



Welcome to the Piedmont Healthcare Office of Research Services (ORS). Click on an area of interest below to go directly to questions and answers related to that area.

<u>Institutional Review Board (IRB)</u>	<u>Pre-Award</u>	<u>Regulatory Affairs</u>	<u>Quality Assurance</u>
---	----------------------------------	---	--

Institutional Review Board (PHCIRB)

The mission of the Piedmont Healthcare Institutional Review Board (PHCIRB) is to enhance and facilitate the ethical conduct of human subjects research conducted by the Piedmont entity. The PHCIRB will perform this mission through its review of human subjects research, its educational and training initiatives, and its compliance oversight and quality improvement programs. The PHCIRB is in compliance with both the Food and Drug Administration (FDA) and Office of Human Research Protections (OHRP) requirements for IRB registration. The PHCIRB is the local designated committee charged with responsibility to provide robust review, approval, and oversight monitoring of research to ensure the protection of the rights, safety, and well-being of human subjects participating in research. The PHCIRB may review industry sponsored, investigator-initiated, student research, and affiliate research proposals. The PHCIRB is established under the authority of the Belmont Report and Common Rule for the purpose of protecting the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of Piedmont Healthcare.

While approval from other Piedmont Healthcare offices or committees may be necessary per institutional policy, the decision of whether to approve or disapprove a submission is made autonomously and is not influenced by potential funding, prestige, or other benefit that may accrue to the Institution.

The PHCIRB is supported by the Institutional Official (IO) and functions administratively through the ORS. This structure provides for administrative coordination of the PHCIRB with various other departments involved in the research process. Direct oversight of the PHCIRB determinations process is under the purview of the PHCIRB Chair to avoid perceived influences of the IO or ORS. The PHCIRB advises and makes recommendations entity wide on all matters related to the use of human subjects in research and applies regulations to both federally funded and federally unfunded research.

How do I locate and contact the IRB? We are located at 1968 Peachtree Road, NW, 95 Building, 3rd Floor, Suite 3025, Atlanta, GA 30309. Phone: 404.605.3638, email: Madeline.Peyton@piedmont.org. The PHCIRB maintains an open door policy for 'drop-in' questions as time and tasks permit.

How frequently does the PHCIRB meet? Monthly. Every 3rd Friday. End of year dates are adjusted to accommodate holiday schedules. Go to <https://www.piedmont.org/research/research-eforms-and-systems> under General Documents to see the calendar for the current year.

Where and what time are IRB meetings held? In addition to online via WebEx and/or teleconference, IRB meetings are held in the 95 building Research Conference Room, 3rd Floor, Suite 3025 at 12:30 pm.

Is there a submission deadline? Yes and No. Submissions requiring full committee review must be in the IRB inbox 3 weeks prior to the next meeting. Note: the ORS submission process is completed prior to submission to the IRB. Submissions not requiring full committee review have no deadline and can be submitted at any time.

What is the composition/membership expertise of the PHCIRB membership? Transplant/Nephrology, Endocrinology, IRB Administration, Jurisprudence, Community Representation, Cardiovascular, Pharmacy, Pathology, Pulmonology, Chaplaincy, Cardiology, Nursing, Hematology/Oncology, and Gastroenterology/Transplant/Hepatology. Note: Membership can and does change often, however, the PHCIRB will maintain sufficient expertise to robustly review submitted proposals OR appropriately solicit the expert opinion from a qualified consultant.

How is member conflict and voting handled? The PHCIRB carefully manages member conflicts in accordance with 21 CFR 46.107(e) and PHCIRB policy #6404 [<https://www.piedmont.org/research/research-eforms-and-systems> under Guidance Documents\ IRB Policies].

Per 21 CFR 46.107 (e), ‘No IRB may have a member participate in the IRB’s initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB’.

Per PHCIRB policy #6404 conflicted members are not given access to the review materials and may not participate in the discussion and vote on applicable research. In these cases the only offering the member may provide is information to the committee and the member must excuse themselves (or be excused) from the deliberations and votes on that protocol.

