VIA E-MAIL AND UNITED PARCEL SERVICE

Dr. Shivprakash Rathnam
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INDIA

Dear Dr. Rathnam:

This letter addresses significant objectionable conditions observed during the U.S. Food and Drug Administration (FDA) inspection conducted at your firm between November 18 and 22, 2019, by FDA personnel Kara A. Scheibner, Ph.D., and Makini Cobourne-Duval, Ph.D., representing the FDA. In addition, based on significant objectionable conditions observed during the inspection, FDA's own data analyses, and other information, FDA issued a General Correspondence Letter (referred to as "FDA's General Correspondence Letter") to you on March 12, 2021, requesting that you provide specific responses to those concerns indicating in FDA's assessment that you had created falsified data that were submitted to FDA. This letter also addresses your April 10, 2021, response to FDA's General Correspondence Letter.

FDA's Inspection

During FDA's inspection of your firm between November 18 and 22, 2019, FDA reviewed the conduct of the following studies:

- **Study** (b)(4), "(b)(4)

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

[redacted]

- **Study** [redacted]

- **Study** [redacted]

- **Study** [redacted]

- **Study** [redacted]

This inspection was conducted as a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to evaluate the conduct of research to help ensure that the rights, safety, and welfare of human subjects have been protected, and to ensure that the data are scientifically valid and accurate.

At the conclusion of the inspection, FDA personnel raised significant concerns about the validity and reliability of bioequivalence and bioavailability data generated at your firm. We acknowledge receipt of your December 9, 2019, response to the inspection, and of your April 10, 2021, response to FDA's General Correspondence Letter.

Based on our review of the FDA Establishment Inspection Report, the documents submitted with that report, your written response dated December 9, 2019, and your April 10, 2021, response to the significant data validity and reliability concerns raised in FDA's General Correspondence Letter, we conclude that you did not adhere to the applicable statutory requirements and FDA regulations governing the conduct of bioavailability and bioequivalence studies at your firm. We wish to emphasize the following:

You failed to demonstrate that the analytical method used in an *in vivo* bioavailability or bioequivalence study to measure the concentration of the active drug ingredient or therapeutic moiety, or its active metabolite(s), in body fluids or excretory products, is accurate and of sufficient sensitivity to measure, with appropriate precision, the actual concentration of the active drug ingredient or therapeutic moiety, or its active metabolite(s), achieved in the body [21 CFR 320.29(a)].

During FDA's inspection of your firm, FDA found unusual and unexplainable study records demonstrating that you engaged in practices and processes that undermined the analytical methods used at your firm. Upon close review of study records from your firm, we conclude that those practices and processes resulted in the submission of falsified study data to the FDA. As a result, FDA has significant concerns about the validity and reliability of bioequivalence and bioavailability data generated at your firm that are submitted to the FDA in support of Abbreviated New Drug Applications (ANDAs) or New Drug Applications (NDAs). Examples include, but are not limited to, the following:

For Study (b)(4): Subjects' pharmacokinetic (PK) study data appeared to separate into two distinct populations, with a change occurring around the midpoint of the study, which would not be expected based on normal subject physiologic variability across a subject population. Specifically, the test product's peak drug concentration (C_{max}) appeared to be higher than the reference product in the first half of the subject population, but the opposite was true for the second half of the subject population.

During FDA's inspection, we asked you to provide a bioequivalence assessment for each cohort independently (Cohort I consisting of Subjects 1-41, and Cohort II consisting of Subjects 42-72), followed by a bioequivalence assessment of the entire study. We also asked you to calculate the C_{max} geometric mean ratios (GMRs) and the area under the plasma concentration-time curve (AUC_{0-t}) GMRs with their respective confidence intervals for the two study subject cohorts independently, to evaluate the overall trends in terms of the bioequivalence endpoints. The calculations resulting from your analysis (see table below) indicated that the (b)(4) GMRs data from Cohort I subjects (Subjects 1-41) were distinct from the GMRs data from Cohort II subjects (Subjects 42-72).

