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ONE HUNDRED EIGHTEENTH CONGRESS

Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-6115
Majority (202) 225-3641
Minority (202) 225-2927

June 21, 2024

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 has been investigating the Food and Drug Administration's (FDA) foreign drug inspection program. The Committee has conducted analysis of the outcomes of FDA inspections in India and China from January 2014 to April 2024. The Committee limited its review to inspectors with ten or more inspections in either China or India.

The results of this analysis were surprising, revealing tremendous variation in inspection outcomes. Some FDA inspectors found compliance issues during all or almost all of their inspections. Other inspectors rarely reported finding a single compliance issue. Two inspectors never found a single compliance issue over the course of a combined 24 inspections in India. Another inspector found zero compliance issues in 20 out of 23 inspections (85 percent) in China while finding compliance issues with almost half of domestic inspections during the same period. These are unusual inspection outcomes, the opposite of what would be expected given the widely reported failures in quality control and lack of adherence to current good manufacturing techniques by drug manufacturing facilities in China and India.[1]

By contrast, 16 FDA inspectors, with over 325 inspections collectively in India, found compliance issues during every inspection they conducted. As a measure of what a pattern of rigorous inspections should look like, the Committee reviewed the inspection outcomes for 3 FDA

[1] Protecting American Health Security: Oversight of Shortcomings in the FDA's Foreign Drug Inspection Program: Hearing before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, 118th Cong. (2024) (Testimony of Dr. Mary Denigan-Macauley, Director of Public Health, Government Accountability Office).

inspectors with a professional reputation for thoroughness who also had at least 10 inspections in China or India during the studied time period. These expert inspectors reported finding no compliance issues during inspections in China at a rate of only 6.7 to 11.4 percent and at a rate of zero to 9.5 percent in India.

Such large variations in inspection outcomes are troubling, and they merit further investigation. At a minimum, the Committee is concerned that these findings suggest vast differences in the skill, thoroughness, and competence of FDA inspectors. The difference in inspection outcomes appears to be just another example of institutional weaknesses and dysfunction in the FDA's foreign drug inspection program.[2] Prior to the pandemic, media reporting found that some FDA inspectors took an inappropriately lenient approach with foreign drug manufacturers with serious compliance violations.[3] There were also reports of, and concerns about, foreign manufacturers attempting to bribe or improperly influence inspectors.[4] The Committee is seriously evaluating the disturbing possibility that some of the variation in inspection outcomes could be the result of bribery or fraud.

As the Committee with jurisdiction over the regulation of drugs and biologics, the Committee needs to understand fully the cause of the institutional weaknesses in the FDA's foreign inspection program in order to respond appropriately. Accordingly, to assist the Committee in our oversight, please respond to the following questions and requests for information by July 8, 2024:

1. Records (including attachments to the Establishment Inspection Reports) of all inspections conducted in India and China from January 2021 to April 2024 by the FDA inspectors listed in the attached non-public document. The listed inspectors are those individuals who have conducted at least ten inspections in India or China and who reported no compliance issues in 70 percent or more of their inspections in India or in 50 percent or more of their inspections in China.

2. Copies of all FDA policy and guidance documents related to the conduct of foreign inspections, including any anti-bribery or gratuity training material, program integrity materials, and performance evaluation metrics for inspectors.

3. Copies of all FDA policy and guidance documents related to any data analytics used to evaluate foreign inspection outcomes and trends.

4. Explain in detail the process for selecting FDA inspectors sent to conduct foreign inspections in China and India, including decisions to send teams of inspectors versus solo

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[2] 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; U.S. GOV'T ACCOUNTABILITY OFFICE, GAO/HEHS-98-21, Food and Drug Administration: Improvements Needed in the Foreign Drug Inspection Program (1998), https://www.gao.gov/assets/hehs-98-21.pdf.
[3] Katherine Eban, *Bottle of Lies: The Inside Story of the Generic Drug Boom* (2019).
[4] *Id.*

inspectors. In addition, provide copies of all relevant policy and guidance documents. For the last 10 years, please provide a list of all inspections in China and India that only involved one inspector, including the name and position of the inspector, the name of the firm, the product under review, the recommended action, and date of inspection.

