Title: **External Regulatory Body Inspections or Audits**	*Applicable to: **Beaumont Health**	Effective Date: **01/12/2018**
		Last Periodic Review Date: **01/12/2018**
Policy Owner: **Administrative Director**	Document Type: **Policy**	Functional Area: **Clinical Research SOP's, 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:

This standard operating procedure (SOP) describes the operations followed at Beaumont Health during an inspection of clinical trial(s) by an external regulatory body, such as the Food and Drug Administration (FDA).

II. SCOPE:

This SOP applies to preparing for an inspection by an external regulatory body of a clinical study conducted at Beaumont Health. It describes the steps followed from the time an inspection is scheduled, until all follow-up activities associated with the inspection have been completed.

III. RESPONSIBILITY:

This SOP applies to all key research personnel and Research Administration staff involved in arranging, managing, or participating in the inspection at Beaumont Health.

IIII. PROCEDURES:

A. **Preparing for the inspection**

1. If notified of an impending inspection by an external regulatory body such as the FDA, the Principal Investigator (PI) or designee must notify the sponsor as soon as possible.

2. The PI or designee must notify Research Administration by contacting the office of the Administrative Director at (248) 551-3792 as soon as possible, upon learning of an impending inspection.
3. The PI or designee should agree to an inspection date to occur within a reasonable period of time.
   a. Starting date and expected duration.
   b. FDA inspector name and contact information.
   c. Who and what is being inspected.
   d. Reason for the inspection.
   e. Requests for specific personnel.
4. The PI or designee must inspect all clinical study records and documentation for accuracy and completeness, including:
   a. Informed Consent and Authorization Forms.
   b. Source documents.
   c. Case Report Forms.
   d. Regulatory documents, including all approvals.
   e. Test article accountability records, including any instances in which emergency breaking of the blind occurred.
   f. Enrollment Log, verifying number of enrolled participants, drop-outs with rationale and evaluable participants.
   g. Documentation related to reporting of unanticipated problems and safety reports.
   h. Documentation with the waiver of eligibility criteria.
   i. Documentation of randomization if applicable.
5. Documents missing from the regulatory binder should be copied from the IRB files and placed in the regulatory binder.
6. The PI or designee should assure all study records are available for review by the inspector.
7. The PI should review records and recall specifics, including the roles of key research personnel and study activities performed by each.
8. Identify an “Inspection Coordinator” and an “Escort.”
   a. The **Inspection Coordinator** is a person from the clinical research department designated to coordinate preparations. The Inspection Coordinator has direct knowledge of the study and is preferably the lead coordinator or research nurse clinician. This person is responsible for arranging the date of inspection, answering study specific questions, arranging space for the Inspector, etc. The PI, with assistance from the Clinical Research Manager (CRM), should identify this individual.

b. The **Escort** accompanies the Inspector throughout the visit. This person serves to assist the Inspector (e.g., making copies). The Escort should be trained and knowledgeable about inspections by external regulatory bodies and familiar with Beaumont and Research Institute (RI) policies, but without direct knowledge of the study. Research Administration and the CRM should identify this person.

9. Select appropriate room(s) to be used as a base for the Inspector. Ideally, the room should afford privacy, access to telephone/fax/ power outlets/photocopier/ restrooms and be away from patient care areas or files of other studies.
10. Assure key research personnel are available during inspection.

B. **During the audit**

I. When the Inspector arrives, the PI, Inspection Coordinator and Escort should be alerted and appear promptly.

II. Interactions with the Inspector should be courteous and in accordance with Beaumont Standards. Personnel must wear their Beaumont ID, and provide business cards (if available).

III. The PI should request to see the Inspector's credentials, and check the photo and descriptors. Their name, number and expiration date should be recorded. For an FDA audit, the Inspector will present an FDA Form 482, "Notice of Inspection" to the PI.

IV. The PI should inquire:
   a. What is the purpose of the inspection?
   b. Who from the external regulatory body will participate?
   c. Expected duration?
   d. Any special records needed?
   e. Request daily debriefing on issues.
   f. Would the Inspector like to meet with the PI throughout the day or at the end of each audit day?

V. The Inspector should be provided with study records and files as requested. The Escort should make copies for the Inspector and stamp them as "copies." The Escort must make two (2) copies of each document requested (1 set to the Inspector and 1 set to the Clinical Research Department).

