CARILION CLINIC INSTITUTIONAL REVIEW BOARD
Standard Operating Guidelines

Title: 2.13: Review of Research: Not Human Subjects Research, QA/QI Submissions, Case Reports	
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Primary Sponsor: Department of Biomedical and Research Ethics/IRB	**Approved By:** Director of Biomedical and Research Ethics and IRB Chair

Objective:

To help investigators determine whether a project is human subjects research or research that is not human subjects research or a study that qualifies for review as a Quality Assurance/Quality Improvement Project. Only activities that are classified as human subjects research are subject to oversight by the Carilion Institutional Review Board (IRB).

General Description:

Research activities that do not meet the definition of human subjects research in the HHS/FDA regulations may qualify for the designation of "Not Human Subjects Research" (NHSR). For example, an activity might not be human subjects research because:

- The activity does not meet the DHHS or FDA definition of "research."
- The activity meets the DHHS or FDA definition of "research," but does not meet the corresponding regulatory definition of "human subject."

The terms Quality Assurance (QA) and Quality Improvement (QI) generally refer to a range of activities conducted to assess, analyze, critique and improve current processes of health care delivery in an institutional setting. QA/QI activities are typically observational and unobtrusive. They involve the collection and analysis of data to which the investigators have legitimate access through their institutional roles. They do not prevent or hinder the delivery of clinically-indicated care to patients, nor do they impose additional risks or burdens (physical or psychosocial) on patients or hospital staff.

Procedure:

It is often difficult to determine whether NHSR/QA and QI activities fall under the jurisdiction of the IRB. In most situations, scientific methodology is used equally. Thus, activities that require IRB review cannot be easily defined by the methods they employ. In addition, other attributes such as publication of findings, methodological design, selection of subjects and hypothesis testing and generating do not necessarily differentiate research from NHSR or QA/QI because these attributes can be shared by both research and non-research activities. This guideline is to assist in determining which activities require IRB review.

What is the federal definition of human subjects?
The IRB is charged with reviewing human subjects research. Therefore, it is important to know the definition of both human subjects and research.

A human subject, as defined by the Common Rule, is a living individual about whom an investigator conducting research: (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. [45 CFR 46.102(e)(1)]

- Living individual – the specimen(s)/data/information must be collected from a live subject. Cadavers, autopsy specimens or specimens/information from subjects now deceased is not human subjects. *Note: Some research in this category, such as genetic studies providing private or medical information about live relatives, may need IRB review. Please contact the Department of Biomedical and Research Ethics (DBRE) for further information.*
- About whom means that the data received from the living individual be about the person. Information received about a product or a service and not about the person would not be human subjects research.
- Intervention includes physical procedures, manipulations of the subject, or manipulations of the subject's environment for research purposes. Interaction includes communication between the investigator and the subject. This includes face-to-face, mail, and phone interaction as well as other modes of communication.
- Identifiable private information includes (1) information about the behavior that occurs in a context in which an individual can reasonably expect that no observation is taking place; and (2) information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public. Identifiable means the information contains one or more data elements that can be combined with other reasonably available information to identify an individual.

What is the federal definition of research?
The Common Rule Defines research as a systematic investigation, including research development, testing, and evaluation designed to develop or contribute to generalized knowledge.

Specifically, what is QA?
The purpose of a QA project is simply to assure known quality. A QA project should present no additional risk to participants. These projects are mechanisms to assure that Carilion functions optimally. Such projects are usually for internal auditing purposes only. QA projects might be used to evaluate direct patient care processes (typically involved in creating clinical practice guidelines), evaluate billing practices, accumulate statistical data for monitoring and clinical performance assessment purposes, and assess community-based outreach programs for delivery of health care.

QA projects must not:

- infringe on a patient's privacy;

- breach a patient's confidentiality; or
- pose additional risk to patients, healthcare providers or staff

Specifically, what is QI?
The purpose of a QI project is to determine quality, improve patient services, and/or improve the provision of medical care. A QI project is generally applied within a defined institutional setting, often a single department or division. It is usually intended to motivate change of practice in a specific location. The intent is to evaluate and alter processes constituting the delivery of health care in the near future, with the expectation that the population of patients usually served in that location will benefit. This is different from research, which is traditionally intended to generate universally applicable knowledge. The experimental method in research is chosen to generate, evaluate or confirm an explanatory theory or conclusion and invite critical appraisal of its stated conclusion by peers through publication and debate.

