03 JAN 2021

Mr. Henry J. Kerner
Special Counsel
US Office of Special Counsel
1730 M St, NW, Suite 300
Washington DC 20036
USA

Re: Comments regarding OSC case DI-019-0931

Dear Mr. Kerner,

In OSC case DI-019-0931, I raised specific concerns that on numerous occasions, the US Food & Drug Administration Agency (hereafter referred to as 'the Agency' or 'FDA') failed to uphold its mission due to gross mismanagement, which led to substantial and specific dangers to public health and safety. OSC formulated questions based on my complaint and submitted questions to the Secretary of the Department of Health and Human Services on 07 FEB 2019. The Agency responded to these questions on 24 JUN 2019. Please find my comments regarding the US Food & Drug Administration's responses to my allegations below.

Unfortunately, OSC refused to share the questions sent to the FDA in their communication of 07 FEB 2019. Had OSC shared these questions prior to issuance, I would have reiterated that the focus of my concerns was the Agency's failure to uphold its mission, namely, to protect and promote the public health. I believe that by focusing on narrow procedural issues, OSC unintentionally subverted the investigation from one of substance into one of procedure.

I will divide my comments into two parts, the first part dealing with OSC's apparent questions regarding the Agency's procedures. The second part will deal with the Agency's gross mismanagement and implementation of policies that present a substantial and specific danger to public health and safety. The Agency's response is egregiously silent with regards to these allegations.

1. National Genetics Institute (FEI 3002082450) – 10-19 JAN 2017

   - Procedural Issues

     The Agency states that a reclassification memo was not required. I do not contest their statement. However, regarding procedural issues, the Agency, per its admission, only reclassified the inspection seven months after the Official Action Indicated (OAI) recommendation.

   - Gross Mismanagement / Danger to Public Health

     National Genetics Institute is responsible for testing plasma to determine if plasma used for biological drug products contains Hepatitis B, Hepatitis C, or human immunodeficiency (HIV) viruses. The firm uses various molecular biological methods to make this assessment. The firm's "product," in this case, is a positive or negative test result. The inspection determined that test results were unreliable due to the multiple systems employed that did not have provisions for data integrity. The firm even instructed analysts to modify raw data. Should analysts incorrectly modify raw data, plasma contaminated with a lethal virus could be used for drug products administered to patients. The Compliance Officer assigned to this case did not have experience or training in molecular biology or data integrity. I contacted the Compliance Officer and made multiple requests to explain how the data could be manipulated and the resulting implications, which I documented in the complaint. I also prepared an Untitled Letter for her use, which was also shared with OSC as part of my complaint. As noted by the Agency, no reclassification memo was issued. As such, there is no objective information describing the reasons the Compliance Officer and Staff Director downgraded this OAI case.

     It is important to note that an OAI recommendation indicates that there is potential for a negative impact on public health. Had the OAI recommendation been upheld, there could have been significant scrutiny into why a substantial public health issue had taken so long to adjudicate.

     Finally, I asked the Staff Director to perform the subsequent inspection in Q1 FY 2019. I explained that it would result in significant savings to the government since the site was 3 miles from my home and would allow me to follow up to determine if the corrections promised had been adequately implemented. Instead, the Staff Director showed fiscal and professional irresponsibility and sent me to inspect a facility in San Diego while simultaneously traveling another Investigator from Seattle to do the Q1 FY 2019 inspection at NGI. I documented this series of events in the initial complaint. Neither the Staff Director nor the Investigator tasked with the re-inspection has training or experience in Molecular Biology or Data Integrity.

2. Baxalta (FEI 3003282293) – 12-26 MAR 2018

   - Procedural Issues

     The Agency provided the (reclassification) Memo to File as part of their response. My review of the Compliance Management System before submitting my complaint in

November 2018 did not uncover this document. The request I sent to the Staff Director regarding this document went unanswered. The 68-page Establishment Inspection Report was issued 13 business days after the inspection. As noted in the Memo to File, the Compliance Officer and Staff Director downgraded the OAI classification six months later.

