April 15, 2015
1:30-3:00 PM

Department of Health
2585 Merchants Row
Conference Rm. 310 A
Tallahassee, Florida 32311

IRB 1 Convened Committee
Meeting Minutes

IRB Attendance:

Sandra Schoenfisch (Chair, Expertise in Subpart D: Children)

Ron Brown (Non-Scientist, Non-Affiliated, Present by Phone)

Karen Reynolds (Non-Affiliated, Expertise in Subpart B: Pregnant Women/Fetus/Neonates; and Subpart D: Children, Present by Phone)

Ovidiu Cotea (Present by phone)

Becky Grigg

Daphne Holden (Absent)

Roland Reis (Non-Scientist)

Other Attendees: Derek Schwabe-Warf, Robert Hood, Ph.D.

Quorum

A quorum **was** present. A quorum is defined as a majority of members present. The quorum also reflected the requirement outlined in 45 CFR 46.108 as well as 21 CFR 56.107. Please note that the number of members present will not always match the total number of votes on items as the total number votes reflects the number of members present in the room at the time of discussion and vote. At least one non-scientist and at least one non-affiliated member were present.

Members present by phone received all pertinent materials prior to the meeting to allow adequate time for review and request of additional information, if needed. Members present by phone actively and equally participated in the discussion of all protocols.

Conflict of Interest:

Conflict of Interest: None declared

Members did not report any:

- Compensation or payments for services (e.g., consulting fees, lecture payments, bonus, royalties, paid authorship, honoraria, gifts, or in-kind products or services) related to the research of any value, except as otherwise excluded by this policy.

- Compensation or payments for services where an arrangement has been entered into such that the amount of compensation will be affected by the outcome of the research.
- Equity interests (stocks, stock options, security, or other ownership interests) related to the research of any value.
- Equity interests whose value when aggregated for the individual and the individual's immediate family represents more than a five percent ownership interest in any single entity.
- Equity interest related to the research in a non-publicly traded corporation of any value by the individual or a member of the individual's immediate family
- Equity interest related to the research of any amount to the researcher or any member of the researcher's immediate family where an arrangement has been entered into such that the amount of compensation will be affected by the outcome of the research.
- Intellectual property rights and interests (patents, copyrights, royalties, licensing agreements, and any other proprietary interest related to the research).
- Board or executive relationship related to the research, regardless of compensation.
- Involvement or participation in the design, conduct, or reporting of the research, including providing advice on Department registry data systems.
- Serving as the immediate supervisor of a researcher within the last year
- Any other interest that the IRB member believes would interfere with his or her ability to objectively review a protocol.
- Any travel related to research

Education:

Robert Hood presented an overview of the expected timeline for AAHRPP re-accreditation as well as the step 1 responses. There were only three Elements that required modification. He informed the board that some but not all IRB committee members will be interviewed in addition to staff (Robert and Derek), legal counsel, the deputy secretary, the state surgeon general, data program staff, and researchers.

Research Site/Protocol:	**Principal Investigator:**	**Summary of Non-Compliance:**
Florida Department of Health in Orange County/EGRIFTA Diabetic Retinopathy	Ewa Szczypinksa, MD	Site failed to redact patient identifier before sending in report of patient hospitalization to sponsor.

The sponsor monitor informed study staff in early March 2015 of a violation of the sponsor protocol and breach of confidentiality involving an unauthorized release of data from the research site. The research coordinator forwarded the notice from the sponsor on March 16, 2015 to IRB staff. An email from the study coordinator confirmed that patient chart, containing a barcode, was released to the sponsor without being redacted, as required by the sponsor protocol. Staff forwarded the report to the IRB chair on March 20, 2015, who determined non-compliance was present in fact on March 20, 2015, and required review by the convened IRB. The information that was released is considered protected health information. Therefore IRB determined that failure to follow the protocol constituted serious non-compliance in fact since unauthorized access to PHI could potentially harm a patient's reputation or

financial standing. Based on information provided by the site, subsequent reports have been appropriately redacted.

