1. PURPOSE

1.1. This policy establishes the Carilion Clinic's Human Research Protection Program (HRPP) and its commitment to protect the rights and welfare of human subjects.

2. GUIDELINE

2.1. Scope

2.1.1. The HRPP applies to:

2.1.1.1. All <Human Research> which engages Carilion Clinic as defined by "WORKSHEET: Engagement (HRP-422)."
2.1.1.2. All <Human Research> submitted to the IRB for review.

2.1.2. <Human Research> may not commence until IRB approved.
2.1.3. Activities that are not <Human Research> do not require IRB review unless there is uncertainty whether the activity is <Human Research>.
2.1.4. Direct questions about whether an activity (such as classroom research, quality improvement, case reports, program evaluation, or surveillance activities) represents <Human Research> to the IRB. The IRB provides written determinations in response to written requests.
2.1.5. Direct questions about whether Carilion Clinic is engaged in <Human Research> to the IRB. The IRB provides written determinations in response to written requests.
2.1.6. After a study is completed, Carilion Clinic does not consider the return of results to former subjects to be <Human Research>.

2.2. Ethical Principles

2.2.1. Carilion Clinic follows the ethical principles described in the report "Ethical Principles and Guidelines for the Protection of Human Subjects of Research" also known as "The Belmont Report." (see Reference 1)
2.2.2. Carilion Clinic applies its ethical principles to all <Human Research> regardless of support or geographic location.

2.2.2.1. Policies and procedures applied to research conducted domestically are applied to international research.

2.2.3. The following categories of individuals are expected to abide by these ethical requirements:

2.2.3.1. Investigators (whether professional or student)
2.2.3.2. Research staff
2.2.3.3. IRB members, IRB chairs, and IRB vice-chairs
2.2.3.4. HRPP staff members
2.2.3.5. Carilion Clinical Institutional Official
2.2.3.6. Employees and agents

2.2.4. Clinical trials should be conducted in accordance with the ethical principles in Reference 1 that have their origin in the Declaration of Helsinki and are consistent with good clinical practice and the applicable regulatory requirements.

2.3. Review and Oversight Requirements

2.3.1. The Carilion Clinic applies FDA regulations, the <Original Rule>, the <Revised Rule>, and 45 CFR §46 Subparts B, C, and D as described in the Tables in the References section.

2.3.2. Carilion Clinic applies the following requirements to non-exempt <Human Research as Defined by HHS> that is conducted, supported, or otherwise subject to regulation by the following federal departments or agencies:

2.3.2.1. DOD: 10 USC 980, DOD Instruction 3216.02, OPNAVINST 5300.8B, and SECNAVINST 3900.39D
2.3.2.2. DOE: DOE Order 443.1A and used "Checklist for IRBs to Use in Verifying That HS Research Protocols Are in Compliance with the Department of Energy (DOE) Requirements".
2.3.2.3. DOJ: 28 CFR §22 and 28 CFR §512.
2.3.2.4. ED: 34 CFR §97 Subpart D (equivalent to 45 CFR §46 Subpart D), 34 CFR §98, 34 CFR §99, and 34 CFR §356.
2.3.2.5. EPA: 40 CFR §26 and EPA Order 1000.17 Change A1.

2.3.3. Carilion Clinic applies 45 CFR §46 Subparts B, C, and D to the extent required by OHRP[1] to all non-exempt <Human Research as Defined by HHS>.
2.3.4. Carilion Clinic commits to apply the "International Conference on Harmonisation – Good Clinical Practice E6." (ICH-GCP) to <Human Research> evaluating the safety or effectiveness of a drug or biologic.
2.3.5. Carilion Clinic applies all policies and procedures applied to research conducted domestically to research conducted in other countries, including:

2.3.5.1. Confirming the qualifications of investigators for conducting the research
2.3.5.2. Conducting initial review, continuing review, and review of modifications to previously approved research
2.3.5.3. Post-approval monitoring
2.3.5.4. Handling of complaints, non-compliance, and unanticipated problems involving risks to subjects or others
2.3.5.5. Consent process and other language issues
2.3.5.6. Ensuring all necessary approvals are met
2.3.5.7. Coordination and communication with local IRBs
2.3.5.8. Encompassing activities that are "research involving human participants" as defined by local laws.

2.3.6. Carilion Clinic prohibits payments to professionals in exchange for referrals of potential subjects ("finder's fees").
2.3.7. This IRB reviews payments designed to accelerate recruitment that are tied to the rate or timing of enrollment ("bonus payments") and does not allow them unless the possibility of coercion and undue influence is minimized.

