OFFICE OF RESEARCH OVERSIGHT

Report to the

Office of Special Counsel

OSC File Number DI-12-1098

Department of Veterans Affairs

VA Boston Healthcare System Boston, MA

Status Report of April 1, 2013

V. Required Actions

1. The VABHS must ensure that all research currently involving the PI and SC adheres to the IRB-approved protocol and complies with all applicable VA research requirements by implementing an appropriate monitoring plan for their research.

VABHS ACTION PLAN: The Research Compliance Officer (RCO) will audit each study involving the Principal Investigator (PI) once a month for a period of six months beginning the week of October 15, 2012. Results of each audit will be presented for discussion to the Institutional Review Board (IRB) and the Research and Development Committee (R&DC) for their input and determinations about the need for modifications in the research and/or PI sanctions as applicable in association with any serious or potentially serious findings identified at the time of audit. At the end of the six month period (following the final audit of March 15, 2013) the RCO will provide a final report to the IRB and R&DC who will jointly determine whether or not the monitoring period needs to be extended.

VABHS STATUS NOVEMBER 30, 2012: The Research Compliance Officer (RCO) has audited PI study files and noted no reportable findings of non-compliance. Therefore, no actions have been required to date on the part of the IRB and/or R&DC.

ORO RESPONSE: Progress satisfactory. Please submit next Progress Report by February 1, 2013, detailing the status of the required action with supportive documents, i.e., R&DC and IRB meeting minutes documenting review and evaluation of the progress.

VABHS STATUS FEBRUARY 1, 2013: The Research Compliance Officer (RCO) has continued audits of PI study files and submitted her most recent report to the VABHS HRPP Office today. No reportable findings were noted and the report will be reviewed at the IRB Meeting on February 4, 2013 and at the R&DC Meeting on February 13, 2013.

VABHS STATUS APRIL 1, 2013: VABHS provides a clarification to ORO's correspondence dated February 5, 2013 in which it was stated that "*A total of 0.8 (32 hours) additional FTEE has been allocated toward research compliance.*" The actual amount of additional FTEE provided toward research compliance is 8 hours for .2 FTEE.

The final RCO audit report of [redacted] studies was submitted to the IRB and the R&DC for their respective reviews.

2. The VABHS must ensure that all of its research studies are conducted according to the IRB-approved protocols and all relevant Federal regulations and VHA Policies.

VABHS ACTION PLAN: The VABHS Research and Development Service (R&D) will provide new educational programs to the VABHS Research Community that includes topics of relevance pertaining to (findings of non-compliance) regulatory requirements associated with the conduct of drug studies/clinical trials. VABHS will perform more frequent audits of PI reports of "***Unanticipated Problems Involving Risks to Subjects and Others***" and "***Adverse Events***" to be followed by PI/protocol specific for cause audits in the event that patterns of noncompliance are identified. Results of these audits will be brought forward to the IRB and R&DC for their determinations and subsequent implementation of remedial action plans. The PI will be instructed to establish permanent weekly lab meetings with research personnel under her supervision and to provide minutes of those meetings to the IRB and R&DC for a period of six months for their review and consideration. Based on their review of the minutes, the IRB and/or R&DC may require the PI to implement changes in research practice. In such instances they will require the PI to provide evidence of having implemented all required changes in the lab. The RCO who will be auditing all PI studies once a month will include in those audits certification that all IRB and R&DC required changes (as applicable) have been implemented. At the end of the six month period (following the final audit the week of March 15, 2013) the RCO will provide a final report to the IRB and R&DC who will jointly determine whether or not the PI needs to continue to provide minutes of weekly lab meetings to them for their review. Of note, a total of .8 (32 hours) additional FTEE has been allocated toward research compliance (supported by the Office of the Medical Center Director).

VABHS STATUS NOVEMBER 30, 2012: (A) R&D has scheduled live training for investigative staff on January 18, 2012 and February 23, 2012. (B) To date the IRB and the R&DC have not reviewed evidence from lab meetings between the PI and her research personnel that warranted recommendations for changes in laboratory practice. (C) VABHS historically audited PI reports of "***Unanticipated Problems Involving Risks to Subjects and Others***" and "***Adverse Events***" on an annual basis and has modified their practice to require auditing on a quarterly basis. The first quarterly audit will be conducted in January 2013 and reflect all reports submitted between 10/1/12 through 12/31/12.