5. Explain in detail any background checks or periodic personnel reviews of foreign inspectors conducted by the FDA and provide copies of all relevant policy and guidance documents.

6. Explain in detail the FDA's policy or practice of issuing import alerts for facilities in India and China that refuse to allow an inspection by the FDA. As part of the response, explain in detail how a facility could be placed on import alert for failing to follow current good manufacturing processes (cGMP) without FDA conducting an onsite inspection.

7. Explain in detail why the number of routine inspections in India and China remain down 38 and 64 percent respectively from their 2019 levels. Explain how FDA plans on increasing the number of routine inspections in these countries.

8. The Committee is concerned that FDA's fear of triggering additional drug shortages is driving the decreased rate that FDA issues warning letters and Other Action Indicated (OAI) classifications to facilities in the Asia Pacific region as compared to pre-pandemic. For example, in 2019, 15.9 percent of "for-cause" inspections resulted in a warning letter. In 2023, the rate was only 4.4 percent. In 2019, 39.7 percent of "for-cause" inspections resulted in an OAI classification. In 2023, that rate was only 17.8 percent.

   Explain in detail the FDA's understanding for why the rates of Warning Letters and OAI classification for facilities in Asia Pacific China and India have dropped since the COVID-19 pandemic. As part of the agency's response, please identify the number of inspections where the initial findings of an inspector were downgraded by FDA personnel who were not present for the inspection.

9. Explain in detail the FDA's plans for retaining and expanding the number of inspectors available to conduct foreign inspections. Include in the response information on any plans to utilize the FDA's Title 42 salary authority or other financial incentives.

10. Explain in detail the role of the FDA's Office of Criminal Investigations (OCI) and the FDA's Office of Internal Affairs (OIA) in protecting the integrity of FDA's foreign inspection program. Include in the response, the number of investigators assigned to the foreign inspection program, a list of all civil or criminal prosecutions related to the FDA's foreign inspection program, and whether the FDA's OCI would investigate allegations of bribery involving a firm or a firm's agent, or whether the FDA OIA would investigate allegations of bribery involving FDA personnel, related to a foreign inspection.

In addition to the above questions, please provide answers to the following outstanding questions and document requests from the Committee's July 18, 2023, letter:

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

2. In the last 10 years, for each year, what percentage 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*

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

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

5. 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.

6. 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.

7. 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.[5] 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.

[5] 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.

It is important for the Committee to understand exactly how and when the FDA was made aware of Intas' plans to halt voluntarily 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 halt voluntarily production at the Ahmedabad plant closure.

*Inspections in China*

8. 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.

9. 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?

    - **Additional follow-up:** Does the FDA notify the State Department in advance when FDA personnel are going into China?

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

    - **Additional follow-up:** Does the FDA get information from foreign agency counterparts about potential difficulties or safety issues related to certain Chinese drug firms? If not, why not?

11. Provide copies of all communications between the FDA or any other federal agency or federal official on behalf of FDA, and the Government of China regarding in-person inspections of drug manufacturing facilities in China from January 2020 to the present.

12. 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.

13. 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.

14. 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 a federal criminal violation under 18 U.S.C. §1001. In addition, the Committee believes that interviews with FDA officials and employees about this matter may be

necessary. Finally, in the event that the FDA fails to begin production of the requested documents by the deadline specified above, the Committee will consider utilizing compulsory process given the importance of protecting the health and safety of the American people.

If you have any questions, please contact the Committee on Energy and Commerce Majority staff at (202) 225-3641. Thank you for your attention to this request.

Sincerely,

Cathy McMorris Rodgers
Chair
Committee on Energy and Commerce

H. Morgan Griffith
Chair
Subcommittee on Oversight and Investigations

Brett Guthrie
Chair
Subcommittee on Health

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