Study (b)(4)				
Subjects	***Parameter***	***GMR Point Estimate***	***GMR 90% Confidence Interval***	***Bioequivalence Determination***
1-41 (n=41)	C_{max}	1.3555	1.1553 - 1.5904	NOT BE
	AUC_{o-t}	1.2298	1.1007 - 1.3741	NOT BE
42-72 (n=31)	C_{max}	0.7354	0.6053 - 0.8936	NOT BE
	AUC_{o-t}	0.7524	0.6333 - 0.8938	NOT BE
Full Study	C_{max}	1.035	0.903 - 1.1862	BE
	AUC_{o-t}	0.9901	0.8886 - 1.1032	BE

You suggested during the inspection that your analysis and the study results were correct even though they appear aberrant based on normal subject physiologic variability. We note that during the inspection and in your December 9, 2019, written response, you provided no acceptable justification for the unusual PK trends in the study data to resolve FDA's concerns about the validity of data for Study (b)(4). Specifically, you failed to explain the presence of two distinct populations around the midpoint of the study, which would not be expected based on normal physiologic variability across a subject population.

During the inspection, we also requested and reviewed the complete concentration profiles for all subjects in Study (b)(4). Our review of the data found that a significant number of different subjects had highly similar plasma drug profiles that shared unique characteristics within their curves between pairs of subjects. That finding is not expected based on physiological differences and is indicative of subject sample substitution. In total, we identified 16 subject pairs with nearly identical concentration-time profiles, some with the same treatment sequence and some with opposing sequences. Each of the subject pairings consisted of one subject from Cohort I (Subjects 1-41) and one subject from Cohort II (Subjects 42-72).

Significantly, our inspection found uncontrolled and loose source documentation at your firm; in particular, we found a notebook documenting the exact subject pairs for 14 of the 16 pairs that your analysis showed had nearly identical concentration-time profiles for Study (b)(4). During our inspection, we discussed what the phrase "((b)(6) B.F.)" meant after the last subject pair listed in that record; you indicated that it likely meant a batch failure occurred for the run analyzing Subjects (b)(6) and (b)(6) The run analyzing Subjects (b)(6) and (b)(6) was confirmed as the only batch failure listed in the data for Study (b)(4) submitted to FDA.

During the inspection, you provided a comparison for 14 of the 16 subject pairs with nearly identical concentration profiles, based on the actual numerical difference between sample concentrations. You claimed that these differences were significant, and therefore the data profiles were not identical. We disagree with your assessment because your analysis is not consistent with the repeat analysis criteria described in your standard operating procedures SYN/BA-101-06, "Incurred Sample Re-analysis," and SYN/BA-071-12, "Repeat Sample Analyses," which are based on percentage difference. Specifically, for each of the 16 subject pairs, the percentage difference for the majority of concentration points between each pair would satisfy your firm's acceptance criteria for repeat analysis (that is, the results of a reanalysis of a subject's samples are sufficiently consistent with the original results), suggesting that the subject pairs are identical or highly similar.

We recognize that the findings discussed above were not listed on the Form FDA 483; however, these items were discussed in detail during the inspection. We note that your December 9, 2019, response, and your explanations during the inspection, provided no substantive explanation for the observed data anomalies in Study (b)(4), and did not clarify why your firm had documentation listing multiple subject pairs in Study (b)(4) (b)(4) with overlapping concentration-time profiles.

Response to FDA's Inspection Concerns in the General Correspondence Letter

FDA's General Correspondence Letter specifically asked you to provide an explanation for the observed data anomalies (the divergent PK data trends and the nearly identical concentration-time profiles) in Study (b)(4), if the subject samples were not substituted or falsified, and why your firm had documentation listing multiple subject pairs in Study (b)(4) with overlapping PK profiles. (See request for response numbers 1 and 4 in FDA's General Correspondence Letter.)

Divergent PK trends and overlapping PK profiles: Your April 10, 2021, response acknowledged FDA's observations, and stated that you performed an investigation of the clinical, bioanalytical, and statistical conduct at your firm to understand the reasons for the trends in the results. You indicated that your investigation identified no discrepancies in the conduct of the study and found no errors to explain FDA's observations.

In addition, your response provided your conclusions from the PK and statistical analyses that were performed after FDA's inspection. You indicated that for Study (b)(4) you found no differences between the two cohorts that would require separate analyses. You stated that you did not observe a statistically significant cohort or sequence effect for the C_{max} or AUC values. You concluded that the difference in cohorts may be due to the PK parameters of (b)(4) exhibiting high intra-subject variability, and you provided published literature to support the expected high intra-subject variability of (b)(4)

PK parameters. Thus, while you agreed that the PK data between the two cohorts were divergent, you stated that the range of PK parameters (the minimum and maximum values for C_{max} and AUCs) was similar for the cohorts. To further support that claim, you identified four additional studies with divergent PK trends (b)(4), (b)(4), (b)(4) (b)(4) and (b)(4)) to argue that because you observed divergent PK trends in these studies, the divergent PK trend in Study (b)(4) is possible, not anomalous, and can be expected from a group of healthy volunteers. You also provided the results of your reanalysis of samples requested by the World Health Organization (WHO) during a 2019 inspection (we note that WHO's inspection coincided with FDA's 2019 inspection), to support your argument that your firm generates reliable study data.

