U.S. FOOD & DRUG ADMINISTRATION

VIA E-MAIL

February 26, 2025

Xiaoming (Diana) Hong
President
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Dear Xiaoming (Diana) Hong:

This letter addresses significant concerns the U.S. Food and Drug Administration (FDA or the Agency) has notified you of regarding the reliability and validity of biocompatibility testing and animal safety and performance testing studies conducted at your testing facility.

Based on FDA's data analyses communicated to you in a General Correspondence Letter (GCL) on December 30, 2024, and your subsequent response to the GCL on January 29, 2025, it is FDA's conclusion that your testing facility copied the results of another study or created falsified or otherwise invalid data that was submitted to FDA.

As described in the December 30, 2024, GCL, FDA identified multiple test reports from studies conducted at your testing facility that have raised concerns, including cytotoxicity studies that contain identical or nearly identical results from different dates, sensitization studies (Guinea Pig Maximization Tests) that contain identical sets of guinea pig pretreatment body weights for different groups on different dates, and a large animal safety and performance study for a staple line reinforcement device that contains implausible bleeding assessments and pre-to-post-procedure weight gains in Bama pigs. As discussed more fully in the December 30, 2024, GCL, generating identical/nearly identical data for the different cytotoxicity and sensitization studies is highly improbable and the data trends for the animal and safety performance study are not consistent with normal physiological responses and variations in a healthy animal model. Thus, our analysis shows that you have, in several instances, created results that were copied from the results of another study or were otherwise falsified or invalid.

As also described in our December 30, 2024, GCL, accurate study data in a premarket submission is necessary to enable FDA to fully and properly assess the overall safety of a device. For example, patient or user exposure to a medical device could result in adverse health effects such as cytotoxicity, allergic reactions, skin irritation or inflammation, fever, toxicity that leads to loss of tissue/organ function or failure, and anaphylaxis. These adverse health effects represent a clear risk to patients and clinical practitioners. Accurate biocompatibility data to determine the potential for such an adverse biological response resulting from direct and/or indirect contact with a medical device is important. Data that are copied from the results of another study or were otherwise falsified or invalid raise concerns about the reliability and validity of associated premarket submissions and impede FDA's ability to assess the safety and risk of a device, which may put public health and safety at risk.

In our December 30, 2024, GCL, we requested that you provide a complete response within 30 days by providing the following information:

1) explanation for the anomalous data identified by FDA with respect to the studies discussed in the GCL;
2) explanation of why your testing facility failed to identify and assess the data anomalies;
3) explanation of how your overall system of process and procedures contributed or permitted multiple studies conducted at your testing facility to have numerous instances of anomalous data;
4) whether any other studies conducted at your testing facility have similar data anomalies, and if so, an assessment of the impact of each study, if any, and a systemic root cause analysis for any identified data anomalies; and
5) any reason why the evidence of copied or otherwise falsified or invalid data discussed in the December 30, 2024, GCL should not raise questions about the reliability and validity of all data reported by your company and provided in past, pending, and future submissions to FDA.

Your Response to the General Correspondence Letter

FDA has reviewed your response to the December 30, 2024, GCL. Your response states, in part, that you "have developed a preliminary path forward to address the issue in the [GCL]" and "opened an investigation with support from the highest levels of our organization to thoroughly investigate the concerns described in the December 30 letter. The investigation aims to identify (1) the root cause(s) of the apparently unreliable data submitted to the Agency and (2) the reason why our Quality Assurance controls did not detect and correct these anomalies. We assure the Agency that the investigation data and reports will be verified by an independent third party." Your response further notes that "Mid-Link intends to:

- Conduct a comprehensive investigation of the issues described in the December 30, 2024 letter from FDA. Mid-Link will look at the issues described in the letter wholistically and

expand our investigation to include our entire operations to determine if there are other suspected instances of unreliable data.

