorically you, could have looked at that and said this is a pretty safe drug, and people could take it for heartburn.

I guess I am asking, since that would save lots of money for patients, lots of money for patients if they could buy those drugs—OTC as opposed to having to see a physician. Is there something Congress can do to expedite that, or do you have all the tools that you need to actually generate a kind of more aggressive approach to the Rx to OTC method?

Dr. CORRIGAN-CURAY. Thank you. So, in the case of that drug, we certainly would say first, yes. Does it look like it has a safety profile that we time—we have enough experience? But then we do have to have the information saying that the consumers can self-

select. We are always happy if you have ideas to work with you on those.

The CHAIRMAN. Senator Kaine.

Senator KAINE. I am such an OMUFA nerd that I am going to stay for the whole hearing. So I am going to yield to Senator Kim and take my questions later.

Senator KIM. Okay. Thank you. Thank you for coming on out. I wanted to ask you, it was raised in the opening remarks about some of the reduction in force. So I guess I just wanted to ask you, are you able to tell us if any of the staff in the Office of Non-Prescription Drugs were terminated under the reduction in force efforts?

Dr. CORRIGAN-CURAY. Yes, thank you for that question. Unfortunately, and consistent with our policy, when there is something that is a subject of litigation, we don't comment on the specifics. And as you know, there is a preliminary injunction around the reduction in force, so I can't go into any details at this point.

Senator KIM. When you are able to provide answers——

Dr. CORRIGAN-CURAY. Yes, we would be happy.

Senator KIM. Yes, I would like to know how many staff have been let go or resigned from the Office of Non-Prescription Drugs and how many of those were funded by user fees.

Also I want to talk about the commitments that the FDA made with the OTC industry as part of the OMUFA commitment letter, specifically the agreement that FDA would hire 11 new full-time employees over the length of the reauthorization.

I understand that there is currently a hiring freeze at the FDA. First, is that the case? And second, if so, will the FDA be able to stand by this commitment of hiring 11 additional full-time staff?

Dr. CORRIGAN-CURAY. Yes, thank you for that question. Yes, there is a hiring freeze, but I know as Dr. Makary has indicated, he is working to allow us to hire the reviewers that we need for all aspects, and so I am confident that he will be working with us to give us the resources we need to be successful under OMUFA II.

Senator KIM. Okay. I want to just kind of hone in on a particular example to try to get a sense of how OMUFA is moving forward and how it is performing. So, for instance, sunscreen.

This is something where we understand that the United States has continued to lag behind other countries in terms of UV filters that are approved for use in sunscreens. And the FDA has not approved a new filter, a UV filter, since 1999. Is that correct?

Dr. CORRIGAN-CURAY. That is correct. Although we do have a new OTC monograph order under review for a new sunscreen ingredient.

Senator KIM. Well, I guess I would just like to hear a little bit more from you because despite Congress creating this new pathway and then several years overhauling the entire OTC monograph order process so, yet we still have no new sunscreen ingredients formally approved. You said there's something in the works?

Dr. CORRIGAN-CURAY. Yes.

Senator KIM. But I guess I just want to kind of ask you like how do we try to address this? How do we try to make sure that we are moving forward and addressing these main challenges of approving new ingredients?

Dr. CORRIGAN-CURAY. Yes. So I would like to explain a little bit about the sunscreen market. Sunscreens for us, they are considered drugs because they are used to protect against the damages of sun and skin cancer. And any drug that we approve that is topical but that has systemic absorption, we need to make sure that the systemic absorption has no untoward effects.

Those could include things like disrupting the endocrine system or even abnormal growth of cells or tumors. And we do know that certain ingredients in the literature have been highlighted for potential endocrine disruption. So to do that we would ask a company to do those tests, just like for any other drug that we approve.

We have laid out the data that we think would be necessary for us to do an assessment. And we are waiting for more companies to come to us with that data, and then we would be happy to review it and work on that. I would also like to note that I know that there are additional sunscreens in different countries.

Not all of them are under—treated as a drug. But I would also like to say that there is no data that those are more effective or that we don't have effective sunscreens on the market here in the United States.

Senator KIM. I want to just switch gears a little bit, just sort of another angle. I am a father of a 7-year-old and a 9-year old. A lot of parents in the bleary early mornings of a sick child try to wander off, try to figure out what we can do for our kids.

I understand that the FDA has stated its intention to develop pediatric weight-based for acetaminophen during the next user fee authorization. I guess I want to know for myself if I am giving my kids the right dosage here.

Could you explain to the Committee what staff resources are needed to make that change happen? How do we ensure that we are able to move that forward promptly?

Dr. CORRIGAN-CURAY. Yes, thank you. We will be asking for new staff in OMUFA II to continue to put out our orders and guidance. But this is a priority for us. We do know that there have been improvements in the way the acetaminophen—concentrations on the shelf, but we need to address this weight-based, and we will put that as a priority. It is on our agenda.

Senator KIM. Well, I just raise this as another example of just the importance that we have staff. That the experts there are able to process this. And when we see so much slashing of employees and staff, I worry that these types of direct benefits to people will be cast to the side. And with that, I will yield back.

The CHAIRMAN. Senator Marshall.

Senator MARSHALL. All right. Thank you, Mr. Chairman. And welcome to our guest today. Let's talk about measuring success. My question is, how do you measure success? I assume that from a safety standpoint, every month you are reviewing things that will—did we get anything wrong and how come?

But beyond that, how do measure success from the standpoint of the ones that are coming into the system? Is there a set amount of time you would like to have them out by? What percentage of those made it through the process in that amount of time? How do you measure success?

Dr. CORRIGAN-CURAY. Thank you. I think in OMUFA I, we have measured success in that we have stood up the program. We have provided those foundational guidance. We have created an electronic, efficient way for companies to communicate with us.

Then we have the first new proposed order in that we are reviewing. We are also making all of our commitments on meetings. So we are meeting with companies. And so, our success will be to continue to move those development programs——

Senator MARSHALL. All those are you trying to improve success, but I don't hear you measuring success. In the standpoint of you run a hospital, you run a bank. Every month you look to these key metrics to say, are we hitting these measures.

Dr. CORRIGAN-CURAY. Yes. For us, we will be putting out our agenda, and that is the plan 3-year agenda, and that will tell you the successes of getting these orders out. So, for example, the new order that we just put out, which will allow for changes in the dosage forms, and we think that is very innovative and will help——

Senator MARSHALL. You don't have a monthly dashboard of metrics that you are looking at to see if we are meeting them?

Dr. CORRIGAN-CURAY. We are tracking all of the things that we are doing in terms of proposed orders, that we are meeting our timelines on reviews. And when there is an——

Senator MARSHALL. Can you share your dashboard with us?

Dr. CORRIGAN-CURAY. I don't know if it is an electronic dashboard, but we are tracking what we are doing and our commitments.

Senator MARSHALL. Okay. I would love to see how you are measuring success, so if it is not a dashboard——

Dr. CORRIGAN-CURAY. Sure. We should get back to you.

Senator MARSHALL [continuing]. I would encourage you to get one. Let's talk about inactive ingredients. As you know, the OTC monographs only list active ingredients. A lot of Omaha moms out there are concerned about inactive ingredients, artificial flavors, sweeteners, etcetera.

What is going on in the world of over-the-counters as far as identifying those inactive ingredients, and is there an effort to get the ones that are not safe out of these over-the-counters?

Dr. CORRIGAN-CURAY. Thank you for that question. We certainly, anytime we identify that there is an issue with an inactive ingredient, we would review it, and we would look to make changes in that inactive ingredients.

We do have ways and guidance. We just did one on color additives to allow firms to—a pathway if they want to change their inactive ingredients or their color additives. And we can get back to you with more information on that.

Senator MARSHALL. Is there a way—isn't it going to be pretty simple for your monographs to include the inactive ingredients?

Dr. CORRIGAN-CURAY. I think I might have to get back to you on that question about could we just do that, if you don't mind. Thank you.

Senator MARSHALL. All right. Let's talk, about studies. More and more, it would seem that AI can replace animal studies, and probably be even more accurate. So often, you read what works—what happens in monkeys and dogs has nothing at all to do with the biology of human beings. Is there any effort in your department to convert over to AI and doing less animal studies?

Dr. CORRIGAN-CURAY. Thank you. We are engaged on the new initiative to reduce animal studies in the monoclonal antibodies. And we had—previously, we have been working on looking for alternatives to animal studies.

We already do—we no longer use animal studies for eye irritation or skin irritation, and we certainly will—are looking at both AI as we are looking at these non-animal approaches.

There are still challenges in coming out with validated studies when you are looking—you are looking for an effect that would affect multi-organ systems. That doesn't mean that we won't get there, and we will continue to work on that.

Senator MARSHALL. Okay. Again, if there is a way that you could measure that and show us. We were doing so many animal studies 5 years ago. This is how many we had last year. This is how many we are doing this year. Prove to me that you are making progress in that. That would be very helpful.

Dr. CORRIGAN-CURAY. We can get back to you. Thank you.

Senator MARSHALL. Thank you so much, Chairman. I yield back.

The CHAIRMAN. Senator Kaine.

Senator KAINE. Senator Hickenlooper.

Senator HICKENLOOPER. Thank you, Mr. Chairman. Thank you, doctor, for being with us and for your service and hard work over there. And I know there are hard times. Several of us are working on a bill we call Skinny Labels, Big Savings—the *Skinny Labels, Big Savings Act*.

Senators Collins, and Cotton, and Welch, and I are trying to address the endless procession of lawsuits against generic drug manufacturers who obtain the skinny label FDA approvals. I think if we can encourage more generic drugs to come to market through this legislation, we are going to lower costs widely for the American consumers.

Dr. Corrigan-Curay, are you willing to commit to work with us to advance this legislation so that we can lower drug costs? And as the Acting Director of the Center for Drug Evaluation and Research, what else are you working on to try and create more competition, more generic competition?

Dr. CORRIGAN-CURAY. Thank you for that question. Absolutely, we support additional generic competition. We know that generics make up 90 percent of the prescriptions in the United States. We

think the skinny labeling, we are happy to work with you on that legislation.

Other things that we are doing. We are continuing to put out our guidance, our product specific guidance which are a roadmap for developers. In addition, it is very important as we see more opportunities in complex generics that we work with industry and academia to develop the science to allow those to come forward. So we have a very robust regulatory science program.

In fact, our science meeting on generics is ongoing today, and then we put guidance. We also seek to meet all of our goals. And I would just note, I believe in 2024, we approved about 59 first generics. So those are generics drugs for which there was no generic competition before we approved.

Senator HICKENLOOPER. That is great. I appreciate that. I will come back also to AI, because you are touching on AI there as well. This week you launched ELSA, this new AI tool. And Commissioner Makary stated that ELSA was designed to expedite, to review processes at the agency with the goal of making them shorter, and yet more successful, better.

He stated, “all information stays within the agency and the AI models are not being trained on data submitted by the industry.” And so, can you share with us a little bit, Dr. Corrigan-Curay, some of the additional details about how exactly the FDA is going to ensure that the data within ELSA remains secure? I mean, I view ELSA as a tool, but like any tool, we have got to make sure we handle it safely.

Dr. CORRIGAN-CURAY. Yes, thank you. We are very excited about the initiative that Dr. Makary is leading on AI, because we do see there is utility to this tool in our work. And we are not training it on the data.

What we are doing in AI, this type of AI could be very helpful when we have got a number of documents and we want to summarize them, and we have to summarize for one of our reviews. We still have to check it, and we have to make sure it is right.

But the confidentiality and privacy of data within the FDA is one of our top priorities. I mean people—we are trusted to keep that, and we will continue to work on that, even as we incorporate new tools into our review processes.

Senator HICKENLOOPER. Well, I appreciate that, and I support that 100 percent. Let’s talk a little bit about transparency at the FDA. Secretary Kennedy, Commissioner Makary both sat in your seat and committed during their confirmation that transparency would be a priority for them and for the entire agency.

Yet, FDA appears to have attempted to gut the team that responds to the freedom of information requests. In other words, those requests for the transparency, everyone disappeared—everyone was let go or encouraged to retire. Also, the FDA bypassed the Advisory Committee on Immunization Practices, ACIP, in the recent COVID vaccine guidance, taking one of the few forums we have for clear and open debate on vaccines, and they kind of skipped right over it.

Does any of this promote transparency? How do we reconcile the public commitments to transparency with some of these opaque actions. At least they appear to me and to many of us. And how can we course correct and make sure that Americans feel confident that they are getting transparency, they are seeing what is coming, and that they can believe in these actions?

Dr. CORRIGAN-CURAY. Thank you for that. At CDER, we are very committed to being transparent. We held an Advisory Committee, I believe, about a month ago on our opioid PMRs. We continue to communicate. And we will continue to keep that transparency and communication open with the public.

In OMFDA, we have several initiatives that we will be doing in terms of webinars, posting not only the firms that didn't pay, but the firms that did pay to provide transparency around that, transparency around exclusivity. So we will continue to do that.

Senator HICKENLOOPER. Appreciate that. Thank you, Mr. Chairman. I yield back.

The CHAIRMAN. Senator Tuberville.

Senator TUBERVILLE. Thank you. Thank you, doctor, for being here. We know Secretary Kennedy is all into modernization. While we are waiting for these user fees to be reauthorized, what are we doing in the meantime of getting ready for dealing with the atmosphere that we are in today? What are you doing?

Dr. CORRIGAN-CURAY. Thank you. Are you asking me how we are preparing for the user fee negotiations?

Senator TUBERVILLE. Yes. Right.

