# POLICY
# Research Requiring IRB Approval and Oversight

**This Policy is Applicable to the following Spectrum Health sites:**
Continuing Care, Corporate, Gerber (Newaygo County General Hospital Association), Outpatient/Physician Practices, Priority Health, Reed City (Reed City Hospital Corporation), SH GR Hospitals (Spectrum Health Hospitals), SHMG, United/Kelsey (Spectrum Health United; Spectrum Health Kelsey Hospital), Zeeland (Zeeland Community Hospital)

**Applicability Limited to:** N/A

**Reference #:** 2056

**Version#:** 3

**Effective Date:** 11/26/2021

**Functional Area:** Research

**Department Area:** Research

## 1. Purpose
To clearly describe the types of activities that qualify as human subjects research or clinical investigations and thus require the review and approval of the Spectrum Health IRB (SH IRB) prior to implementation.

## 2. Policy
In accordance with federal regulations and Spectrum Health policies, the SH IRB must approve activities involving the use of *human subjects in research prior to initiation*.

Before employees or agents of Spectrum Health undertake activities that might be considered human-subjects research or a clinical investigation involving human subjects as defined by this policy, they should, consult the Spectrum Health Office of the IRB as necessary to ensure that they are reviewed prospectively by the SH IRB.

### A. Definitions

A.1. DHHS/Common Rule (45 CFR §46.102)

A.1.1. Research: a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

A.1.2. Human Subject: a living individual *about whom* an investigator (whether professional or student) conducting research *obtains* information or biospecimens through intervention or interaction with the individual *and* uses, studies, or analyzes the information or biospecimens; - or - obtains, uses,

studies, analyzes or generates identifiable private information or identifiable biospecimens.

A.1.2.1. Intervention: includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

A.1.2.2. Interaction: includes communication or interpersonal contact between investigator and subject.

A.1.2.3. Private Information: includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., medical record).

A.1.2.4. Identifiable private information: private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

A.1.2.5. Identifiable biospecimen: a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

A.1.3. Clinical trial: a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

A.1.4. Public health authority: an agency or authority of the United States, a state, a territory, a political subdivision of a state or territory, an Indian tribe, or a foreign government, or a person or entity acting under a grant of authority from or contract with such public agency, including the employees or agents of such public agency or its contractors or persons or entities to whom it has granted authority, that is responsible for public health matters as part of its official mandate

A.2. U.S. Food and Drug Administration (FDA) (21 CFR §56.102)

A.2.1. Clinical Investigation: any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the act, or the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. *The application for research or marketing permits are further defined at 21 CFR §56.102(b).*

If the research involves any of the following, FDA Regulations, 21 CFR §50 and §56 apply and require IRB approval prior to implementation:

- Any use of a drug in research other than the use of an FDA approved Drug in the course of medical practice; or
- Any use of a medical device in studies where the purpose is to determine safety or effectiveness of the device.

A.2.2. Human subjects: an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient. A human subject includes an individual on whose specimen a medical device is used (regardless if the specimen is coded or all identifiers were/are removed).

A.3. DHHS Office for Civil Rights (OCR) - Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule (45 CFR §164.501)

A.3.1. Research: a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

A.3.2. Protected Health Information (PHI) (45 CFR §160.103): individually identifiable health information, held or maintained by a covered entity or its business associates acting for the covered entity, that is transmitted or maintained in any form or medium. This includes identifiable demographic and other information relating to the past, present, or future physical or mental health or condition of an individual, or the provision or payment of health care to an individual that is created or received by a health care provider, health plan, employer, or health care clearinghouse.

**B. Non-Human Subjects Research**

The SH IRB may determine that an activity does not meet the criteria for research involving human subjects as defined in the federal regulations. Projects that do not involve "human subjects" and/or are not considered "research," as described above, do not require review and approval by the SH IRB. Submissions to the IRB determined not to meet both criteria will be issued a "Not Human Subjects Research" determination letter.

OHRP considers private information or specimens to be individually identifiable as defined at 45 CFR §46.102(f) when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

Research involving *only* coded or de-identified private information or specimens is considered non-human subjects research when the private information or specimens cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. OHRP does not consider research involving only coded private information or specimens to involve human subjects as defined under 45 CFR §46.102(e) if the following conditions are both met:

- the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and
- the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:
    - the investigators and the holder of the key entered into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased;
    - there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

Non-human subjects research does not require an exempt determination by the SH IRB as it does not constitute research involving human subjects as defined in 45 CFR §46.102(e)).

When the activity is determined to be Research Involving Human Subjects, the investigator must submit an application for initial review to the SH IRB.

Investigators who have questions related to this policy, such as what is considered identifiable information or are unsure of whether their research involves human subjects, should contact the Spectrum Health Office of the IRB for guidance.

### C. Case Reports / Case Series

Case reports may or may not be considered research. Case reports generally involve the collection and presentation of detailed information about a particular patient to highlight an interesting condition, treatment, presentation or outcome. There is no intent to test a hypothesis via systematic analysis, analyze data or add to generalizable knowledge. Thus, a case report that documents the clinically indicated care of a single patient does not generally meet the regulatory definition of research.

A single summary of a treatment, presentation, or outcome of a patient, does not typically constitute research. As such, it would not be considered a research activity when a case report is presented to share information for medical educational purposes, or to request advice from colleagues on the clinical care of a patient or group of patients during a departmental meeting, conference, or other accepted venue for discussion of clinical management.