IRB staff met with the Privacy Officer and reviewed to determine if the breech required reporting under HIPAA, and concluded that the event did not require reporting. Department policy regarding information security and protected health information requires reporting to the Office of Civil Rights under HIPAA in the event of a reportable breech, but that was determined not to be the case here.

The IRB required a corrective action plan. The site must schedule education by IRB staff; concerning adequate protections for confidentiality of information and unauthorized PHI disclosures and their potential impact on patient well-being; and staff must conduct an additional site visit by June 30, 2015 to verify provisions are in place to protect confidentiality of data. A letter will be sent to the FDA in accordance with DOH policy.

Total votes for approval of the corrective action plan: Affirmative: 6 Negative: 0 Recusal: 0 Absent: 0

Letter: Researchers and research staff must attend education on adequate protections for confidentiality of data to be conducted by HRPP staff before May 29, 2015.

Research Site/Protocol:	**Principal Investigator:**	**Summary of Non-Compliance:**
Florida Department of Health in Hillsborough County/GS-0112	Todd Wills, MD	Patient was brought in for visit 1.5 months before the patient was supposed to be seen.

The sponsor monitor informed study staff of a violation of the sponsor protocol. The study coordinator forwarded the notice from the sponsor on March 2, 2015 to IRB staff. An email from the study coordinator confirmed that a patient was brought in for their 36-week study visit a month and a half early: on June 9, 2014 instead of July 29, 2014. Staff forwarded the report to the IRB chair on April 6, 2015, who determined non-compliance was present in fact on April 6, 2015, and required review by the convened IRB. The IRB determined that failure to follow the protocol in fact constituted serious non-compliance since the patient was placed in potential risk by not being seen during their protocol scheduled visit.

The IRB required documentation of an education plan by IRB staff for all study staff and management. In addition the IRB required documentation of a plan for implementation of a quality assurance/quality improvement plan and process by the site and a site visit by IRB staff. A letter will be sent to the FDA in accordance with DOH policy.

Total votes for approval of the corrective action plan: Affirmative: 6 Negative: 0 Recusal: 0 Absent: 0

Letter: Describe a plan for education of all researchers and research staff on adequate protections for confidentiality of data to be completed by May 29, 2015. Describe plans for a monitoring program, to be implanted by May 29, 2015.

Protocol Title: (A5332) Randomized Trial to Prevent Vascular Events in HIV REPRIEVE

Submission:	**Principal Investigator:**	**Presenters:**
Initial Review	Charurut Somboonwit, MD	Ovidiu Cotea
		Becky Grigg

Meeting Discussion:

This is a new study looking at cardiovascular disease in HIV positive patients. Immune activation from HIV infection may contribute to increased cardiovascular disease morbidity and mortality compared with uninfected people. This study looks at pitavastatin 4 mg (stage 4) as a prevention strategy for cardiovascular disease events in HIV positive patients. Looks at efficacy of pitavastatin via LDL levels and incidence of major cardiovascular disease events, and safety in HIV subjects via routine health indicators such as blood pressure. Both men and women who have been on ART for 6 months or more and who do not meet current guidelines for statin initiation will be eligible. One arm (experimental) involves pitavastatin while the other arm involves placebo (control). Patients in both the treatment and control arm will continue with their normal HIV antiretroviral therapy. The study will be conducted at the Florida Department of Health Hillsborough County. The plan is to enroll up to 6500 patients across all sites. The study will last for 72 months. The study is conducted by Charurut Somboonwit, a well-known board licensed infectious disease physician.