Based on the explanations and information provided in your April 10, 2021, response, your response to the FDA's General Correspondence Letter is inadequate because you failed to resolve FDA's concerns related to data anomalies between two distinct subject populations. FDA agrees that your study records were complete; however, the concerns that FDA raised during the inspection were not about the completeness of your records, but how the validity of those records can be ensured, given the significant PK data anomalies we observed across multiple studies conducted at your firm.

We disagree with your suggestion that the PK and statistical results showing divergent PK data trends between cohorts may be attributed to expected high intra-subject variability for (b)(4) PK parameters. We would not expect high intra-subject variability for (b)(4) to produce PK trends like those observed in Study (b)(4) Specifically, we would expect high intra-subject variability to occur across a study population, rather than being concentrated in sub-groups or cohorts, as we observed in that study. Further, we would expect the high intra-subject variability of (b)(4) to increase the differences between subject concentration-time profiles, making it less likely that the concentration-time profiles of 16 subject pairs would be nearly identical, as we observed in that study.

Additionally, your focus on similar ranges of minimum and maximum C_{max} and AUC values within a cohort does not explain the divergent PK trends for Study (b)(4). Examining minimum and maximum values for PK parameters within a cohort is not representative of the overall mean T/R ratios that are at issue for a specific cohort. As such, this argument fails to explain the non-physiologic PK trends in Study (b)(4) that deviate significantly from the normal population distribution in a group of healthy volunteers.

We also disagree with your claim that because you observed patterns of abnormal, non-physiologic PK trends in Studies (b)(4), and (b)(4) (all of which were identified as studies with significant concerns in our March 12, 2021, letter) similar to those in Study (b)(4), the PK trends in Study

(b)(4) are in fact not anomalous and could occur in a normal healthy study population. In fact, your argument highlighting the PK anomalies in multiple studies conducted at your firm only heightens our concern about the manner in which you conduct studies, and to us, is more supportive of the possibility that the data reliability concerns for Study (b)(4) and for those studies you cited are systemic rather than isolated issues. Of note, FDA assessed other bioequivalence studies conducted at different firms for (b)(4) (b)(4) and (b)(4), and did not observe divergent PK trends like those in studies conducted at your firm, which further undermines your argument.

We also note that the results of the reanalysis for Study (b)(4) that your firm performed at the request of the WHO inspector do not provide any additional information to explain the observed PK anomalies in Study (b)(4).

Documentation of overlapping PK Profiles: You noted in your April 10, 2021, response that the freezer custodian responsible for the notebook found during FDA's inspection was on leave. You stated that the custodian had indicated that the notebook was used for training, tracking, and reference purposes to identify, distinguish, and verify samples he retrieved from the freezers. Your investigation into the notebook documenting the subject numbers for 14 of the 16 sample pairs with overlapping PK profiles resulted in your confirming that the subject numbers were "pre-dose samples that required repeat analysis" for Study (b)(4) (b)(4), which you confirmed based on the (b)(6) B.F." notation on the notebook page. You came to that conclusion despite noting that the notebook page with the suspected subject pairs did not have a study number, sample IDs, or dates that would link to Study (b)(4)-(b)(4). As we explained above and discussed with you during our 2019 inspection, we found that the "(b)(6) B.F." annotation on the notebook page correlates with the batch failure of a run containing subjects (b)(6) and (b)(6) reported in Study (b)(4) and thus we agree with your assessment connecting the study numbers to Study (b)(4).

Based on the information in your response, you did not provide a legitimate, scientifically valid reason why your firm would have a notebook page detailing the exact subject number pairs for 14 of the 16 subject pairs with nearly identical concentration-time profiles for Study (b)(4). In fact, your response does not address why the subject numbers are listed in pairs if the samples were not being manipulated or falsified. Your response focuses on suggesting that the subject numbers recorded on the notebook identified those subjects with pre-dose samples from Study (b)(4) that required repeat analysis, without providing any evidence to support how you came to this conclusion. This is especially concerning because the numbers listed in pairs in the notebook match subject numbers for 14 of the 16 pairs with nearly identical concentration-time profiles observed in Study (b)(4) (b)(4), which to us does not align with your conclusion that the numbers represent subject-specific pre-dose samples.

