Title: **Investigational Device Studies**	*Applicable to: **Beaumont Health**	Effective Date: **03/16/2018**
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***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 ensure Beaumont Health (Beaumont) is in accordance with Food and Drug Administration (FDA) regulations, which mandate all research involving the use of an investigational device, must be reviewed and approved by an Institutional Review Board (IRB) prior to the implementation of such research activities.

II. SCOPE:

This policy applies to investigators, key personnel, IRB members and staff. **The Beaumont Health (Beaumont) IRB serves as the primary Institutional Review Board for human participant research conducted at Beaumont (for information about the use of external IRB's, see policy *Review by an External Institutional Review Board*).** Except where noted, the policy requirements apply to all Beaumont research involving investigational or study agents, regardless of a study's IRB of record.

III. GENERAL:

A. The use of a test article is defined as an unapproved device, drug or biologic typically part of a clinical trial designed to test the safety and /or efficacy of the test article. These clinical trials require prior IRB review and approval. The majority of clinical trials are conducted under an Investigational Device Exemption (IDE) or an Investigational New Drug (IND) exemption obtained from the FDA, which require the research protocols to be filed with the FDA prior to initiation.

B. An investigational device exemption (IDE) allows an investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support a Premarket Approval (PMA) application or a Premarket Notification [510(k)] submission to the Food and Drug Administration (FDA). All clinical evaluations of investigational devices, unless exempt, must have an approved IDE before the study is initiated. An IDE is also required when evaluating an FDA approved device for a new indication.

C. Clinical evaluation of devices which have not been cleared for marketing requires:
   1. An IDE approved by an IRB. If the study involves a significant risk device, the IDE must also be approved by the FDA.
   2. Informed consent for study participation from all patients.
   3. Labeling indicating the device is for investigational use only.
   4. Monitoring of the study.
   5. Well documented study records.
   6. Regular reporting of study activities to the IRB and, if a significant risk device, to the FDA.

D. If the study involves the *use* of a device and meets criteria to undergo expedited review, the IRB will consult with Clinical Engineering to confirm the non-significant risk determination or have the determination made at a full board meeting.

IV. DEFINITIONS:

A. **Device -** A device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:
   1. Recognized in the official National Formulary, or the United States Pharmacopoeia, or any other supplement to them;
   2. Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or,
   3. Intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

B. **Implant -** An implant is a device placed into a surgically or naturally formed cavity of the human body and is intended to remain there for a period of 30 days or more. In order to protect public health, the FDA may determine a device placed in participants for shorter periods are also implants.

C. **Investigational Device -** An investigational device is a device, including a transitional device which is the object of an investigation.

D. **Investigational Device Exemption -** An Investigational Device Exemption **(**IDE) refers to the regulations under 21 CFR 812. An *approved* IDE indicates the IRB (and FDA for significant risk devices) has approved the sponsor's study application and all requirements under 21 CFR 812 are met.

E. **Investigational Device Exemption for Non-Significant Risk (NSR) Device Study** - The FDA is not required to review research involving NSR; however, IRB submission and oversight are required.

F. **Non-Significant Risk (NSR) Device Study -** The study of a device which does not meet the definition of a significant risk device and does not present the potential for serious risk to the health, safety, or welfare of participants. NSR device studies should not be confused with the concept of "minimal risk". Once a device is determined to meet the definition of NSR device it is subject to abbreviated requirements as stated in 812.2(b).

G. **Significant Risk (SR) Device Study -** Significant risk device is an investigational device: (1) intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a participant; (2) for use in supporting or sustaining human life and represents a potential for serious risk to the health, safety, or welfare of a participant; (3) for a use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a participant; or (4) otherwise presents a potential for serious risk to a participant.

H. **Sponsor/Investigator -** An individual who both initiates and actually conducts, alone or with others, a clinical investigation (i.e., under whose immediate direction the investigational device is administered, dispensed or used). The term does not include any person other than an individual. The regulatory obligations of a sponsor/investigator include both those of an investigator and those of a sponsor.

I. **Unanticipated Adverse Device Effect -** Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with a device, if effected problem or death was not previously identified in nature, severity, degree of incidence, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of participants in the investigational plan or IRB application.