- Gross Mismanagement / Danger to Public Health
  The inspection uncovered 12 significant inspectional observations and ten discussion points documented in the Form FDA 483 "Inspectional Observations" and Establishment Inspection Report (EIR), provided as part of the initial complaint. The most significant inspectional observation was the failure of a batch that had already been released to patients to maintain its potency throughout the product's shelf life. The firm had averaged Out of Specification (OOS) results and retested product into compliance, a practice explicitly proscribed in FDA's guidance "Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Production," written to help firms correctly interpret the requirements of 21 CFR 211. Although the firm determined that 10 out of 27 samples (approximately 37% of samples) failed to meet the potency requirements in their license, the firm did not notify FDA of these failures per the requirements of 21 CFR 600.14 and had not followed the conditions of their license in this respect, breaching 21 CFR 601.12(b).

  The firm claimed that the method's high variability led to high variability in test results; however, the evidence provided as part of their Biological License Application (BLA) indicated that their test results were robust and had significantly lower variability. The previous inspection, conducted in February 2016, noted the same inspectional observation. The firm had failed to correct the observation as promised in their previous response to the Agency.

  The inspectional team reviewed Baxalta's responses to the Inspectional Observations and issued a memo to the Compliance Officer on 01 MAY 2018; I provided this memo of the initial complaint. We concluded that:

  > "…the response does not increase our level of confidence in the site to remediate all the inspectional observations we found. In some cases, the firm does not portray our observations factually … Other responses do not provide enough information to adequately determine if their course of action will correct the issues we discovered … Finally, we have determined that the firm's responses … are inadequate … Taken together, the overwhelming impression we get from the firm's responses is that they do not, either through ignorance or will, understand the potential significance of the observations with respect to patient impact."

  I contacted the Compliance Officer in July 2018, asking him if the case had progressed. In an email sent on 31 JUL 2018, the Compliance Officer informed me that he had drafted an Untitled Letter in May and was still waiting to get comments back from the Staff Director and the Deputy Director of the Office of Biological Products Operations (OBPO). I provided this email in the initial complaint. Four months after the Compliance Officer drafted the Untitled Letter, the Staff Director asked him to issue the reclassification memo. The reclassification memo reiterates

Baxalta's responses to the inspectional observations, the same responses that all three Investigators had previously determined were inadequate.

This case, initially classified as OAI, indicated a significant potential for a negative impact on public health. Had the OAI recommendation been upheld, there could have been considerable scrutiny into why a significant public health issue had taken so long to adjudicate.

3. CSL Behring GmBH (FEI 3003098680)

- Procedural Issues

  The Agency's response included the EIR cover page, issued on 14 JUN 2018, and a reclassification memo issued by CBER's Biological Drug and Device Compliance Branch of the Office of Compliance and Biologics Quality. CBER issued the reclassification memo on 13 JUL 2018. My review of the Agency's Compliance Management System prior to sending my complaint did not uncover this reclassification memo. Similarly, my email request to the Staff Director, sent on 20 Sep 2018, requesting further information about the issuance of a reclassification memo for this inspection went unanswered. I included this email in my initial complaint.

  The Staff Director's rapid decision making (7 calendar days) stands in direct contrast with her performance in the other cases in this complaint. In all cases where she took significantly more time, she downgraded the initial classification.