Carilion Clinic NHSR and QA/QI Categories

NHSR 1. Health Care Delivery Improvement, including Quality Improvement, Process Improvement, or Performance Improvement

In order for NHSR 1 to apply, all the following criteria must be applicable:

- The activity is intended to improve the process/ or delivery of care while decreasing inefficiencies within a specific setting
- The activity is intended to evaluate current practice and/or implement practices and interventions within Carilion that are consensus-based or evidence-based
- The activity is conducted by individuals who are responsible for the practice change in the institutions where the activity will take place
- The methods for the activity are flexible and include approaches to evaluate rapid and incremental changes
- The activity will involve a sample of the population (patients/participants) ordinarily seen in the institution where the activity will take place
- Future patients or employees at the institution where the planned activity will be implemented will potentially benefit from the project
- There is no additional risk to patients/participants and participating in the activity is acceptable and expected in order to implement practice changes within a healthcare environment
- The activity could be considered part of the usual care and therefore will not require additional consent from participants
- **If this work is to be published, you must place the following statement in your methods section: "*This project was undertaken as a Health Care Delivery Improvement Project, and as such was not reviewed as Human Subjects Research.*"**

NHSR 2. Establishment of a database for clinical care or quality assurance/quality improvement ONLY. A subsequent decision to extract data for research will require submission of a regular IRB application.

In order for NHSR 2 to apply, all the following must be applicable:

- The primary reason for establishing this database is for clinical purposes or future improvement projects (e.g. Health Care Delivery Improvement, including Quality Improvement, Process Improvement, or Performance Improvement)
- Only those involved with the care of the patient will have access to the data and this data must be stored in a secure location
- A subsequent decision to extract data for research will require submission of a regular IRB application and IRB approval. Contact the IRB Office if you have questions.

NHSR 3. Evidence-based Medical Practice

For NHSR 3 to apply, all the following must be applicable:

- The primary reason for this work is to integrate the best available research-based evidence with clinical expertise and patient values to improve outcomes
- The process involves asking a relevant clinical question, finding the best evidence to answer it, applying the evidence to practice, and evaluating the evidence based on clinical outcomes
- **IRB approval of a protocol IS required if you wish to do research contributing to generalizable knowledge. Contact the IRB office if you have questions.**

NHSR 4. Use of Public Data Sets

In order for NHSR 4 to apply, all the following must be applicable:

- Research will NOT involve merging any of the data sets in such a way that individuals might be identified
- Researcher will NOT enhance the public data set with identifiable, or potentially identifiable data
- Researcher will NOT use data from the NIH GWAS (Genome Wide Association Studies) data repository
- The data host does not require the researcher or the researcher's institution to sign a Data Use Agreement.

NHSR 5. Research using Coded Data/Specimens

In order for NHSR 5 to apply, data or specimens will not be submitted to the FDA and all the following must be applicable:

- The data/specimens being accessed by or provided to the Carilion researchers will not contain any of the 18 HIPAA identifiers
- The entity releasing the data/specimens will retain a code or link which may be used to re-identify the donor, however, the key to the code will not be shared with the Carilion researchers
- The data/specimens were collected for purposes other than this project
- The person providing the data/specimens to the researcher will not otherwise be involved in this project (such as interpretation or analysis of data or preparation of a manuscript)
- No data will be returned to the source of the specimens/data
- Specimens do not include newborn dried blood spots or fetal tissue
- A Material Transfer Agreement (MTA) will be obtained through the Office of Research and Development prior to receipt of data or specimens
- If anyone on the research team unexpectedly learns the identity of a living individual or wishes to identify the individual(s) from the coded data/specimens, the research will require further IRB review.
- One of the following must be true:
    - A signed agreement will be executed between the person releasing the specimens/ data and the researcher receiving the specimens/data stipulating that the key to the code will never be released to any member of the research team
    - Confirmation of the data/specimen provider's IRB approval of written policies and operating procedures for a repository or data management center that prohibit the release of the key to the researchers under any circumstances
    - There are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

