The **Office of Human Research Protection (OHRP)** provides an internal monitoring function and educational forum for Georgia Health Sciences University (GHSU) to assure that all research studies utilizing human subjects and/or human derived materials comply with federal, state and institutional regulations and policies to protect research subjects, the university and the research team.

**History**

The OHRP was formed in 1997 by the Board of Regents to provide oversight and closely monitor clinical research at GHSU. The GHSU holds a Federal Wide Assurance (FWA) issued by the Department of Health and Human Services (DHHS) Office of Human Research Protections (OHRP). This requires GHSU to assure that there are procedures that monitor compliance with human research subject protection requirements. Conducting study compliance assessments provides one such mechanism for meeting this requirement. The study compliance assessments are used to improve the quality of human research subject’s protections program and to increase the awareness of regulatory compliance. The compliance assessments are intended to be proactive, non-punitive and focused on educating investigators and research staff of their ethical and regulatory responsibilities. Currently OHRP employs two full time compliance auditors.

**Function**

- To assure that research using human subjects and/or human derived materials is conducted according to conditions approved by the institutional review boards (IRB) known as the Human Assurance Committee (HAC), National Cancer Institute (NCI) CIRB or Chesapeake Research Review, Inc. (CRRI).
- To assure that data are appropriately managed so that any aspect (institutional review board approval, subject recruitment, financial records) of the study can be reviewed in a timely manner.
- To assure that the faculty and staff conducting research are well trained and aware of the policies and procedures. The findings of the compliance assessments conducted by the Clinical Trials Compliance Auditors (CTA) drive the education and training program offered by the OHRP.

**Goals**

- To ensure subject safety, verify accurate data collection, identify problem areas, and take corrective action when necessary. This process includes verifying eligibility and protocol and regulatory compliance according to GHSU policy, the International Conference on Harmonisation (ICH) Good Clinical Practice, the Food and Drug Administration (FDA) as well as the Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP) Regulations and Guidelines.
- To work closely with members of the GHSU community to improve the overall quality of clinical research and to facilitate the application and approval process.
The compliance assessments being conducted by OHRP will be based on a quality systems approach. There are three levels that encompass seven controls that will be assessed during the compliance assessment. These seven controls are listed below with a breakdown of the specific information to be reviewed during the compliance assessment.

SEVEN QUALITY CONTROLS

Level One

Management Controls

- Organizational structure and personnel
- Procedures and policies
  - Investigator SOPs
  - Institutional SOPs
  - IRB SOPs that the investigator has to follow
- Corporate systems and quality systems
  - Institutional or PI system of QA/QC
- Management oversight and supervision
- Monitoring oversight

Personnel Controls

- Education, training, and expertise of Investigative staff
- Personnel involvement and impact on compliance
- Deviations (type and scope)

Facility and Equipment Controls

- External facility
- Internal facility
- Equipment

Level Two
**Investigational Product Controls**

- Investigator selection/receipt process
- Distribution
- Dispensing
- Use
- Return
- Reconciliation

**Safety Controls**

- Adverse event reporting
- Medical oversight
- Appropriate or over delegation
- Physician involvement in I/E, etc.
- Laboratory and specialty testing
- Vendor, including Clinical Investigator and/or IRB/IEC, selection and management
- Human research subject safety/ethics
- Informed Consent
- Protocol deviation management
- Data Safety Management Board process, if applicable.

**Records, Documents, and Revision Controls**

- Case report form design and control process
- Data collection, including source data credibility and integrity and data management process
- Data delay
Data accuracy / acquisition issues

Regulatory approval process and tracking.

Approvals, lapses, required reporting issues

Regulatory document process

Trial master file process

Delegation of Authority and training records

**Level Three**

**Corrective and Preventative Action Controls**

- Internal quality assurance and quality control
- Monitoring process and controls (here or above)
- Internal assessment capabilities
- Risk management

**Compliance assessment Types**

Currently the OHRP conducts 6 types of compliance assessments as described below:

- **Routine compliance assessments** – This type of compliance assessment is routinely conducted as part of the Human Subjects Protection Program (HSPP). Active studies are routinely selected throughout the year by querying the HAC database.

- **Rotational Compliance assessments** – This type of compliance assessment is conducted every 4-6 weeks for each division of Oncology (Adult, Pediatric, Women’s Health, Prevention). Oncology studies are selected by a query of the HAC database.

- **“For cause” compliance assessments** – This type of compliance assessment is conducted in response to known or suspected information regarding research non-compliance. “For cause” compliance assessments are given priority over all other compliance assessments.

- **Investigator invitation compliance assessments** – This type of compliance assessment is conducted in response to a request from the PI. Investigator invited compliance assessments may be requested to help a site prepare for a FDA audit,
or in order to help a PI or study coordinator organize the regulatory documents for a study.

- HAC internal file compliance assessment – A compliance assessment of the HAC internal files is conducted for each routine compliance assessment selected by the CTA. These compliance assessment reports are sent to the Assistant Director of the OHRP. A compliance assessment response is completed by the HAC office specialist and returned to the CTA.

- HAC meeting minutes audit – An audit of the monthly HAC meeting minutes is conducted on a monthly basis. The audit is conducted to make sure the minutes are compliant with all Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP) recommendations.