Dr. CORRIGAN-CURAY. Yes, thank you. So as we do every cycle for the user fees—obviously for OMFDA we are here to talk about the reauthorization. For the other user fees, we do have internal processes that we undertake to think about the next agreements and what we would like to propose.

Of course, those would be discussed with Dr. Makary. I believe the notices of our public meetings for July are already out, and so we will have those public meetings and engage the public on those user fees.

Senator TUBERVILLE. Thank you. We have already talked a little bit about dyes, some things like sweeteners that go into a lot of our over-the-counter drugs. You go into these places and the drug stores look like a candy store, and they are enticed to be marketed in certain ways because of the color.

Do we have—what kind of priorities do we have on labeling of, No. 1, what goes into some of the over-the-counter drugs? Where they are made. I have looked at a lot of bottles and things inside our stores, and you can't find out whether they are made in Korea, whether they are made in China, or whether they were made in the United States. Shouldn't that be a priority?

Dr. CORRIGAN-CURAY. Thank you for that question. One thing when we think about where a drug is made, we are committed to making sure that wherever the drug is made and if it is being marketed that it's safe, that we apply the same standards, whether it is made domestically or it is made internationally.

We certainly are very supportive. I know the Administration is looking to onshore pharmaceutical manufacturing, and that would be for prescriptions or for OTC. And we are very supportive of that, and we will work with them in terms of our regulatory frameworks to help make that happen.

But right now we don't have a labeling on the drug for where it is made. We are happy to work with you, if that is a priority.

Senator TUBERVILLE. Well, I think in the future, with the problems we are having worldwide, I think it will probably be a good suggestion that people, when they go in and they find out where it is made—we found out during COVID, we don't make much anymore. Most of it comes from China, and we really don't know what is in it.

We are just finding out now a lot of metals and things are in a lot of the drugs and even the foods that we have. Another question I had about sunscreen. Most of us use sunscreen. I don't know how it is evaluated, but over the years, last 50 years, melanoma and skin cancers have almost quadrupled.

I don't know whether people don't use it, or it is not working, or we get some kind of skin cancer from ingredients that are in sunscreen. All of us used it at some point. It doesn't really feel safe every time I put it on, but I put it on because sometimes you look at the worst case scenario. So what are your thoughts on that?

Dr. CORRIGAN-CURAY. Yes, thank you for that. First of all, we are very aware that skin cancer risk is a very serious problem. And the sunscreens we have, the testing does say they are effective if used properly. And some of our tests, when we are testing for systemic absorption, is how you use them.

We do have two sunscreens that are mineral sunscreen, that are grass. They are not absorbed. For those that are absorbed we have asked for additional tests just to assure their safety. That any systemic absorption has no untoward effects.

Senator TUBERVILLE. Are we looking into the ingredients that are so-called cancer causers? I would hope we would be—and read it all the time.

Dr. CORRIGAN-CURAY. Yes—sorry to interrupt. Yes, and part of the testing that we want to do whenever a drug is absorbed, and it reaches systemic levels is a test for tumor formation.

Senator TUBERVILLE. Thank you. I yield back.

The CHAIRMAN. Senator Kaine.

Senator KAINE. Senator Markey.

Senator MARKEY. Thank you, Mr. Chairman. The Trump administration has fired 3,500 Federal employees at the Food and Drug Administration out of 20,000, and 800 out of the 7,500 people at your Center for Drug Evaluation and Research.

Despite assurances from Commissioner Makary that slowdowns would not happen, I have heard from researchers and companies that the drug review process has slowed down to a crawl and many have been stuck in limbo for months waiting on reviews and approvals to be completed.

Up in Massachusetts in a survey released by MassBio, in May, 67 percent of biopharma firms surveyed were highly concerned that workforce reductions will delay drug approvals, and at least 50 percent were already feeling the impacts from the FDA layoffs. So this is not a good situation for all these biotechs up in my state and across the country.

The Trump administration's actions have guaranteed that every stage of developing life-saving drugs, from research, to clinical trials, to approvals is slowed down or stopped. We are witnessing in real time a giveaway of our global leadership in drug research, in development, in biomedical innovation, and firing FDA officials responsible for drug approvals and evaluation is part of the problem.

My question is, obviously there have been many essential employees who have left as part of this reduction in workforce. And the goal has to be to increase, obviously, the timeliness of the review processes. So what is your plan, doctor, to replace the institutional knowledge that was lost from long-time FDA employees being fired or resigning?

Dr. CORRIGAN-CURAY. Thank you for that question. I know we can't really discuss details around the RIF about the litigation, but our reviewers are——

Senator MARKEY. Can you pull over the microphone a little bit, please?

Dr. CORRIGAN-CURAY. Sorry. Our reviewers are in place. And I would say that we are meeting our timelines. I know that occasionally——

Senator MARKEY. The timelines to do what?

Dr. CORRIGAN-CURAY. The timelines for approval and for our—— approval of our drugs. We do occasionally miss timelines. If you look at our——

Senator MARKEY. I have 50 percent of my companies who are already saying they are feeling the impacts of the FDA layoffs. So they are already feeling it.

Dr. CORRIGAN-CURAY. We certainly will look into that. I would note that, we are approving drugs and making our timelines.

There are certain times all of our agreements, we have 90 percent, not 100 percent because sometimes there are issues that come up that are complex and scientific issues that we would rather take a little bit more time if we need to, to make sure we get them right.

But we are also going to work with Dr. Makary. We have turnover in our review staff on a routine basis every year and Dr. Makary——

Senator MARKEY. I appreciate that, but you are down 800, which is a lot, in the real time that these companies have to get some answers. So what was your role in the firing of the 800 employees at the Center for Drug Evaluation and Research?

Dr. CORRIGAN-CURAY. Again, I apologize, but because of the ongoing litigation, I can't comment a lot about the RIF and the employees, and the reduction of employees.

Senator MARKEY. Was DOGE involved in the firings at the FDA?

Dr. CORRIGAN-CURAY. Again, because of the ongoing litigation, I am not able to comment on that.

Senator MARKEY. In a lawsuit that was filed by Federal workers yesterday, a Federal worker stated that on March 31st, 2025, just 2 months ago, a group of DOGE employees visited the FDA's office. And that day, someone dressed in a business attire yelled, this is DOGE, and this is your last supper as an FDA employee.

Doctor, can you walk me through what happens when someone at the Center for Drug Evaluation and Research is fired, in terms of who signs off on the termination paperwork, and how the notification is sent to employees?

Dr. CORRIGAN-CURAY. Again because the RIF is involved in litigation, I can't comment further on the process, and I am not aware of that incident.

Senator MARKEY. Yes, well, obviously, you are in a difficult position, which I appreciate—I appreciate that. But whether it is Makary, or Kennedy, or DOGE who are calling the shots, it is obviously going to ripple down into very negative consequences for the bio-pharma industry, but for people across our Country and nation who are waiting for these drugs to be available to help their families.

It is really—it is a crisis. And combined with all of the cuts in NIH research funding, we might as well gift wrap the biotech sector as a gift to the Chinese government because this is just an absolute tragedy in real time that is unfolding in our Nation, and it is just completely unnecessary. So, I thank you so much.

The CHAIRMAN. Senator Moody. Husted, I am sorry.

Senator Husted.

Senator HUSTED. Thank you. Appreciate you joining us today. The realm of my question is really around the idea that health care costs are the most inflationary costs in the 21st century in the American economy. And that time is money.

The faster we can do things, we can lower costs and improve access to consumers. And whether it is moving from prescription to over-the-counter, whether it is approval of generics, whether it is decreasing the time development and approval process, parallel approval tracks, all of those things, give me your thoughts on how we can go faster, maintain quality, but also in everything that FDA touches to reduce the cost of delivery ultimately within the economy to our consumers, our patients.

Dr. CORRIGAN-CURAY. Yes, thank you for that. I think there is a number of different things we do. For example, on the innovative drug side, when we approve a new molecular entity, a new drug, a novel drug that has an unmet need, it often undergoes priority review. So, we speed up that review.

In 2024, we approved 50 new drugs. 52 percent were for rare diseases. And of those, 56 percent we did priority review. So, shaving off the time. We also realize that our role in this is really to increase competition. So as I spoke, our generic program is very robust and we seek to get generic drugs on the market by working to provide clarity on the pathway, by working on regulatory science that can make a difference.

Then the other younger program is a biosimilar, but we are seeing that accelerate with the number of approvals we have. And again, we have been working on thinking about this—the biosimilar to interchangeable that in most cases you don’t need any additional study.

We also have convened a meeting with the public and our international regulators to think more on how we can rely on analytic rather than clinical studies because we know those take the longest and are the most expensive. So those are some of the areas that we are working on.

Senator HUSTED. I know that the issue of AI has been discussed in terms of process refinement, but what quantum computing and other tools are being used in the health care sector to speed development. Do you have any comments or thoughts on that and how that can enhance the time?

Dr. CORRIGAN-CURAY. Yes, we have—yes, thank you. We do have a program called Model and Foreign Development in which we do modeling, and we use machine learning to look at how we can accelerate a review program, maybe looking at different doses through modeling.

Our biostatisticians also do a lot of modeling if they are doing complex statistical modeling to see how we work on the development program. So we are very committed to using AI. Some of our research, I believe, in the generic industry is also—in the generic science program also focuses on some AI approaches. We can give you more information if you would like.

Senator HUSTED. Yes, that would be great. And again, I didn’t hear you really touch on generic approval and generics—approval of generics and timeframe around that. Is there any thoughts on that?

Dr. CORRIGAN-CURAY. Again we do have two different tiers in the generic. So if it is a first generic or there is not a lot of competition, again, we speed up those timelines to really try and meet the need.

We have been meeting the timelines that we have agreed with industry, and we will be looking for efficiencies. I think the AI, in terms of summarizing some of the paper and administrative tasks that are involved, we will try and work on that.

Senator HUSTED. I am going to give you an opportunity to give us some advice. What laws exist that are inhibiting you from going faster, and what should we change?

Dr. CORRIGAN-CURAY. Well, in the generic industry, I think one thing would be to make the ingredients transparent so that they wouldn’t have to ask us the ingredient and the amount. That is what we call the Q1, Q2. I think we have put forth legislation because we often have to go back and forth on that topic. So that would be very helpful. I think what was spoken about with the skinny labeling is very helpful to give certainty in that area and bring generics. And I think in the biosimilar area we have talked about not having this biosimilar interchangeable classification and have everything that is a biosimilar be interchangeable. I think that would also be quite helpful.

Senator HUSTED. Great. Thank you.

The CHAIRMAN. We did have a drug bill last December before you came in, John, that addressed the Q1, Q2, and so we do hope to get that back up.

Senator HUSTED. Great. Thank you, Mr. Chairman.

The CHAIRMAN. Senator Kaine.

Senator KAINE. Senator Hassan.

Senator HASSAN. Thank you, Senator Kaine and Chairman Cassidy. And Senator Husted, Senator Paul and I have the Q1, Q2 bill that the witness was just talking about, and we would love it if you would take a look at it too. Dr. Corrigan-Curay, thank you for being here today, and thank you for your work at the FDA from one Administration to the next. It is really important work.

Before 2015, FDA used a labeling system that made it hard for pregnant women to understand the health risks of different medications. For example, the old system labeled two very different kinds of medications under a single category, medications where animal studies suggested risks for pregnant women and medications where the risk for pregnant women hadn't been studied at all.

The FDA replaced this system back in 2015, but as of earlier this year, there were still several drugs on the market using the old, including common medications like antibiotics. Senator Budd and I wrote to the FDA in January urging the agency to address this issue. Doctor, has the Center for Drug Evaluation and Research brought all prescription drug manufacturers into compliance with pregnancy labeling standards?

Dr. CORRIGAN-CURAY. Yes, thank you. We now have submissions from all of the drugs that were outstanding to put into the PLLR labeling.

Senator HASSAN. Thank you. That is really good progress, and I appreciate it very much. Now, I understand that over-the-counter drugs sometimes have pregnancy warnings on the label, but the FDA does not have a specific standard for pregnancy safety labeling for over-the-counter drugs. Is the FDA working to improve the labeling process for over-the-counter drugs as well?

Dr. CORRIGAN-CURAY. I know we do have—in our proposed order, we are going to be looking at some labeling for pregnancy. I believe it is around the NSAIDs, but we can take that under advisement.

Senator HASSAN. I think that would be a really important thing to look at, and I would look forward to working with you on that. At Commissioner Makary's confirmation hearing, he and I discussed lowering drug prices by increasing generic drug competition, something we were just talking about.

Pharmaceutical companies currently use loopholes in the patent system to build so-called patent walls around their products. The patent walls can block low-cost generic versions of medications for decades.

What steps is the FDA taking—you talked about this a little bit with Senator Husted. What steps is FDA taking to improve its coordination with patent regulators in the United States to facilitate more access to low-cost generics?

Dr. CORRIGAN-CURAY. Thank you. We have started meeting with the Patent and Trade Office and sharing our expertise with them. As well as we are cooperating. As you know, the FTC has sent some letters about certain products in the Orange Book. We are not the experts in this, but we certainly will work with the other agencies on these issues.

Senator HASSAN. Well, thank you. I appreciate that. I have a bipartisan bill that would improve access to generic drugs by closing a loophole through which drug makers currently exploit a lack of coordination between the FDA and the Patent Office. The bill would allow patients to access lower cost medication sooner and would save taxpayers \$100 million over a decade.

I am hopeful that the Chairman and my colleagues on this Committee will work with me to advance the legislation. Families across the country rely on over-the-counter medications to stay healthy, especially during bad cold and flu seasons like the one we just had. Unfortunately, in recent years, we have seen vulnerabilities in our supply of common medications such as children's cold and flu medications.