NHSR 6. Research using De-identified Data/Specimens

In order for NHSR 6 to apply, all the following must be applicable:

- The data/specimens were collected for purposes other than this project.
- The data/specimens will be provided to the researcher without any HIPAA identifiers or other personally identifiable information.
- **No codes or links of any sort exist with either the researcher or by the person releasing the data/specimens.**
- Specimens do not include newborn dried blood spots or fetal tissue.

- A Material Transfer Agreement will be obtained through the Office of Research and Development prior to receipt of data or specimens.

NSHR 7. A case series involving no more than three Carilion patients

A case report is the external reporting (publication, poster presentation, verbal presentation, etc.) of an interesting clinical situation or medical condition of a single patient or a series of patients. Case reports normally contain detailed information about patient(s) and may include demographic information and information on diagnosis, treatment, response to treatment and follow-up after treatment, as well as a discussion of existing relevant literature. **The patient information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience and the medical record review is done by persons involved in the patient's care.**

The Carilion Clinic IRB considers the retrospective analysis of three or fewer clinical cases to be a medical/educational activity that does not meet the federal regulatory definition of research. These regulations define research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Case reports are generally carried out by retrospective review of records and highlight a unique treatment, case, or outcome. As the collection and organization of information for such reports usually involves no data analysis or testing of a hypothesis, they do not involve a systematic investigation designed to contribute to generalizable knowledge. **No changes may be made in the patient's care and/or no testing is added for the purpose of reporting the case. The case report may not include investigational use of a drug, device, or biologic.**

When a larger series of patients are being reported, investigators usually begin to ask specific research questions and formal systematic collection of data occurs, moving these activities closer to prospectively designed research. Therefore, a case report of four or more clinical cases is considered human subjects research that needs IRB review and approval.

Going beyond one's own clinical practice to seek out and report cases seen by other clinicians (even combining cases with colleagues within one's department) creates the appearance of a systematic investigation with the intent to contribute to generalizable knowledge. Therefore, it also would be considered research and would require IRB review and approval.

Teaching and/or soliciting colleagues' advice on clinical care of a specific patient or group of patients during presentation of a case at departmental conferences does not require IRB review. Generalized commentary by a clinician on the outcome of their clinical care of patients in accepted venues for discussions of clinical management also is not considered human subjects research requiring IRB review if there is no prospective research plan and no formal, systematic prospective collection of information. This type of communication may occur at hospital or practice meetings or in continuing education venues where comments are explicitly identified as personal experience and not formal clinical research.

If it is unclear whether a particular case report requires IRB approval or IRB approval is required for publishing purposes, the case report should be submitted to the IRB office for review prior to conducting the activity. **The IRB will not issue a determination letter after activities have been completed.**

Although a case report involving up to three patients may not require IRB review, certain HIPAA provisions may apply and ethical concerns can arise if identifiable information is published. The use of protected health information to prepare such a case report does not require IRB review for Privacy Rule purposes. However, anyone who wishes to publish information that includes HIPAA identifiers or may identify the patient due to the description of a unique disease, condition or outcome should confer with the Carilion Clinic Privacy Officer. Additionally, those publishing such case reports are strongly advised to obtain informed consent from any patients about whom information will be published. In the case of deceased individuals, consent should be sought from the patient's legally authorized representative.

In order for NHSR 7 to apply, all must be applicable:

- Any health information in the case series must be de-identified per HIPAA regulations
- For all case reports and case series, a signed HIPAA authorization should be obtained from the patients or their legally authorized representatives for the use and disclosure of their Protected Health Information. The only exception to the requirement for obtaining authorization is if the author of a case report or case series believes that the information is not identifiable; in this case, the author must consult with the HIPAA Privacy Officer to seek an expert opinion about the magnitude of the risk of identifying an individual.