- Danger to Public Health

  The inspection at CSL Behring GmBH was conducted by myself, another Team Biologics Investigator, and a CBER Senior Staff Fellow. During the inspection, we uncovered, amongst other violations, the systematic contamination of Water for Injection manufactured at the site with Silicone Oil. The firm had known about this contamination for approximately ten years. It had done nothing to investigate the concentration of the adulterant, the proportion of vials in a lot that could be affected by the impurity, and most importantly, the potential effect the contaminant could have on patient health/product quality. This issue was the most significant of a 13-item, 14-page Form FDA 483 "Inspectional Observations" issued to the firm listing all the significant deviations from Good Manufacturing Practice regulations that the Agency has jurisdiction over and is responsible for enforcement. After the inspection, the entire inspection team, including the CBER Senior Staff Fellow, agreed that this inspection should be classified as Official Action Indicated. ORA sent this recommendation to CBER.

  CBER's response in the reclassification letter states:

  > "We determined that the observations were less than what would normally result in an OAI inspection classification."

CBER does not state in the memo what exactly they meant by "less than what would normally result in an OAI inspection classification." It is unclear if 20 years of manufacturing adulterated products would have been more persuasive or if an additional 13 observations would have somehow convinced them that the OAI classification was justified.

Furthermore, CBER notes in the memo that two of the responses made by the firm were inadequate.

Without a specific and objective discussion describing how the Biological Drug and Device Compliance Branch made their decision, this memo, which could have been used as a tool for better communication between CBER and ORA, is of minimal value. The Agency has a duty to make public health decisions based on objective criteria; there is no evidence that the Agency made this decision objectively.

4. Merck Sharp and Dohme (FEI 3006525584) – 22 – 30 OCT 2018

- Procedural Issues
  While the FDA did not specify the procedural issues mentioned in their response, the initial complaint filed with OSC included the following issues:

  - The inspection was inadequately resourced, with insufficient staffing and time dedicated to this inspection.
  - The Staff Director did not provide the letter from the Merck whistleblower promptly.
  - I was not given sufficient training on handling a Confidential Informant.

  FDA responded:

  > "In the inspection of Merck Sharp and Dohme, Complainant was provided support from ORA management in the form of an inspection plan specifically designed by ORA management to direct Complainant on critical areas to review and evidence to collect to narrow the focus of his inspection and attempt to substantiate the CI's [Confidential Informant] complaint. Complainant himself was unable to corroborate the information provided by the CI."

  This response does not address any of the procedural points above and additionally is patently false on its face. As with the responses to the other cases, the FDA completely disregards its responsibility and stated mission to protect the public health.

  Inspection Resources - Even before the inspection began, I sent an email to the Staff Director, noting that Merck produced both Active Pharmaceutical Ingredients and Finished Vaccines in a facility that covered over 850,000 sq. ft. In my email, I noted that this was the first time this facility would be inspected by only one Investigator

and asked for 14 days to conduct the inspection by myself. The Staff Director was unmoved and replied:

> Your assigned inspections are all Level 2, which should only include coverage of Quality plus one system. I would think you should be able to conduct a systems based Level 2 inspection in no more than seven days. These firms do not have violative histories.

Since the Staff Director has never actually performed an inspection at a vaccine manufacturing site, her supposition regarding the length of time required to perform an adequate inspection has no basis in reality. Furthermore, after the Staff Director sent me the Confidential Informant's [CI] letter, she widened the scope of the inspection but did not give me any further resources to conduct this already inadequately resourced inspection, despite my urgent request:

> I believe that we're talking about a criminal case at this stage and I want to move forward as expeditiously as possible. He [the CI] wants to sit down and talk. I told him that it's our procedure to have two people present so that one person can engage him and the other scribe the details of the conversation, in line with the IOM.
>
> I have been in touch with Susan and Deb, and they're both available and interested in helping. I am requesting that Deb with her understanding of criminal cases, and Susan having been at the firm recently join me ASAP to ensure a successful outcome for patients worldwide and for the Agency. Once they're here, I'll be able to focus on the CI and data integrity issues. I want to emphasize that we still have time for them to get them here and make a difference.

At 19:55 on 23 OCT 2018, after the second day of the seven-day inspection, the Staff Director responded:

> I have talked with --- and --- [the Staff Director's supervisors] about the issue and we all feel that additional CSOs onsite will not be necessary and that you are capable of following up on this complaint with [offsite] support from Helen and I.