Additionally, your records reviewed during the FDA inspection do not support your claims that the numbers on the notebook page represent the sample custodian's tracking of pre-dose samples. Based on the custodian's retrieval of samples and sample analysis for Study (b)(4) (b)(4): (1) pre-dose samples from 66 subjects required repeat analysis, but only 28 numbers were listed on the notebook page, leaving 38 subjects unaccounted for if tracking is the purpose of the list; and (2) the sample custodian who you argue created the list to track pre-dose samples, did not retrieve pre-dose samples for 13 of the 28 subject numbers listed on the notebook page from the freezer. Thus, your study records do not support your claim that the notebook was used merely to track pre-dose samples.

Based on FDA's inspection findings of anomalous PK study data at your firm, including a record documenting multiple specific subject pairs with overlapping PK profiles, and based on your responses' failure to adequately address or refute FDA's significant concern that subject samples in Study (b)(4) were substituted or falsified, the facts support that your firm engaged in practices and processes that undermine the reliability and validity of the analytical methods used at your firm and the study data generated by your firm.

Post-Inspection FDA Data Analyses

In addition, FDA's General Correspondence Letter identified similar and significant anomalous PK data trends to those described above in a number of other studies performed at your firm, which were submitted to the Agency in support of certain ANDAs. Specifically, the letter raised concerns about unexpected, non-physiologic PK data from six studies: (b)(4) (b)(4); and (b)(4).

For those studies, FDA asked you to provide an explanation for the anomalous PK data identified; that is, to explain the study data (1) showing multiple pairs of subjects with overlapping time-concentration profiles; (2) showing distinct groups of subjects where the T/R ratio for C_{max}, AUC_{0-t}, or $AUC_{0-\infty}$, among other parameters, for most subjects in the subgroups is above or below 1; or (3) having both concerns. (See request for response number 2 in FDA's March 12, 2021, letter.)

In your April 10, 2021 response, you acknowledged the observations regarding PK data anomalies from FDA's inspection and FDA's General Correspondence Letter. You stated that you investigated the clinical, bioanalytical, and PK-statistical conduct for all studies. (Only bioanalytical investigations were performed for studies (b)(4) and (b)(4), because the clinical and PK- statistical portions were not done by your firm). You indicated that your investigations confirmed the accuracy of the clinical and bioanalytical study records for those studies, similar to your review for Study (b)(4) described above, and you did not identify any discrepancies or errors to explain the anomalous data. Thus, you concluded that

there were no errors to explain the FDA's observations related to PK anomalies or overlapping concentration-time profiles.

Regarding the PK-statistical investigations, you provided reviews of all statistical procedures used, a sample-by-sample comparison of concentration differences, and an assessment of all T1/T2, R1/R2, and T/R ratios for C_{max} and AUCs. You concluded from those analyses that the ratios of PK parameters for different test formulations (T1/T2) and different reference formulations (R1/R2) showed trends either above or below 1.0 in the distinct subject groupings, which, you claimed, mitigated concerns that the divergent PK parameter T/R ratios were anomalous, and therefore they would be expected in a normal study population.

Finally, for studies with anomalous overlapping time-concentration profiles (that is, for studies (b)(4), and (b)(4)), similar to your analysis for Study (b)(4) described above, you assessed the minimum and maximum differences between comparable timepoints for subject pairs with overlapping PK profiles, and you performed a complete analysis of all timepoints. Based on those assessments, you argued, "there is in fact a noticeable percentage difference in concentrations at respective periods" for the subject pairs that FDA identified with overlapping profiles. Thus, you concluded that the data were not aberrant.

Divergent PK trends: Based on the information provided in your response, we do not agree with your conclusion that your analysis of the T1/T2 and R1/R2 ratios for studies (b)(4) (b)(4) and (b)(4) mitigates our significant concerns regarding the distinct sub-group trends observed for T/R ratios for C_{max} and AUC in those studies. Our analyses did not identify distinct sub-group trends in the distribution of T1/T2 and R1/R2 ratios, despite observing the distinct, divergent sub-group T/R ratios for C_{max} and AUC. Regarding studies (b)(4) and (b)(4), we also note that we assessed another (b)(4) study conducted at a different contract research organization, and that study did not show the unusual PK data trends seen in studies (b)(4) and (b)(4). We also did not observe subjects with nearly identical concentration-time profiles similar to those studies conducted at your firm, which further undermines your argument that the data are not anomalous.