2.4. Components of the HRPP

2.4.1. Carilion Clinical Institutional Official

2.4.1.1. Carilion Clinical Institutional Official is the leader of the HRPP.
2.4.1.2. The Carilion Clinical Institutional Official is authorized to:

2.4.1.2.1. Allocate HRPP resources
2.4.1.2.2. Appoint and remove IRB members, IRB chairs, and IRB vice-chairs
2.4.1.2.3. Bind HRPP policies on the Carilion Clinic
2.4.1.2.4. Determine what IRBs the Carilion Clinic will rely upon
2.4.1.2.5. Disapprove, suspend, or terminate <Human Research>

[1] OHRP has indicated that for research not conducted, supported, or otherwise subject to regulation by a federal department or agency, OHRP will not review reports (e.g., unanticipated problems, non-compliance, suspensions, terminations), will not provide secretarial review of not otherwise approvable research under Subparts B and D, and will not certify prisoner research under Subpart C.

2.4.1.2.6. Hire and fire HRPP staff members
2.4.1.2.7. Limit or condition privileges to conduct <Human Research>
2.4.1.2.8. Determine that information represents <Serious Noncompliance>, <Continuing Noncompliance>, an <Unanticipated Problem Involving Risks to Subjects or Others>, a <Suspension of IRB Approval>, or a <Termination of IRB Approval>
2.4.1.2.9. Act against employees related to <Serious Noncompliance> or <Continuing Noncompliance>
2.4.1.2.10. Sign IRB authorization agreements
2.4.1.2.11. Suspend or terminate <Human Research>

2.4.1.3. Carilion Clinical Institutional Official is responsible to:

2.4.1.3.1. Oversee the HRPP
2.4.1.3.2. Ensure the independence of the review process
2.4.1.3.3. Ensure that complaints and allegations regarding the HRPP are appropriately handled
2.4.1.3.4. Ensure that the HRPP has sufficient resources, including IRBs, appropriate for the volume and types of <Human Research> reviewed, so that reviews are accomplished in a thorough and timely manner
2.4.1.3.5. Establish a culture of compliance with HRPP requirements
2.4.1.3.6. Investigate and correct allegations and findings of undue influence on the <Human Research> review process
2.4.1.3.7. Investigate and correct systemic problems related to the HRPP
2.4.1.3.8. Periodically review HRPP policies and procedures
2.4.1.3.9. Periodically review HRPP resources
2.4.1.3.10. Review and sign federal assurances (FWA) and addenda

2.4.2. All employees and agents of the Carilion Clinic:

2.4.2.1. All employees and agents of the Carilion Clinic ultimately report to the Carilion Clinical Institutional Official for HRPP issues.
2.4.2.2. All employees and agents of the Carilion Clinic are responsible to:

2.4.2.2.1. Be aware of this policy.
2.4.2.2.2. Be aware of the definition of <Human Research>.
2.4.2.2.3. Consult the IRB when there is uncertainty about whether an activity is <Human Research>.
2.4.2.2.4. Not conduct <Human Research> without IRB approval.
2.4.2.2.5. Report allegations of undue influence related to the HRPP.
2.4.2.2.6. Report <Allegations of Noncompliance> or <Findings of Noncompliance>.

2.4.3. IRB members and HRPP staff members

2.4.3.1. IRB members, IRB chairs, IRB vice-chairs, and HRPP staff members are responsible to:

2.4.3.1.1. Follow HRPP policies and procedures
2.4.3.1.2. Undergo initial training, including training on specific federal agency requirements (e.g., DOD) when such research is reviewed
2.4.3.1.3. Participate in continuing education activities at least annually, including training on specific federal agency requirements (e.g., DOD) when such research is reviewed
2.4.3.1.4. Respond to contacts from participants or others

2.4.3.1.5. Ensure contacts from participants or others are reported to the IRB when required by the IRB's written procedures
2.4.3.1.6. Ensure research submitted to an external IRB meets local requirements
2.4.3.1.7. Ensure research approved an external IRB has all local approvals before being conducted

2.4.3.2. IRB chairs are authorized to suspend or terminate <Human Research>.
2.4.3.3. IRB members and HRPP staff members ultimately report to the Carilion Clinical Institutional Official for HRPP issues.

