Title: **Clinical Research Quality and Process Improvement Program**	*Applicable to: **Beaumont Health**	Effective Date: **03/16/2018** Last Periodic Review Date: **03/16/2018**
Policy Owner: **Administrative Director**	Document Type: **Policy**	Functional Area: **Research Administration, Research Institute**

***For This Document, Beaumont Health Includes**:
Beaumont Corporate Shared Services
Beaumont Hospital, Dearborn
Beaumont Hospital, Farmington Hills
Beaumont Hospital, Grosse Pointe
Beaumont Hospital, Royal Oak
Beaumont Hospital, Taylor
Beaumont Hospital, Trenton
Beaumont Hospital, Troy
Beaumont Hospital, Wayne
Beaumont Medical Group
Beaumont Pharmacy Solutions
Post Acute Care

I. PURPOSE:

The purpose of this policy is to provide an overview of the Clinical Research Quality and Process Improvement Program (CRQIP) at Beaumont Health (BH).

II. GENERAL:

The CRQIP represents BH's quality improvement plan for clinical research and serves to periodically assess the compliance of BH's Human Research Protection Program. The CRQIP goals are to:

A. Assess and maintain compliance with federal, state, local and institutional research regulations in order to protect the rights and well-being of BH's human research participants.

B. Assess and maintain the integrity and quality of data generated by BH's researchers.

C. Assess the capacity of existing policies and associated systems to facilitate an efficient and effective human research protection program (HRPP).

III. SCOPE:

This policy applies to all clinical research conducted at Beaumont Health.

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IV. POLICY:

A. The CRQIP objectives are:
   1. To conduct a range of clinical study audits, Institutional Review Board (IRB) operational audits, and Research Administrative operational audits to assess participant safety, compliance, data quality, and system effectiveness/efficiency.
   2. To report findings/observations to HRPP members, including the IRB of record and collaborate on policy refinement/development, continuous process improvement activities and educational strategies.

B. Related measures include but are not limited to:
   1. Number of level 1 non-compliance episodes.
   2. Percentage of investigator-initiated studies with major protocol deviations related to eligibility or protocol adherence at first participant monitoring visit.
   3. Percentage of studies with conflict of interest management plans in full compliance with management plan.
   4. Percentage of consent-related major protocol deviations per executed consents.

V. TYPES OF AUDITS:

All clinical research projects conducted under the auspices of BH may be monitored or inspected. Audits may be conducted routinely, as part of the Research Institute (RI) Compliance Plan, based on a special monitoring focus, or conducted upon request of the RI Directors, or the IRB of record, or a BH oversight committee. Audit types include but are not limited to those listed below.

A. **First Participant Monitoring Visits for Investigator-Initiated Research -** Investigator-initiated projects reviewed via full board or via expedited procedures and involving face-to-face contact with participants are audited after enrollment of the first participant, with a focus on compliance with consenting, eligibility and record keeping.

B. **Consent Audits -** All executed informed consent and authorization documents are audited by a clinical research manager (CRM) or their designee within twenty-four (24) business hours for compliance with RI policies. Immediate feedback is provided by the CRM to consent providers.

C. **Conflict of Interest (COI) Management Plan Audits** - All studies with a conflict of interest management plan are audited to assess compliance with the management plan. Audits are

generally conducted annually, although this schedule may be revised on a study-by-study basis, dependent on such factors as anticipated enrollment patterns, etc.

D. **"For Cause" Audits -** "For Cause" audits may be conducted upon request of the RI Vice President or Administrative Director, IRB of record, or a BH oversight committee. Reasons for requesting inspections may include:
   1. IRB concerns including potential high risk to participants related to the research, vulnerable populations, frequency or seriousness of protocol deviations, or investigator compliance with IRB policies and procedures.
   2. Probability of audit by external regulators, such as the Food and Drug Administration (FDA).
   3. Concerns from sponsors, expressed in monitoring reports or other means.
   4. Past or current performance issues related to key research personnel.
   5. Special monitoring foci related to possible regulatory changes or concerns in the research community about a particular test article, vulnerable population, etc.
   6. Research potentially conducted out of compliance with federal, state or local laws or regulations or with RI policies and procedures.
   7. Concerns expressed by individuals, such as actual or potential participants, key research personnel, other Beaumont personnel, or members of the community.

E. **Studies Related to the United States Department of Defense -** Studies associated with the Department of Defense are subject to additional regulatory oversight as described in the *Requirements for Research Involving or Supporting by the Department of Defense* document posted on the RI website. These studies are monitored to assess compliance with the additional regulatory requirements.