ORO RESPONSE: Progress satisfactory. Please submit next Progress Report by February 1, 2013, detailing the status of all required actions with supportive documents, i.e., R&DC and IRB meeting minutes documenting review and evaluation of the progress.

VABHS STATUS FEBRUARY 1, 2013: (A) R&D has re-scheduled live training for investigative staff on February 14, 2013 and March 18, 2013 due to scheduling conflicts of speakers and lack of available conference rooms. (B.) The IRB and the R&DC await more detailed reports of (minutes) lab meetings between the PI and her research personnel in order to determine whether or not changes in laboratory practice need to be recommended. R&DC is satisfied with the frequency of lab meetings, although the content of discussions needs to be clarified before formal conclusions can be drawn about the adequacy of the meetings. (C) The first quarterly audit of the PI reports of "***Unanticipated Problems Involving Risks to Subjects and Others***" and "***Adverse Events***" reflecting all reports submitted between 10/1/12 through 12/31/12 has not yet been completed due to the absence of HRPP staff because of illness (the flu). We anticipate the audit to be completed by the end of February, 2013.

VABHS STATUS APRIL 1, 2013:

(A) R&D presented live training for investigative staff on February 14, 2013 and March 18, 2013.

(B) The IRB and the R&DC continued to review minutes of weekly lab meetings between the PI and her research personnel and felt the minutes did not contain information to suggest that the PI was not in compliance with regulations. The R&D Committee felt that review of the minutes was not the best way for them to ascertain PI compliance and that review of RCO audits was a more appropriate means for doing so. Therefore, the R&DC decided to authorize the PI to discontinue submitting weekly lab minutes for their review.

(C) An audit of the PI reports of "***Unanticipated Problems Involving Risks to Subjects and Others***" and "***Adverse Events***" reflecting reports submitted between 10/1/12 through 12/31/12 was completed and compared with annual audits of those reports conducted in 2011 and 2012, results of which were discussed with the IRB who has a result of the information presented to them is in the process of revising their SOP for PI self-reporting. Going forward audits will be completed by the RCO on a quarterly basis with the next audit due by the end of April (covering January through March of 3013).

3. The VABHS must ensure that pharmacy personnel dispense study medications only when prescribed by authorized prescribers.

VABHS ACTION PLAN: Beginning in October 2012 for a period of six months the Research Pharmacist will submit monthly Drug Accountability Reports verifying that only authorized prescribers have dispensed study medications to the Institutional Review Board (IRB) and the Research and Development Committee (R&DC) for their review. In addition, beginning in November 2012 the RCO will audit pharmacy records on a bimonthly basis in order to validate Drug Accountability Reports submitted by the Research Pharmacist. Results of those audits will be submitted to the IRB and R&DC for their review and determinations about the need for modifications in pharmacy procedure and/or record keeping as necessary to remain compliant with regulations that govern dispensing of research drugs. At the conclusion of the six month period following the RCO's third bimonthly pharmacy audit (March 2013) the RCO will provide a final report to the IRB and R&DC who will jointly determine whether or not the monitoring period needs to be extended and/or whether or not VABHS needs to modify pharmacy practices in order to remain compliant with applicable regulations.

VABHS STATUS NOVEMBER 30, 2012: The Research Pharmacist has verified that only authorized prescribers have dispensed study medications as documented through Drug Accountability Reports. Pharmacy audit of drug accountability logs revealed that for CSP # 562 thirty-right bottles of sunscreen

were inventoried and those that have expired will be destroyed. It was noted that five bottles are sunscreen remain unaccounted for when compared to shipping logs. Efforts to account for these five bottles have been initiated and this will be reported to the IRB at their next regularly scheduled meeting on 12/3/12 and subsequently to the R&DC at their next regularly scheduled meeting on 12/12/12.

ORO RESPONSE: Progress satisfactory. Please submit next Progress Report by February 1, 2013, detailing the status of required actions with supportive documents, i.e., R&DC and IRB meeting minutes documenting review and evaluation of the progress.

VABHS STATUS FEBRUARY 1, 2013: The Research Pharmacist has verified through oral conversations with the HRPP office and the RCO that only authorized prescribers have dispensed study medications as documented through Drug Accountability Reports. His next audit report is due to the R&DC for review at their meeting of February 13, 2013 following which minutes documenting the continuing review of dispensing logs will be available.