V. POLICY:

In accordance with federal regulations and Beaumont policies, IRB review is required for all projects involving an investigational device.

A. **Exemptions from IDE Requirements -** A device may be exempt from the IDE requirements. There are seven (7) exemption categories which may be claimed. Full information regarding the seven exemption categories may be found in the FDA regulations 21 CFR Sec. 812.2(c).

1. A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.
2. A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976 determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.
3. A diagnostic device, if the sponsor complies with applicable requirements in 809.10(c) and if the testing:
   a. Is non-invasive; and
   b. Does not require an invasive sampling procedure that presents significant risk; and
   c. Does not by design or intention introduce energy into a participant; and
   d. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
4. A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put participants at risk.
5. A device intended solely for veterinary use.
6. A device shipped solely for research on or with laboratory animals and labeled in accordance with 812.5(c).
7. A custom device as defined in 21 CFR §812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

The sponsor or sponsor/investigator must provide sufficient justification to support the exemption category being claimed. The principal investigator (PI) must reference the exemption category being claimed in the IRB Application. An exemption from the IDE requirement is **not** an exemption from the requirement for prospective IRB review or informed consent.

B. **Significant Risk (SR) versus Non-Significant Risk (NSR) Devices -** Unless exempt by the IDE regulations, an investigational device must be categorized as either an SR device or an NSR device. The sponsor makes the initial risk assessment, but an IRB must make a formal determination regarding the appropriate SR/NSR category. The determination of SR/NSR must occur at a fully convened IRB meeting. The SR/NSR decision by the IRB is important to the FDA since the IRB serves as the FDA's surrogate with respect to review and approval of NSR studies. The IRB's determination applies only to studies under their jurisdiction.

1. Examples of SR/NSR determinations include:
   a. A sponsor protocol includes an indwelling dual port catheter for administration of pain medication for 24-36 hours as an NSR device. The IRB did not agree with the sponsor's NSR justification and determined this is an SR study requiring IDE approval from the FDA. The IRB however, was willing to allow the FDA to weigh in as the final arbiter of this conflict. Upon review by the FDA, it was determined the catheter was of significant risk due to the length of time it was indwelling. A NSR device according to the FDA is a single port catheter implanted for less than 24 hours.
   b. A study was submitted to the IRB involving a nasal turbinate device manufactured outside of the U.S. and labeled in a foreign language as an NSR device. After consulting with Clinical Engineering, the IRB determined the device was an SR device and required an FDA issued IDE prior to accepting the study submission.
   c. An IRB application for a randomized study comparing a bare metal stent approved by the FDA for use in native vessels to a drug eluting stent approved by the FDA for use in native vessels was submitted. Since both stents are FDA approved for the indication being studied they are considered Exempt devices satisfying 812.2(c)(2), for the purposes of this study.
   d. A data collection study surrounding the standard of care use of a cardiac stent for an approved indication would not undergo an SR/NSR determination since the study does not involve the actual *use* of a device, just collection of data.

Research involving the use of an SR device must be conducted in full accordance with FDA requirements and must have an approved IDE from the FDA.

C. **IDE for NSR Device Studies -** If the sponsor identifies a study as NSR, the sponsor must provide the reviewing IRB an explanation of its determination (21 CFR812.2(b)(1)(ii)) and should provide any other information which may help the IRB in evaluating the risk of the study e.g., a description of the device, reports of prior investigations with the device, the proposed investigational plan, participant selection criteria, and other information the IRB may need.

The FDA considers an investigation of an NSR device to have an approved IDE, when an IRB concurs with the NSR determination and approves the study. The IRB may require a letter from the FDA indicating full FDA review is not required. The sponsor also must comply with the IDE requirements under §812.2 (b)12.