Has the PHCIRB ever been FDA audited and what were the results? FDA audits were conducted in 2007, 2015, and 2018. The PHCIRB has never been issued a 483.

What is the PHCIRB Federalwide Assurance Number? FWA00000662.

What is the PHCIRB Registration Number? IRB0000809.

What are the investigator reporting responsibilities? See PHCIRB policy # 6434 at <https://www.piedmont.org/research/research-eforms-and-systems> under Guidance Documents\ IRB Policies.

What is the research education training requirement and to whom does it apply? See PHCIRB policy # 6423 at <https://www.piedmont.org/research/research-eforms-and-systems> under Guidance Documents\ IRB Policies. NOTES: 1) Research education training offered through the WCG Academy is also required of the IRB membership. 2) On a case-by-case basis, certification through the CITI program may initially be accepted, however, prior to expiration of certification the trainee must complete the Piedmont entity training requirement offered through WCG Academy.

Does the PHCIRB use a protocol tracking database? Yes, it is called IRBNet. The IRBNet system is fully compliant with the technology requirements for Electronic Records per 21 CFR Part II, Section 11.10 – Controls for Closed Systems, and the technology requirements for Electronic Signatures per 21 CFR 11 Subpart C – Electronic Signatures.

Do IRB fees apply? Yes. IRB fees are for review services and are not contingent upon approval of submissions. Go to <https://www.piedmont.org/research/research-eforms-and-systems> under General Documents\IRB Fee Schedules.

What is some of the most commonly used terms in research? Go to <https://www.piedmont.org/research/research-eforms-and-systems> under General Documents\Glossary.

What are the ABCs of IRBs? Go to <https://www.piedmont.org/research/research-eforms-and-systems> under Guidance Documents\ABCs of IRBs.

Are there other IRB review committee options? Yes. Piedmont allows IRB review through several central review committees: 1) Western IRB (WIRB). WIRB is an independent central IRB that offers the full range of regulatory and ethics review services for research. In 2014 Piedmont Healthcare executed a contract with WIRB that effectively made WIRB the first consideration for IRB of record for all new industry sponsored research. The agreement afforded Piedmont physicians with the option to use WIRB or the local IRB (PHCIRB) and eliminated the need for dual review. WIRB has been inspected by FDA 17 times over the past 33 years and has no outstanding issues. The last inspection was in November 2014 and was classified as VAI (voluntary action indicated) for a single-item 483 regarding a consent form approved in 2008. 2) Central Institutional Review Board for the National Cancer Institute. This entity serves institutions conducting NCI sponsored research. NOTE: Researchers can access either committee above via ORS@piedmont.org.

Compliance? The PHCIRB is a duly constituted IRB through its Federalwide Assurance and registration with the Office for Human Research Protections (OHRP). The Piedmont Healthcare IRB complies with all US regulatory requirements and state laws related to the protection of human research participants. Specifically, the PHCIRB complies with 45CFR 46 subparts A through E, as well as 21 CFR parts 11, 50, 54, 56, 312, 803, 812, and 814. Components of Piedmont Healthcare are inclusive of: Piedmont Athens Regional, Piedmont Atlanta, Piedmont Columbus Regional-Midtown, Piedmont Columbus Regional-Northside, Piedmont Fayette, Piedmont Henry, Piedmont Mountainside, Piedmont Newnan, Piedmont Newton, Piedmont Rockdale, Piedmont Walton, Piedmont Physicians Group, Piedmont Heart Institute, Piedmont Cancer Center, and Piedmont-Georgia Lung Associates.

Pre-Award

What does Pre-Award mean? Pre-Award is a term used to describe activities that occur before the contract is executed or finalized. At Piedmont Healthcare, these activities are split up between individuals who work together simultaneously to do what is needed to get enrollment started on a study.

What is going on simultaneously during the pre-award process?

- Regulatory documents are being completed, signed, and filed. Examples: 1572, financial disclosure forms, CV updates.
- IRB document preparation, submission, and approvals are completed.
- The Medicare Coverage Analysis is completed.
- The study budget is negotiated and finalized.
- The clinical trial agreement (CTA) is negotiated and finalized.
- Companies sponsoring (paying for) the trials are vetted to ensure they are in good standing.
- Investigators on the trial are vetted to make sure they do not have a financial conflict of interest that could cause bias.

