Verbal Remarks - Dinesh S Thakur at the Hearing of the Subcommittee on Oversight and Investigations of the United States House Committee on Energy and Commerce

On

Protecting American Health Security: Oversight of Shortcomings in the FDA's Foreign Drug Inspection Program

Chairman Griffith, Ranking Member Castor and distinguished members of the Subcommittee, I thank you for convening this hearing on a topic which impacts each and every one of us and for giving me the opportunity to appear before you today. My name is Dinesh Thakur, I am here to offer my testimony on the effectiveness of the Foreign Inspection Program of the US Food & Drug Administration (US FDA).

My background and training are documented in my written statement. I was the whistleblower in the prosecution of a generic drug company by the US DOJ in May 2013, where Ranbaxy pled guilty to seven counts of criminal felony and agreed to pay penalties of $500 million to the US DOJ[1].

While I have made substantive recommendations in my written statement which I have submitted to this Subcommittee, I would beg your indulgence today to let me provide some concrete examples of the issues which I refer to in my statement. I have intentionally picked examples that are not technical; I have a whole stack of these investigation reports here that have much more damning data which requires a chemist to understand and interpret. I am happy to hand over this stack to the subcommittee.

In July, 2014, US FDA inspectors Peter Baker and Joanne King inspected a pharmaceutical manufacturer in India which makes medicines that treat hypertension including **Metoprolol Tartrate and Furosemide**. In their inspection report, which is called Form 483, the inspectors made the following observation:

- Our review of the QC data package found that the **raw data files had been manipulated** ...
- **Result was deleted** from the system and was not available for review
- We observed two different analysts actively **backdating/falsifying** "Temperature" record logbooks. Upon questioning, one of the analysts stated that **she had been "forced" to falsify the record** by her direct supervisor.

[1] https://www.justice.gov/opa/pr/generic-drug-manufacturer-ranbaxy-pleads-guilty-and-agrees-pay-500-million-resolve-false

A few months later, in October 2014, investigators Peter Baker and Dipesh Shah made the following observations upon inspecting another facility of the same manufacturer.

- We noted what appears to be the laboratory practice of **overwriting and deleting raw data** files.
- During our review of your firm's electronic FTIR data, we noted **duplicate results** for the same sample. Our review of the QC data package found that the **original result was not included/reported...**
- During our walk-through inspection of your manufacturing unit, we identified **partially shredded Training Evaluation Forms for multiple operators** that had been completed and signed on 09/23/2014.

Five years go by. In August 2019, investigators Arsen Karapetyan and Pratik Upadhaya go back to inspect the same manufacturer. They record the following observations in their inspection report (Form 483):

- The firm **compromised the integrity of OOS investigation by changing the HPLC system**..... A **repeat analysis** was performed .... That resulted in a **passing test**.
- Your firm's quality unit allows the **destruction of draft and interim lab investigation** reports using **shredders** maintained in your Quality Assurance area. The Logbook maintained for controlling the destruction of documents showed several entries pertaining to **destruction of interim investigation reports.**
- It is observed that the recycle bin is available without restriction to all production operators during real time compression activities.

Five years between the two sets of inspections and the investigators find and document more egregious behavior.

Let me give you another example. Last year, we had a shortage of drug used to treat cancer, Cisplatin. The manufacturer of this particular drug, an India based company was inspected in July 2023, last year. These are the observations made by the investigators on Form 483:

- Our investigators observed **plastic bags and torn and discarded original cGMP documents** in your Quality Control **scrap area under a stairwell**, in your general parental scrap room, and **on a truck outside your facility**.

- An analyst destroyed cGMP records by **pouring acetic acid in the trash bin** containing analytical balance slips for testing of ... A QC employee stated he observed the same analyst destroy KF titration curves and balance print outs.

In November of last year, not that long ago, US FDA investigators made the following observations on their Form 483 after conducting an inspection of this same manufacturer's facilities.

- Since 2001, **visual inspectors manipulated particle and other defect counts** on manual visual inspection records "**to keep the category wise rejection within limits to avoid a deviation and investigation**"

Two more quick examples and then I will stop with these.

In November 2023, investigators Pratik Upadhaya and Saleem Akhtar made the following observation on Form 483 during an inspection of another company, NATCO Pharma in India

Upon putting together some of the torn pieces of documents with the help of your employees, your quality unit management stated that the torn pieces belonged to an original record, raw data and meta data....

