DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:
Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive - MSC 7982
Bethesda, Maryland 20892-7982
Home Page: http://grants.nih.gov/grants/olaw/olaw.htm

FOR EXPRESS MAIL:
Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive
Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 402-7065

September 18, 2017

Re: Animal Welfare Assurance
#A3086-01 (OLAW Case F]

Dr. Mark G. Lewis
Chief Executive Officer and President
BIOQUAL, Inc.
9600 Medical Center Drive
Rockville, MD 20850

Dear Dr. Lewis,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your September 13, 2017 letter reporting two instances of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at BIOQUAL, Inc. According to the information provided, OLAW understands that a Principal Investigator administered a higher dose of test article to five guinea pigs in a pilot study without prior IACUC approval. In addition, post-procedural analgesia was not administered to animals as approved in the protocol. It was not stated if the associated animal activity was PHS funded.

The corrective actions consisted of the Principal Investigator resubmitting a proposal for a secondary pilot study inclusive of the appropriate USDA pain and distress category and associated scientific justification, training the Principal Investigator on regulatory compliance and enhancing post approval monitoring of the pilot study.

Based on the information provided, OLAW is satisfied that appropriate actions have been taken to investigate, correct and prevent recurrence of the noncompliance. We appreciate having been informed about this matter and find no cause for further action by this Office.

Sincerely,

(b) (6)

for Neera V. Gopee, DVM, PhD, DACLAM, DABT
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Chair

A3086-F

BIOQUAL, Inc.

BIOQUAL Institutional Animal Care and Use Committee
12301 Parklawn Drive
Rockville Maryland 20852
301-881-8824 (f) 301-881-9175

Wednesday, September 13, 2017

Director of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 260, MSC 7982
6705 Rockledge Drive
Bethesda, Maryland 20892-7982

RE: Deviation from Approved IACUC Protocol
D16-00052 (A-3086-01)

The BIOQUAL, Inc Institutional Animal Care and Use Committee has identified deviations from IACUC Approved Protocol, **17-052P** with title "**Development of a Guinea Pig Model for Vaginal HSV-2 Infection.**" This pilot protocol was approved for the use of twelve (12) SPF Hartley (Strain Code: 051) Guinea Pigs (*Cavia porcellus*) to establish the HSV-2 guinea pig model for future vaccine and therapeutics testing at BIOQUAL Inc.

The protocol approved the use of two strains of HSV-2 MS, one from Merck and the other from Virapur, each at the dose of $5x10^5$ PFU. The study was split into three groups, the two strain groups with five (5) animals, and a control group of two (2) animals to receive a placebo. However, prior to the start of the pilot study, the second strain listed, Virapur, became unavailable. The Investigator then instead ordered the use of a higher dose of the Merck strain (at $1x10^6$ PFU) in group three, alongside the original dose of the Merck strain in group two, and the placebo group (group one). The investigator failed to notify the IACUC of this change and did not amend the protocol accordingly.

Secondly, the protocol in question was designated USDA Pain Categories C (for the control group), and D (for the study groups). According to the approved protocol, "In the event an animal requires temporary relief from pain or distress, they will be administered an analgesic per the attending veterinarian following SOP RD-021," as is appropriate for a Category D study. However, while the animals did receive anesthesia (Ketamine and Xylazene) prior to the IVAG HSV-2 challenge, the animals did not receive analgesic measures to reduce their pain and distress during the course of the study.

The IACUC has identified these deviations and has met twice, on September 5th, and again on September 12th, to discuss this protocol. Principle Investigator training on regulatory requirement and IACUC communication is in development and will be implemented pending IACUC approval at the upcoming

scheduled meeting of the IACUC on October 27th, 2017. Furthermore, an updated plan for Post Approval Monitoring is in the final stages of approval and will also be reviewed at the aforementioned meeting.

The following corrective action plan has been proposed:

1. The Principle Investigator has been asked to resubmit a proposal containing a secondary pilot study to either be run as a USDA Category E study with scientific justification as to why the analgesia is withheld, or as another Category D study with the use of appropriate analgesic measures in the known case of animal pain and distress.
2. The Principle Investigator will complete the forthcoming IACUC training
3. The pilot study described in (1) will be subject to the improved Post Approval Monitoring plan.

BIOQUAL Inc. is committed to protecting the welfare of animals used in research and appreciates the guidance and assistance provided by OLAW in this regard. Should you have any questions regarding this report, please contact Dr. Wendeline Wagner, DVM, IACUC Chair.

Thank you for your consideration of this matter.

Sincerely

(b) (6)

Mark G. Lewis,
Institutional Official
President, CEO
BIOQUAL, Inc.

(b) (6)

Wendeline L. Wagner, DVM
IACUC Chairperson
Director, Parklawn Drive
BIOQUAL, Inc.

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Thursday, September 14, 2017 7:51 AM
To: (b) (6) OLAW Division of Compliance Oversight (NIH/OD)
Cc: Lewis, Mark; Dr Wagner
Subject: RE: Report of Deviation from Approved IACUC Protocol

Thank you for this report. We will send an official response soon.

Sincerely, Brent Morse

Brent C. Morse, DVM, DACLAM
Acting Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

From: (b) (6) @bioqual.com]
Sent: Wednesday, September 13, 2017 4:35 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Lewis, Mark <mlewis@bioqual.com>; Dr Wagner <wwagner@bioqual.com>; (b) (6) @bioqual.com>
Subject: Report of Deviation from Approved IACUC Protocol

Good afternoon,

On behalf of the BIOQUAL, Inc. Institutional Animal Care and Use Committee,

Attached is the September 13th, 2017 report from BIOQUAL, Inc. regarding a recently discovered deviation from an Approved IACUC Protocol.

A parallel report has also been issued to USDA APHIS.

Thank you for your consideration of this matter,

Please contact Dr. Mark Lewis, President, CEO – mlewis@bioqual.com;
Dr. Wendeline Wagner, IACUC Chairperson, Director – wwagner@bioqual.com,
or myself,

(b) (6)