In the winter of 2023, many families, including my own, could not find children's Tylenol or Motrin on the shelf due to extreme increased demand and strain on the supply chain. How can Congress help the FDA identify and address vulnerabilities in our over-the-counter drug supply chains so we can ultimately stop these shortages from happening?

Dr. CORRIGAN-CURAY. Yes, thank you. And that was a very unfortunate time where we had a very rapid increase in demand for those medications, and our shortage staff have really worked and worked very hard to resolve it like they do with other shortages.

I think one thing that we do have a lot of—we do reporting, and you gave us this authority, when there is an interruption supply, for example, for manufacturing or a lack of API, but we don't have the same required reporting for increased demand. So in that case whether we could get—if we can get an earlier signal that increased demand could lead to a shortage, that is when we can take action.

Each year—last year in 2024, there were 11 new shortages. That is unfortunate. We would like that to be zero. But we prevented over 250 shortages. And it is that early action that allows us to start doing things quickly in terms of getting new suppliers, getting new API. So, demand would be great.

Senator HASSAN. No, that would be something I would be really interested in working on. There is nothing like watching a child's temperature go up and up and up and not have the medication you need to not only get that child comfortable but prevent further risks and complications. So, thank you so much. Thank you, Mr. Chairman.

The CHAIRMAN. Senator Moody.

Senator MOODY. Thank you, Mr. Chairman. Thank you for being here and thank you for your service. We are grateful to you. I am from the Sunshine State. I am Ashley Moody. I am the newest Sen-

ator in the Sunshine State. Sunscreens are really important to our almost 24 million citizens.

This is a topic that I want to get into, and I know that speed and delay has been addressed with you. That is an issue across Federal agencies. What I am really loving about this new Administration, they are focusing on efficiency and getting back to the mission of these agencies.

I am hopeful that we are going to see that on some of these issues. I know in your testimony you talked about sunscreen and how we can move forward. I think we are basing—trying to get new products on the market that may be more effective, and it is adding some ingredients.

Do you expect that to be addressed quickly? Because I cannot tell you how important it is to all the golfers, and all the beach goers, and all of the Florida folks, and all of the tourists by the way—we broke another record in tourism in Florida this year—to have that looked at. We want people to be safe obviously but is that going to be expeditiously approved?

Dr. CORRIGAN-CURAY. Yes, so we are very excited to be reviewing the first new sunscreen, and we will review that on time. We will get the order out and get the public comment. And we will meet our goals on that hopefully. It will be a special—

Senator MOODY. What is that—what is that timeline? What is your goal?

Dr. CORRIGAN-CURAY. When something—I would have to look at exactly when it was submitted. Our timeline for a new ingredient is 17 months, which seems long, but it is quite different than our other UFAs. So it would have—because it has a public comment period, because the public is so involved in this process. And so, we have a 45-day comment period, and then we get those comments.

Often the public wants to provide us a lot of comment. We have to make sure that we take that comment into respect when we then move forward with the final order. And I think what is different in the OMUFA and why the timelines look a little bit longer is when we are in the PDUFA or GDUFA, it is one company, one drug. When we are the OTC monograph, it is one monograph that could be many and thousands of drugs.

We have to make sure that we really get that right when we issue that final order. And again we are committed to working with companies. They get us that data, as you said, so we make sure any of those ingredients that were absorbed are safe. We are also looking at alternative test methods to see if they are validated and we can use them.

Senator MOODY. I think that is one of the key things. And one of the key issues you have been addressing today, I think, is speed. We want to make sure we are protecting the health, safety, and welfare of Americans, obviously, but we need to also make sure bureaucracy is not weighing down what is meant to be a protection mechanism.

It would be my preference, as not just a United States Senator but as an American, that Government stay out of our business as much as possible. In fact, I think that—if that can be achieved,

that is what promotes a thriving, successful populist country. Only when it is necessary to protect rights or safety of our citizens.

Even there, at the bare minimum. As Attorney General in Florida, I once had to fight the Biden administration because they wanted to put masks on 2-year-olds while they were outside. I mean, it made absolutely no sense. They wanted to involve themselves in every facet of American life.

I, for one, believe that the first thing that should cross a bureaucrat's mind when they are going to act is, do we really need to be involving ourselves in this issue or in Americans' lives? The majority of the time it should be no. But when they do, it should be minimized, and we should deliver and act as efficiently as possible. And one of the things that I am happy about is how quickly we were able to get Naloxone to the market. I know that you have been happy about that.

You used both the monograph drug user fee program and other things to make sure that was done. And I believe that is significantly contributing to the decrease in deaths as it relates to the opioid crisis. In fact, I think nationally we saw over a 12 month period a 27 percent decline nationwide.

In Florida, we exceeded that number, a 30 percent decline. But it was not just about interdiction efforts or getting people to seek treatment, it was also about access to Naloxone and people being able to get that over-the-counter.

Thank you for that. Was there anything that you can learn from working with the drug sponsor, getting information quickly, getting that through the process, that we can apply to how we are moving forward to making sure we are streamlining this program? Because the deadline to reauthorize it is coming up quickly, I know.

If we are going to have a program that is supposed to push things forward quicker, if Government is going to involve itself in the lives of Americans to protect them, how do we do that quicker? Is there something you learned from that in the FDA approval of the Naloxone drug to over-the-counter that we can apply to this program?

Dr. CORRIGAN-CURAY. Yes, thank you. And just to clarify, the OTC—Naloxone was not under the monograph program because they are not monographs, but yes. One of the things that we are introducing in OMUFA II is we need to make sure, when we are working with a company and they are meeting with us, that we are maximizing that time and getting them on the right path.

One of things that we will do, we will expand those meetings if it is complex. We will make sure that we give them advice on their protocol synopsis if they need it. And if we give them advice and they are still not sure what to do, they have the opportunity to ask us to clarify that advice.

I think making sure that when we interact, it is very clear to the company what our expectations are. And I 100 percent agree with you, we want to streamline. We want to take a risk-benefit approach to every action that we do and to try and get products to the market that are—to meet an unmet need as quickly as possible.

The CHAIRMAN. Thank you.

Senator Kaine.

Senator KAINE. Senator Alsobrooks.

Senator ALSOBROOKS. Thank you so much. Good morning, Dr. Corrigan-Curay. And thank you so for being here today. And I also want to just thank you for your service. It is really—it is unfortunate, because I know you have been thrust in the position today, to answer for many of the very reckless decisions of political leadership at the Federal Drug Administration.

But the reality is that this Administration really has been unable to answer basic questions about their so-called Reduction In Force. Just this week, Commissioner Makary canceled a meeting with the Maryland delegation.

We were just simply asking about the impact of the Administration's cuts to my state. I have been waiting, for example, for 7 weeks now for specific answers from the department, and we just need to know how many staff at FDA have received a RIF notice.

We would like to know how many participated in the Deferred Resignation Program, were terminated on the basis of their probationary status, or are concurrently on administrative leave pending termination. I don't like the term Reduction In Force because it softens, I believe, the reality of what has happened.

It is the very heartless and cruel firing of thousands of very critical civil servants without cause and without an ounce of thought about the potential consequences to public health and safety.

Public health and safety is what brings us here today. I know that we are here to talk about reauthorizing the over-the-counter monograph drug user fee program to keep Americans safe, and we also know that the Administration has terminated 3,500 staffers from the FDA, including at the Center for Drug Evaluation and Research, which undermines its ability to do—to really operate.

I want to just make very clear to the public, because these staffing cuts have really been—they have been framed as duplicative or administrative staff that have no bearing on public health, but the truth of the matter is that these staff members really contribute to the core functions of the FDA to keep humans safe.

Each of them makes sure that, for example, pharmaceutical advertising is accurate, that the public is aware of potential risks, that drug shortages are mitigated, and that approvals are conducted in a timely manner.

I understand that you are not able to answer specific questions about the so-called Reduction In Force. But instead, I hope that you can demonstrate today the importance of the work that the civil servants do every day and to talk generally about the implications of it.

Just quickly, can you briefly share what the Center, for example, for Drug Evaluation and Research does every day?

Dr. CORRIGAN-CURAY. Yes, thank you. So, in the Center for Drug Evaluation and Research, we oversee several different programs, including obviously the OMUFA program and the OTC.

Our Office of Non-Prescription Drugs, I can tell you, we have had very little loss in that office. That is the office that is primarily. We review new drugs that are coming through. We work with the sponsors.

We have meetings on development programs. We review safety data in the post-marketing and make sure that the labels were up to date. We do review direct-to-consumer advertising and make sure promotion.

As I said, we work on generic drugs. That is a big priority to get additional generic drugs in competition. In the biosimilar space, we are reviewing biosimilars and we have a regulatory science program under that to develop the science to bring those drugs to the forefront sooner.

Then we need to—we always communicate what we are doing. We are putting out. We have Advisory Committees when needed to bring further transparency and get additional expertise to inform our decisions.

Senator ALSOBROOKS. These are critical staff. The Center's Office of Pharmaceutical Quality, can you just talk to us about what those staff members—I know you said there have been very few cuts, but cuts in any of these areas I think really do impact public health. So can you just tell us what the Center—the Center's Office for Pharmaceutical Quality does?

Dr. CORRIGAN-CURAY. Yes, and I am sorry. I should have mentioned that because they are really core to all our programs. They are responsible for looking at the manufacturing of—and the quality of the drug manufacturing.

Under—for example, under OMuFA II, we are going to put more resources so that when a facility comes and starts to market an OTC monograph, that we quickly evaluate that facility. That we get those records requests out there. That we are going to update our risk model to make sure we are taking appropriate—and selecting the facilities that we need to do an inspection on.

They do carry that out for our biosimilars and for our generics and our new drugs as well. And they are also working—just sort of be very forward-working. So when we—there is a priority by the Administration to try and bring our manufacturing back and for supply chain reasons, and we have been thinking about that and understand that companies would probably want to use advanced manufacturing to be more competitive.

Several years ago we started a special program to work with manufacturers. So when they want these new technologies, they can come talk to us early and we can give them advice and get them on the right path.

Senator ALSOBROOKS. Thank you so much. So the work you do is critical. All of these staff are critical as well. Just making the point that they are not wasteful. These are critical to our public health and safety. Thank you so much. I yield.

The CHAIRMAN. Senator Banks.

Senator BANKS. Thank you, Mr. Chairman. Doctor, what improvements will the public see in the products on their drug store shelves if Congress reauthorizes OMuFA for another 5 years?

Dr. CORRIGAN-CURAY. Yes, thank you for that question. I think the first thing I would mention, the order that we just did, which would allow certain drugs to be changed from just a tablet or a capsule into an oral dissolving or a chewable capsule or a film. And I think that will be a lot of innovation that will make these drugs more accessible to children and for those who have trouble swallowing.

As I said, the more that we innovate with the industry by providing them further guidance, by meeting with them and making sure they have clarity on our expectations. We are going to do some webinars on the GRAS standard and talk to them about confidentiality guidance when they are doing a new ingredient.

All those things we think are going to speed up innovation, and we hope to see additional OTC orders come out on new products.

Senator BANKS. On that point, the monographs and user fees are supposed to streamline the FDA's process to approve over-the-counter drugs so better products come to market faster. But that only happens when the FDA uses that authority. How are you going to make better use of the OMUFA authority over the next 5 years to encourage that type of innovation?

Dr. CORRIGAN-CURAY. Again, the commitments that we have agreed to is really to make the meetings with our companies, make them as productive as possible, extend them if we need to, give them advice on their protocol synopsis so they get their products.

We are also going to ask to create a new tier two so they can update their test methods, and that may be more efficient. We are going to continue to give them education on the GRAS standards, on how to submit their orders and what should be in there, and their eligibility for that.

We are going to also make sure that we are being very transparent in all of this, including all the historical documents that will be up on the web so everyone can learn from those. They can learn all the issues that we identify in the quality, and we will do some work on good manufacturing practices so that the expectations are clear. And when the expectations are clear, I think that allows for innovation.

Senator BANKS. On another point, I am curious, why doesn't the FDA inspect more overseas facilities that export over-the-counter drugs to the U.S.?

Dr. CORRIGAN-CURAY. Right now we do use a risk-based model to determine where our inspections, and we do inspections overseas and domestically. And we can get you those exact numbers. I don't have them off the top of my head.

One of the things we will do is we are going to update our risk-based model and make sure it is taking into account any factors that may be specific to OTC monograph facilities, and that would determine inspections. We are also going to more rapidly do those record requests to assess the facilities that might need an inspection that are coming.

Senator BANKS. Do you think, are there loopholes there that allow for some overseas facilities not to be as inspected as much?

Dr. CORRIGAN-CURAY. In terms of if we can do the inspection, what is different in the OTC monograph space is in the other UFAs, there is a time point in which we can do the inspection before the product comes to the market.

Whereas in this, in the OMUFA, there isn't that one time point. They can come into and register with us and start to distribute, and then we start the assessment of that facility.

Senator BANKS. Mr. Chairman, contaminated, non-sterile eye drops coming from China and other countries have been a problem for years. I would like to enter three different letters, FDA warning letters to these companies into the record.

The CHAIRMAN. Without objection.

[The following information can be found on page 35 in Additional Material:]

Senator BANKS. Doctor, how do you determine whether these over-the-counter drugs actually follow the monographs and are safe or whether they are safe, or whether they are fraudulent and dangerous?

Dr. CORRIGAN-CURAY. Again, we looked for reports with the eye drops. We did do—we had adverse events, and we followed up on them. We issued the warning letters.