This is back from back in 2014, but it is for one of the largest manufacturer of generic drugs for the US market from India. Investigators Peter Baker, Dipesh Shah and Dr Carmelo Rosa signed this Form 483 which states:

The presence of the ____ laboratory facility ("CQC") was only discovered during our review of the HPLC audit trials on 11/20/2014, which introduced a significant delay in our ability to perform a comprehensive review of the electronic cGMP chromatography data. No explanation was provided regarding the failure to facilitate the review of cGMP data collected within the "CQC" laboratory.

On 11/17/2014, **numerous bags described as waste material** was observed in your firm's waste area containing **copies of issued/unused batch records, raw data, analytical results**, stability summary reports and controlled documents.

Five retests were conducted obtaining passing results, which led to your conclusion that the final result (**5th of the 5 retest** injection results) would be final **reported results**.

Imagine if this behavior was observed and documented at a financial services firm. That records demonstrating illegal behavior were destroyed by pouring acid into the waste bin. In my brief tenure at Ranbaxy back in 2014, I was told that the company had a "steam-room"; where freshly minted documents asked by the US investigators would be aged over night to appear look like old documents before handing them over to the investigators the following day. Could you imagine making Enron pay a large fine, which is akin to what the US FDA does with an import alert and let both Ken Lay and Jeff Skilling go scott-free? That is precisely what we are doing today.

And then we wonder why these erring pharma manufacturers don't learn. Why the US FDA inspectors continue to observe and document this same fraudulent behavior year after year. It has become cost of doing business for foreign manufacturers. Putting the lives of US patients at risk has become acceptable to these foreign manufacturers because there is no fear of individual prosecution.

As the statement of my co-panelist from the GAO notes, in 2022, the US FDA inspected 6% of approximately 2800 foreign manufacturers, and if you look closely at the facilities in India, that number is even smaller, just 3%. Yes, it was that small because of the challenges to international travel during the Covid Pandemic. But is that acceptable?

In my written statement submitted to the subcommittee, I have made three recommendations for you to consider.

A. **Mandatory end-user testing:** We have accepted as Gospel that once a pharma manufacturer secures a market authorization from the US FDA, its generic drug formulations can interchangbly be used to treat patients. There is a lot of anecdotal data today that this is not true. There is significant batch to batch variability for the same formulation. Patients notice it, bring it up to their doctor only to be told its all in their head. Why? Because the US FDA approved the formulation. Well, we need an independent assessment of how true this is. The DOD pilot will give us an initial assessment soon. In April. But we need a legal a legal mandate to put in place a mandatory testing program for all drugs entering the United States from countries where past inspections have demonstrated a consistent pattern of data fraud and GMP violations.

B. **Criminal prosecution to introduce a deterrent effect:** The second, is to investigate the US FDA's prosecution practices when its drug inspectors discover brazen criminality during foreign inspections.

In the last 18 years, in addition to Ranbaxy, I know of only one Indian pharmaceutical company being fined $50 million[2,3] for destroying critical quality related data - such data is at the heart of the GMP model of regulation adopted by the US to monitor quality manufacturing practices in the pharmaceutical industry. The European Union employs a model where a Qualified Person (QPPV)[4] needs to be the resident of the EU and be accountable for drug safety and is therefore amenable to prosecution if gross violations of EU laws are discovered. The Subcommittee should consider such a model where an officer of the foreign manufacturing company needs to be a resident of the US and is therefore accountable for our drug quality and gross violations of the US regulatory code. I would request the Committee to summon data on criminal prosecutions from the US FDA specifically in relation to its foreign inspection program.

C. **A bilateral solution:** Lastly, this issue needs to be escalated at the diplomatic level between the US and India. We need the Indian Government to assure us that such blatantly criminal behavior cannot continue under its oversight. The US spends billions of dollars buying drugs from India every year. As a customer and an strategic ally, the United States is in a strong position to demand that it receive quality drugs from Indian manufacturing facilities.

I thank you again, Chairman Griffith, Ranking member Castor and all the other members of this subcommittee for this opportunity to appear before you and offer this testimony. I am happy to answer any questions you may have.

[2] https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/press-releases/indian-cancer-drug-manufacturer-pay-50-million-concealing-and-destroying-records-advance-fda
[3] https://www.bloomberg.com/news/features/2019-02-01/the-4-3-billion-deal-that-blew-up-over-shoddy-drug-production
[4] https://www.gov.uk/guidance/guidance-on-qualified-person-responsible-for-pharmacovigilance-qppv-including-pharmacovigilance-system-master-files-psmf