In contrast, a case report that plans to incorporate a systematic data analysis of treatments and outcomes to allow possible extrapolation of the results to a larger population may satisfy the federal definition of research and requires SH IRB review.

When a case series is developed, and investigators begin to ask specific questions and a systematic collection of data occurs, or there is an intent is to evaluate a specific hypothesis (e.g., a hypothesis is generated in advance of a retrospective records review), this activity may constitute research.

It is recommended that prior to writing a case report, the authors should determine to which peer-reviewed journals the case report will be submitted and the journals' requirements for documentation from their local IRB. The SH IRB may provide a letter documenting the determination that the case report/case series did not meet the definition of human subjects research and does not require IRB review.

#### C.1 HIPAA Requirements for Case Reports

The SH IRB regards a limited case report preparation as an educational activity, and thus it is permissible under the Privacy Rule (HIPAA) as a part of health care operations (45 CFR §164.501). Authors who remove HIPAA identifiers from the case report data prior to disclosure of the data (e.g., prior to submission of the case report to a journal) do not need to obtain a signed privacy authorization from the subject of the case report.

If the author of the case report removes all HIPAA identifiers, but the information associated with the subject of the article includes a "unique characteristic" which would make it identifiable to the subject, or the author has actual knowledge that the information about the subject could be used alone or in combination with other information to identify the subject, the author must seek a signed privacy authorization prior to publication. In addition, if an

investigator wishes to use a photo or illustration in the case report that could lead to identification of the patient, the author must seek a signed privacy authorization prior to publication.

Authors who wish to publish a case report that is not completely deidentified to the standards of the HIPAA Privacy Rule (i.e., that contains any direct or indirect identifiers), must first obtain each patient's signed privacy authorization. It is not necessary to submit this authorization form to the SH IRB for review.

### D. Quality Improvement Projects

There is often confusion in determining whether Quality Improvement (QI)/ Quality Assurance (QA) activity falls under the jurisdiction of the SH IRB. In order to determine whether QI/QA activities involving human participants or individually identifiable data constitute research, the investigator and IRB must consider the definition of research as put forth by the federal regulations. As above, research is defined as "a systematic investigation, including research development, testing, and evaluation, designed to develop and contribute to generalizable knowledge." QI/QA activities tend to focus on improving systems and organizational performance based on findings from internal quality assurance activities (internal audits/gap analysis) with the intention to improve outcomes to benefit current patients. Research activities tend to focus on creating new knowledge for the scientific community to benefit future patients.

QI/QA activities are intended and designed to improve the quality of the health care patients receive locally by identifying opportunities for improvement in the delivery system through audits of the current state and then addressing the identified problem areas based on existing knowledge in the literature. QI/QA is a continuous process of evaluating the current state, identifying problem areas, proposing solutions, (e.g. changing internal processes, staff re-education), and then re-evaluating if the change made an improvement.

A group of leaders convened by the Hastings Center to address ethical requirements for QI/QA defined quality improvement as a systematic, data-guided activity, designed to bring about immediate improvements in health care delivery in particular settings. QI/QA is an intrinsic part of normal health care operations and informed consent is not generally required since patients expect their health care provider to continually improve the quality of care provided. In addition, as an academic institution that is accredited by the Accreditation Council for Graduate Medical Education (ACGME), Spectrum Health is required to continually evaluate and improve our training activities through quality assurance and performance improvement.

The intent to publish and share the data from an internal quality improvement project does not automatically make the activity human subjects research. Other hospitals and health care systems may benefit from learning how Spectrum Health addressed a specific institutional problem. Thus, QI/QA activities may be published and presented to other external parties without the requirement of initial SH IRB approval and oversight.

Investigators may submit a Request for Determination for review by the SH IRB in order to obtain a formal determination. Investigators are also to inform the Office of the IRB if changes occur to a QI/QA activity that may alter this initial determination.

Additional Regulatory Definitions utilized in determining QI/QA activities:

- 42 CFR §480.101(b): *Quality review study* is defined as an "assessment, conducted by or for a Quality Improvement Organization, of a patient care problem for the purpose of improving patient care through peer analysis, intervention, resolution of the problem and follow-up."

- 45 CFR §164.501(2): The HIPAA regulations define *health care operations* to include "conducting quality assessment and improvement activities, including outcomes evaluation and development of clinical guidelines, provided that the obtaining of generalizable knowledge is not the primary purpose of any studies resulting from such activities; population-based activities relating to improving health or reducing health care costs, …"

### E. Research that is Excluded from IRB Review and Approval

In revising the Common Rule in 2018, OHRP identified four categories of activities that are not to be considered research and are thus, *excluded* from the requirements to obtain IRB approval. The four categories pertain to certain scholarly and journalistic activities, public health surveillance activities, criminal justice activities, and authorized operational activities in support of national security missions.

If the activities included one or more of the following, SH IRB approval and oversight is not required (45 CFR §46.102):

- (1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
- (2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow *a public health authority* to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
- (3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
- (4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

## 3. Revisions

Spectrum Health reserves the right to alter, amend, modify or eliminate this policy at any time without prior written notice.

## 4. Policy Development and Approval

**Document Owner:**
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Not Assigned

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Not Assigned

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**5. Keywords**

research, research approval, requirements for approval, student research, sh-admin-res-008quality improvement, quality assurance, nhsr