Overlapping PK profiles: FDA disagrees with your response's conclusions and general explanation that there were noticeable percentage differences between corresponding time points of the subjects with overlapping profiles for studies (b)(4) (b)(4) and (b)(4). First, we disagree with your approach of assessing individual concentration points as a marker of differences between subject pairs, because such an assessment is not representative of the entire PK profile. We find it particularly inappropriate to do so for highly variable drug products (such as (b)(4) in Study (b)(4) (b)(4)) or drug products with a concentration-time profile exhibiting multiple peaks (such as

(b)(4) in studies (b)(4) and (b)(4)), where any overlapping PK profiles for subjects would be unexpected. Thus, your approach fails to appropriately focus on the entire PK profile and does not resolve our concern about multiple subject pairs across multiple studies showing overlapping PK profiles.

Second, our analysis of the percentage difference in concentration points does not support your claim that "there is in fact a noticeable percentage difference in concentrations at respective periods," and does not support your conclusion that the study data are not abnormal. Specifically, our analysis of those studies demonstrates that, for a majority of the subject pairs with overlapping PK profiles, the differences between subject pair concentration data are insignificant, given that for incurred sample reanalysis, the general standard is that a difference less than or equal to 20% between the original and the repeat sample analysis indicates that the concentrations are comparable and that the analytical method is reproducible. Thus, our analysis, which mirrors that described for Study (b)(4), showed high similarity in concentration points between the subject pairs in those studies, which concurs with your firm's acceptance criteria for incurred sample re-analysis (see SOP #SYN/BA-101-06) and contradicts your conclusion.

We remain concerned about your failure to provide an adequate justification or explanation for why data generated at your firm show the unexpected overlapping PK profiles for multiple pairs of study subjects across multiple studies.

Taken together with your response to FDA's inspection findings for Study (b)(4), as noted above, your April 10, 2021, response fails to provide adequate explanation(s) for the observed anomalous time-concentration overlaps and PK trends (that is, distinct groups of subjects in which T/R ratios for C_{max}, AUC_{0-t}, and $AUC_{0-\infty}$ are above or below 1.0) to resolve our concerns. As such, FDA's concerns regarding study data generated by your firm remain, because your study data are inconsistent with normal variation or distribution found in a healthy population, and these data are not expected to occur by chance across the significant number of Synchron studies identified by FDA.

FDA Specific Request for Responses

We also note that FDA's General Correspondence Letter specifically asked you to explain the following (listed in the FDA's General Correspondence Letter as request for response number (3) and numbers (5) through (7)):

(1) Why your firm failed to identify and assess the data anomalies observed during the inspection

(2) How multiple studies conducted at your firm could have numerous instances of overlapping subject sample concentrations and unusual PK trends that deviate significantly from normal population distribution of data in a group of healthy volunteers

(3) Whether any other bioequivalence or bioavailability studies conducted at your firm have similar PK data anomalies, and if so, an assessment of the impact of each study, if any, and the root cause for any identified data anomalies

(4) Any reason why the evidence of falsification of data discussed in this letter should not raise questions about the validity of all data reported by your firm

Regarding those requests, your April 10, 2021, response stated that your firm has "impressive world-class facilities" that have provided contract services for over 22 years, that you have trained and qualified staff, and that you comply with all GCP and GLP standards. Based on your firm's multiple inspections from regulatory agencies (including FDA) that have not made similar observations, you stated your surprise at the inspection observations regarding the concentration-time profile similarities and anomalous PK trends in Study (b)(4) (b)(4). We acknowledge that you referenced your detailed responses to FDA's General Correspondence Letter (described above) and restated the results of your investigations, and that you verified study conduct in all clinical, bioanalytical, and statistical assessments.

We note that your response of April 10, 2021, also acknowledged FDA's concerns raised during the inspection regarding your poor documentation practices, and stated that documents from current and previous studies were stored in the deep freezer room for ease of access by study staff. Further, you acknowledged that several processes described in your established standard operating procedures (SOPs) were not followed regarding documentation controls, including the return of sample retrieval request templates for each study to analysts for filing, and document reconciliation.