D. **Device Labeling -** A label is required on each device, regardless of risk determination (SR/NSR), with the name of the manufacturer and the risks/warnings associated with the device. The device must be labeled in accordance with the labeling provisions of the IDE regulation and must bear the statement "CAUTION - Investigational Device. Limited by Federal (or United States) law to investigational use". The labeling must not contain any information claiming safety or effectiveness.
   1. IRB Approval - The sponsor must obtain and maintain IRB approval throughout the investigation as an NSR device study.
   2. Informed Consent - The sponsor must assure investigators obtain and document informed consent from each participant, unless the IRB has waived the requirement in accordance with regulations.
   3. Monitoring - All investigations must be properly monitored to protect the human participants and assure compliance with approved protocols (§812.46). Guidance on monitoring investigations can be found in Guideline for the Monitoring of Clinical Investigations.
   4. Records and Reports - Sponsors are required to maintain specific records and make certain reports as required by the IDE regulation.
   5. Investigator Records and Reports – The sponsor must assure the participating investigators maintain records and make reports as required.
   6. Prohibitions – Commercialization, promotion, test marketing, misrepresentation of an investigational device, and prolongation of the study are prohibited (§812.715).

E. **PI Responsibilities for Investigational Device Studies -** PI requirements for the use of an investigational device in research include:
   1. The investigational device must be used only by the PI or approved sub-investigators under his/her direct supervision; **and**
   2. The investigational device must be used only for the approved indications and under the conditions approved by the FDA and as described in the current IRB approved protocol; **and**
   3. The PI must not supply the investigational device to any persons not authorized under the IDE; **and**
   4. Informed consent from the participant or the participant's legally authorized representative must be prospectively obtained, unless waived by the IRB; **and**

5. Device storage must be under lock and key and disposal or return of the investigational devices must be appropriate and according to the sponsor's instructions; **and**
6. The PI must maintain complete and accurate records related to the device, including records of receipt, use or disposition, records of each participant exposure to the device, dates and reasons for any deviations from the protocol and dates and descriptions of any device malfunction.

F. **Sponsor/Investigator Responsibilities for Device Studies in Investigator Initiated Research (IIR) -** The PI functions as the sponsor and the investigator for IIR studies involving investigational devices. Additional responsibilities associated with being a sponsor/investigator includes:

1. Reporting Unanticipated Problems (UPs) to the study Safety Committee or DSMB, per the protocol. In addition, reporting Unanticipated Adverse Device Effects (UADE) to the FDA within ten (10) working days of PI knowledge. The sponsor/investigator is required to conduct an immediate evaluation of an UADE and must report the results of the evaluation to the FDA, all reviewing IRB's and participating investigators within ten (10) working days after the sponsor first receives notice of the effect.
2. Reporting any protocol deviation made to protect the life or physical well-being of a participant in an emergency, to the IRB and the FDA within five (5) working days.
3. Reporting any use of the investigational device without obtaining prior informed consent to the FDA, IRB and the Safety Committee within five (5) working days after such use.
4. Monitoring the device shipping, use, disposition and final disposal of devices. Upon completion or termination of the study, the sponsor/ investigator is required to document disposition of all devices shipped out during the study, including the return, destruction or other disposition of unused devices.
5. Submitting a Progress Report to the FDA, IRB and the Safety Committee no less than annually.
6. Upon completion of the study, submitting a final report to the FDA, IRB and the Safety Committee within three (3) months.
7. Any further information requested by the FDA or the IRB regarding any aspect of the study is required to be reported promptly.
8. IDE regulations strictly prohibit the promotion and commercialization of a device not cleared or approved by the FDA for marketing. This encompasses the following activities:
   a. Promotion or test marketing of the investigational device.
   b. Charging participants for the device a price greater than is necessary to recover the costs of manufacturer research development and handling.
   c. Prolonging an investigation beyond the point needed to collect data required to determine whether the device is safe and effective.

d. Representing that the device is safe or effective for the purposes for which it is being investigated.

Questions about an FDA IDE application should be directed to the FDA. The FDA will keep IDE records confidential and not disclose the existence of the IDE unless:

1. FDA determined the information had been previously disclosed to the public;
2. FDA approves a PMA for a device subject to an IDE; or
3. A notice of completion of a Product Development Protocol (PDP) is in effect.

G. **Additional Reporting Requirements -** A PI or sponsor who determines an adverse device effect presents an unreasonable risk to participants, must terminate or suspend all parts of studies presenting the risk(s) as soon as possible. If the device is an SR device, a terminated or suspended study may not resume at Beaumont without FDA and IRB approval. If the device is an NSR device, a terminated or suspended study may not resume at Beaumont without IRB approval and, if the study was terminated or suspended for an UADE which presented an unreasonable risk to participants or others, FDA approval.

