U.S. FOOD & DRUG ADMINISTRATION

June 24, 2019

Mr. Henry J. Kerner
Special Counsel
U.S. Office of Special Counsel
1730 M Street, N.W., Suite 300
Washington, D.C. 20036-4505

Re: OSC File No. DI-19-0931

Dear Mr. Kerner:

Please accept this letter and the enclosed Report of Investigation (ROI) as the Department of Health and Human Services' response to your February 7, 2019 correspondence, in which your office referred for investigation several allegations of improprieties in inspection activities in the Food and Drug Administration, Office of Regulatory Affairs (ORA). Specifically, the Office of Special Counsel requested that the agency investigate the following:

- The inspection conclusion report for the 2017 National Genetics Institute inspection (FEI 3002082450) was designated as Official Action Indicated (OAI) and was subsequently reclassified as Voluntary Action Indicated (VAI) without a reclassification memorandum;
- The inspection conclusion report for the 2018 Baxalta US, Inc. inspection (FEI 3003282293) determined that the case should be considered OAI, with a recommended Untitled Letter. This was later downgraded to VAI without a reclassification memorandum;
- The inspection conclusion report for the 2018 CSL Behrin GmBH inspection was entered as OAI and was subsequently downgraded to VAI without a reclassification memorandum; and
- During the 2018 inspection of Merck Sharpe and Dohme (FEI 3006525584), the complainant discovered evidence that the company was intentionally destroying evidence of possible violations, which was confirmed by a Confidential Informant. The complainant asserted that FDA procedures for responding to the receipt of this information were not followed.

Pursuant to your letter, ORA investigated the allegations and the findings of the investigation are set forth in the enclosed ROI. A legend is included to identify the specific parties involved.

In summary, the results of ORA's investigation revealed that in the three (3) inspections where improper reclassification was alleged, the reclassifications were conducted in compliance with governing procedures. In the fourth allegation, the complainant

received instruction and support from ORA management throughout the course of the inspection but was unable to substantiate the information provided by the confidential informant. Please note that this matter involves information received from a confidential informant that should not be publicly released. FDA will be happy to work with OSC to identify appropriate redactions if OSC plans to transmit the report and its attachments to either Congress or the public.

If you have any further questions, please do not hesitate to contact my office at (240) 402-7562.

Sincerely,

Glenda F. Barfell

Glenda F. Barfell
Director, Office of Management
Office of Regulatory Affairs

Subject: Investigation of Allegation of Violations of Law and Gross Mismanagement under 5 U.S. Code § 1213; OSC File No. DI-19-0931

This report summarizes the findings of an investigation conducted by the US Food and Drug Administration (FDA), Office of Regulatory Affairs, into the allegations made by Complainant. These allegations were detailed in a February 7, 2019 letter from the US Office of Special Counsel.

FINDINGS:

The allegations of improper downgrading of inspection conclusion reports without the filing of classification memoranda was investigated for inspections at National Genetics Institute, Baxalta US, Inc. and CSL Behring GmBH. The facts show that the reclassification from Official Action Indicated (OAI) to Voluntary Action Indicated (VAI) in each case was conducted per governing procedures.

In addition, the information provided by the confidential informant could not be verified by the complainant during the inspection of Merck Sharp and Dohme. Therefore, there is no merit to these allegations.

ALLEGATIONS:

The allegations are as follows:

Complainant disclosed that Team Biologics Manager improperly downgraded several inspection conclusion reports without filing reclassification memoranda, as required in Food Drug Administration's Regulatory Procedures Manual. The allegations to be investigated include:

- The inspection conclusion report for the 2017 National Genetics Institute inspection (FEI 3002082450) was designated as Official Action Indicated (OAI) and was subsequently reclassified as Voluntary Action Indicated (VAI) without a reclassification memorandum;
- The inspection conclusion report for the 2018 Baxalta US, Inc. inspection (FEI 3003282293) determined that the case should be considered OAI, with a recommended Untitled Letter. This was later downgraded to VAI without a reclassification memorandum;
- The inspection conclusion report for the 2018 CSL Behring GmBH inspection was entered as OAI and subsequently downgraded to VAI without a reclassification memorandum; and

- During the 2018 inspection of Merck Sharpe and Dohme (FEI 3006525584), the complainant discovered evidence that the company was intentionally destroying evidence of possible violations, which was confirmed by a confidential informant. The complainant asserted that FDA procedures for responding to the receipt of this information were not followed.