We do inspections to see. So we do monitor the safety of the products on the market, and that is how we do a risk-based approach to that.

Senator BANKS. Okay. I would like to dig into that further at another time. Thank you, Mr. Chairman. I yield back.

The CHAIRMAN. Thank you. Senator Kaine.

Senator KAINE. Thank you, Dr. Corrigan-Curay. I am going to focus my 5 minutes on transparency, which has been mentioned by many of my colleagues and you have mentioned it in your testimony.

I think it needs to be a hallmark of this particular program, and it also matches up with the values that Secretary Kennedy talked about when he has been here before us. And I have been troubled that while transparency is a goal, there is this one area where we just can't get answers.

I asked Secretary Kennedy about people, the number of people who have been RIF or took the Fork in the Road Initiative and he could not answer. At the time, he didn't have the number at his fingertips. But when I did a follow-up letter, I still have not gotten a response.

That was kind of an interesting contrast to how customer-focused Secretary Kennedy was in my questioning of him when he was recently before us. I raised the issue of his response to some of my constituents who were writing in about concerns and they were getting response from HHS—it was actually a CMS response saying because of the change in Administration, we can no longer entertain these kinds of questions.

When I showed that, Secretary Kennedy went back and he found that was an improper response, and he told me that it was, and he said he was going to correct it, and this wasn't authorized. So

he actually responded to my concern about that. And I think Senator Murray had a particular constituent concern that she raised, and he was very solicitous, we want to respond to that.

It seems like there is this sort of gag order on talking about the number of people that are employed or the number of people that are RIF. And for an Oversight Committee that is trying to exercise oversight over these programs, or even trying to decide what is the right way to reauthorize a program so that it can be effective, more effective, if we can't get an answer about kind of this basic issue, it hobbles us in our ability to do our job.

I know that policy decisions of this kind are probably not yours, but let me just ask if you could answer this question, within the Center for Drug Evaluation and Research, how many people were subject to the RIF issued by Secretary Kennedy?

Dr. CORRIGAN-CURAY. Again, because it is under litigation, I am not allowed to, or I can't discuss specifics, but we would be very happy when that litigation is resolved to come back and provide you those numbers.

Senator KAINE. I am assuming you would answer the same way if I ask you the question about how many of these folks who were RIF were veterans.

Dr. CORRIGAN-CURAY. Um—

Senator KAINE. You would answer the same way?

Dr. CORRIGAN-CURAY. I would answer the same way.

Senator KAINE. You and I both went to law school. And I have had to give a lot of advice to witnesses about not talking about pending litigation. And so, I didn't ask you who was involved in the discussion, who was involved the decision, what was the rationale for the decision. Were there different rationales.

I haven't asked you any of that. All I have asked you is the factual question, which is public—it should be public information because the public is paying for all of this, about the numbers of people.

The fact that I can't get that answer from you, from Secretary Kennedy. We have similar questions of folks who have been here from the Department of Labor. Nobody wants to answer the question, how many people have been laid off and what percentage of veterans.

Now, the veterans issue matters to me as a Virginian because we are such a veteran heavy state. I have asserted, based on what I have been able to cobble together, that this Administration has fired more veterans than any Administration in the history of the United States. That is based on what I have been able to cobble together. I would like to be proven wrong.

Maybe if I got the answers to my questions, I am making an assertion that is incorrect. But I think I am entitled to the information. I know you have been instructed not to answer it. It is not that you can't, and it is not that you won't. It is that you have been instructed not to. But I will say, pending litigation is not really an excuse for not answering a basic factual question the knowledge of which is within the ambit of the Administration.

On transparency, I do have some proposals about the reauthorization. You did a good job in your testimony of kind of laying out, if this program is not reauthorized, here are some bad things that can happen.

But also, I know the Chairman is very much into this idea, if you are going to reauthorize, we don't just reauthorize as is. We should reauthorize and improve. There have been obviously longer-standing, more established user fee programs where there is lessons learned about how we can improve.

I have been getting feedback from groups about how this particular OMUFA program can be improved. With the updates that I am proposing that are in the transparency space, we would be able to have question answers to questions like how many OTC monographs were filed and approved during a fiscal year.

Which drug facility and contract manufacturing organizations have actually paid their user fees instead of only having visibility into those who haven't paid their users fees. How is the FDA addressing post-market safety for OTC products.

I think a lot of the questions today have kind of wrapped around that important topic, including how the agency responds to individual reports of adverse events. My hope is that we will do this bill. I think it is going to be bipartisan. I think we cannot only reauthorize but improve by taking some of the lessons from the other similar programs.

Pro-transparency initiatives are things that I think are going to get pretty nice support on both sides of the dais here. With that, I yield back.

The CHAIRMAN. I have a couple of follow-ups. How many Rx to OTC drugs in the last 1 year, 2 year, 3 years, how many have actually made that transition from being a prescription only to be an OTC?

Dr. CORRIGAN-CURAY. Thank you for that question. I know that the Naloxone would have been in 2023. And I think the Opil was also around that time. I would have to go back further and get you the details on the rest of the drugs.

The CHAIRMAN. Marshall asked about a dashboard, but that seems to be rubber hits the road. We have only had three drugs in the last two and a half years that have gone from Rx to OTC.

Dr. CORRIGAN-CURAY. I believe that is correct. For some reason, I think I am forgetting one, but I will get back to you.

The CHAIRMAN. That just seems like a not very productive record.

Dr. CORRIGAN-CURAY. Again, I think the issue is we do need to find drugs—drugs are safe—that are safe for a population, for anyone to walk in, and look at that drug facts label, and appropriately self-select and use that drug.

We need to look at the drugs that we have and think if that is appropriate and look at the development programs. And I think that is why the new rule that we have coming out is really meant to try and open up that space more.

Because for any drug, it may be relatively safe in this population, and it may, but we are—sometimes a drug fact label is not sufficient for just those folks to understand that is a drug for them, and it is not for others.

The CHAIRMAN. That is true of everything. Non-steroidals, you shouldn't take if you have a history of active peptic ulcer disease.

Dr. CORRIGAN-CURAY. Right.

The CHAIRMAN. Yet we have approved non-steroidals all over the place. And so, we are willing to accept that somewhat of a risk. And so, for the greater good. And turns out we have—it worked out. Not that many people are taking non-steroidals and exacerbating their peptic ulcer disease.

Dr. CORRIGAN-CURAY. Right, that is true. We did—

The CHAIRMAN. I just want to lean into this because, I mean, this costs consumers a heck of a lot of money to go to a doctor to get a prescription for something which they could safely take OTC.

Dr. CORRIGAN-CURAY. Yes, I agree. And we are going to look for opportunities. And as I said, I think the new rule in which we can sort of just—it is adding something in the self-selection to the drug facts label has the real potential to open up for other conditions that could be for chronic conditions and open up consumer choice. And so we are going to work with—to finalize that rule and work on development programs that could come under that rule.

The CHAIRMAN. I asked this earlier, but I didn't quite follow the answer, so I will finish with this. Do you feel as if this final rule—that you have the tools, particularly with this final rule, to expedite the transition from Rx to OTC, or does Congress need to do something to kind of light a fire?

Dr. CORRIGAN-CURAY. I think with this rule, that we have a new tool that is going to be very powerful and effective for us to move things from Rx to OTC.

The CHAIRMAN. Would you expect the new rule to be implemented?

Dr. CORRIGAN-CURAY. The rule was—the implementation was delayed. I think it should be the end of May, but I need to check. There was a delay after we had the transition.

The CHAIRMAN. Okay. Yes?

Senator KAINE. I have a follow-up just based upon the Chairman's questions.

To what degree was the fact that there have only been three or four Rx to OTC in the relevant time period he was discussing, to what degree is that a function of just sheer personnel or resources within CDER versus the regulatory structure that shapes what can be approved?

Dr. CORRIGAN-CURAY. I would say in the last 5 years, it is more about the regulatory structure and what can be appropriately put over-the-counter and selected.

Senator KAINE. Hopefully this new rule, when it becomes effective, will help you accelerate.

Dr. CORRIGAN-CURAY. Yes.

Senator KAINE. Thank you.

The CHAIRMAN. Okay. For any Senator wishing to ask additional questions, questions for the record will be due on 10 business days on June 18th at 5.00 p.m.. Thank you very much, Dr. Corrigan-Curay.

Dr. CORRIGAN-CURAY. Thank you.

The CHAIRMAN. The Committee stands adjourned.

ADDITIONAL MATERIAL

WARNING LETTER

Hubei Kangzheng Pharmaceutical Co., Ltd.

MARCS-CMS 616581 — November 23, 2021

Delivery Method:

Email

Product:

Drugs

Recipient:

Mr. Chen Tianzhong

CEO/General Manager

Hubei Kangzheng Pharmaceutical Co., Ltd.

No. 88 Hexi Jinquan Road Anlu City Hubei Sheng, 432600 China

Issuing Office:

Center for Drug Evaluation and Research | CDER

United States

Warning Letter 320-22-05

November 23, 2021

Dear Mr. Chen:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Hubei Kangzheng Pharmaceutical Co., Ltd., FEI 3010580682, located at No. 88 Hexi Jinquan Road, Anlu City, Hubei Province, China, from June 16 to 24, 2021.

This warning letter summarizes significant violations of Current Good Manufacturing Practice (CGMP) regulations for finished pharmaceuticals. See Title 21 Code of Federal Regulations (CFR), parts 210 and 211 (21 CFR parts 210 and 211).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drug product is adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

In addition, pi yen chin is an unapproved new drug in violation of section 505(a) of the FD&C Act, 21 U.S.C. 355(a), and is misbranded under sections 502(x) and (ee) of the FD&C Act, 21 U.S.C. 352(x) and (ee). Introduction or delivery for introduction of such products into interstate commerce is prohibited under sections 301(d) and (a) of the FD&C Act, 21 U.S.C. 331(d) and (a). These violations are described in more detail below.

We reviewed your June 28, 2021, response to our Form FDA 483 in detail and acknowledge receipt of your subsequent correspondence.

During our inspection, our investigator observed specific violations including, but not limited to, the following.

1. Your firm failed to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes (21 CFR 211.113(b)).

You failed to demonstrate that your manufacturing process is capable of preventing microbial contamination of your over-the-counter (OTC) drug product, pi yen chin ophthalmic redness reliever drops, containing naphazoline hydrochloride (HCl) 0.1%. For example,

- You manufactured pi yen chin as a non-sterile drug product in a Grade D clean area without appropriate controls to prevent microbial contamination.
- You failed to establish and validate a process that is suitable for the manufacture of a sterile drug product.
- You failed to establish and follow appropriate written procedures for sterilizing equipment used for manufacturing your ophthalmic drug product.
- You failed to establish an adequate system for monitoring environmental conditions to ensure the suitability of the areas used to manufacture your ophthalmic drug product.
- You distributed batches of pi yen chin to the U.S. market without conducting sterility testing or testing for particulate and foreign matter prior to release.

In your response, you stated that because you manufactured and released pi yen chin as non-sterile nasal drops, the requirements for producing a sterile drug product do not apply. You also stated that sterility testing and visual inspection for particulate and foreign matter are not needed. In addition, you stated that environmental monitoring (EM) in the manufacturing area should be conducted **(b)(4)**.

Your response is inadequate. Your drug product is labeled as an ophthalmic and includes the instruction to apply into eyes. Therefore, your interpretation that this drug product is not required to be sterile is incorrect. See 21 CFR 200.50(a)(1).

See FDA's guidance document *Sterile Drug Products Produced by Aseptic Processing - Current Good Manufacturing Practice* to help you meet the CGMP requirements when manufacturing sterile drugs using aseptic processing at <https://www.fda.gov/media/71026/download>.

We acknowledge that your firm initiated a voluntary recall for all the batches distributed in the U.S. market within expiry.

In response to this letter, provide:

- A comprehensive risk assessment of all contamination hazards with respect to your aseptic processes, equipment, and facilities, including an independent assessment that includes, but is not limited to:
 - o All human interactions within the ISO 5 area
 - o Equipment placement and ergonomics
 - o Air quality in the ISO 5 area and surrounding room
 - o Facility layout
 - o Personnel Flows and Material Flows (throughout all rooms used to conduct and support sterile operations)
- A detailed remediation plan with timelines to address the findings of the contamination hazards risk assessment. Describe specific tangible improvements to be made to aseptic processing operation design and control.
- A detailed summary of your validation program for ensuring a state of control throughout the product lifecycle for your (b)(4) drug product, along with associated procedures. Describe your program for process performance qualification, and ongoing monitoring of both intra-batch and inter-batch variation to ensure a continuing state of control.
- A timeline for performing process performance qualification for your marketed drug product.
- Include your process performance protocol(s), and written procedures for qualification and sterilization of equipment.
- A comprehensive summary of your media fill program that ensures an appropriate simulation of the worst-case conditions of commercial manufacturing. In addition, describe in detail how you examine units for presence of growth and how you perform batch yield reconciliation. Include all related standard operating procedures.

- Smoke studies conducted under static and dynamic conditions to fully evaluate air flow patterns on the aseptic processing line. Provide an independent assessment of the smoke studies.
- Updated EM procedures that include appropriate:
 - o Frequency, location, and duration of sampling; sample size; specific sampling equipment and techniques
 - o Action and alert limits for each location, and a description of its function and ISO classification
 - o Instructions regarding investigation of out-of-limit EM results
 - o Identification of microorganisms detected in EM samples
- Appropriate microbiological batch release specifications (i.e., total counts, identification of bioburden to detect objectionable microbes) for your ophthalmic drug product.
- All chemical, physical, and microbial test methods used to analyze your ophthalmic drug products.