2.4.4. IRB

2.4.4.1. Carilion Clinic may rely upon the IRB of another organization provided an Authorization Agreement for IRB review (IAA) is in place
2.4.4.2. The IRB has the authority:

2.4.4.2.1. To approve, require modifications to secure approval, and disapprove all <Human Research>.activities overseen and conducted by Carilion Clinic
2.4.4.2.2. To suspend or terminate approval of <Human Research> not being conducted in accordance with HRPP requirements or that had been associated with unexpected serious harm to participants
2.4.4.2.3. To observe, or have a third party observe, the consent process and the conduct of the <Human Research>.
2.4.4.2.4. Determine whether an activity is <Human Research>.
2.4.4.2.5. Determine whether Carilion Clinic is engaged in <Human Research>
2.4.4.2.6. To decide whether financial interests <Related to the Research> and the management, if any, allow approval of the <Human Research>.

2.4.4.3. Carilion Clinic cannot approve <Human Research> that the IRB has not approved.
2.4.4.4. External organizations relying on Carilion Clinic's IRB to can expect the Carilion Clinic's IRB to do the following and when the Carilion Clinic relies on an external IRB the Carilion Clinic expects the IRB to do the following:

2.4.4.4.1. Determine whether an activity is <Human Research>.
2.4.4.4.2. Determine whether <Human Research> engages the Carilion Clinic.
2.4.4.4.3. Determine which persons are considered engaged (agents) in the <Human Research>.
2.4.4.4.4. Assure all IRB members, IRB Chairs and Vice Chairs are trained in accordance with applicable IRB SOPs.
2.4.4.4.5. Evaluate scientific or scholarly validity of proposed research.
2.4.4.4.6. For clinical trials, assure ICH-GCP guidelines are met, including whether the available non-clinical and clinical information on an investigational product is adequate to support the clinical trial.
2.4.4.4.7. Identify any relevant local, state, or international requirements related to <Human Research>, and apply AAHRPP criteria to international research.
2.4.4.4.8. Make contact information for the IRB available to current and former subjects.

2.4.4.4.9. Explain to subjects how to contact someone independent of the investigator for questions, concerns, complaints, or subject rights, or to offer input.

2.4.4.4.10. Assure individuals with knowledge of community-based participatory research attend meetings where such research is reviewed.

2.4.4.4.11. Evaluate and manage <Unanticipated Problems Involving Risks to Subjects or Others>, <Noncompliance>, <Serious Noncompliance> and <Continuing Noncompliance>, including when necessary to conduct an audit.

2.4.4.4.12. Determine whether each allegation of noncompliance has a basis in fact and whether each incident of noncompliance is serious or continuing, including when necessary to conduct an audit.

2.4.4.4.13. Manage <Unanticipated Problems Involving Risks to Subjects or Others>, <Noncompliance>, <Serious Noncompliance> and <Continuing Noncompliance>, <Suspension of IRB Approval> and <Termination of IRB Approval>.

2.4.4.4.14. When appropriate, collaborate with the Carilion Clinic to Manage <Unanticipated Problems Involving Risks to Subjects or Others>, <Noncompliance>, <Serious Noncompliance> and <Continuing Noncompliance>, <Suspension of IRB Approval> and <Termination of IRB Approval>.

2.4.4.4.15. Notify the FDA of any <Unanticipated Problems Involving Risks to Subjects or Others>, <Serious Noncompliance> and <Continuing Noncompliance>, <Suspension of IRB Approval> and <Termination of IRB Approval.

2.4.4.4.16. Collaborate with the Carilion Clinic to notify regulatory agencies other than the FDA of any <Unanticipated Problems Involving Risks to Subjects or Others>, <Serious Noncompliance> and <Continuing Noncompliance>, <Suspension of IRB Approval> and <Termination of IRB Approval>

2.4.4.4.17. Conduct independent IRB review to manage organizational conflict of interest related to the research.

2.4.4.4.17.1. The relying organization is responsible to identify organizational conflicts of interests.

2.4.4.4.18. Identify and manage financial conflicts of interest of investigators and research staff and upon request, review and incorporate the relying organization's management plan.

2.4.4.4.19. Evaluate and confirm test articles have appropriate regulatory approval (e.g., IND or IDE, meet exemption requirements)

2.4.4.4.19.1. The relying organization is responsible to have and follow written policies and procedures to ensure that the handling of investigational or unlicensed test articles conforms to legal and regulatory requirements.