**Compliance Assessment Plan**

The auditor will conduct:

- 20-25 routine or rotational compliance assessments
- As needed “For-Cause” and investigator initiated compliance assessments
- 20-25 compliance assessments of HAC internal files
- Monthly HAC minutes audits

**How the Compliance Assessment System Works**

Routine Compliance assessments:
The routine compliance assessments are selected by a pre-determined criteria based on assessment of regulatory risk, including the funding source, the number and type of studies conducted by an investigator, studies involving vulnerable populations, investigators holding Investigational New Drug Applications (IND), and investigator initiated studies.

Our primary focus will be the following types of studies:

- Phase 0
- Phase I Protocols in which a GHSU faculty member is the IND holder
- Phase I Protocols
- Phase I-III Oncology Protocols
- Pediatric Protocols
- Investigator Initiated Protocols
- Device Protocols (to include IDE)

Routine compliance assessments are conducted by querying the IRB database. The CTA will contact the Principal Investigator (PI) and/or Study Coordinator (SC) two to three weeks in advance via email or telephone to schedule the compliance assessment. Each PI and research team will be given adequate time to prepare for the compliance assessment.
to ensure that required documentation is available for review, to arrange for downtime out of the clinic or teaching, as needed and to be available for the entrance and exit interviews. The research team members are not required to be present during the actual compliance assessment.

A follow-up letter or email serves as the formal compliance assessment notification, which describes the compliance assessment proceedings and how to prepare for the compliance assessment. The notification also confirms the data and documents that will be assessed and the logistics of the compliance assessment, such as time, date and place as agreed upon during the scheduling phone call. At this time, the PI and/or SC will be requested to provide the following:

- a copy of the screening and/or enrollment log
- a copy of delegation of duties log
- the most recent monitoring report.

All research subject consent documents will be reviewed for studies with an enrollment of less than 10 participants. For large studies with enrollment greater than 100 or for those studies with multiple treatment/research arms, 5-10% of the subject population will be selected. An additional random selection may be on site if the auditor determines that additional measures are necessary.

The OHRP auditor will request that the PI and/or research team, have the research records for selected subjects to be made available for the compliance assessment. Access to all selected subjects’ research records, Case Report Form (CRF) or Data Collection Tools (DCT) records and associated documents should be provided to OHRP at the research site. The number of subject records that will be reviewed during a compliance assessment will be based on the complexity of the protocol and the number and type of issues identified by the auditor.

The hospital medical records will be reviewed by the CTA to verify the presence of the informed consent document.

During the compliance assessment, the PI and/or the study coordinator should be available to assist the CTA as needed.

The exit interview will take place upon completion of the compliance assessment, with the PI and study staff. During the exit interview, the PI and the study staff will have an opportunity to respond to the findings, recommendations, or questions that have arisen during the compliance assessment. Information provided from this process is included in the final report.

a. The CTA completes the compliance assessment report and letter listing the findings discussed in the exit interview and any other findings that may be found after the compliance assessment. Depending on the issues identified, the CTA may consult with the HAC Chairman or OHRP director for further recommendations. The complete final compliance assessment report is e-mailed to the PI and the study coordinator within two weeks of the exit
interview. If this time line cannot be met, the PI and study coordinator will be sent a summary report and notification when the final report will be sent. The HAC Chair, Vice Chair, OHRP Director, Assistant Director and Department Chair will also receive a copy of the compliance assessment report. If the study is conducted at the Veterans Administration Medical Center (VAMC), the Chief of Research and Development, and Administrative Officer will also receive a copy of the compliance assessment report. If NCI CIRB or CRRI is the IRB of record, they will also be sent a copy of the report.

b. Any for cause compliance assessment or routine compliance assessment that have findings that are classified as critical will be sent to the Institutional Official and the Vice President of Research. The PI is asked to reply with a written corrective action plan as needed within one month. Also the CTA will schedule a re-audit within 6 months of the date of the original assessment to verify that all corrective actions have been implemented.

The CTA will review the compliance assessment response from the PI. If any items need further clarification, the CTA will correspond with the PI until all issues are resolved. Once all the compliance assessment items have been addressed satisfactorily, an compliance assessment close-out letter will be sent to the PI indicating that the study compliance assessment is now complete.

The timeline may vary per compliance assessment.

Selecting Protocols for Routine Compliance Assessments

The CTA selects two protocols per month. All active protocols are eligible for a compliance assessment, including industry-sponsored studies. The following guidelines are used for prioritizing protocols to assess:

- A protocol is eligible for an OHRP compliance assessment after IRB approval
- The CTA attempts to distribute the compliance assessments evenly among the various protocols.
- Although unlikely, a PI who is routinely assessed once during the year may be routinely assessed a second time during the year on a different protocol.

Selecting Protocols for Rotational Compliance Assessments

Each division of Oncology (Adult, Pediatric, Women’s Health, and Prevention) will be assessed every four to six weeks to ensure protocol compliance.
Cooperative Group Compliance Assessments

The cooperative group studies are audits every three years but may be audited at any time by the respective cooperative group. These studies will be assessed by OHRP as part of the rotational compliance assessments and we will no longer be providing preparatory audit assistance. Any compliance assessment findings identified during an OHRP compliance assessment should applied to all other studies to ensure that all studies are audit ready at the time of the cooperative groups scheduled audit. Our office can be contacted if assistance with audit preparation is needed due to extenuating circumstances. The Assistant Director will make the final decision if resources are available.