- Signatures for all parties to the contract are obtained.
- The clinical trial management system is set up for each study.
- The electronic medical record is built out to recognize research patients for each study.
- Local CMS (Centers for Medicare & Medicaid Services) submissions are made to link device trials in the Medicare billing system.

What is a Medicare Coverage Analysis (MCA)? The MCA is a roadmap for the budgeting and billing process. It indicates whether a charge generated by the medical care of a participant in a clinical trial is billed to the patient's insurance, the study, or neither.

Why is a MCA important? The ultimate goal of a MCA is to ensure compliance with billing regulations.

How does one know what can and cannot be billed to Medicare? Medicare has published guidelines that indicate what can and cannot be billed to them. There are national guidelines (National Coverage Determinations or NCDs), local guidelines (Local Coverage Determinations or LCDs), National Comprehensive Cancer Network (NCCN) guidelines, and research-specific guidelines.

Where can I find the guidelines? <https://www.cms.gov/medicare-coverage-database/overview-and-quick-search.aspx> This database allows you to search LCDs, NCDs, or both. Guidelines for oncology are located at: <https://www.nccn.org/>. Access to both databases is free.

What if a study procedure is not part of a guideline? If there is not a guideline saying you cannot bill Medicare and the patient is on a clinical trial with an IDE (Investigational Device Exemption) or IND (Investigational New Drug) number assigned by the Food & Drug Association (FDA), the service can fall into a "catch all" category. For drug studies, this catch all category is NCD 310.1. For device trials, this is covered by Chapter 14 of the Medicare Benefits Processing Manual. Coverage with Evidence Development or CED can also be referenced at the link below.

<https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/index.html>

What is considered routine care? Routine care is a service or test a physician would normally order in their usual practice of medicine if the patient was not in a clinical trial.

After the MCA is complete, then what? The MCA is sent to Research Finance for budget development.

What is a Local Medicare Contractor? The United States is split into regions that administer federal Medicare funds. Piedmont's local Medicare Contractor is Palmetto GBA. All the billing for Medicare patients goes through this office.

What is the difference between a device and drug study in the pre-award process? Drug studies fall under NCD 310.1 for guidance. Device studies fall under Chapter 14 of the Benefits Processing Manual. Device trials must be submitted to the local CMS office. This allows billing to flow unencumbered electronically. Devices also need to be submitted to Piedmont's Supply Chain where they are registered in EPIC and can be billed appropriately when used. If you would like to view more specific information on these guidelines, you can visit:

https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/ncd103c1_Part4.pdf

Who is Piedmont's legal counsel? HuZu Law based in Savannah, Georgia represents Piedmont Healthcare's research interests.

What is a Master Agreement? A Master Agreement serves as an avenue to improve the clinical trial agreement process. Many terms are universal among clinical trials. These are negotiated in the Master Agreement leaving only a few terms applicable to a specific study needing review and negotiation.

What is a Professional Services Agreement? This type of agreement applies when Piedmont contracts services from another professional or medical group to provide services for a specific purpose.

What is a Statement of Work? A Statement of Work or SOW defines the specific procedure or service needed for a specific clinical trial and is a part of a Professional Services Agreement or a Master Agreement.

What do I do with an unsigned Confidentiality or Non-disclosure agreement? Please send it to ORS@piedmont.org. ORS will ensure specific terms required by Piedmont Healthcare are present in the document before it is fully signed.

What does it mean when I hear sanctions and COI are needed? Just before Piedmont signs off on any legal document, a request is made by ORS to run a sanctions and COI check. This request is managed by Piedmont's Compliance Department. They have access to a national database that is up-to-date. Sanctions will denote if a sponsor is in poor standing with a regulatory body. COI is Conflict of Interest and will show if a study physician has more than the allowed financial interests in a company.