VI. Only individuals with direct knowledge of the study should answer the Inspector's study-specific questions. If in doubt, questions should be referred to the PI. When responding to questions posed by the Inspector:
   a. Be concise; only answer only the question that was asked.
   b. Try to be as clear as possible.
   c. Answer as honestly and openly as you can.
   d. DO NOT volunteer any additional information.

e. DO NOT argue with the inspector.
f. If you don't know an answer to a question you were asked, say so, write down the question and refer it to the correct person.
g. The designated escort should keep a list of questions asked by the Inspector.

VII. At the end of each audit day, the Escort and Inspection Coordinator should summarize events in a daily email. This summary should be distributed to the PI, the CRM, the RI Directors and the IRB Chair.

C. **Following up after the audit**

a. The PI, the Inspection Coordinator, the Escort and the CRM should participate in the exit interview with the Inspector. If this is an FDA inspection, the Inspector may provide an FDA Form 483 documenting "Inspectional Observations".
b. Provide a copy of the "Inspectional Observations" or any other documentation provided by the Inspector to the IRB and RI Administrative Director.
c. The PI, with assistance from the CRM and Research Administration should provide written response to the Inspectional Observations, within fifteen (15) days. The PI response is taken into consideration by the regulatory body as they consider further actions or sanctions. For FDA audits, the FDA Inspector will prepare a written Establishment Inspection Report (EIR). The EIR, FDA Form 483, copies of materials collected and the principal investigator's response are evaluated by the appropriate FDA center in considering an inspection outcome.
d. The Regulatory Body will provide a formal letter to the PI indicating the inspection outcome classification. For an FDA audit, the responsible FDA Center provide one of the following types of letters to the PI:
    i. A letter that generally states that FDA observed basic compliance with pertinent regulations. A letter is not always sent when FDA observes no significant deviations.
    ii. An Informational or Untitled Letter that identifies deviations from statutes and regulations that do not meet the threshold of regulatory significance for a Warning Letter.
    iii. A Warning Letter that identifies serious deviations from applicable statutes and regulations. A Warning Letter is issued for violations of regulatory significance. Significant violations are those violations that may lead to enforcement action if not promptly and adequately corrected. Warning Letters are issued to achieve voluntary compliance, and include a request for correction and a written response to the agency. Warning letters are posted on the FDA website and include the PI's name.

VIII. All inspection outcome letters are addressed with a written response within fifteen (15) days. The PI, with assistance from Research Administration and Legal Affairs, will:

a. Address each particular observation or finding, point by point.

b. Determine if a finding was an oversight/one-time occurrence or systemic, where a change of procedure is indicated.
c. Delineate corrective and preventive action, including justification of why the proposed response will remediate the issue and a realistic timeline for implementation and evaluation.

IX. All correspondence with the regulatory body is provided by the PI to Research Administration. When related to a specific IRB study, the correspondence is submitted to the IRB as a study amendment.

V. SPONSOR REQUESTS FOR FDA AUDIT DOCUMENTATION:

If an inspected study is externally sponsored, information about the inspection may be shared with the study sponsor, consistent with the clinical trial agreement. Additional funding to cover inspection related expenses may be requested from sponsors, when appropriate. Prospective sponsors may request inspection documentation as part of their site assessment process. **Specific information about external inspections involving other sponsors and Beaumont investigators is confidential and may not be shared. Sharing documentation from past audits, such as copies of FDA Form 483's or correspondence between the FDA and PIs, is prohibited.**

A central log and archive of correspondence related to each audit by an external regulatory body will be maintained within Research Administration by the Administrative Manager of Research Education and Process Improvement. At sponsor request, a summary of inspection activity may be provided, omitting identifying details, such as PI and sponsor names.

VI. APPLICABLE REGULATIONS AND GUIDELINES:

21 CFR 312.60 General responsibilities of investigators
21 CFR 312.62 Investigator recordkeeping and retention
21 CFR 312.64 Investigator reports
21 CFR 312.66 Assurance of IRB review
January 1988 Guidelines for the Monitoring of Clinical Investigations
September 1993 FDA Compliance Program Guidance Manual 7348.811: Clinical Investigators
May 9, 1997 International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline

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VII. REFERENCES TO OTHER APPLICABLE SOPs:

All current Beaumont Research Institute policies and procedures

Policy and Procedure Standards on Unannounced Surveys

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.