Reviewers determined the application was greater than minimal risk study and is consistent with sound research design and does not unnecessarily expose subjects to risk. The risks of statins are well understood and statins are generally well-tolerated. The statin in this study is not contraindicated for patients undergoing HIV drug therapy. The design of the study is consistent with scientific standards, is double-blinded. Risks are reasonable in relation to anticipated benefits because the study provides important knowledge which could not be obtained in an alternative fashion and does not significantly compromise the welfare or rights of participants. Statins are standard of care for patients with hyperlipidemia, but are poorly tolerated or contraindicated in patients on certain HIV medications. The study evaluates a statin that is not contraindicated to see if it reduces incidence of major cardiovascular disease events. Selection of subjects is equitable because subjects are selected based on inclusion criteria which is based on disease characteristics rather than selecting participants based on race or sex. The researcher has chosen a long form written consent, which is appropriate for this study. The consent document includes all required disclosures. Committee members discussed the safety monitoring plan in

the application and determined that adequate provisions were made for safety monitoring. The sponsor's plan for safety monitoring is appropriate. A data and safety monitoring board is reviewing the research, and will report findings to the IRB. In addition, the local health department director has authorized the study and is aware it will be ongoing. Committee members discussed the provisions protecting privacy interests and determined that adequate provisions were in place due to use of a private exam room. Committee members discussed the provisions protecting confidentiality and determined that adequate provisions were made to protect the confidentiality of data because file drawers housing hard copies of records are locked and password protected computers are utilized. Study is HIPAA compliant. No vulnerable populations are enrolled in the study.

Total votes for approval for not more than 12 months: Affirmative: 6 Negative: 0 Recusal: 0 Absent: 0

Protocol Title: GS-1160 A Phase 3b, Randomized, Double-Blind Study to Evaluate Switching from a Regimen Consisting of Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate (EFV/FTC/TDF) Fixed Dose Combination (FDC) to Emtricitabine/Rilpivirine/Tenofovir Alafenamide (FTC/RPV/TAF) FDC in Virologically-Suppressed, HIV-1 Infected Subjects

Submission:	**Principal Investigator:**	**Presenters:**
Initial Review	Todd Wills, MD	Ovidiu Cotea
		Daphne Holden

Meeting Discussion:

This is an initial review of a new study looking at a novel HIV treatment for HIV treatment experienced patients. The control arm involves an approved medication EFV/FTC/TDF fixed dosed combination therapy while the experimental arm involves switching to FTC/RPV/TAF fixed dose combination therapy. The experiment looks at the non-inferiority of switching to the experimental therapy via HIV-1 RNA copies. Also, the experimental therapy is thought to be safer in terms of bone mineral density than the control treatment. This will be ascertained primarily through X-ray absorptiometry. The study will be conducted at the Florida Department of Health Hillsborough County. The plan is to enroll up to 15 patients at the site and will last for 48 months. The study will be conducted by Dr. Todd Wills, a physician board certified in infectious disease with appropriate qualifications and expertise due to his prior research experience.

Reviewers determined that one or more criteria for approval was not met. Risks are reasonable in relation to anticipated benefits because the study provides important knowledge which could not be obtained in an alternative fashion and does not significantly compromise the welfare or rights of participants. The other drugs in the same class are well understood, and side effects are expected to be similar, and the investigational drug is expected to have lower loss of bone density. Selection of subjects is equitable because subjects are selected based on inclusion criteria which is based on disease

characteristics rather than selecting participants based on race or sex. The researcher has chosen a long form written consent, which is appropriate for this study. The consent document includes all required disclosures. Committee members discussed the safety monitoring plan in the application and determined that adequate provisions were made for safety monitoring. The sponsor's plan for safety monitoring is appropriate. A data and safety monitoring board is reviewing the research, and will report findings to the IRB. The local health department director is aware of the study and has devoted adequate resources to the research. Committee members discussed the provisions protecting privacy interests and determined that adequate provisions were in place due to use of a private exam room. Committee members discussed the provisions protecting confidentiality and determined that adequate provisions were made to protect the confidentiality of data because file drawers housing hard copies of records are locked and password protected computers are utilized. Study is HIPAA compliant. No vulnerable populations are enrolled in the study.