We acknowledge that your response also provided eight additional studies that you had assessed to determine whether those bioequivalence or bioavailability studies conducted at your firm had similar PK data anomalies, including those identified by FDA in FDA's General Correspondence Letter. In addition, you provided the results of the sample reanalysis of WHO data from study (b)(4) (also discussed above) and stated that your firm has conducted multiple failed bioequivalence studies; you provided a table of these failed bioequivalence studies. We note regarding this table of failed bioequivalence studies that you provided no information to allow us to determine the significance of the studies listed in terms of your assessment of their relevance to the data anomalies raised during the inspection and in our March 12, 2021, letter.

Your April 10, 2021, response described corrective actions that you indicated had been or would be implemented by your firm. Specifically, among other things, to address the data anomalies we identified, you: (1) revised multiple SOPs (including SOP SYN-BM-029-06, "Criteria for Considering Concentration Values for Investigation"; SOP SYN-BA-120-05, "Bioanalytical Failure Investigation Procedure"; and SOP SYN-QA-023-05, "Quality Control Procedure for Bioanalytical Department"); (2) indicated that you instructed various staff not to document study-related information in undocumented notebooks, and removed spiral notebooks from the analytical department; and (3) provided training to staff on Good Documentation Practice.

Regarding your firm's documentation practices, your response acknowledged inconsistencies in documentation practices that left critical source documents uncontrolled, but you did not provide specific assessments for how your firm's poor documentation controls affected or did not affect studies conducted by your firm. Despite your recognition of those facts, your investigations recognized no errors in study conduct or data reporting, concluding that the PK trends for the multiple studies identified were not anomalous and would be expected from a normal study population. We do not agree with that conclusion, and we are unable to verify whether your firm's lack of adherence to your established controls and documentation practices affected study conduct or reliability, and we cannot confirm the number of studies affected.

We acknowledge the corrective actions your firm has taken or will take specific to the implementation of system improvements in response to the significant concerns raised by FDA's inspection and FDA's General Correspondence Letter.

Your response to FDA's General Correspondence Letter is inadequate because you failed to address: (1) FDA's concerns about what caused the anomalous PK trends; (2) why multiple studies conducted at your firm could have overlapping subject concentration-time profiles and unusual PK trends without being identified before FDA's inspection or the inspections performed by other international regulators; and (3) any legitimate, scientifically valid reason why the evidence of falsification of data discussed in FDA's General Correspondence Letter should not raise questions about the validity of all data generated by your firm. This failure raises significant concerns because it suggests that you failed to perform a comprehensive evaluation of all bioequivalence and bioavailability studies conducted at your firm to date for similar PK anomalies.

Your failure to identify and address how numerous studies could each have multiple instances of overlapping subject sample concentrations and/or anomalous PK trends raises significant concerns about the bioavailability and bioequivalence data generated at your firm that is submitted to FDA in support of ANDAs or NDAs. Your firm engaged in practices and

processes that undermined the reliability and validity of the analytical methods used at your firm and the study data generated by your firm.

This letter is not intended to be an all-inclusive list of deficiencies regarding bioavailability and bioequivalence studies conducted at your firm. It is your responsibility to ensure adherence to each requirement of the law and relevant FDA regulations, and to ensure the integrity of all data generated at your firm that is submitted to the FDA in ANDAs or NDAs.

The manner in which Synchron conducted the studies noted above makes FDA believe that the reliability and validity of study data generated by your firm cannot be ensured. Put simply, because you have been responsible for the creation of false data in the studies discussed here, we have no reason to believe that any data you have generated is reliable. Therefore, FDA has determined that study data from studies conducted at your firm must be rejected.

Please be advised that we are not requesting a response to this letter. You are responsible to ensure that your firm adheres to each requirement of the law and relevant FDA regulations if you are involved in the conduct of studies that are submitted to FDA. You should address any deficiencies and establish procedures to ensure that any ongoing or future studies comply with FDA regulations. This may include, among other things, that your firm documents your implementation of and adherence to processes and procedures that are sufficient to promptly identify, assess, and resolve any aberrant study data from studies conducted at your firm, including issues similar to those identified by the FDA as discussed above. Note that we may conduct a future inspection to verify your corrective actions and compliance with FDA regulations.

We appreciate the cooperation shown to FDA personnel Kara A. Scheibner and Makini Cobourne-Duval during the inspection.

Should you have any questions regarding this letter, please e-mail Sean Kassim at sean.kassim@fda.hhs.gov or David Burrow at david.burrow@fda.hhs.gov, or write to:

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Sincerely yours,

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