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Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
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July 18, 2023

The Honorable Robert M. Califf, M.D., MACC
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20903

Dear Dr. Califf,

Pursuant to Rules X and XI of the U.S. House of Representatives, the Committee is conducting oversight of the Food and Drug Administration's (FDA) foreign drug inspection program. As you are aware, members of the Committee have expressed concern regarding the effectiveness of the FDA's foreign drug inspection program at two separate hearings before the Subcommittee on Oversight and Investigations and the Subcommittee on Health.[1]

The Committee is particularly concerned about foreign drug inspections conducted in India and China. The FDA's recent decision to address shortages of critical drugs by allowing the temporary import of otherwise unapproved drugs from India and China makes having effective foreign inspection programs in those countries critical.[2] Chinese and Indian manufacturers receive the most FDA Warning Letters.[3] These violations have included carcinogens in medicines, destroying or falsifying of data, and non-sterile manufacturing processes. Given that approximately 32 percent of generic drugs and 45 percent of active pharmaceutical ingredients (APIs) are from these two countries, we are worried that the United States is overly reliant on

[1] *Examining the Root Causes of Drug Shortages: Challenges in Pharmaceutical Drug Supply Chains: Hearing Before the Subcomm. on Oversight & Investigation of the H. Comm. on Energy & Commerce*, 118th Cong. (May 11, 2023); *Preparing for and Responding to Future Public Health Security Threats: Hearing Before the Subcomm. on Health of the H. Comm. on Energy & Commerce*, 118th Cong. (May 11, 2023).
[2] Joseph Keenan, *FDA to Allow Temporary Overseas Production to Shore up Supplies of Chemo Drug*, Fierce Pharma (June 6, 2023), https://www.fiercepharma.com/manufacturing/fda-allow-temporary-overseas-production-shore-supplies-chemo-drug.
[3] *Preparing for and Responding to Future Public Health Security Threats: Hearing Before the Subcomm. on Health of the H. Comm. on Energy & Commerce*, 118th Cong. (May 11, 2023).

sourcing from foreign manufacturers with a demonstrated pattern of repeatedly violating FDA safety regulations.[4]

The Committee is not alone in voicing concerns. The Department of Defense recently announced that it will begin independently testing the quality and safety of imported generic drugs.[5] The non-partisan Government Accountability Office (GAO) also criticized the FDA's foreign inspection program in a report published last year, noting that the FDA faced "unique challenges" and that it is inadequate at holding foreign manufacturers accountable for repeatedly violating regulations.[6] In particular, the GAO was concerned that the FDA's practice of conducting preannounced foreign inspections is ineffective and raises "questions about the equivalence of foreign to domestic inspections."[7]

From 2014 to 2015, the FDA conducted a pilot program in India that eliminated extended advance notice for inspections. Instead, the FDA conducted short notice or unannounced visits and selected sites for the program that the agency believed had significant issues. The pilot program appears to have been successful at exposing widespread misconduct and significant violations of FDA regulations, including falsified quality records.[8] Despite the pilot program's success, the FDA elected to discontinue it.[9]

The COVID-19 pandemic stopped most in-person inspections of foreign drug manufacturers from March 2020 until April 2022. In lieu of in-person inspections, the FDA resorted to alternatives and workarounds, such as remote interactive inspections of drug manufacturing facilities on a voluntary basis. Once FDA inspections resumed, they did so at a much lower level than before the pandemic. One analysis found that out of approximately 2,800 foreign manufacturing facilities, the FDA inspected only 6 percent of them, with just 3 percent of Indian manufacturers being inspected.[10]

In many respects, China presents a more dangerous situation than India. Between fiscal years (FY) 2020 and 2022, the FDA conducted only 40 inspections in China as compared to 131