2. Your firm failed to establish and follow an adequate written testing program designed to assess the stability characteristics of drug products and to use results of stability testing to determine appropriate storage conditions and expiration dates (21 CFR 211.166(a)).

During the inspection, you acknowledged that you do not have a written stability program for your pi yen chin drug product, and were unable to provide data to demonstrate that its chemical, physical, and microbiological properties, including sterility, will remain acceptable throughout the labeled three-year expiry period.

In your response, you stated that you have established a stability protocol to support a three-year expiration date for future drug product batches.

Your response is inadequate. You did not provide the stability protocol and details, including all relevant quality attributes, acceptance criteria, and stability indicating methods.

In response to this letter, provide:

- A comprehensive, independent assessment and corrective action and preventive action (CAPA) plan to ensure the adequacy of your stability program. Your remediated program should include, but not be limited to:
 - o Stability indicating methods
 - o Stability studies for each drug product in its marketed container-closure system before distribution is permitted
 - o An ongoing program in which representative batches of each product are added each year to

the program to determine if the shelf-life claim remains valid

- o Detailed definition of the specific attributes to be tested at each station (timepoint)
- All procedures that describe these and other elements of your remediated stability program.

3. Your firm failed to thoroughly investigate any unexplained discrepancy or failure of a batch or any of its components to meet any of its specifications, whether or not the batch has already been distributed (21 CFR 211.192).

Your firm failed to thoroughly investigate unexplained discrepancies and out-of-specification (OOS) results. For example,

- You did not initiate an investigation when the infrared (IR) spectrum of naphazoline HCl active pharmaceutical ingredient (API) lot (b)(4) was found to be different from the standard. You used this API lot to manufacture pi yen chin drug product batches (b)(4), which were distributed to the U.S. market.
- You did not perform an investigation when unknown peaks were detected during release assay testing for batches (b)(4).

In your response, you stated that a new external laboratory IR test result for naphazoline HCl API lot (b)(4) conformed to the standard. You also stated that you contacted a qualified laboratory to characterize the unknown peaks for the finished drug product batches.

Your response is inadequate. We acknowledge that you recently initiated a deviation for the IR test result discrepancy involving your API sample. However, you have not provided any scientific justification to invalidate the original OOS result. In addition, you did not initiate an investigation to determine a root cause for the unknown peaks that were detected in your finished drug product batches and implement a CAPA to prevent reoccurrence.

For more information about handling failing, OOS, out-of-trend, or other unexpected results and documentation of your investigations, see FDA's guidance document *Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Production* at <https://www.fda.gov/media/71001/download>.

In response to this letter, provide:

- A retrospective, independent review of all invalidated OOS (including in-process and release/stability testing) results for U.S. product and a report summarizing the findings of the analysis, including the following for each OOS:
 - o Determine whether the scientific justification and evidence relating to the invalidated OOS result conclusively or inconclusively demonstrates causative laboratory error.
 - o For investigations that conclusively establish laboratory root cause, provide rationale and

ensure that all other laboratory methods vulnerable to the same or similar root cause are identified for remediation.

o For all OOS results found by the retrospective review to have an inconclusive or no root cause identified in the laboratory, include a thorough review of production (e.g., batch manufacturing records, adequacy of the manufacturing steps, suitability of equipment/facilities, variability of raw materials, process capability, deviation history, complaint history, batch failure history). Provide a summary of potential manufacturing root causes for each investigation, and any manufacturing operation improvements.

4. Your firm failed to clean, maintain, and, as appropriate for the nature of the drug, sanitize and/or sterilize equipment and utensils at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements (21 CFR 211.67(a)).

Your cleaning validation and verification program for manufacturing equipment is inadequate to prevent cross contamination. For example,

- Your cleaning validation lacked the study of a (b)(4) agent for the equipment train used in the manufacturing of your ophthalmic drug product.
- You used reusable, non-sterile wipes for cleaning equipment used for manufacturing your ophthalmic drug product.
- Apparent rust was observed in the (b)(4) that attaches from the (b)(4) tank (F-219-01-001) to the filling line ((b)(4)), which comes into direct contact with your ophthalmic drug product. In addition, fraying of a conveyor belt on the filling line was observed.

In your response, you stated that you removed the rust from the (b)(4) and repaired the fraying parts of the conveyor belt. You also stated that you manufactured pi yen chin as nasal drops, therefore, a study of a (b)(4) agent is not required for cleaning validation. In addition, you stated that there is no need to use sterile wipes for equipment cleaning.

Your response is inadequate. You failed to provide a comprehensive CAPA plan to address the deficiencies and prevent recurrence. As previously noted, your pi ye chin drug product is intended for ophthalmic use and must be manufactured accordingly.

In response to this letter, provide:

- Your CAPA plan to implement routine, vigilant operations management oversight of facilities and equipment. This plan should ensure, among other things, prompt detection of equipment/facilities performance issues, effective execution of repairs, adherence to appropriate preventive maintenance schedules, timely technological upgrades to the equipment/facility infrastructure, and improved systems for ongoing management review.

- A comprehensive, independent retrospective assessment of your cleaning effectiveness to evaluate the scope of cross-contamination hazards. Include the identity of residues, other manufacturing equipment that may have been improperly cleaned, and an assessment whether cross-contaminated products may have been released for distribution. The assessment should identify any inadequacies of cleaning procedures and practices, and encompass each piece of manufacturing equipment used to manufacture more than one product.

Unapproved New Drug and Misbranding Violations

Pi yen chin is a “drug” as defined by section 201(g)(1)(B) of the FD&C Act, 21 U.S.C. 321(g)(1)(B), because it is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease, and/or under section 201(g)(1)(C) of the FD&C Act, 21 U.S.C. 321(g)(1)(C), because it is intended to affect the structure or any function of the body. Specifically, this product is intended for use as an ophthalmic vasoconstrictor (redness reliever).

Examples of claims observed on the pi yen chin product label and labeling that provide evidence of the intended use (as defined in 21 CFR 201.128) of the product include, but may not be limited to, the following:

“Ophthalmic Redness Reliever Drops . . . Drug Facts ...**Uses** Temporarily relieves redness due to minor irritation of eyes.”

This ophthalmic vasoconstrictor product is a “new drug” within the meaning of section 201(p) of the FD&C Act, 21 U.S.C. 321(p), because it is not generally recognized as safe and effective (GRASE) for use under the conditions prescribed, recommended, or suggested in its labeling. New drugs may not be introduced or delivered for introduction into interstate commerce without prior approval from FDA, as described in section 505(a) of the FD&C Act, 21 U.S.C. 355(a), unless they are lawfully marketed under section 505G of the FD&C Act (which is not the case for this product, as further described below), or under other exceptions not applicable here. No FDA-approved application pursuant to section 505 of the FD&C Act, 21 U.S.C. 355, is in effect for this drug product, nor are we aware of any adequate and well-controlled clinical studies in the published literature that support a determination that your pi yen chin drug product is GRASE for use under the conditions suggested, recommended, or prescribed in its labeling. Accordingly, this product is an unapproved new drug marketed in violation of sections 505(a) and 301(d) of the FD&C Act, 21 U.S.C. 355(a) and 331(d).

Section 505G of the FD&C Act addresses nonprescription drugs marketed without an approved application. Under section 505G(a)(1) of the FD&C Act, 21 U.S.C. 355h(a)(1), category I drugs that were subject to a final monograph (FM) issued under 21 CFR Part 330 are deemed to be GRASE and not “new drugs,” as long as they are in conformity with the relevant conditions of use outlined in the applicable FM and comply with all other applicable requirements. We note

that OTC ophthalmic products were addressed in the FM for Ophthalmic Drug Products for OTC Use (ophthalmic final monograph), see 21 CFR Part 349.

Under 505G(b)(8) of the FD&C Act, 21 U.S.C. 355h(b)(8), the FM for Ophthalmic Drug Products for OTC Use is deemed to be a final administrative order. However, your pi yen chin product does not conform to the final administrative order, because it is inconsistent with the applicable FM or any other applicable TFM or proposed rule, and it accordingly does not meet the conditions under section 505G(a)(1) of the FD&C Act for marketing without an approved application under section 505.

Specifically, your product's labeled concentration for the active ingredient naphazoline HCl exceeds the allowable concentration for this active ingredient as specified in the ophthalmic FM. Pi yen chin is labeled to contain naphazoline HCl 0.1% and the ophthalmic FM requires that naphazoline HCl be present at 0.01% to 0.03%, per 21 CFR Part 349.18(b). Thus, such a product formulated and labeled as pi yen chin does not conform with the ophthalmic FM described above.

In addition, pi yen chin is misbranded under section 502(x) of the FD&C Act, 21 U.S.C. 352(x), because the product label fails to disclose a complete domestic address or domestic telephone number through which the responsible person may receive a report of a serious adverse event with such drug.

Lastly, this product is misbranded under section 502(ee) of the FD&C Act, 21 U.S.C. 352(ee), because pi yen chin is a nonprescription drug subject to section 505G of the FD&C Act, 21 U.S.C. 355h, but does not comply with the requirements for marketing under that section and is not the subject of an application approved under section 505 of the FD&C Act, 21 U.S.C. 355.

The introduction or delivery for introduction of a misbranded drug into interstate commerce is prohibited under section 301(a) of the FD&C Act, 21 U.S.C. 331(a).

Drug Production Ceased

We acknowledge your commitment to cease production of drugs for the U.S. market. In response to this letter, clarify whether you intend to resume manufacturing drugs for the U.S. market at this facility in the future.

If you plan to resume manufacturing drugs for the U.S. market, notify this office before resuming your operations.

Conclusion

The violations cited in this letter are not intended to be an all-inclusive list of violations that exist at your facility. You are responsible for investigating and determining the causes of any violations and for preventing their recurrence or the occurrence of other violations.

FDA placed your firm on Import Alert 66-40 on November 4, 2021.

Correct any violations promptly. FDA may withhold approval of new applications or supplements listing your firm as a drug manufacturer until any violations are completely addressed and we confirm your compliance with CGMP. We may re-inspect to verify that you have completed corrective actions to any violations.

Failure to address any violations may also result in the FDA continuing to refuse admission of articles manufactured at Hubei Kangzheng Pharmaceutical Co., Ltd., at No. 88 Hexi Jinquan Road, Anlu City into the United States under section 801(a)(3) of the FD&C Act, 21 U.S.C. 381(a)(3). Articles under this authority that appear to be adulterated or misbranded may be detained or refused admission, in that the methods and controls used in their manufacture do not appear to conform to CGMP within the meaning of section 501(a)(2)(B) of the FD&C Act, 21 U.S.C. 351(a)(2)(B) and are misbranded under section 502 of the FD&C Act, respectively.

This letter notifies you of our findings and provides you an opportunity to address the above deficiencies. After you receive this letter, respond to this office in writing within 15 working days. Specify what you have done to address any violations and to prevent their recurrence. In response to this letter, you may provide additional information for our consideration as we continue to assess your activities and practices. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion.

Send your electronic reply to CDER-OC-OMQ-Communications. Identify your response with FEI 3010580682 and ATTN: Qin Xu.

Please identify your response with FEI 3010580682.

Sincerely,
/S/

Francis Godwin
Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research

WARNING LETTER

Kilitch Healthcare India Limited

MARCS-CMS 672956 — March 28, 2024

Delivery Method:

VIA Electronic Mail

Product:

Drugs

Recipient:

Mr. Paresh Mehta

Managing Director

Kilitch Healthcare India Limited

902-B, Godrej Coliseum, Behind Everard NagarOff. Eastern Express Highway, Nr. Priyadarshani
CircleSion (E.), Mumbai 400022India

Issuing Office:

Center for Drug Evaluation and Research | CDER

United States

Warning Letter 320-24-29

March 28, 2024

Dear Mr. Mehta:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Kilitch Healthcare India Limited, FEI 3011853060, at R - 904 905 T T C Industrial Road, Navi Mumbai from October 12 to October 20, 2023.

This warning letter summarizes significant violations of Current Good Manufacturing Practice (CGMP) regulations for finished pharmaceuticals. See Title 21 Code of Federal Regulations (CFR), parts 210 and 211 (21 CFR parts 210 and 211).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drug products are adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

Because your drug products were prepared, packed, or held under insanitary conditions, whereby they may have become contaminated with filth or rendered injurious to health, your drug products are also adulterated within the meaning of section 501(a)(2)(A) of the FD&C Act, 21 U.S.C. 351(a)(2)(A).

We reviewed your November 10, 2023 response to our Form FDA 483 in detail and acknowledge receipt of your subsequent correspondence.

During our inspection, our investigators observed specific violations including, but not limited to, the following.

Insanitary Conditions

Your drug products are adulterated under section 501(a)(2)(A) of the FD&C Act because they were prepared, packed, or held under insanitary conditions. FDA investigators observed your facility to be in a state of disrepair, poorly cleaned and maintained as evidenced by:

- (b)(4) residue on the (b)(4) adjacent to the HEPA filters in the ISO 5 area.
- Multiple barefoot employees in an ISO 8 area, without required gowning, including gloves, while handling materials being transferred into the ISO 7 manufacturing area.
- Operators used visibly dirty restricted access barrier system (RABS) (b)(4) for interventions on the filling line.