2.4.4.4.20. Evaluate and permit emergency uses of a test articles and assure uses follow FDA requirements.

2.4.4.4.21. Assure that emergency uses of a test articles are not considered <Human Research as Defined by HHS> and prohibit use of data obtained from an emergency use for <Human Research as Defined by HHS>.
2.4.4.4.22. Assure investigators and research staff are trained on DOD requirements when research is DOD-regulated, note the potential for additional training, and the possibility of DOD oversight of the educational program.
2.4.4.4.23. Assure that IRB members, IRB Chairs and Vice Chairs are trained in accordance with applicable IRB SOPs on DOD requirements when research is DOD-regulated.
2.4.4.4.24. Evaluate DOD research for scientific merit.
2.4.4.4.25. For DOD research, determine that the investigator has permission to conduct research in that country by certification or local ethics review.
2.4.4.4.26. For DOD research, determine that the investigator will follow all local laws, regulations, customs, and practices.
2.4.4.4.27. Assure the IRB consent has the requirements of DOD Instruction 3216.02 when reviewing non-exempt classified DOD research.
2.4.4.4.28. Report serious or continuing noncompliance with DOD research to the DOD human research protection officer.
2.4.4.4.29. Assure all DOE requirements of 10 CFR 745 and DOE Order 443.1.B. are met.
2.4.4.4.30. Assure all DOJ requirements of 28 CFR 22 and 512 are met.
2.4.4.4.31. Evaluate DOJ research to assure there is an adequate research design and it contributes to the advancement of knowledge about corrections.
2.4.4.4.32. Assure all ED requirements of 34 CFR 98, 99 and 356 are met.
2.4.4.4.33. Assure EPA requirements of 40 CFR 26 and EPA Order 1000.17 Change A1 are met, and to flag research that collects data intended to be submitted to EPA as subject to EPA regulations.
2.4.4.4.34. Provide equivalent protections for participants in non-funded research.
2.4.4.4.35. Ensuring concordance between any applicable grant in the IRB application, when required by regulators.
2.4.4.4.36. Assure that investigators and research staff are appropriately trained.
2.4.4.4.37. For international research:

2.4.4.4.37.1. Ensure appropriate expertise and knowledge of the country(ies) either through IRB members or consultants.
2.4.4.4.37.2. Ensure knowledge of local laws.
2.4.4.4.37.3. Ensure knowledge of cultural context.
2.4.4.4.37.4. Confirm the qualifications of the researchers and research staff for conducting research in that country.
2.4.4.4.37.5. Conduct initial review, continuing review, and review of modifications to previously approved research.
2.4.4.4.37.6. Conduct post-approval monitoring.

2.4.4.4.37.7. Handle complaints, noncompliance, and unanticipated problems involving risk to participants or others.
2.4.4.4.37.8. Manage consent process and document and other language issues.
2.4.4.4.37.9. Coordinate and communication with local IRBs when appropriate.

2.4.4.4.38. Should the relying organization terminate reliance on the IRB, the IRB will continue oversight of active studies until closure or a mutually agreed-upon transfer of the studies.

2.4.5. Upon request or when required by law, the Carilion Clinic will execute an Authorization Agreement with the relying organization, which documents respective authorities, roles, responsibilities, and communication between this Carilion Clinic and the relying organization.
2.4.6. Investigators and research staff ultimately report to the Carilion Clinic Institutional Official for HRPP issues and are to follow the obligations described in "POLICY: Investigator Obligations (HRP-070)."
2.4.7. The [Chief Compliance Officer] works with the Carilion Clinical Institutional Official]on HRPP issues and is responsible to:

2.4.7.1. Determine who is a <Legally Authorized Representative>, <Child>, and <Guardian>
2.4.7.2. Provide legal advice related to the HRPP to the Carilion Clinical Institutional Official, IRB, and investigators
2.4.7.3. Determine who is an agent for purposes of engagement
2.4.7.4. Identify relevant state and international laws
2.4.7.5. Resolve conflicts among applicable laws

2.4.8. Grants and Contracts Office works with the Carilion Clinical Institutional Official on HRPP issues.

2.4.8.1. The Grants and Contracts Office is responsible to review contracts for compliance with HRPP requirements.

2.5. Written Procedures

2.5.1. The Carilion Clinic makes written materials describing the HRPP available to all members of the Carilion Clinic through its Web site at https://www.carilionclinic.org/institutional-review-board.
2.5.2. The Carilion Clinic makes written materials describing the HRPP available to sponsors, CROs, and investigators upon request when those materials apply to the requestor.
2.5.3. When written materials are changed, the Carilion Clinic communicates to affected individuals through one or more of the following actions:

2.5.3.1. Email communications
2.5.3.2. Web-site postings
2.5.3.3. Direct outreach at organizational meetings
2.5.3.4. Training
2.5.3.5. PRIS3M On-line IRB submission system

2.6. <Reliance Agreements>

2.6.1. For federally funded research that must follow the <Revised Rule> (with the exception of exempt research for which IRB review is not required by regulation) that takes place at an institution in which IRB oversight is conducted by an IRB that is not operated by the institution, the institution and the organization operating the IRB must document the institution's reliance on the IRB for oversight of the

research and the responsibilities that each entity will undertake to ensure compliance with the requirements of this policy.