Regulatory Affairs

The Regulatory Affairs department of the Piedmont Healthcare Office of Research Services (ORS), is responsible for the maintenance of regulatory documentation pertaining to the conduct of all clinical trials ongoing at any Piedmont Healthcare facility. Regulatory documentation means the preparation of documents for submission to an Institutional Review Board for review, creation of documents for signature by a study investigator or clinical research coordinator, as well as maintenance of an electronic or paper record of all non legal or financial documents pertaining to the trial as indicated below:

- Preparation, submission, and maintenance of regulatory documents required by the Piedmont Healthcare Institutional Review Board (PHC IRB), the Western Institutional Review Board (WIRB) and/or other Institutional Review Boards used by Piedmont Healthcare, Food and Drug Administration (FDA), study sponsor, and related local and federal agencies.
- Informed consent development and submission to review committees.
- Tracking and maintaining regulatory documentation in electronic & non-electronic formats.

How do I submit something to the regulatory affairs department of ORS? Please email all required documents to ors@piedmont.org. This will generate a ticket to get the items you have submitted into the work queue.

What needs to be submitted to the ORS email for handling by regulatory affairs? Documents for any new study that you want to open at a PHC Facility. Documents which will require submission to an IRB for any ongoing study at a PHC Facility. The following is a list of many of the items that need to be submitted to

ors@piedmont.org for IRB submission. A ticket must be created before any work will begin. This is not an all-inclusive list:

New Study:

- New study documents
- CV (for each study team member, hand signed and dated within 2 years)
- Medical License (as applicable for each study team member)
- Proof of WCG Academy training completion (for each study team member). Other human subjects training may be accepted.
- Protocol (if a non Pharmaceutical study please request the Piedmont IRB protocol template)
- Consent template (if a non Pharmaceutical study please request the Piedmont IRB consent template)
- Completed ORS In-Take form (will be provided to you)
- Any patient facing materials (advertisements, questionnaires, etc.)
- Any other information/documents pertaining to the conduct of the study (Investigator Brochures, FDA letters, etc.)
- Forms that will need to be signed (if applicable)

Ongoing Study:

- Anything that needs IRB approval
- Protocol amendments
- Investigator Brochure revisions
- Consent revisions (including patient stipend changes)
- Patient-facing materials (ex. advertisements, questionnaires, etc.)
- Monitor visit dates and follow-up letters
 - If paper binder, send to ORS for filing
 - If e-binder, upload to eReg binder in IRBNet
- Newsletters
 - If paper binder, send to ORS for filing
 - If e-binder, upload to eReg binder in IRBNet
- Any personnel change requests (PI's, Sub-I's, coordinators, etc.), include current signed and dated [within 2 years] CV and current medical license for any new to research personnel
- Study closure and impending close-out visit
- Request for change to target enrollment
- Request for patient transfer
- Annual study status reports, DSMB letters, etc.

- Study documents downloaded from the study portal (if applicable)
- Anything the sponsor requires to be submitted to the IRB.
- Sponsor requests that will require IRB submission or regulatory document revisions

What if I'm not sure it needs to be submitted to Regulatory Affairs? If you aren't sure if something needs to be submitted to the Regulatory Affairs department please send to ors@piedmont.org. We will be able to review what was sent and process accordingly. If it isn't something that would be handled by Regulatory Affairs, we would be able to provide guidance on where to send the information.

What documents are study coordinators responsible for maintaining in the regulatory binder (paper or eReg Binder)?

- Study specific training logs
- CVs/MLs on the M drive
 - M:\ORS General\Staff\CVs (Signed & Dated) and MLs
- DOA logs
- Drug/device accountability logs
- Temperature logs
- Sponsor/coordinator correspondence
 - Anything that does not require IRB submission

Quality Assurance

What is Quality Assurance?

A program for the systematic monitoring and evaluation of the various aspects of a project, service, or facility to ensure standards of quality are met.

What is the purpose of internal auditing?

The primary purpose of the internal audit process is to ensure the protection of human subjects, verify the validity and accuracy of data collection, identify non-compliance, and take corrective action when necessary. The audit process involves verifying subject eligibility, protocol adherence, and regulatory compliance according to FDA, ICH Good Clinical Practice, Piedmont research policies and procedures, and all other applicable regulations. The internal auditing of clinical trials will promote continuous improvement opportunities by providing an increased awareness of policies to researchers and staff as well as education of best practices to ensure the institution is conducting consistent high quality research.