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[4] Drug Shortages Task Force, U.S. Food & Drug Admin., Drug Shortages: Root Causes and Potential Solutions (2019), https://www.fda.gov/media/131130/download.
[5] Anna Edney & Riley Griffin, *US Military Is So Worried About Drug Safety It Wants to Test Widely Used Medicines*, Bloomberg (June 7, 2023), https://www.bloomberg.com/news/articles/2023-06-07/drug-safety-fears-spur-pentagon-plan-to-test-widely-used-meds#xj4y7vzkg.
[6] U.S. Gov't Accountability Office, GAO-22-103611, Drug Safety:
FDA Should Take Additional Steps to Improve Its Foreign Inspection Program (2022), https://www.gao.gov/products/gao-22-103611.
[7] *Id.*
[8] Sidley, *Proposed Bill Seeks to Eliminate Preannounced Foreign Drug Inspections*, Sidley (Jan. 31, 2022), https://www.sidley.com/en/insights/newsupdates/2022/01/proposed-bill-seeks-to-eliminate-preannounced-foreign-drug-inspections.
[9] *Securing the U.S. Drug Supply Chain: Oversight of FDA's Foreign Inspection Program: Hearing Before the Subcomm. on Oversight & Investigation of the H. Comm. on Energy & Commerce*, 116th Cong. (Dec. 10, 2019), https://www.govinfo.gov/content/pkg/CHRG-116hhrg44495/html/CHRG-116hhrg44495.htm.
[10] Irena Hwang, *After Pandemic Delays, FDA Still Struggling to Inspect Foreign Drug Manufacturers*, ProPublica (Apr. 19, 2023), https://www.propublica.org/article/fda-drugs-medication-inspections-china-india-manufacturers.

inspections in FY 2019 alone.[11] On January 8, 2023, the Government of China ended its requirement that international arrivals quarantine for two weeks upon entry to the country.[12] However, the FDA only began in-person inspections in China in April 2023.

Moreover, there have been recent, troubling political developments in China that the Committee believes may jeopardize the viability of the FDA's in-person inspections there. Last month, the ruling Communist Party of China announced a reinterpretation of its already sweeping National Security Law to expand the scope of the law beyond state secrets to cover "data, materials, or items related to … national interests."[13] The law's new interpretation is so broad that it would allow officials to arrest FDA inspectors or block access to manufacturers' records if officials deem it in the national interest.[14] Authorities have already raided the offices of companies that specialize in collecting market information in China and detained employees.[15]

Accordingly, to assist the Committee in our oversight, please respond to the following questions by August 1, 2023:

Foreign Inspections Generally

1. Section 3112(e) of the CARES Act gave the FDA additional authority to require manufacturers to report certain supply chain information to it. The FDA's May 9, 2023, letter to the Committee stated that only 44 percent of facilities are reporting the required data to the FDA.[16] Based on the FDA's letter, a disproportionate percentage of noncompliant API and finished dose formula facilities are located outside of the United States. How many regulatory actions has the FDA enforced against noncompliant foreign facilities regarding the CARES Act reporting requirements? Provide a list of all foreign facilities that have been penalized for noncompliance. Include in your response a detailed description of the action taken by the FDA.

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[11] Baker McKenzie, *United States: With China's Re-Opening: Staying Ahead of FDA Drug cGMP Enforcement*, Lexology (Feb. 3, 2023), https://www.lexology.com/library/detail.aspx?g=f20c187f-db67-4a97-8d96-b9b0a665f33c.

[12] U.S. Mission China, *COVID-19 Information*, U.S. Embassy & Consulates in China (Jan. 27, 2023), https://china.usembassy-china.org.cn/covid-19-information/#:~:text=Quarantine%20Information,international%20arrivals%20entering%20the%20PRC.

[13] Chun Han Wong & Dan Strumpf, *China Spy Law Adds to Chilling Effect of Detentions*, Wall St. J. (Apr. 27, 2023), https://www.wsj.com/articles/chinas-expanded-spy-law-adds-to-chilling-effect-of-detentions-ce8cea1a?mod=article_inline; *see also* Jeremy Daum, *Bad as It Ever Was: Notes on the Espionage Law*, China Law Translate (Feb. 05, 2023), https://www.chinalawtranslate.com/en/bad-as-it-ever-was-notes-on-the-espionage-law/.