BACKGROUND:

The U.S. FDA's Office of Regulatory Affairs (ORA) is the FDA inspectorate and the lead office for all agency field activities. ORA inspects regulated products and manufacturers, conducts sample analyses of regulated products and reviews imported products offered for entry into the United States.

The Office of Biological Products Operations (OBPO) consists of a specialized workforce within ORA that conducts inspections, investigations, and compliance activities for blood and tissue products as well as vaccines and other biological products regulated by the FDA's Center for Biologics Evaluation and Research (CBER). CBER (referred to below as "Center") is the Center within FDA that regulates biological products for human use under applicable federal laws, including the Public Health Service Act and the Federal Food, Drug and Cosmetic Act.

Team Biologics Staff (TBS) is a team of specialized investigators within OBPO. They conduct current Good Manufacturing Practice (cGMP) inspections of manufacturers of biological products. In the period covered by the allegations, TBS conducted both investigations and compliance activities. Team Biologics Manager was the TBS Director during that time. Complainant was formerly an Investigator/Consumer Safety Officer (CSO) in the TBS. He has since resigned from federal service.

INSPECTIONS AND INSPECTION CLASSIFICATIONS:

OBPO investigators perform regulatory oversight of the biologics industry by conducting surveillance cGMP inspections of regulated biologics establishments. If an Investigator/CSO identifies objectionable conditions in the firm, they issue to the firm a Form FDA 483 containing inspectional observations. Per ORA's Investigations Operations Manual (IOM) Chapter 5 (5.11.2), the Investigator summarizes inspectional findings in an Establishment Inspection Report (EIR) and recommends an inspection classification which is reviewed by their supervisor who in turn may refer the recommendation to the OBPO compliance group and/or CBER. The supervisor, compliance group and/or CBER may have a role in reclassifying the inspection. Any such reclassification is based on a consideration of several factors including the inspectional findings and the response of the firm to the Form FDA 483 observations.

An inspection may receive a final classification of No Action Indicated (NAI), Voluntary Action Indicated (VAI) or Official Action Indicated (OAI). OBPO makes the final classification decision for all domestic inspections. The Center makes the final classification decision for all foreign inspections. The attached Field Management

Directive (FMD) No. 86 provides information on inspection classifications. As stated in FMD No. 86, the ORA Investigations Branch (IB) recommends an advisory action, but the Compliance Branch evaluates the IB referral and takes the appropriate action. The Center serves as the Compliance Branch for all foreign inspections.

During the time covered by the allegations, neither the Regulatory Procedures Manual (RPM), Chapter 4, nor other FDA policy, required the issuance of an inspection reclassification memorandum when ORA downgraded an inspection.[1] As noted below, however, in the case of Baxalta US, Inc, a memorandum was included in the administrative file. In December 2018, OBPO issued a Standard Operating Procedure that provides that a Compliance Officer "will document the rationale for not undertaking the proposed regulatory action or for changing the proposed classification within 30 working days of receipt of the Establishment Inspection Report (EIR) and supporting documentation…" (See attached SOP "Compliance Branch Evaluation of Investigations Branch Recommendations, 6.1.2, effective date December 13, 2018). Accordingly, consistent with the SOP, OBPO instructs its Compliance Officers to prepare memoranda in cases, such as those that are referenced in the allegations, where classification recommendations are changed.

ASSESSMENT OF ALLEGATIONS:

1. **Complainant alleged Team Biologics Manager improperly downgraded several inspection conclusion reports without filing reclassification memoranda, as required in FDA's Regulatory Procedures Manual.**

   - National Genetics Institute (FEI 3002082450):

   A surveillance inspection of National Genetics Institute, located in Los Angeles, CA, was conducted between January 10, 2017 and January 19, 2017 by TBS Investigators, Complainant and TBS Investigator One. The lead investigator, TBS Investigator One recommended an OAI classification for this inspection on March 2, 2017. The Compliance Officer/Acting Director of the Compliance Branch reviewed the case and final classified this inspection as VAI on October 5, 2017, as documented in the FDA's Field Accomplishments Compliance Tracking System (FACTS) Establishment Inspection Report. This reclassification was not addressed in an ORA reclassification memorandum, nor was a memo required.