Your response is not adequate. While you commit to replacing the (b)(4) that surround the HEPA filtration system, your response does not include an evaluation of the residue on the (b)(4) to determine its identity or investigate the source. You also commit to perform re-training of personnel for gowning requirements and implement a procedure for sterilization of RABS (b)(4), however, you do not evaluate the microbiological impact that lack of proper gowning and unclean RABS (b)(4) has on your classified areas, such as ISO 5, ISO 7, and ISO 8. The potential impact to sterile drug products produced under these insanitary conditions is also not addressed.

CGMP Violations

1. Your firm failed to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes (21 CFR 211.113(b)).

Poor Practices in the Aseptic Processing Areas

In addition to the insanitary conditions described above, during the inspection of your facility, we observed poor practices and behaviors in ISO 5 areas during the manufacturing of sterile drug products. These poor practices included, but are not limited to:

- Operators performing interventions on the filling line in ISO 5 areas using a cloth to wipe the (b)(4) of the filling (b)(4) and the conveyor.
- Operators leaning over the filling line, including open and filled eye drop bottles, blocking unidirectional airflow.
- Operators in the ISO 5 area not wearing goggles and therefore had exposed skin during line set-up and aseptic processing.
- Operators observed placing bags of components that made contact with the walls in the ISO 7 area into the ISO 5 area without the bags being disinfected.

Your response is inadequate because it does not address the lack of oversight for the operators' aseptic behaviors and if the initial training received was sufficient. Further, these poor aseptic practices were not investigated to determine the impact to sterile drug products and aseptic processing areas.

Inadequate Media Fill Program

Your media fills failed to accurately simulate commercial operations. Our inspection found the aseptic operations simulated during your media fills were not sufficiently representative of commercial aseptic manufacturing operations. It is your routine practice not to document interventions of the filling line in the manufacturing batch record during production. Because of this, your program lacks reliable data to determine the quantity and duration of interventions to simulate during media fills. In addition, during the inspection there were numerous interventions performed during routine manufacturing that were either not simulated as part of a media fill, or lacking in quantity and duration in the media fills compared to what was observed during production.

Your response is inadequate. While you commit to document routine interventions during manufacturing, you fail to evaluate the interventions used in your media fill program and whether they represent routine production. Your operators performed numerous, manually intensive interventions during aseptic operations. As such, the quantity and duration of process

simulation interventions should closely resemble the actual manufacturing process. If a media fill program fails to incorporate contamination risk factors and closely simulate actual drug product exposure, the state of process control and sterility assurance cannot be accurately assessed.

Inadequate Smoke Studies

Smoke studies performed by your firm are not adequate to show unidirectional airflow in the aseptic processing areas. Multiple instances of turbulent airflow in critical areas of the (b)(4) filling line were noted, including above the filling (b)(4). In addition, smoke study videos did not include set-up of the aseptic processing line or interventions of the filling line that simulate actual manufacturing.

In your response you commit to repeat smoke studies with defined set-up and interventions. This is not adequate as you do not provide details such as who is performing and evaluating the smoke studies, how you will determine what interventions are included, and how you will address potential deficiencies.

See FDA's guidance document *Sterile Drug Products Produced by Aseptic Processing—Current Good Manufacturing Practice* to help you meet the CGMP requirements when manufacturing sterile drugs using aseptic processing at <https://www.fda.gov/media/71026/download>.

In response to this letter, provide the following:

- Your plan to ensure appropriate aseptic practices and cleanroom behavior during production. Include steps to ensure routine and effective supervisory oversight for all production batches.

Also describe the frequency of quality unit (QU) oversight (e.g., audit) during aseptic processing and its support operations.

- A thorough retrospective review and risk assessment that evaluates how poor aseptic technique and cleanroom behavior may have affected the quality and sterility of your drugs.
- A comprehensive, independent assessment of the design and control of your firm's manufacturing operations, with a detailed and thorough review of all microbiological hazards.
- A detailed risk assessment addressing the hazards posed by distributing drug products with potentially objectionable contamination. Specify actions you will take in response to the risk assessment, such as customer notifications and product recalls.

- Complete investigations into all batches with potential objectionable microbial contamination or an out-of-specification (OOS) microbiological result (whether or not later invalidated). The investigations should detail your findings regarding the root causes of the contamination.
- Comprehensive risk assessment of all contamination hazards with respect to your aseptic processes, equipment, and facilities, including an independent assessment that includes, but is not limited to:
 - o All human interactions within the ISO 5 area
 - o Equipment placement and suitability, including ergonomics for each human interaction.
 - o Air quality in the ISO 5 area, and surrounding room including, but not limited to, air volume, air flow, and microbial/particulate levels
 - o Reduction or elimination of aseptic manipulations and connections (e.g., replacing (b)(4) aseptic connections with (b)(4) system)
 - o Facility layout
 - o Personnel Flows and Material Flows (throughout all rooms used to conduct and support sterile operations)
- A detailed remediation plan with timelines to address the findings of the contamination hazards risk assessment. Describe specific tangible improvements to be made to aseptic processing operation design and control.
- A plan to implement systemic remediations that address a pattern of recurring contamination events and ensure sustainable control of your aseptic processing operations.

2. Your firm failed to ensure that laboratory records included complete data derived from all tests necessary to ensure compliance with established specifications and standards (21 CFR 211.194(a)).

Your firm failed to collect the required amount of environmental and personnel monitoring samples required by your procedures to support the manufacture of sterile drug products. During the inspection, a reconciliation of samples that should have been taken during manufacturing activities and those that were actually taken did not match. Interviews with microbiology laboratory staff and management confirmed that it is your routine practice to fabricate results for samples that were never taken or to alter results for samples that would otherwise fail to meet established specifications.

Batch record information for environmental monitoring (EM) is not recorded at the time of completion. For example, a batch record was being filled out in the microbiology laboratory on October 12, 2023, for batch (b)(4) that was manufactured in March 2023, approximately six

months prior to the recorded date. Data for the microbiological activity in the filtration/filling area in the batch record was blank on October 12, 2023. This includes the air sample and non-viable particulate counting start and end times, activity done by signatures and dates, and the checked by signatures and dates. When the record was later provided on October 19, 2023, the record was filled out with times, signatures, and dates in March 2023.

During our inspection, investigators observed multiple sample collections in the ISO 5 and ISO 7 areas, and on personnel that resulted in plate readings with numerous colony forming units (CFUs). Your firm stated that prior to the start of the inspection, where you admitted routine fabrication of environmental monitoring results, no single action limit excursion had been documented, however, FDA investigators observed the following during the inspection:

- 15 action level excursions for ISO 5 area environmental monitoring samples
- 13 action level excursions for personnel monitoring samples
- 5 action level excursions for ISO 7 area environmental monitoring samples

Laboratory technicians falsified this data which is critical to maintaining an ongoing state of control in your aseptic processing facility. Data integrity is critical throughout the CGMP data life cycle, including in the creation, modification, processing, maintenance, archival, retrieval, transmission, and disposition of data after the record's retention period ends.

Your response states that a new checklist and procedure for oversight will be implemented. This response is not adequate as it does not address the data integrity issues that were identified by FDA. In addition, your response does not include a holistic review of data recording practices at your facility. Further, your corrective action and preventive action (CAPA) of adding a laboratory quality unit (QU) checklist for microbiologist tasks is not adequate to ensure contemporaneous completion of laboratory records.

In response to this letter, provide the following:

A comprehensive, independent assessment of your laboratory practices, procedures, methods, equipment, documentation, and analyst competencies. Based on this review, provide a detailed plan to remediate and evaluate the effectiveness of your laboratory system.

Data Integrity Remediation

Your quality system does not adequately ensure the accuracy and integrity of data to support the safety, effectiveness, and quality of the drugs you manufacture. See FDA's guidance document

Data Integrity and Compliance With Drug CGMP for guidance on establishing and following CGMP compliant data integrity practices at <https://www.fda.gov/media/119267/download>.

We acknowledge that you are using an independent third-party consultant to audit your operation and assist in meeting FDA requirements. In response to this letter, provide:

- A comprehensive investigation into the extent of the inaccuracies in data records and reporting. Your investigation should include:
 - A detailed investigation protocol and methodology; a summary of all laboratories, manufacturing operations, and systems to be covered by the assessment; and a justification for any part of your operation that you propose to exclude.
 - Interviews of current and former employees to identify the nature, scope, and root cause of data inaccuracies. We recommend that these interviews be conducted by a qualified third party.
 - An assessment of the extent of data integrity deficiencies at your facility. Identify omissions, alterations, deletions, record destruction, non-contemporaneous record completion, and other deficiencies. Describe all parts of your facility's operations in which you discovered data integrity lapses.
 - A comprehensive retrospective evaluation of the nature of the testing data integrity deficiencies. We recommend that a qualified third party with specific expertise in the area where potential breaches were identified should evaluate all data integrity lapses.
- A current risk assessment of the potential effects of the observed failures on the quality of your drugs. Your assessment should include analyses of the risks to patients caused by the release of drugs affected by a lapse of data integrity and analyses of the risks posed by ongoing operations.
- A management strategy for your firm that includes the details of your global CAPA plan. Your strategy should include:
 - A detailed corrective action plan that describes how you intend to ensure the reliability and completeness of all the data you generate including analytical data, manufacturing records, and all data submitted to FDA.
 - A comprehensive description of the root causes of your data integrity lapses including evidence that the scope and depth of the current action plan is commensurate with the findings of the investigation and risk assessment. Indicate whether individuals responsible for data integrity lapses remain able to influence CGMP-related or drug application data at your firm.
 - Interim measures describing the actions you have taken or will take to protect patients and to ensure the quality of your drugs, such as notifying your customers, recalling product, conducting additional testing, adding lots to your stability programs to assure stability, drug application actions, and enhanced complaint monitoring.

- o Long-term measures describing any remediation efforts and enhancements to procedures, processes, methods, controls, systems, management oversight, and human resources (e.g., training, staffing improvements) designed to ensure the integrity of your company's data.

- o A commitment to have a qualified consultant conduct extensive annual audits, for at least two years, to assist in evaluating CAPA effectiveness after you have executed your data integrity remediation protocol.

- o Inform FDA if you will be hiring a Chief Integrity Officer who is fully empowered to receive anonymous complaints from employees reporting data integrity concerns and with the authority to ensure any potential breach is promptly investigated (by independent quality assurance function, along with expertise from outside entities whenever needed).

- o A status report for any of the above activities already underway or completed.

3. Your firm failed to perform operations within specifically defined areas of adequate size and to have separate or defined areas or such other control systems necessary to prevent contamination or mix-ups in aseptic processing areas (21 CFR 211.42(c)(10)).

Environmental Monitoring Deficiencies

Your environmental monitoring (EM) program is deficient. Locations selected for EM in critical areas such as the ISO 5 aseptic processing line, do not have scientific justification to support the chosen locations. For example, standard operating procedure (SOP) KHIL/RB/QC/036 "Swab Testing" describes locations such as "(b)(4)" without providing details to ensure samples are taken from the same location each time. When asked to provide justification for sampling locations, no documentation was provided.

Additionally, the materials used to perform environmental and personnel monitoring are inadequate. The media used does not contain a neutralizing agent and operators were observed spraying (b)(4) near open plates. The plates themselves were observed numerous times to have desiccated media pulling away from the sides of the plates and cracking.

Your response is inadequate as you do not include a risk based, scientific study to determine sampling locations for your environmental monitoring. In addition, you failed to evaluate how the growth media and plate deficiencies potentially impact your drug products and facility's state of control for microbial contamination.

Facility Maintenance Deficiencies

During the inspection, numerous instances of your facility being in a state of disrepair or unclean were noted. This includes but is not limited to:

- (b)(4) surrounding the HEPA filters in the ISO 5 area were detached, creating gaps where air from the ISO 7 area could flow into the ISO 5 area.

- Hose connected to a leaking purified water use point was submerged in a bucket of stagnant water.
- Peeling paint, stains, and residue on the ceiling of the (b)(4) room.

Your response is inadequate as you failed to consider that persistently deficient environmental controls (e.g., poor design of processing lines, lack of data integrity, and insufficient environmental monitoring) provide a fundamental lack of meaningful retrospective data to support sterility assurance.

A vigilant ongoing EM program, and supporting laboratory, are essential to detect and respond to potential product contamination hazards in your manufacturing environment in a timely manner. Loss of environmental control in an aseptic manufacturing facility can ultimately pose a serious hazard to patients.

In response to this letter, provide:

- An independent assessment of your EM program including, but not limited to, establishing appropriate limits, sampling frequencies, investigating deviations, and trend analysis. Also ensure the implementation of a comprehensive CAPA plan.
- Your CAPA plan to implement routine, vigilant operations management oversight of facilities and equipment. This plan should ensure, among other things, prompt detection of equipment/facilities performance issues, effective execution of repairs, adherence to appropriate preventive maintenance schedules, timely technological upgrades to the equipment/facility infrastructure, and improved systems for ongoing management review.

4. Your firm's quality control unit failed to exercise its responsibility to ensure drug products manufactured are in compliance with CGMP, and meet established specifications for identity, strength, quality, and purity (21 CFR 211.22).

Your firm's QU failed to adequately execute its responsibilities. For example:

A. Your QU failed to follow approved, written production and process controls. Your firm was manufacturing Multi Action Relief Drops, Polyvinyl Alcohol 0.5%, Povidone 0.6%, and Tetrahydrozoline HCl 0.05% using non-pharmaceutical grade (b)(4) as a preservative. When your customer requested a switch to pharmaceutical grade (b)(4), you proceeded to repeat process validation without opening a change control per SOP KHIL/RB/QA/016/-R07, "Change Control." You also failed to conduct a risk assessment of product that was in the U.S. market with non-pharmaceutical grade (b)(4).