F. **Studies Requiring Compliance with the International Commission on Harmonization Good Clinical Practices -** Sponsors may contractually obligate Principal Investigators (PI) to conduct specific studies in full compliance with the International Conference on Harmonization Good Clinical Practice E6 Guidelines (ICH-GCP), as described in IRB Policy 257, *Clinical Studies Conducted in Full Compliance with ICH-GCP.* A sample of these studies is monitored to assure compliance with the additional regulatory requirements.

G. **IRB Operational Audits IRB Minute Audits and IRB File Audits -** Minutes of each IRB meeting are audited. IRB File Audits are conducted semi-annually; a representative sample of studies from each review type is selected, in addition to a trial conducted in full compliance with ICH-GCP.

H. **Other Operational Audits -** Other operational audits include but are not limited to, Lead Researcher Study Audits, Unanticipated Problem Reporting Process Audits, and Conflict of Interest and Disclosure Process audits.

VI. POLICY:

A. **Monitoring Process: Clinical Studies -** The CRQIP monitor will notify the PI and the clinical research department in advance of the inspection visit, whenever possible. Notification will include the date/time of the monitoring visit and the protocol(s) to be inspected. The monitor may review any study records, including but not limited to the:

1. Regulatory Binder for:
   a. Organization and completeness.
   b. Proper documentation of IRB and sponsor approval(s).
   c. Verification of current protocol, informed consent and authorization document(s) versions.
   d. Confirmation that no changes in research have been implemented prior to amendment submission and IRB approval or prior to sponsor approval.
   e. Correspondence with the IRB and sponsor is filed appropriately.
2. Participant screening and enrollment logs, master identification logs, sponsor-monitoring reports, monitoring record logs.
   a. Original signed consent and authorization documents for completeness and adherence to policies.
3. Participant-specific records, including case report forms, hospital chart, source documentation, case histories, etcetera, to confirm:
   a. Consent process occurred as detailed in the IRB Application and in compliance with policies and procedures.
   b. Participant eligibility.
   c. Participant provided consent prior to initiation of any study-related activities.
   d. Consent procedure appropriately documented in participant case history.
   e. Accuracy of data reported.
4. Stored specimens and related documentation to verify specimens or tissue collected for research purposes is properly authorized by the participant, properly labeled and stored, and used per the IRB-approved protocol.
5. Test article stock, storage, and accountability records, to verify:
   a. Test article is stored securely and in accordance with conditions specified in the protocol and Investigational Drug Service approval.
   b. Test article is dispensed by appropriately prepared and credentialed personnel and in the manner described in the protocol.
   c. Participant has returned any unused test articles and empty packaging.
   d. Test article stock and records are reconciled.

e. Blinding and randomization are maintained as described in the protocol.
f. Unused test article is returned to the sponsor or destroyed per sponsor and institutional policies.

6. Records and reports to the IRB and sponsor to confirm all were submitted in accordance with policies, including:
   a. Unanticipated Problems, Serious Adverse Events and/or Adverse Events.
   b. Protocol Deviations.
   c. Continuing Review Reports.
   d. Data Safety Monitoring Board Reports.

In addition to reviewing the study records, other evaluations may be conducted and may include:

7. Verifying the consent process was conducted as described in the IRB-approved study application and verifying participants were fully informed and voluntarily signed the informed consent and authorization document. This evaluation may involve participant telephone contact.
8. Verifying study records are being stored properly and securely, to protect privacy and confidentiality of participants and in accordance with Beaumont and RI policies.
9. Assessing mechanisms for participant recruitment to identify potential discrimination or exploitation.

The PI, CRM, and other key personnel as appropriate will be contacted for information and kept abreast of audit progress during the process.

B. **Post Inspection Process**

1. The CRQIP monitor will provide a written report of observations and recommendations to the PI, the CRM overseeing involved research personnel, the IRB, the chairperson of the committee requesting the inspection, and/or the RI Administrative Director. Results will also be reported to the RI Compliance Committee and provided to the Corporate Compliance Office as part of the Corporate Compliance Status Report. Observations suggestive of potential non-compliance and/or research misconduct are promptly reported to the Institutional Official, the IRB, and the Research Compliance Coordinator, consistent with IRB Policy *Contacts, Complaints, Allegations of Non-Compliance and Confirmed Non-Compliance in Clinical Research* and IRB Policy *Inquiries and Investigations of Alleged Research Misconduct* . The PI is encouraged to provide feedback or make corrections/clarifications as necessary on the report before returning the signed audit report.
2. The IRB will provide the PI with a written response in follow up to the audit report. The IRB will endorse or modify the recommendations outlined in the audit report, impose additional corrective actions up to and including halting the research, require

education/process improvement or require additional audit activity. The RI Directors may also impose corrective action or administrative reporting as appropriate.