[14] Wenxin Fan, *China Detains Japanese Employee from Drugmaker Astellas*, Wall St. J. (Mar. 27, 2023), https://www.wsj.com/articles/china-detains-japanese-employee-from-drugmaker-astellas-abb01d27?mod=article_inline.

[15] Nathaniel Taplin, *Beijing's Bain Raid, Espionage Law Are Self-Sabotage*, Wall St. J. (Apr. 28, 2023), https://www.wsj.com/articles/beijings-bain-raid-espionage-law-are-self-sabotage-40f87276?mod=article_inline; Yoko Kubota & Miho Inada, *In China, a Detention and a New Espionage Law Have Businesses Worried*, Wall St. J. (Apr. 28, 2023), https://www.wsj.com/articles/in-china-a-detention-and-a-new-espionage-law-have-businesses-worried-78fc88b1?mod=article_inline.

[16] Letter from Hon. Robert Califf, FDA Commissioner, to Hon. Cathy McMorris Rodgers, Hon. Morgan Griffith, and Hon. Brett Guthrie (May 9, 2023) (on file with Committee).

2. The FDA ensures the quality of drugs and other pharmaceutical products through manufacturers' compliance with facility registration and Current Good Manufacturing Practice (CGMP) regulations. The Food and Drug Administration Safety and Innovation Act (FDASIA, P.L. 112-144) contained several provisions providing the FDA greater insight into the original sources of excipients, API, and finished dosage products. Specifically, Section 703 requires that drug manufacturers identify the name and place of business of all establishments involved in the production of drug excipients, while Section 711 revises CGMP regulations to require oversight over the production of any raw materials for the manufacture of a drug. The FDA has indicated in its recent requests for additional authorities over supply chain information that it does not currently have access to original sources for API and other drug excipients, notwithstanding these and other provisions providing such authorities.

    a. Given its authorities under FDASIA, why does the FDA take the position that it does not have visibility into where API and drug excipients are sourced?

    b. Explain in detail, how the FDA processes information received under Sections 703 and 711. As part of your response, explain how has the data received under Sections 703 and 711 informs FDA's foreign inspections programs and drug shortage response efforts?

3. Was the FDA consulted by the Department of Defense regarding its decision to independently test the quality and safety of generic drugs it purchases? If yes, provide communications and documents related to the consultation.

4. Has the FDA considered a plan to end preannounced inspections of foreign manufacturing facilities? If no, explain in detail why not? If yes, provide copies of any such plans.

5. How many FDA inspectors are currently conducting domestic inspections?

6. How many FDA inspectors are currently conducting foreign inspections? Include in your response how many of these inspectors are operating in each country.

7. How many positions are currently open for foreign inspections? Include in your response what country the open position is for and how long the position has been unfilled.

8. The FDA has noted there is a backlog in conducting foreign inspections. How large is the backlog and what progress has the FDA made in closing it? Include in your response a complete list of the foreign facilities in the backlog.

9. In the last 10 years, for each year, what percent of FDA inspections of foreign facilities have been preannounced and what was the lead time given for each preannounced inspection?

10. In the last 10 years, for each year, what percent of the FDA's inspections of U.S. domestic facilities have been preannounced and what was the given lead time was given for each preannounced inspection?

Inspections in India

11. Explain in detail why the FDA ended the unannounced inspection pilot program conducted in India between 2014 to 2015.

12. Does the FDA plan to reinstate the unannounced inspection program in India? If not, explain in detail why not.

13. For foreign facilities in India that have received a Warning Letter in the last 10 years, provide a list of which of these facilities have been inspected in-person, inspected remotely, or not inspected at all since the Warning Letter was issued.

14. In the last 10 years, how many times has a foreign manufacturer in India been inspected and had their Warning Letter lifted before the FDA investigator filed a report, allowing the company to get approval for a drug shortage product or its abbreviated new drug application (ANDA)? Provide a list of these companies, dates of approval, and the product that was approved.