On 24 OCT 2018, the third day of the inspection, the Staff Director held a meeting at 08:00 to share an inspection plan, the only support that she offered throughout this inspection. By increasing the inspection scope without increasing the resources available, she and her supervisors failed to adequately support this inspection.

That evening at 22:57, I put in one final plea for adequate resourcing of this inspection, noting that a similar case had included four investigators and 21 inspectional days:

> Dear [redacted]
>
> I just got off the phone with the CI to ask for some clarifications about EM procedures and processes he has seen/heard about. He was very helpful and he reminded me that he is willing to go on the record and that people who have worked at Merck in the past are also willing to go on the record to corroborate the issues he's identified

(and others). He also reminded me that people currently working at Merck are willing to corroborate his version of the events in his letter.

He also let me know that:

1. They have removed the biohazard garbage (see attached picture) so I am blocked as to being able to ask further on this point

2. He heard that apparently Justin was looking in the shred bins during his inspection in Virginia (which fits Justin's MO). As a result, the shredding service came at 06:45 this morning to empty the site's shred bins; he noted that they never come to the site this early, so I am blocked from pursuing this avenue of review as well.

If I had any question before this, I now fully believe that this firm is not interested in pursuing corrective actions and not interested in pursuing manufacture of quality product. They are interested in hiding things from us and now, with the disappearance of one definite source and one potential source of valuable information gone, it appears that they have been successful.

I fully appreciate that we have to accomplish the workplan to fulfill our mission to protect and promote the Public Health, however, I wonder if somewhere along the line we've forgotten that the workplan is a means to an end, not the end goal itself.

Please consider the below as an example of how OPQO [the Office of Pharmaceutical Quality Operations] handled an inspection related to CIs (which I happened to receive in my inbox today). My pleas for resources seem insignificant when compared to the 4 investigators and 21 investigational days that were allotted for the Akorn inspection.

If there are to be any changes to the inspectional team / inspection duration and / or if you want me to pursue affidavits or a visit to the garment service provider please let me know.

[redacted]

After business hours on 25 OCT 2018, the fourth day of the inspection, the Staff Director responded to this email. She denied my request for additional staffing or an extension of the inspection a third time.

Handling of CI Letter –CBER's Biological Drug and Device Compliance Branch received the CI's letter on 13 SEP 2018. It was in OBPO personnel's hands, including the Director, the Deputy Director, the Program Division Director, and the Staff Director on or before 11 OCT 2018. Although the Staff Director was fully aware of my inspection schedule, she did not provide the letter to me until the end of the first day of the inspection, on 22 OCT 2018. She did not involve OBPO compliance before the inspection, and this delayed handoff prevented me from adequately preparing for the inspection.

The CI's letter, dated 31 AUG 2018, noted that this was his second letter; he included a copy of the first letter he prepared on 01 JAN 2016. Although received by the FDA, the first letter was never given to the inspection team that performed the previous inspection in November 2016. FDA's records state, however, that the complaint associated with this letter had been closed.

Whistleblowers/Confidential Informants risk their jobs/livelihood and place their trust in the FDA to enforce regulations that protect the public health. The mishandling of two CI letters for the same facility is unconscionable and represents gross mismanagement.

Training on Handling a Confidential Informant – This was my first case handling a Confidential Informant (CI). I followed the instructions in Investigations Operations Manual (IOM) to the best of my ability and prepared an affidavit based on the information the CI related through his letter and our discussions. Since my request for additional investigators from Team Biologics was rebuffed, I contacted the Raleigh, NC Resident Post. I spoke with the Supervisory Consumer Safety Officer (SCSO) stationed in Raleigh to ask if he could provide me with an additional Investigator to work on the affidavit together, in line with the IOM. The SCSO rebuffed my request. I attached the draft Affidavit to my OSC complaint.