VI. PROCEDURES:

A. **When the Beaumont IRB Serves as the IRB of record:**
All studies with Beaumont Sponsor/Investigators must be reviewed by the Beaumont IRB; they may not be submitted to an external IRB. Greater than minimal risk, investigator initiated studies will require the PI or co-investigator to participate in the IRB meeting introduction of the project and to answer committee questions, in order to facilitate review. The Clinical Engineering Committee will review the research information submitted to the IRB. Upon completion of their review, signoff on the IRB application or a letter to the IRB documenting their review will be required.

B. When submitting a study involving a device to the Beaumont IRB, a subset of questions regarding use of the device must be completed within the iMedRIS initial IRB submission application. Responses should provide the IRB with adequate information to determine whether the study is exempt from IDE requirements or includes an NSR or SR device. The PI must provide the IRB with information such as the device manual, reports of prior investigations conducted with the device, the proposed investigational plan, a description of participant selection criteria, monitoring procedures, a risk assessment and the rationale used in making the device risk determination.

C. The risk determination should be based on the proposed research use of a device, and not on the device alone. The IRB will consider the following, when evaluating a device for risk determination:

1. The nature of the harm which may result from use of the device. Studies where the potential harm to participants could be life threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to body structure should be considered SR.
2. If the participant must undergo a procedure as part of the study (e.g., a surgical procedure), the IRB must consider the potential harm which could be caused by the procedure in addition to the potential harm caused by the device.

D. **If the IRB determines the device is Significant Risk and the sponsor has not yet obtained an IDE from the FDA,** the IRB will:
1. Notify the PI of the SR decision.
2. Complete IRB review of the study after the sponsor obtains the IDE from the FDA.

The study may not begin until the FDA approves the IDE and the IRB approves the study.

E. **If the IRB determines the device is Non-Significant Risk,** the study may be reviewed and approved by the IRB without submission to the FDA. The sponsor and PI must comply with the "abbreviated IDE requirements".

1. To assure risks to the participant are reasonable in relation to the anticipated benefits, the risks and benefits of the study should be compared to the risks and benefits of alternative devices or procedures. This differs from the judgment about whether a study poses an SR or NSR, which is based solely upon the seriousness of the harm which may result from the use of the device.

2. Minutes of the IRB meetings must document the rationale for determining SR/NSR decisions for the study.

3. The FDA considers the IRB the review body to make the risk determination for all device studies at a fully convened IRB meeting. Thus, full board IRB review is required for all studies involving SR/NSR devices. Once the risk assessment of the investigational device has been made with the initial IRB review, NSR device studies may qualify as a minimal risk device and be reviewed under IRB expedited review procedures going forward.

F. **Unanticipated Problem Involving Risk to Participants or Others** - UPs must be reported to the IRB per IRB policy *Reporting an Unanticipated Problem Involving Risk to Participants or Others*. Additionally, UADE's must be reported by the PI to the sponsor and the IRB of record. If the IRB determines the new information changes its risk assessment of the device used in the study, the IRB may reconsider a prior NSR decision and request FDA review.

G. **Protocol Deviation Reporting -** Protocol deviations related to device studies must be reported to both the IRB and, for externally sponsored trials, the sponsor, in compliance with IRB policy 229, *Protocol Deviations.*

VII. APPLICABLE REGULATIONS AND GUIDELINES:

21 CFR 50 – Protection of Human Subjects
21 CFR 56 – Institutional Review Boards
21 CFR 812 – Investigational Device Exemption
21 CFR 814 – Pre-Market Approval of Medical Devices FDA
Guidance on IDE Policies and Procedures
IDE Enforcement of Good Clinical Practices (GCP) Regulations
Guidance for Clinical Investigators, Sponsors, and IRB's Adverse Event Reporting to IRB's
Improving Human Subject Protection
Device Advice FAQ's

VIII. REFERENCES TO OTHER APPLICABLE POLICIES:

IRB Policy *Reporting an Unanticipated Problem Involving Risk to Participants or Others*
IRB Policy *IRB Initial Review of Research Protocols*
IRB Policy *Protocol Deviations*
IRB Policy *Emergency Use of a Test Article*
IRB Policy *Review by an External Institutional Review Board*

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.