B. Your QU released drug product batches of Equate Hydration Polyethylene Glycol 400 and Propylene Glycol Eye Drops **(b)(4)** before the process validation was completed, as required in your SOP KHIL/RB/QA/081 "Process Validation." Your QU stated that due to a customer request they released the product for distribution before the studies were completed (21 CFR 100(a)).

C. Your QU failed to ensure that adequate stability data supported your drug expiration dates. Equate Hydration Polyethylene Glycol 400 and Propylene Glycol Eye Drops **(b)(4)** was released with a **(b)(4)** expiration date based on only three months of accelerated stability data. (21 CFR 211.166(b)).

D. Your sampling plan to test for diethylene glycol (DEG) and ethylene glycol (EG) in polyethylene glycol is not representative. For example, when receiving the same vendor lot of polyethylene glycol multiple times, only the first shipment of the lot is sampled and tested for DEG and EG. Subsequent shipments with the same vendor lot are not sampled and tested for DEG and EG (21 CFR 211.84).

Your response is inadequate for the following:

A. You failed to review all formulations to ensure that when required, United States Pharmacopeia (USP) grade materials are used to manufacture drug products for the U.S. market and that change controls are opened when required by your procedure.

B. Procedural updates are not sufficient to address the QU disregarding what was written in the previous version of the SOP to release product without completed process validation.

C. A review of expiration dates and the stability data that support them was not included as part of your response.

D. A plan for testing to verify that DEG and EG was at acceptable levels in all lots of raw materials and finished drug products was not included as part of your corrective action plan.

In response to this letter, provide the following:

- A comprehensive assessment and remediation plan to ensure your QU is given the authority and resources to effectively function. The assessment should also include, but not be limited to:
 - A determination of whether procedures used by your firm are robust and appropriate.
 - Provisions for QU oversight throughout your operations to evaluate adherence to appropriate practices.
 - A complete and final review of each batch and its related information before the QU disposition decision.

o Oversight and approval of investigations and discharging of all other QU duties to ensure identity, strength, quality, and purity of all products.

- A comprehensive, independent assessment of your change management system. This assessment should include, but not be limited to, your procedure(s) to ensure changes are justified, reviewed, and approved by your quality unit. Your change management program should also include provisions for determining change effectiveness.

The use of ingredients contaminated with DEG or EG has resulted in various lethal poisoning incidents in humans worldwide. See FDA's guidance document *Testing of Glycerin, Propylene Glycol, Maltitol Solution, Hydrogenated Starch Hydrolysate, Sorbitol Solution, and Other High-Risk Drug Components for Diethylene Glycol and Ethylene Glycol* to help you meet the CGMP requirements when manufacturing drugs containing ingredients at high-risk for DEG or EG contamination at <https://www.fda.gov/media/167974/download>.

In response to this letter, provide:

- A commitment to provide DEG and EG test results, no later than 30 calendar days from the date of this letter, from testing retains for all lots of high-risk drug components used in the manufacture of drug products. Alternatively, if a retain of a component lot is unavailable, perform retain sample testing of all implicated finished drug product batches for the presence of DEG and EG.
- A full risk assessment for drug products that are within expiry which contain any ingredient at risk for DEG or EG contamination (including, but not limited to, glycerin). Take prompt and appropriate actions to determine the safety of all lots of the component(s) and any related drug product that could contain DEG or EG, including customer notifications and product recalls for any contaminated lots. Identify additional appropriate CAPA that secure supply chains in the future, including, but not limited to, ensuring that all incoming raw material lots are from fully qualified manufacturers and free from unsafe impurities. Detail these actions in your response to this letter.
- A description of how you will test each component lot for conformity with all appropriate specifications for identity, strength, quality, and purity. If you intend to accept any results from your supplier's certificate of analysis (COA) instead of testing each component lot for strength, quality, and purity, specify how you will robustly establish the reliability of your supplier's results through initial validation as well as periodic revalidation. In addition, include a commitment to always conduct at least one specific identity test for each incoming component lot. In the case of glycerin, propylene glycol, and certain additional high-risk components we note that this includes the performance of parts A, B, and C of the USP monograph.

- The chemical quality control specifications you use to test each incoming lot of high-risk drug components to determine acceptability for use in manufacturing.
- A comprehensive, independent review of your material system to determine whether all suppliers of components, containers, and closures, are each qualified and the materials are assigned appropriate expiration or retest dates. The review should also determine whether incoming material controls are adequate to prevent use of unsuitable components, containers, and closures.

Ineffective Quality System

Significant findings in this letter demonstrate that your firm does not operate an effective quality system in accord with CGMP. In addition to the lack of effective management oversight of your production and laboratory operations, we found your quality unit is not enabled to exercise proper authority and/or has insufficiently implemented its responsibilities. Executive management should immediately and comprehensively assess your company's global manufacturing operations to ensure that your systems, processes, and products conform to FDA requirements.

Delay in Drug Product Recall

FDA held a teleconference with your firm and your U.S. Agent on October 25, 2023, to discuss our concerns regarding your sterile ophthalmic drug products. During this call, we recommended that you recall all drug products within expiry due to the insanitary conditions at your facility and other egregious violations, as described in this letter.

Due to the potential public health risks associated with the situation at your facility, the Agency released their own announcement on October 27, 2023 (<https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-consumers-not-purchase-or-use-certain-eye-drops-several-major-brands-due-risk-eye>). Despite numerous attempts by the Agency to obtain your recall decision, your firm did not initiate a recall until November 15, 2023 (<https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/kilitch-healthcare-india-limited-issues-voluntary-nationwide-recall-various-eye-drops-potential>), approximately three weeks after the initial discussion.

Drug Production Suspended

We acknowledge your commitment to suspend production of all drugs for the U.S. market. In response to this letter, clarify whether you intend to resume manufacturing drugs for the U.S. market at this facility in the future.

If you plan to resume any manufacturing operations regulated under the FD&C Act, notify this office before resuming your drug manufacturing operations. You are responsible for resolving all

deficiencies and systemic flaws to ensure your firm is capable of ongoing CGMP compliance. In your notification to the Agency, provide a summary of your remediations to demonstrate that you have appropriately completed all corrective action and preventive actions (CAPAs).

CGMP Consultant Recommended

Based upon the nature of the violations we identified at your firm, you should engage a consultant qualified as set forth in 21 CFR 211.34 to evaluate your operations and to assist your firm in meeting CGMP requirements if your firm intends to resume manufacturing drugs for the U.S. market. The qualified consultant should also perform a comprehensive six-system audit¹ of your entire operation for CGMP compliance and evaluate the completion and efficacy of your corrective actions and preventive actions before you pursue resolution of your firm's compliance status with FDA. Your use of a consultant does not relieve your firm's obligation to comply with CGMP. Your firm's executive management remains responsible for resolving all deficiencies and systemic flaws to ensure ongoing CGMP compliance.

Conclusion

The violations cited in this letter are not intended to be an all-inclusive list of violations that exist at your facility. You are responsible for investigating and determining the causes of any violations and for preventing their recurrence or the occurrence of other violations.

FDA placed your firm on Import Alert 66-40 on October 23, 2023.

Correct any violations promptly. FDA may withhold approval of new applications or supplements listing your firm as a drug manufacturer until any violations are completely addressed and we confirm your compliance with CGMP. We may re-inspect to verify that you have completed corrective actions to any violations.

Failure to address any violations may also result in the FDA continuing to refuse admission of articles manufactured at Kilitch Healthcare India Limited, T T C Industrial Road, Navi Mumbai into the United States under section 801(a)(3) of the FD&C Act, 21 U.S.C. 381(a)(3). Articles under this authority that appear to be adulterated may be detained or refused admission, in that the methods and controls used in their manufacture do not appear to conform to CGMP within the meaning of section 501(a)(2)(B) of the FD&C Act, 21 U.S.C. 351(a)(2)(B).

This letter notifies you of our findings and provides you an opportunity to address the above deficiencies. After you receive this letter, respond to this office in writing within 15 working days. Specify what you have done to address any violations and to prevent their recurrence. In response to this letter, you may provide additional information for our consideration as we continue to assess your activities and practices. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion.

Send your electronic reply to CDER-OC-OMQ-Communications. Identify your response with FEI 3011853060 and ATTN: Sarah Rhoades.

Sincerely,
/S/

Francis Godwin
Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research

WARNING LETTER

Similasan AG

MARCS-CMS 658878 — September 11, 2023

Delivery Method:

Via Email

Product:

Drugs

Recipient:

Urs Lehmann

CEO

Similasan AG

Industriestrasse 276060 SarnenSwitzerland

Issuing Office:

Center for Drug Evaluation and Research | CDER

United States

WARNING LETTER

September 11, 2023

RE: 658878

Dear Urs Lehmann and Dan Quail

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Similasan AG, FEI 1000110034, at Chriesiweg 6, Jonen, from March 27 to April 4, 2023. This letter is to advise you that FDA reviewed the information related to the inspection, including Similasan's response to the FDA Form 483 and follow-up that Similasan submitted on June 19,

2023 in response to FDA's request for information, which included product labels for multiple drug products. We also reviewed Similasan's website at the Internet address <https://www.similasanusa.com/>. The FDA has observed that your website directs consumers in the United States (U.S.) to the linked websites of U.S. retailers where your drug products can be purchased, including "Similasan Dry Eye Relief," "Similasan Complete Eye Relief," "Similasan Allergy Eye Relief," "Similasan Kids Allergy Eye Relief," "Similasan Red Eye Relief," "Similasan Pink Eye Relief," "Similasan Kids Pink Eye Relief," "Similasan Aging Eye Relief," "Similasan Computer Eye Relief," "Similasan Styte Eye Relief," "Similasan Pink Eye Nighttime Gel," and "Similasan Dry Eye Nighttime Gel" (hereinafter "your ophthalmic products"). Based on our review, these products are unapproved new drugs under section 505(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 355(a). As explained further below, introducing or delivering these products for introduction into interstate commerce violates sections 301(d) and 505(a) of the FD&C Act, 21 U.S.C. 331(d) and 355(a).

This warning letter also summarizes significant violations of Current Good Manufacturing Practice (CGMP) regulations for finished pharmaceuticals. See Title 21 Code of Federal Regulations (CFR), parts 210 and 211 (21 CFR parts 210 and 211).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drug products are adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B). We reviewed your April 21, 2023 response to our Form FDA 483 in detail and acknowledge receipt of your subsequent correspondence.

Your unapproved ophthalmic drug products are especially concerning from a public health perspective, particularly given your firm's significant violations of CGMP regulations. Ophthalmic drug products, which are intended for administration into the eyes, in general pose a greater risk of harm to users because the route of administration for these products bypasses some of the body's natural defenses.¹

Unapproved New Drugs

Based on a review of your product labeling, including on your website, your ophthalmic products are drugs under section 201(g)(1) of the FD&C Act, 21 U.S.C. 321(g)(1), intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease, and/or intended to affect the structure or any function of the body. Examples of claims from your product labeling, including on your website <https://www.similasanusa.com/>, that provide evidence of the intended use of these products as drugs include, but may not be limited to, the following:

Similasan Dry Eye Relief

- "Use As Often As Needed For •Dryness •Redness •Soothes •Moisturizes"

- “[T]emporarily relieve minor symptoms such as: •dry eye •redness of eyes and lids •reflex watering secondary to dry eye”

Similasan Complete Eye Relief

- “Use As Often As Needed For •Redness •Burning •Watering •Grittiness •Dryness •Irritation”
- “[T]emporarily relieve minor symptoms such as: •redness of eyes and eye lids •dry eye •reflex watering secondary to dry eye •sensation of grittiness •sensation of burning”
- “Similasan Complete Eye Relief is designed for temporary multi-symptom relief from redness, burning, watering, grittiness, dryness, and irritation”

Similasan Allergy Eye Relief

- “Use As Often As Needed For •Itching •Burning •Watering •Redness”
- “[T]emporarily relieve minor eye allergy symptoms such as: •itching •burning •excessive watering •redness of eyes and lids”

Similasan Kids Allergy Eye Relief

- “Use As Often As Needed For •Itching •Burning •Watering •Redness”
- “[T]emporarily relieve minor eye allergy symptoms such as: •itching •burning •excessive watering •redness of eyes and lids”

Similasan Red Eye Relief

- “Use As Often As Needed For •Redness •Stinging •Irritation •Watering”
- “[T]emporarily relieve minor eye symptoms such as: •itching •burning •redness of eyes and lids •stinging •excessive watering •irritation”

Similasan Pink Eye Relief

- “Use as often as needed for •Redness •Burning •Watery Discharge •Sensation of Grittiness”
- “[T]emporarily relieve minor eye symptoms such as: •excessive watery (clear) discharge •sensation of grittiness •redness and burning”
- “Similasan eye drops soothe and provide temporary relief of the following symptoms: •Redness •Burning •Watery discharge •Sensation of Grittiness”

Similasan Kids Pink Eye Relief

- “Use As Often As Needed For •Redness •Burning •Dryness •Stinging •Grittiness •Watering”
- “[T]emporarily relieve minor symptoms such as: •redness of the eyes •irritation, dryness, and burning •sensation of grittiness, stinging •excessive watering (clear)”

Similasan Aging Eye Relief

- “Multi-Symptom Relief •Blurred Vision •Eyestrain •Tearing due to Dryness”
- “[T]emporarily relieve minor symptoms such as: •Blurred vision •Eye Strain •Tearing due to dryness”
- “Eye drops for symptoms of aging eyes such as cloudy or blurry vision”

- “Similasan Aging Eye Relief eye drops are specially designed to support corneal and macular health, and [...] provide temporary relief for dryness”