However, although the design of the study minimizes risk, and risks are reasonable given the anticipated benefits, if any, of the research, the local procedures for dispensing medications are not adequate. Currently study staff dispense medications, which is inconsistent with the Department policy and state law. The board determined risks are not minimized because unlicensed, untrained staff who are not knowledgeable about Department policies are dispensing investigational drugs.

Total votes to approve study for 12 months pending minor changes: Affirmative: 6 Negative: 0 Recusal: 0 Absent: 0

Letter: Confirm that a licensed physician or pharmacist dispenses investigational medications for all research.

Protocol Title: GS-1216 A Phase 3b, Randomized, Double-Blind Switch Study to Evaluate the Safety and Efficacy of Emtricitabine/Rilpivirine/Tenofovir Alafenamide (FTC/RPV/TAF) Fixed Dose Combination (FDC) in HIV-1 Positive Subjects who are Virologically Suppressed on Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate (FTC/RPV/TDF)

Submission:	**Principal Investigator:**	**Presenters:**
Initial Review	Todd Wills, MD	Ovidiu Cotea
		Ron Brown

Meeting Discussion:

This is a new study looking at a novel HIV treatment for HIV treatment experienced patients. The study involves a different combination of medications than the previous study. The control arm consists of an approved medication Complera (FTC/RPV/TDF) fixed dose combination therapy while the treatment arm involves (FTC/RPV/TAF) Fixed Dose combination therapy. The study aims to determine the non-

inferiority of switching to the experimental arm from the control arm by measuring HIV-1 RNA copies throughout the course of the study. The secondary object is to look at bone and mineral density via X-ray absorptiometry. The study will be conducted at the Florida Department of Health Hillsborough County. The plan is to enroll up to 15 patients at the site. The study will last for 48 months. The study will be conducted by Dr. Todd Wills, a physician board certified in infectious disease with appropriate qualifications and expertise due to his prior research experience. Since the researcher is allowing study staff without a medical degree to dispense medications, the board moved to approve the study after confirmation from the site that only physicians or designated nurses will dispense medication is obtained.

Reviewers determined the application was greater than minimal risk study and is consistent with sound research design and does not unnecessarily expose subjects to risk because design of the study is consistent with scientific standards. Risks are reasonable in relation to anticipated benefits because the study provides important knowledge which could not be obtained in an alternative fashion and do not significantly compromise the welfare or rights of participants. The study involves a different combination of drugs, involving the unapproved tenofovir alafenamide. TAF is similar to existing forms of tenofovir, but is absorbed more readily, and is anticipated to protect bone density compared with TDF. Selection of subjects is equitable because subjects are selected based on inclusion criteria which is based on disease characteristics rather than selecting participants based on race or sex. The researcher has chosen a long form written consent, which is appropriate for this study. The consent document includes all required disclosures. Committee members discussed the safety monitoring plan in the application and determined that adequate provisions were made for safety monitoring. The sponsor's plan for safety monitoring is appropriate. A data and safety monitoring board is reviewing the research, and will report findings to the IRB. The county health department director is aware of the study and has devoted adequate resources. Committee members discussed the provisions protecting privacy interests and determined that adequate provisions were in place due to use of a private exam room. Committee members discussed the provisions protecting confidentiality and determined that adequate provisions were made to protect the confidentiality of data because file drawers housing hard copies of records are locked and password protected computers are utilized. Study is HIPAA compliant. No vulnerable populations are enrolled in the study.

However, although the design of the study minimizes risk, and risks are reasonable given the anticipated benefits, if any, of the research, the local procedures for dispensing medications are not adequate. Currently study staff dispense medications, which is inconsistent with the Department policy and state law. The board determined risks are not minimized because unlicensed, untrained staff who are not knowledgeable about Department policies are dispensing investigational drugs.

Total votes for approval study for 12 months pending minor change: Affirmative: 6 Negative: 0 Recusal: 0Absent: 0

Letter: Confirm that a licensed physician or pharmacist dispenses investigational medications for all research.

Next Meeting: May 20, 2015

Other Business:

Meeting Adjourned: 2:55