- Leverage input from our third-party experts who have assisted Mid-Link in addressing the concerns in the FDA 483 observations and those listed in the Warning Letter.
- Perform a comprehensive assessment of our FDA 483 observations and Warning Letter CAPAs to ensure the controls implemented after the FDA 483 and FDA Warning Letter post-date the issues identified in the December 30, 2024 FDA letter and that they are effective in assuring the integrity of data generated by our laboratory.
- Engage a qualified, third-party expert, to perform a comprehensive gap assessment of how Mid-Link generates, stores, and controls GLP laboratory data."

Your response[1] does not resolve FDA's data integrity concerns regarding the data generated by your firm. While you have expressed a commitment to investigating the issues described in the December 30, 2024, GCL, the concerns in the FDA 483 observations, and the Warning Letter violations,[2] you have not provided a complete response that addresses any of the five items requested in our December 30, 2024, GCL. You did not provide any explanation of why your testing facility failed to identify and assess the data anomalies. You did not provide any explanation of how your overall system of process and procedures contributed or permitted multiple studies conducted at your testing facility to have numerous instances of anomalous data. You did not provide any additional information on whether any other studies conducted at your testing facility have similar data anomalies, and if so, an assessment of the impact of each study, if any, and a systemic root cause analysis for any identified data anomalies. And you did not provide any reason why the evidence of copied or otherwise falsified or invalid data discussed in the December 30, 2024, GCL should not raise questions about the reliability and validity of all data reported by your company and provided in past, pending, and future submissions to FDA.

FDA's Conclusions

Your response does not adequately address FDA's concerns discussed in the December 30, 2024, GCL, including regarding the cause of significant data anomalies present in your studies. In addition, your response does not alter FDA's conclusion that your testing facility copied the results of another study or created falsified or otherwise invalid data that was submitted to FDA. Further, your response does not indicate you have resolved the issues regarding the reliability and validity of biocompatibility testing and animal safety and performance testing studies conducted at your testing facility or provided any reason why the evidence of copied or otherwise falsified or invalid data discussed in FDA's December 30, 2024, GCL should not call

[1] Your response states that you will continue to service your current customers under contracts already executed. For any studies conducted for current customers, FDA would have the same concerns about your testing facility's conduct of all biocompatibility studies and animal safety and performance testing studies and the reliability and validity of all study data from your testing facility as identified in the December 30, 2024, GCL and this letter.

[2] Your September 30, 2024, November 18, 2024, and January 29, 2025, responses to the September 30, 2024, Warning Letter are currently under review. Because those responses are not directly relevant to the December 30, 2024, GCL, FDA will assess the adequacy of those responses in a separate communication.

into question the validity of all data generated by your firm and provided in past, pending, and future submissions to FDA. Therefore, your response does not resolve FDA's concerns regarding the data generated at your testing facility.

Mid-Link's conduct of the studies cited in the December 30, 2024, GCL causes FDA to 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 copying of results of another study or creation of falsified or otherwise invalid data that was submitted to FDA in the studies discussed in the GCL, we have no reason to believe that any data that you have produced are reliable. Thus, based on FDA's data analyses, FDA has determined that all study data from all studies conducted at your firm will be rejected until you have demonstrated that the issues described in the December 30, 2024, GCL have been adequately addressed. This may include, among other things, your firm's documentation of your implementation and following of procedures that are sufficient to prevent the use of copied or otherwise falsified or invalid data – similar to those identified by FDA in studies conducted at your firm. Note that we may conduct a future inspection to verify your corrective actions.

We acknowledge that your response requested a meeting with FDA "to discuss the progress and gather feedback on our investigation and remediation plans to date." We do not believe a meeting would be beneficial at this time because your firm has not substantively responded to the concerns included in the December 30, 2024, GCL. We, therefore, decline your request at this time. However, FDA would consider a future request for a meeting after you have completed your investigation into the issues described in the December 30, 2024, GCL.

Should you have any questions regarding this letter, please email the Office of Product Evaluation and Quality (OPEQ) Regulation, Policy, and Guidance (RPG) Team at RPG@fda.hhs.gov.

Sincerely,

ANGELA C. KRUEGER -S

Digitally signed by ANGELA C. KRUEGER -S
Date: 2025.02.26 09:29:54 -05'00'

Angela C. Krueger
Deputy Director for Regulatory Policy
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