Similasan Computer Eye Relief

- “Use As Often As Needed For •Aching Eyes •Eye Strain •Burning •Redness”
- “[T]emporarily relieve minor symptoms such as: •aching eyes •burning •redness •strained eyes (Computer, TV, reading, driving)”
- “[T]emporarily relieve the symptoms of eye strain that may include blurred vision, hypersensitivity to light, and dry eyes”

Similasan Styte Eye Relief

- “Multi-Symptom Relief •Redness •Burning •Tearing”
- “[T]emporarily relieve minor symptoms such as: •redness •burning •eyelid redness •tearing”
- “[T]emporarily relieve symptoms of styes, such as redness, burning, and tearing”

Similasan Pink Eye Nighttime Gel

- “Use As Often As Needed For •Redness •Burning •Watery Discharge •Sensation of Grittiness”
- “[T]emporarily relieve minor eye symptoms: •excessive watery (clear) discharge •sensation of grittiness •redness and burning”
- “Pink Eye Nighttime Gel is a thicker formula made for overnight relief from pink eye symptoms: •Redness •Burning •Watery discharge • Sensation of Grittiness”

Similasan Dry Eye Nighttime Gel

- “Use As Often As Needed For •Dryness •Redness”
- “[T]emporarily relieve minor eye symptoms such as: •dry eye •redness of eyes and lids •reflex watering secondary to dry eye”
- “Dry Eye Nighttime Gel is a thicker gel formula made for nighttime and overnight relief of dry eye symptoms: •Dryness •Redness •Soothes & moisturizes”

Your ophthalmic products are not generally recognized as safe and effective (GRASE) for their above referenced uses and, therefore, these products are “new drugs” under section 201(p) of the FD&C Act, 21 U.S.C. 321(p). With certain exceptions not applicable here, a new drug may not be introduced or delivered for introduction into interstate commerce without an approved application from FDA in effect, as described in sections 505(a) and 301(d) of the FD&C Act, 21 U.S.C. 355(a) and 331(d). No FDA-approved application pursuant to section 505 of the FD&C Act, 21 U.S.C. 355, is in effect for your ophthalmic products. Accordingly, the introduction or delivery for introduction into interstate commerce of these products violates sections 301(d) and 505(a) of the FD&C Act, 21 U.S.C. 331(d) and 355(a).

We recognize that your ophthalmic products are labeled as homeopathic drugs with active ingredient(s) measured in homeopathic strengths. Under section 201(g)(1) of the FD&C Act, 21

U.S.C. 321(g)(1), the term “drug” includes articles recognized in the official Homeopathic Pharmacopeia of the United States (HPUS), or any supplement to it. Homeopathic drug products are subject to the same statutory requirements as other drugs; nothing in the FD&C Act exempts homeopathic drugs from any of the requirements related to adulteration, misbranding, or FDA approval.

We note that Similasan’s information submission to FDA in June 2023 included product labels for additional ophthalmic products (i.e., “Similasan Children’s Allergy Eye Relief,” “Similasan Children’s Pink Eye Relief,” and “Similasan Irritated Eye Relief”) that are not currently listed on Similasan’s U.S. website. Please be advised that the violations and safety concerns outlined above also apply to these products if introduced into U.S. commerce.

CGMP Violations

During our inspection, our investigators observed specific violations including, but not limited to, the following:

1. Your firm failed to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes. (21 CFR 211.113(b))

The written procedures for your media fills were not appropriate because they failed to accurately simulate commercial manufacturing. Our inspection found that aseptic interventions simulated during your media fills were not sufficiently representative of commercial aseptic manufacturing. For example, the number of interventions conducted during your manually intensive commercial operations exceeded the number performed during your media fills as follows,

- (b)(4), batch (b)(4), documented 38 interventions in the cap (b)(4) area during manufacture and 14 interventions were simulated during your supportive media fill
- (b)(4), batch (b)(4), documented 40 interventions in the cap (b)(4) area during manufacture and 23 interventions were simulated during your supportive media fill

Your inadequate media fill studies compromise your ability to accurately assess the state of validation and process control. To ensure a valid assessment, it is critical that media fill studies accurately simulate the number and type of interventions that occur during commercial manufacturing.

Furthermore, interventions may increase contamination risks during aseptic manufacturing.

Your response states that you plan to include these and other interventions in the next media fill simulation, scheduled for June 2023. Your response failed to include a risk assessment or

investigation to determine whether the safety of your drug products are impacted by the excessive manual interventions during aseptic operations.

You may refer to FDA's guidance document *Sterile Drug Products Produced by Aseptic Processing—Current Good Manufacturing Practice* to help you meet the CGMP requirements when manufacturing sterile drugs using aseptic processing at <https://www.fda.gov/media/71026/download>.

In response to this letter, provide:

- Comprehensive risk assessment of all contamination hazards with respect to your aseptic processes, equipment, and facilities, including an independent assessment that includes, but is not limited to:
 - o All human interactions within the ISO 5 area
 - o Equipment placement and ergonomics
 - o Air quality in the ISO 5 area and surrounding room
 - o Facility layout
 - o Personnel Flows and Material Flows (throughout all rooms used to conduct and support sterile operations)
- A detailed remediation plan with timelines to address the findings of the contamination hazards risk assessment. Describe specific tangible improvements to be made to aseptic processing operation design and control.

2. Your firm failed to establish laboratory controls that include scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity. (21 CFR 211.160(b))

You failed to establish and conduct 100% visual inspections of your ophthalmic drug products to ensure that each container is essentially free of visible particulates. Since at least June 23, 2022, your established in-process inspection procedure for in-process inspection for visible particulates was limited to acceptable-quality-limits (AQLs). The use of AQL sampling is intended as an additional analysis routinely conducted as part of the quality release processes only after performing 100% visual inspection. Your failure to conduct 100% visual inspection increases the risk for the release of ophthalmic drug product with visible particulate contamination.

Your response states that your (b)(4) particle inspection system's imaging processing, that you qualified in 2022 and utilized for 100% visual inspection, "was too slow" and the rejection rate was too high with "false positive[s]" so you suspended its use and implemented manual visual

inspections using AQLs, with no 100% visual inspection. As a corrective action, you planned to re-introduce the (b)(4) system on May 1, 2023.

Your response is inadequate. There is no commitment to conduct a retrospective review for your released drug products that only relied on the AQL sampling to try and assure product quality and limit patient risk. Additionally, your response did not include supportive documentation for routine osmolarity testing of your ophthalmic drug products.

In response to this letter, provide:

- Improved in-process testing and monitoring to enhance detection of variation during production of each batch. Include remediated in-process quality standards, including but not limited to enhanced sampling, that will more robustly monitor (b)(4) process control. Describe how the improvements will ensure early detection of process variation and manufacturing defects, and prevent consumer exposure to substandard quality drug products.
- Given that your container closure system uses an (b)(4) vial, provide data supporting that your (b)(4) particle inspection system can adequately detect particles within your container closure.
- For all batches that you have not conducted 100% visual inspection, conduct 100% visible inspection of your retain samples. If you obtain out-of-specification (OOS) results, conduct investigations and provide your completed investigations, including conclusions and take appropriate market action for all batches of drug products confirmed not meeting specifications.
- Supportive documentation clarifying whether you are conducting routine osmolarity testing for your topical ophthalmic drug products for release and stability testing.

3. Your firm failed to ensure that laboratory records included complete data derived from all tests necessary to ensure compliance with established specifications and standards. (21 CFR 211.194(a))

Your laboratory records do not include complete testing data to support the analysis performed. For example, negative controls for sterility testing are not documented at the time of performance. The absence of concurrently performed negative controls during sterility testing does not allow full assessment of the suitability of the testing performed.

All CGMP-related data must be retained to enable appropriate assessments and decisions by the QU and to demonstrate ongoing control. The lack of complete testing records compromises the integrity of the testing results.

In your response, you state that you will implement new test method records for standard preparations. You also state that you will follow your test procedures in accordance with the compendial method, and finished product test results reported by the quality control unit for sterile drug products will be accurately recorded. Your response is inadequate because there is no commitment to conduct retrospective reviews for tested products and training of employees to correct deficient practices.

In response to this letter, provide:

- A complete assessment of documentation systems used throughout your manufacturing and laboratory operations to determine where documentation practices are insufficient. Include a detailed CAPA plan that comprehensively remediates your firm's documentation practices to ensure you retain attributable, legible, complete, original, accurate, contemporaneous records throughout your operation.
- Your action plan to address any product quality or patient safety risks for your drug products in U.S. distribution, including potential customer notifications and recalls.

4. Your firm failed to establish an adequate quality unit and the responsibilities and procedures applicable to the quality control unit are not in writing and fully followed (21 CFR 211.22(a) and 211.22(d)).

Your quality unit (QU) did not provide adequate oversight for the manufacture of your drug products. For example, your QU failed to ensure:

- Adequate procedures for that are designed to prevent microbiological contamination of drug products purporting to be sterile (21 CFR 211.113(b)).
- Adequate procedures to establish laboratory controls that include scientifically sound and appropriate specifications, standards, and sampling plans sampling plans, and test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality, and purity (21 CFR 211.160(b)).
- Adequate procedures to ensure that laboratory records included complete data (21 CFR 211.194(a)).
- Adequate QU oversight to ensure the use of harmless components¹ in your drug products.

Your firm's quality systems are inadequate. You may refer to FDA's guidance document *Quality Systems Approach to Pharmaceutical CGMP Regulations* for help implementing quality systems and risk management approaches to meet the requirements of CGMP regulations 21 CFR, parts 210 and 211 at <https://www.fda.gov/media/71023/download>.

In response to this letter, provide:

- A comprehensive assessment and remediation plan to ensure your QU is given the authority and resources to effectively function. The assessment should also include, but not be limited to:
 - A determination of whether procedures used by your firm are robust and appropriate
 - Provisions for QU oversight throughout your operations to evaluate adherence to appropriate practices
 - A complete and final review of each batch and its related information before the QU disposition decision
 - Oversight and approval of investigations and discharging of all other QU duties to ensure identity, strength, quality, and purity of all products
 - Also describe how top management supports quality assurance and reliable operations, including but not limited to timely provision of resources to proactively address emerging manufacturing/quality issues and to assure a continuing state of control.
 - Take prompt and appropriate actions for all batches of drug products that contain unacceptable levels of ingredients that could cause them to be harmful, including customer notifications and other applicable market actions for any batches containing harmful ingredients. Detail these actions in your response to this letter.

CGMP Consultant Recommended

Based upon the nature of the violations we identified at your firm, you should engage a consultant qualified as set forth in 21 CFR 211.34 to evaluate your operations and to assist your firm in meeting CGMP requirements if your firm intends to resume manufacturing drugs for the U.S. market. The qualified consultant should also perform a comprehensive six-system audit of your entire operation for CGMP compliance and evaluate the completion and efficacy of your corrective actions and preventive actions before you pursue resolution of your firm's compliance status with FDA.

Your use of a consultant does not relieve your firm's obligation to comply with CGMP. Your firm's executive management remains responsible for resolving all deficiencies and systemic flaws to ensure ongoing CGMP compliance.

Products Containing Glycerin and Sorbitol Solution

You manufacture multiple drugs that contain glycerin or sorbitol solution. Identity testing for these and certain other high-risk drug components² includes a limit test in the United States Pharmacopeia (USP) to ensure that the component meets the relevant safety limits for levels of diethylene glycol (DEG) or ethylene glycol (EG).

The use of ingredients contaminated with DEG or EG has resulted in various lethal poisoning incidents in humans worldwide. See FDA's guidance document *Testing of Glycerin, Propylene Glycol, Maltitol Solution, Hydrogenated Starch Hydrolysate, Sorbitol Solution, and Other High-*

Risk Drug Components for Diethylene Glycol and Ethylene Glycol at <https://www.fda.gov/media/167974/download>, to help you meet the CGMP requirements when manufacturing drugs containing ingredients at high-risk for DEG or EG contamination.

Conclusion

The violations cited in this letter are not intended to be an all-inclusive statement of violations that may exist in connection with your products and at your facility. You are responsible for investigating and determining the causes of any violations and for preventing their recurrence or the occurrence of other violations. It is your responsibility to ensure that your firm complies with all requirements of federal law, including FDA regulations.

FDA placed all products from your establishment in Switzerland on Import Alert 66-40 on July 24, 2023.

Correct any violations promptly. FDA may withhold approval of new applications or supplements listing your firm as a drug manufacturer until any violations are completely addressed and we confirm your compliance with CGMP. We may re-inspect to verify that you have completed corrective actions to any violations.

This letter notifies you of our concerns and provides you an opportunity to address them. Failure to adequately address this matter may result in legal action including, without limitation, seizure and injunction. In addition, please note that unapproved new drugs are subject to refusal of admission into the United States, and such products may be subject to detention without physical examination. For more information about detention without physical examination, see Import Alert 66-41.

Please notify FDA in writing, within fifteen working days of receipt of this letter, of the specific steps you have taken to correct any violations. Include an explanation of each step being taken to prevent the recurrence of violations, as well as copies of related documentation. If you believe that your products are not in violation of the FD&C Act, include your reasoning and any supporting information for our consideration. If you cannot complete corrective action within fifteen working days, state the reason for the delay and the time within which you will complete the correction. Your response should be sent to U.S. Food and Drug Administration, CDER/OC/Office of Unapproved Drugs and Labeling Compliance by email to FDAAdvisory.

Sincerely,
/S/

Jill Furman
Director

[Whereupon, at 11:22 a.m., the hearing was adjourned.]