C. **Monitoring Process: IRB Audits**
IRB audits (both minute and file audit reports) are provided to the IRB manager. The manager reviews the findings and observations provide clarifications. Deficiencies and process improvements are discussed with the IRB chairperson, members and staff.

D. **Process Improvement Opportunities**
Observations and recommendations made during the monitoring of a single study are frequently common to other studies and research departments, and may present process improvement opportunities. As part of the RI Process Improvement Program, findings from inspections of specific research projects are used to evaluate associated processes, policies, procedures, practices, and educational efforts. The response may include development of new policies or procedures, revisions or clarifications of existing policies and procedures, additional targeted educational offerings and multi-dimensional communications. A multi-dimensional communication plan may involve review at the CRM meeting, RI Newsletter articles, changes to the RI Website on *Inside Beaumont*, and inclusion in corporate communications. All individuals, including investigators and other key research personnel, are expected to participate in process improvement activities.

E. **Corrective and Preventive Action Plans**
A Corrective and Preventive Action Plan (CAPA) is a structured, systematic approach focused on investigation of the root causes of identified problems or identified risks in an attempt to prevent their recurrence (for corrective action) or to prevent occurrence (for preventive action). A CAPA may be initiated in response to, but not limited to, the following:
1. noncompliance, complaints and/or concerns
2. internal or external audit findings
3. risk assessment of particular studies
4. study conduct or data integrity concerns
5. operational concerns
6. management concerns
7. PI, research staff or sponsor performance concerns.

A formalized CAPA may be required by a BH oversight committee or RI leadership, based upon human participant protection, data integrity or organizational regulatory risks. A systematic CAPA process standardly includes the following stages; issue(s) identification; causal analysis; preventive and/or corrective action plan development; plan implementation; effectiveness evaluation; closure.

F. **CAPA Development**

1. Most CAPAs are study-specific, though some may be designed to address wider-reaching situations. Actions may be applied institution-wide, as part of continuous process improvement. When a CAPA is required by a BH oversight committee or RI Leadership, it is developed by that body, in collaboration with the PI and research team. The CRQIP manager will provide CAPA consultation as requested, may participate in each stage of the CAPA process, and may be called upon to generate the CAPA document and track CAPA progress. Actions are planned to mitigate or eliminate specific causes and must be:
   S - specific
   M - measureable
   A - attainable
   R - realistic, and
   T - timely.
2. Actions should include what will be done, who will do it, and a target date for completion.
3. CAPAs are approved by the Research Institute Compliance Committee (RICC). The PI serves as CAPA owner and is responsible for CAPA execution and resolution of each issue identified. The CAPA owner is responsible for effective implementation and reporting CAPA progress or barriers to the RICC.

G. **Escalation Process**

When a CAPA process is not adhered to, does not progress or the established CAPA fails to address the issues identified, an escalation process occurs. CAPA responsibility escalates from the PI to the Department Chair and from the clinical research manager to the RI Directors. Once escalated, it becomes the responsibility of those to whom it is escalated to ensure necessary action occurs and risk is mitigated.

H. **Community Outreach Activities Evaluation**

Community outreach activities are planned in order to enhance the understanding of human research by prospective participants, participants and the community. A working group meets on quarterly basis to evaluate the effectiveness of current activities, which include but are not limited to educational material on the external customer website, searchable clinical trials listings, and participation at community based events to promote human participant protections awareness. Additionally, a larger group which includes the VP of Research, Research Administrative Director, and IRB Chairperson meet annually to evaluate current activity and propose program enhancements.

VII. ASSOCIATED REGULATIONS, GUIDANCES, AND REFERENCES:

Guidance for FDA Staff and Industry, Compliance Policy Guide
Clinical Investigators: "FDA Access to Results of Quality Assurance Program Audits and Inspections"

VIII. ASSOCIATED POLICIES AND DOCUMENTS:

RI Compliance Plan
Research Administration Policy *Inquiries and Investigations of Alleged Research Misconduct*
Research Administration Policy *Contacts, Complaints, Allegations of Non-Compliance and Confirmed Non-Compliance in Clinical Research*
IRB Policy, *Administrative Holds, Suspensions and Terminations*

CORPORATE AUTHORITY:

Beaumont Health ("BH") as the corporate parent to William Beaumont Hospital, Botsford General Hospital, and Oakwood Healthcare Inc., ("Subsidiary Hospitals") establishes the standards for all policies related to the clinical, administrative and financial operations of the Subsidiary Hospitals. The Subsidiary Hospitals, which hold all health facility and agency licenses according to Michigan law, are the covered entities and the providers of health care services under the corporate direction of BH. The Subsidiary Hospitals' workforces are collectively designated as BH workforce throughout BH policies.