Why should an organization have internal auditing?

Internal auditors provide recommendations for improvement in those areas where opportunities or deficiencies are identified.

What are QA responsibilities?

QA conducts site audits throughout the course of a trial to assess protocol and regulatory compliance and to ensure that the safety and welfare of subjects are addressed. The QA team ensures that data generated during the study reflect what is specified in the source records.

What are good clinical practices (GCP)?

GCP is defined as a standard for the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of clinical trials or studies. GCP is an international quality standard that is provided by the International Conference on Harmonisation (ICH).

What is monitoring?

Act of overseeing the progress of a clinical trial and ensuring that it is conducted, recorded, and reported in accordance with the Institutional Review Board (IRB) approved Protocol, Standard Operating Procedures (SOPs), and applicable regulatory requirements and Health Insurance Portability and Accountability act (HIPAA).

What are the steps to an internal audit?

Selection/Initiation

- New study enrollments
- Random selection
- Risk based monitoring

Pre-Inspection Process

- The study staff will receive a notification of upcoming audits
- The auditor/inspector will meet with the lead study coordinator to discuss preliminary questions (e.g., current status of the study; how many patients have been enrolled, randomized, completed or withdrawn; who identifies and contacts patients; and the auditor inquires about number of protocol deviations)

Auditing Process

- At the request of QA, study coordinator will provide the QA analyst with the current version of the Study Protocol, Informed Consent, and Case Report Forms
- QA will meet with the study coordinator to discuss the study's enrollment progress
- QA will thoroughly review selected enrolled study participants study charts and CRFs
- If a major finding is identified, QA reserves the right to review additional enrolled patients up to 25% of total enrolled subjects
- QA will draft a report documenting the review findings which will include the category, classification, detailed findings, responsible staff, and due date
- QA will schedule and meet with key research personnel to review report findings and review an action plan for resolution as needed
- QA review can be requested at any time throughout the life of a study

Close-out Report and Follow Up

- Following the audit, the inspector will review a summary of findings with the study coordinator. The study team will respond to any findings/observations before the final report generated. The auditor reviews the report and corrective actions will be completed prior to report finalization.

What is reviewed during routine audits?

The reviewer will typically randomly select a pre-determined number of patients (usually ~20%) to complete source document verification. This involves checking the patient chart against the research records:

- Informed consent process
- Proper data entry to CRFs
- Proper documentation and follow-up of SAEs and AEs
- Investigational product
- Withdrawal procedures
- Good documentation practices

Non-patient essential documents. Examples include:

- Investigator's brochure
- Signed protocol & amendments
- Contractual agreements - IRB approval/correspondence/annual reviews
- Regulatory approvals/amendments
- CVs/training records
- Relevant communications (emails, meeting agendas, etc.)
- Delegation of authority log
- IP accountability

What are the types of findings?

- **Major Finding:** A finding that threatens the safety of participants, the confidentiality of participants' information, or quality of the clinical trial outcome or results. Requires timely corrective action and typically indicates the lack of a management tracking system or a systematic failure pattern. It may also include a repeat observation that was previously identified as a deficiency. A process deviation may also be upgraded to major.
- **Minor Finding:** A finding that does not affect the participant safety, confidentiality of information or quality of the clinical trial. However, the finding could potentially indicate a fault in a process, which could lead to major or critical impact if repeated or escalated. Should be corrected at the earliest opportunity (typically an isolated occurrence with no systematic pattern).
- **Observation:** A finding that, while the safety confidentiality, quantity or outcome of the trial is not likely to be affected and/or may not represent a compliance issue, a recommendation is made to ensure continuing process improvement.

What is a corrective action plan?

A corrective action plan (CAP) is a step-by-step plan of action that is developed to achieve targeted outcomes for resolution of identified errors in an effort to:

- Develop and implement a plan of action to improve processes or methods so that outcomes are more effective and efficient
- Achieve measurable improvement in the highest priority areas
- Eliminate repeated deficient practices