2.7. Questions, Concerns, and Feedback

2.7.1. The Carilion Clinic solicits questions, concerns, and feedback by making the document "BROCHURE: Should I Take Part in Research (HRP-900)" available on its Web site and available to investigators to provide to the public.

2.7.2. Individuals should address questions, suggestions, concerns, or complaints about the IRB or human research protection program; allegations of undue influence, <Allegations of Noncompliance> or <Findings of Noncompliance> orally or in writing to:

Carley Emerson, MS, CIP, CCRP
Human Protections Administrator
2001 Crystal Springs Ave, Suite 202
Roanoke, VA 24014
540-981-8097
caemerson@carilionclinic.org

2.7.3. Individuals may also contact the Carilion Clinical Institutional Official at:

Daniel Harrington, M.D.
Vice President for Academic Affairs
Riverside 2 M124
Roanoke, VA 24014
540-526-2521
DPHarrington@carilionclinic.org

2.7.4. The Carilion Clinic takes steps to protect employees and agents who report in good faith from retaliation and harassment. Immediately reports such concerns to the Carilion Clinical Institutional Official.

3. REFERENCES

3.1. "Ethical Principles and Guidelines for the Protection of Human Subjects of Research," The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, April 18, 1979, (http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html)

4. APPROVAL AND REVISIONS

4.1. 1/18/19: IRB Director, Carley Emerson, originally created and approved

4.2. Table of Applicability of Regulatory and Policy Requirements by Category of Research

Category of Research	Research initially reviewed, determined exempt, or waived:	
	Before Jan 21, 2019	On or after Jan 21, 2019
FDA regulated research that is NOT emergency use[2], compassion use, or device research on anonymous tissue specimens[3]	• FDA regulations • <Original Rule> • Subparts B, C, D	• FDA regulations • <Original Rule> • Subparts B, C, D
Emergency use, compassion use, and device research on anonymous tissue specimens[4]	• FDA regulations	• FDA regulations
Research regulated by federal department or agency other than DOJ or CPSC	• <Original Rule>[5] • Subparts B, C, D	• <Revised Rule> • Subparts B, C, D
Research regulated by DOJ or CPSC	• <Original Rule> • Subparts B, C, D	• <Original Rule> • Subparts B, C, D
Unregulated research[6]	• <Original Rule>[7] • Subparts B, C, D	• <Hybrid Rule> • Subparts B, C, D

[2] This includes emergency use as defined in 21 CFR 56.102(d) and described in 21 CFR 50.23(a) and (b). This does not include waiver of consent for planned emergency research.

[3] <Research Involving Human Subjects as Defined by FDA> that is also <Research Involving Human Subjects as Defined by HHS>

[4] <Research Involving Human Subjects as Defined by FDA> that is NOT <Research Involving Human Subjects as Defined by HHS>

[5] On or after January 21, 2019, sponsors can request that the research in this category initially reviewed, determined exempt, or waived before January 21, 2019 be re-reviewed under the <Revised Rule>

[6] <Research Involving Human Subjects as Defined by HHS> that is NOT subject to regulation by either FDA or a federal department or agency

[7] On or after January 21, 2019, sponsors can request that the research in this category initially reviewed, determined exempt, or waived before January 21, 2019 be re-reviewed under the <Hybrid Rule>

4.3. Table of Applicability of Regulatory and Policy Requirements by Requirement

Requirement	Research initially reviewed, determined exempt, or waived:	
	Before Jan 21, 2019	On or after Jan 21, 2019
FDA regulations	• FDA regulated research	• FDA regulated research
<Original Rule>	• Research regulated by a federal department or agency • FDA regulated research that is NOT emergency use, compassion use, or device research on anonymous tissue specimens	• Research regulated by DOJ or CPSC • FDA regulated research that is NOT emergency use, compassion use, or device research on anonymous tissue specimens
<Revised Rule>	NA	• Research regulated by federal department or agency other than DOJ or CPSC
<Hybrid Rule>	NA	• Unregulated research[8]
Subparts B, C, D	• All research except, emergency use, compassion use, and device research on anonymous tissue specimens[9]	• All research except, emergency use, compassion use, and device research on anonymous tissue specimens

5. APPROVAL AND REVISIONS

5.1. 1/18/19: IRB Director, Carley Emerson, originally created and approved

[8] <Research Involving Human Subjects as Defined by HHS> that is NOT subject to regulation by either FDA or a federal department or agency

[9] <Research Involving Human Subjects as Defined by HHS> including FDA regulated research that is also <Research Involving Human Subjects as Defined by HHS>