NHSR 8. Decedent research (all potential subjects are deceased)

In order for NHSR 8 to apply, all must be applicable:

- If the work will entail reviewing medical records of former patients, you must first consult with the Carilion Privacy Officer at (540) 981-7000 or privacy@carilionclinic.org.
- Any published health information must be de-identified per HIPAA regulations.
- If using specimens, the specimen is NOT fetal tissue.

NHSR 9. Contributing data/specimens for research outside of Carilion

In order for NHSR 9 to apply, all the following criteria must be met:

- Individuals releasing the data/specimens are NOT working in collaboration with the recipients on the research project (ie: have not been involved in the design of the research and will not be involved with the conduct beyond providing data, analysis or publication of the research). The data/specimen, in its entirety, was collected for purposes other than the research project to be done by those with whom you are sharing the data/specimens.
- If the original data/ specimens were collected for research purposes, the study team confirms the secondary use does not disagree with language in the consent under which the data/specimens were obtained.
- Data/ samples must meet the HIPAA criteria of Limited Data Set or completely de-identified data at the time of release, unless you are contracting with the recipients outside of Carilion to de-identify the data or partially de-identify it to create a Limited Data Set. If so, contact the Carilion Compliance Office in order to execute a HIPAA Business Associate Agreement (BAA) with the recipient for this purpose.
- Study team must obtain a Material Transfer Agreement with the Research & Development Office prior to sending Limited Data Set or completely de-identified data/specimens.
- If the data/specimens meet the criteria of a Limited Data Set, Research & Development will incorporate a HIPAA Data Use Agreement into the Material Transfer Agreement.

NHSR 10. Public Health Practice

In order for NHSR 10 to apply, all the following must be applicable:

- Intent is to prevent or control a disease or injury and improve health or to improve a public health program or service through such activities as disease surveillance, program evaluation, and outbreak investigation
- Focused on improving the health of a specific population or group
- There is a specific legal authorization for conducting the activity or governmental duty to perform the activity to protect the public's health and there may be direct performance or oversight of the activity by a governmental public health authority (or authorized partner) accountable to the public

Examples of projects that are human subjects research:

- A project that involves interventions, procedures or tests beyond what is routine for patient care and then collects data or gathers information about the interventions, procedures or tests.

- A project that compares prospective interventions that are deliberately administered or made available (through randomization or other process) to some patients and not to others. This does not include a QI process of a small percent of patients at Carilion first to ensure feasibility, before introducing it to the entire patient population.

- A project that utilizes test subjects for new devices, products, drugs or materials.

- A project that collects sensitive data through intervention or interaction with individuals. Examples: internet surveys about alcohol consumption, research involving risky behaviors or attitudes, studies requesting information on HIV status.

- A project involving deception.

- A project utilizing open-ended interviews with minors that contributes to generalizable knowledge.

- A project that uses bodily materials such as cells, blood, urine, tissues, organs, hair or nail clippings; even if one did not collect these materials for the study.

- A project that produces generalizable knowledge about categories or classes of subjects from individually identifiable information.

- A project involving the use of human beings to evaluate environmental alterations. Examples: weatherization options or habitat modifications to their living or working space or test chamber.

- A project involving care practices, interventions or treatments that are not standard.

- A project involving more than minimal risk to subjects.

Examples of projects that are not human subjects research:

- A project that collects only data for internal departmental, school or other Carilion administrative purposes. Example: teaching evaluations, customer service surveys.

- A project involving only service surveys issued or completed by Carilion patients, students or staff for the intent and purpose of improving services and programs of Carilion or for developing new services and programs, as long as the privacy of the subjects is protected, the confidentiality of individual responses are maintained and survey participation is voluntary.

- A project involving only information-gathering interviews where questions focus on things, products or policies rather than people or their thoughts regarding themselves. Example: canvassing nurses about a new hand-washing policy.

- A project involving only court-related activities designed specifically for education or teaching purposes, where data is collected from and about human subjects as part of a class exercise or assignment, and not intended for use outside of the classroom.