Throughout the inspection, I tried to be conscious of the CI's anonymity by not revealing everything shared with me in the CI's letter. I was given no support in determining what to include within the Form FDA 483 "Inspectional Observations" and what would constitute a danger to the CI's anonymity and livelihood. As a result, and since I had not seen the Biohazard Waste Bin (the firm removed it before I entered the gowning area), I chose to omit the presence of the Biohazard Waste Bin as an observation. Instead, I noted it in the EIR as a discussion point and discussed it further in Attachment 7 to the EIR.

FDA Response – FDA's response states that "an inspection plan specifically designed by ORA management to direct Complainant on critical areas to review and evidence to collect." The inspection plan reflects the Staff Director's lack of experience in performing inspections since numerous points were not implementable. For example, the Staff Director advised me to "Observe gowning (in and out)." However, since I was not qualified to gown into a Grade A or B area, I would not have had access to a gowning room to observe individuals gowning. These areas do not typically have a viewing window to allow individuals to view gowning activities.

The FDA's response continues: "specifically designed by ORA management … to narrow the focus of his inspection". No instruction was given to me that would indicate that the focus of the inspection had somehow narrowed.
Finally, the FDA's response concludes: "Complainant himself was unable to corroborate the information provided by the CI." I include Attachment 7 to the Establishment Inspection Report, entitled "Memo 05 MAR 2019," which details all the points that I had substantiated from the CI's letter, including:

- The presence of a Biohazard Bin where uniforms soiled with Urine, Feces, and Blood were disposed
- The transition of personnel between cleanrooms and non-classified/ mechanical spaces without a gowning change
- Failure to perform work documented in the firm's batch records, with specific reference to environmental/personnel monitoring

As a result, this part of the FDA's response is patently false. As I noted numerous times in the Attachment, I could not substantiate more of the CI's claims due to the lack of resources allocated to this inspection.

- Danger to Public Health

  The Form FDA 483 "Inspectional Observations" that I issued at the end of the inspection contains four observations. The first observation indicates a significant departure from data integrity. Specifically, I determined that personnel monitoring that had been documented as performed, had in fact, not been performed. This observation puts the safety of the batches produced in question.

  Furthermore, although I was able to substantiate a number of the CI's claims, the Staff Director downgraded the inspection to Voluntary Action Indicated and has not followed up with another inspection.

  Merck's facility in Raleigh produces vaccines for some of the most vulnerable populations, including infants/children and elderly people. In line with my responsibilities, I gathered evidence showing significant breaches of Good Manufacturing Practices. Yet, FDA, the agency responsible for enforcement, did absolutely nothing to assure that the Merck facility produces quality products.

Conclusion

Prior to my resignation, I was advised by HHS OCG that I could resign without affecting my permanent record if I were to withdraw the OSC complaint. As I wrote in my letter of resignation:

> My conscience does not allow me to waive the OSC complaint I made in November and I refuse to violate the public trust by rescinding the complaint.

In contrast, the former Staff Director of Team Biologics, who has subsequently been promoted to a Branch Director, noted recently that she had had "sleepless nights" as a result of the potential that her name might appear in one of the news articles recently published about my experiences in the FDA. If only she had had sleepless nights with regards to some of the sites/inspections listed in the complaint, I am confident I would not have needed to file a complaint to begin with.

Through gross mismanagement, the FDA has broken their promise to American consumers and has allowed firms that produce biologic medical products that do not meet the requirements of the Good Manufacturing Practice to continue unfettered.

It has been my hope from the beginning of filing this complaint that the FDA examines its recent practices and the supervisory personnel assigned to Team Biologics to assure that the Agency as a whole is capable of delivering upon its promise to the American consumer, of protecting and promoting the public health. It is my sincere hope that the Agency elects to do this before patients are injured (or worse) by substandard biologic medical products.

Sincerely,