15. As early as November 2022, the FDA was aware of significant, repeated quality control failures at Intas Pharmaceuticals' Ahmedabad, India manufacturing facility. At the time, this facility was one of only five finished product manufacturers supplying the U.S. market with chemotherapy drugs carboplatin and cisplatin.[17] Intas voluntarily stopped operations at its Ahmedabad plant in response to quality control failures on June 5, 2023.

    During a June 9, 2023, briefing with Congressional staff on cancer drug shortages the FDA stated that it was not aware of the company's plans to halt operations at its Ahmedabad, India, manufacturing facility until after the plant had shut down operations. This lapse in communication is concerning, as the FDA was ostensibly aware of the ongoing quality issues at the plant, as well as Intas' significant U.S. market share for cisplatin and carboplatin and the disruption a plant closure would cause in the supply of these drugs.

    It is important for the Committee to understand exactly how and when the FDA was made aware of Intas' plans to voluntarily halt operations at its Ahmedabad facility. Explain in detail and provide copies of any communications between the FDA and Intas Pharmaceuticals from January 2023 through June 2023 related to the company's decision to voluntarily halt production at the Ahmedabad plant closure.

[17] U.S. Food & Drug Admin., Form FDA 483 (09/08): Inspectional Observations of Intas Pharmaceuticals Ltd. (Dec. 2, 2022), https://www.fda.gov/media/164602/download.

Inspections in China

16. What is the FDA's plan to ensure that inspections in China can continue despite the expanded scope of China's National Security Law? Provide copies of any analysis or relevant documentation related to China's National Security Law and its implications for FDA's foreign drug inspection program and drug safety.

17. What actions will the FDA take in response to an inspector being detained, arrested, or otherwise prevented from completing an inspection of a drug manufacturing facility in China?

18. Has an FDA inspector even been detained, arrested, or otherwise prevented from completing an inspection of a drug manufacturing facility in China?

19. Provide copies of all communications between the FDA and the Government of China regarding in-person inspections of drug manufacturing facilities in China from January 2020 to the present.

20. Does the FDA plan to start an unannounced inspection program in China? If not, explain in detail why not. If yes, provide copies of any such plans.

21. For facilities in China that have received a Warning Letter in the last 10 years, provide a list of which of these facilities have been inspected in-person, inspected remotely, or not inspected at all since the Warning Letter was issued.

22. In the last 10 years, how many times has a foreign manufacturer in China been inspected and had their Warning Letters lifted before the FDA investigator filed a report, allowing the company to get approval for a drug shortage product or its ANDA? Provide a list of these companies, dates of approval, and the product that was approved.

Please be advised that intentional misstatements or omissions in response to the above questions may constitute federal criminal violations under 18 U.S.C. §1001. In addition, the Committee believes that interviews from FDA officials and employees about this matter may be necessary.

Finally, this letter serves as a formal request to preserve all existing and future records and materials in the FDA's possession relating to the topics addressed in this letter. You should construe this preservation notice as an instruction to take all reasonable steps to prevent the destruction or alteration, whether intentionally or negligently, of all documents, communications, and other information, including electronic information and metadata, that are or may be responsive to this congressional inquiry. This instruction includes all electronic messages sent using official and personal accounts or devices, including records created using text messages, phone-based message applications, or encryption software.

If you have any questions, please contact John Strom with the Majority Committee staff at (202) 225-3641. Thank you for your attention to this request.

Sincerely,

Cathy McMorris Rodgers
Chair
Energy and Commerce Committee

Brett Guthrie
Chair
Subcommittee on Health

H. Morgan Griffith
Chair
Subcommittee on Oversight and Investigations

CC: Frank Pallone Jr., Ranking Member, Energy and Commerce Committee
Anna Eshoo, Ranking Member, Subcommittee on Health
Kathy Castor, Ranking Member, Subcommittee on Oversight and Investigations