- A project involving only biography or oral history research involving a living individual that is not generalizable beyond that individual.

- A project involving only an innovative therapy; an intervention designed solely to enhance the well-being of an individual patient or client, with the purpose being to help provide diagnosis.

- A case history when the case is limited to a description of the clinical features and/or outcome of a single patient and does not contribute to generalizable knowledge.

- A project involving only coded private information or biological specimens that were not collected for the currently proposed project and involves only information and specimens that the investigator cannot link back to the individual subjects.

If it is unclear if a project is QA/QI or research, the IRB will review the following questions to determine whether a project qualifies as QA/QI or research:

- Is the project a hospital QA/QI initiative, or presentation/publication of results thereof, that is conducted within Carilion only, and serves to measure or improve Carilion's ability to meet or exceed an existing national standard of care of benchmark (JCAHO, etc.) or develop a standard of care of benchmark for applicability within Carilion?

- Is the project a submission of data to a national or state registry/database that is mandated at the state or federal level; or that directly impacts reimbursements and funding available from the state Department of Health or Federal Centers for Medicare and Medicaid Services (CMS) based on performance and/or clinical or quality outcomes; or that is maintained by an organization formally recognized by Carilion, the principal purpose of which is benchmarking and/or performance improvement, the use of which is for internal Carilion activities?

- Is the project a hospital QA/QI use of data from a registry/database that is mandated at the state or federal level; or that directly impacts reimbursements and funding available from the state Department of Health or Federal Centers for Medicare and Medicaid Services (CMS) based on performance and/or clinical or quality outcomes; or that is maintained by an organization formally recognized by Carilion, the principal purpose of which is benchmarking and/or performance improvement, the use of which is for internal Carilion activities for the purpose of measuring or improving Carilion's ability to meet or exceed an existing national standard of care or benchmark (JCAHO, etc.) or develops a standard of care of benchmark for applicability within Carilion?

- Is the project a hospital QA/QI initiative, conducted within Carilion only, designed to develop a standard of care or benchmark for general applicability (i.e., not only for operations within Carilion, but to outside entities as well)?

- Is the project a QA/QI initiative (including one that proposes to develop an operational standard of care or benchmark) that is investigator-initiated?

- Is the project a submission of data to a registry/database that is not identified as a project a submission of data to a national or state registry/database that is mandated at the state or federal level; or that directly impacts reimbursements and funding available from the state Department of Health or Federal Centers for Medicare and Medicaid Services (CMS) based on performance and/or clinical or quality outcomes; or that is maintained by an organization formally recognized by Carilion, the principal purpose of which is benchmarking and/or performance improvement, the use of which is for internal Carilion activities?

- Is the project the use of data from any registry/database for the purpose of measuring, improving or developing a standard or benchmark, under any condition not covered in Section III above, including the use of registry data for the purpose of research?

- Is the project only using de-identified data and will not be able to reidentify subjects?

Are there other privacy and protection issues that need to be taken info consideration even if the QA/QI project does not require IRB review?

Yes, in order to preserve privacy and mitigate sensitivity of members of the organization to adverse publicity, the following policies should be followed when IRB review is not conducted:

- Any QA/QI or educational survey results must be completely anonymous, and results should be presented as aggregate data. Results must not be aggregated in such a fashion that the identity of respondents can be ascertained (e.g., identification of departments with very small numbers of staff members).

- The survey must not be coercive. Individuals who do not wish to complete the survey may decline without fear of blame or punishment.

Can my QA/QI project be published?

Intrinsic components of QA/QI, educational infinitives and competency assessments are shared learning. It is entirely appropriate to disseminate and replicate QA/QI successes, including through channels that are external to Carilion. This may include presentations at meetings and publications in professional journals. The intent to publish does not obligate IRB review. However, the publication may not refer to the activity as research, and it must make clear that the publication is the result of a QA/QI or educational/competency assessment.

Even though formal IRB review is not required, a letter from the IRB stating the status of a particular project may be required by Health Information Management (HIM) before records are released. Therefore, before beginning a project, a proposal may be submitted to the IRB for issuance of a determination letter.