VABHS STATUS APRIL 1, 2013: The Research Pharmacist confirmed that no study drugs were administered for [redacted] studies more recently than July of 2012 and May of 2012 (VA CIRB/CSP # 562 and VABHS IRB # 2596 respectively). For this reason, following the initial review of pharmacy dispending reports/drug accountability logs through those dates, the R&DC authorized the Research Pharmacist not to generate future reports. The R&DC reiterated that determination at their most recent meeting. In addition, [redacted] has not opened any new research studies involving drugs at VABHS that would require monitoring.

OFFICE OF RESEARCH OVERSIGHT

Report to the

Office of Special Counsel

OSC File Number DI-12-1098

Department of Veterans Affairs

VA Boston Healthcare System Boston, MA

Response October 4, 2012

V. Required Actions

1. The VABHS must ensure that all research currently involving the PI and SC adheres to the IRB-approved protocol and complies with all applicable VA research requirements by implementing an appropriate monitoring plan for their research.

   VABHS ACTION PLAN: The Research Compliance Officer (RCO) will audit each study involving the Principal Investigator (PI) once a month for a period of six months beginning the week of October 15, 2012. Results of each audit will be presented for discussion to the Institutional Review Board (IRB) and the Research and Development Committee (R&DC) for their input and determinations about the need for modifications in the research and/or PI sanctions as applicable in association with any serious or potentially serious findings identified at the time of audit. At the end of the six month period (following the final audit of March 15, 2013) the RCO will provide a final report to the IRB and R&DC who will jointly determine whether or not the monitoring period needs to be extended.

2. The VABHS must ensure that all of its research studies are conducted according to the IRB-approved protocols and all relevant Federal regulations and VHA Policies.

   VABHS ACTION PLAN: The VABHS Research and Development Service (R&D) will provide new educational programs to the VABHS Research Community that include topics of relevance pertaining to (findings of non-compliance) regulatory requirements associated with the conduct of drug studies/clinical trials. VABHS will perform more frequent audits of PI reports of "***Unanticipated Problems Involving Risks to Subjects and Others***" and "***Adverse Events***" to be followed by PI/protocol specific for cause audits in the event that patterns of

noncompliance are identified. Results of these audits will be brought forward to the IRB and R&DC for their determinations and subsequent implementation of remedial action plans. The PI will be instructed to establish permanent weekly lab meetings with research personnel under her supervision and to provide minutes of those meetings to the IRB and R&DC for a period of six months for their review and consideration. Based on their review of the minutes, the IRB and/or R&DC may require the PI to implement changes in research practice. In such instances they will require the PI to provide evidence of having implemented all required changes in the lab. The RCO who will be auditing all PI studies once a month will include in those audits certification that all IRB and R&DC required changes (as applicable) have been implemented. At the end of the six month period (following the final audit the week of March 15, 2013) the RCO will provide a final report to the IRB and R&DC who will jointly determine whether or not the PI needs to continue to provide minutes of weekly lab meetings to them for their review. Of note, a total of .8 (32 hours) additional FTEE has been allocated toward research compliance (supported by the Office of the Medical Center Director).

3. The VABHS must ensure that pharmacy personnel dispense study medications only when prescribed by authorized prescribers.

VABHS ACTION PLAN: Beginning in October 2012 for a period of six months the Research Pharmacist will submit monthly Drug Accountability Reports verifying that only authorized prescribers have dispensed study medications to the Institutional Review Board (IRB) and the Research and Development Committee (R&DC) for their review. In addition, beginning in November 2012 the RCO will audit pharmacy records on a bimonthly basis in order to validate Drug Accountability Reports submitted by the Research Pharmacist. Results of those audits will be submitted to the IRB and R&DC for their review and determinations about the need for modifications in pharmacy procedure and/or record keeping as necessary to remain compliant with regulations that govern dispensing of research drugs. At the conclusion of the six month period following the RCO's third bimonthly pharmacy audit (March 2013) the RCO will provide a final report to the IRB and R&DC who will jointly determine whether or not the monitoring period needs to be extended and/or whether or not VABHS needs to modify pharmacy practices in order to remain compliant with applicable regulations.

4. The VABHS must determine whether any disciplinary action is warranted in light of ORO's findings.

VABHS ACTION PLAN: The need for disciplinary action has not yet been determined. Discussions regarding the need for disciplinary action and what such action would entail will be held among the PI's supervisor (Chief, Medical Service), the Associate Chief of Staff/R&D, the Chief of the Staff and the Medical Center Director and a determination made no later than November 30, 2012.