[1] RPM Chapter 4 provides procedures for developing Warning Letters and Untitled Letters, which could be issued in response to certain inspections, depending on the nature of the findings. Exhibit 4-4-1 of the Chapter provides that, "[t]he Center will also issue a memorandum to the Director of the Compliance Branch that states its reasons for nonconcurrence…" Although the Chapter applies specifically to Warning Letters, in practice, ORA has interpreted the RPM to mean that an inspection classification downgrade by the Center should be accompanied by a memorandum.

- Baxalta US, Inc. (FEI 3003282293):

A surveillance inspection of Baxalta US Inc. was conducted by TBS Investigators, Complainant and TBS Investigator Two, and by OBPO Investigations Branch (IB) Investigator at the firm's Milford, Massachusetts location from March 12 to March 26, 2018. Complainant recommended an OAI classification and this recommendation was endorsed by his supervisor, Team Biologics Manager on April 24, 2018, (See eNSpect Establishment Inspection Report Cover Sheet). The Team Biologics Compliance Officer (retired) reviewed the case and final classified this inspection as VAI on September 18, 2018. This downgrade was endorsed by Team Biologics Compliance Officer's supervisor, Team Biologics Manager on September 18, 2018. The administrative record contains a "Memo to File", dated September 18, 2018, with subject "Change of Classification, EI dated March 12-26, 2018.

- CSL Behring GmBH (FEI 3003098680):

A surveillance inspection of CSL Behring GmbH in Marburg, Germany, was conducted between April 30, 2018 and May 17, 2018 by TBS Investigators, Complainant and TBS Investigator Three, and by CBER Reviewer. The lead investigator, Complainant recommended an OAI inspection classification on June 7, 2018 and this recommendation was endorsed by his supervisor, Team Biologics Manager on June 14, 2018, (See eNSpect Establishment Inspection Report Cover Sheet) after which the inspectional findings were referred to the FDA's Center for Biologics Evaluation and Research (CBER) per FMD No. 86 for final classification. A memorandum signed by CBER Consumer Safety Officer was issued with Subject: "Inspection Reclassification – OAI to VAI". The downgrade memorandum states that "CBER found the firm's response and corrective actions to be generally adequate to prevent recurrence. CBER is re-classifying the inspection to Voluntary Action Indicated (VAI)…"

2. **During the 2018 inspection of Merck Sharp and Dohme (FEI 3006525584), Complainant discovered evidence that the company was intentionally destroying evidence of possible violations, which was confirmed by a Confidential Informant (CI). Complainant asserted that FDA procedures for responding to the receipt of this information were not followed.**

Considering the information provided by the confidential informant, Complainant received specific instructions and support from TBS management and staff throughout the course of the inspection but was personally unable to substantiate the information provided.

CONCLUSION:

Contrary to Complainant's allegation, FDA's Regulatory Procedures Manual (RPM) Chapter 4 does not dictate the issuance of a reclassification memorandum for downgrading an inspection conclusion within ORA. However, the RPM has been interpreted to mean that a reclassification memorandum should be written to the file for non-concurrences by the Center.

Accordingly, a reclassification memorandum was not required for downgrading of domestic inspections at National Genetics Institute and Baxalta. Even so, a reclassification memorandum was generated by the Team Biologics Compliance Officer for the Baxalta inspection and subsequently endorsed by Team Biologics Manager.

There is no reclassification memorandum in the administrative record for the National Genetics Institute inspection. However, the record shows that Compliance Officer/Acting Director of Compliance Branch endorsed a final classification of VAI for this inspection.

In the case of the inspection of CSL Behring in Germany, a reclassification memorandum by the Center was needed, per ORA's interpretation of the RPM. Accordingly, a memorandum was signed by the Center to downgrade the foreign inspection at the CSL Behring GmBH establishment to VAI.

Therefore, the allegation of improper downgrades of several inspection classification recommendations, without documentation in memoranda, is not supported by the facts.

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 complaint. Complainant himself was unable to corroborate the information provided by the CI.

The administrative record was used to conduct this investigation. Complainant was not interviewed due to the sufficiency of the administrative record. Furthermore, Complainant resigned from his position with the federal government effective May 29, 2019 and he now resides in Israel.

INFORMATION ABOUT ACTUAL OR PROJECTED FINANCIAL SAVINGS AS A RESULT OF THE INVESTIGATION:

It is not anticipated that this investigation will result in financial savings as our findings do not indicate the need to enact policy modifications or other changes.