



Handbook for Investigators: A Guide to the IRB and Human Research Protection Program

**Division of Research
IRB Administration Office**

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*The format of this handbook is based on the University of Oklahoma's Investigator Manual
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Chapter 1: **Background on the IRB and the HRPP**

This Handbook for Investigators is designed to provide direction and assistance to faculty, staff, students or other personnel who are conducting human participant research at Wayne State University (WSU) or any of its affiliated institutions. The content of the Handbook is based on policies and procedures of the WSU Human Research Protection Program (HRPP). It is essential that investigators and key personnel familiarize themselves with applicable policies, procedures, and federal regulations before submitting documents to the Institutional Review Board (IRB) and before beginning their proposed research. In addition to referring to this Handbook, investigators have access to educational and training resources through the IRB Administration Office and website, as well as through on-line training modules from the Collaborative Institutional Training Initiative at <https://www.citiprogram.org/Default.asp>.

Most of the links referenced in this document are located on the IRB's website at www.irb.wayne.edu where additional information is available. Contact the IRB Administration Office for further assistance at 313-577-1628.

Until July of 2011, the IRB was also known as the "Human Investigation Committee" or "HIC". While some polices, forms, templates and other documents may still retain references to the HIC, these should be considered to be synonymous with "IRB" as it is used in the federal regulations.

Location and Contact Information

The WSU HRPP is overseen by the Office of Research Compliance within the WSU Division of Research. The Research Compliance Office can be reached at 577-9064. The WSU IRB Administration Office is located between Woodward Avenue and John R on the North side of Canfield. The address and contact information are as follows:

Address: 87 E. Canfield, 2nd floor
Detroit, MI 48201
Phone: 313-577-1628
Web Address: www.irb.wayne.edu
Hours: 8:30 AM – 5:00 PM
(closed from 12 Noon – 1:00 PM)

Join the IRB Info Listserv:

Please join the WSU IRB Info listserv that has been created for all researchers and research staff who are using the WSU IRB. This listserv provides a means for us to occasionally share information, make announcements, advertise the training calendar, share answers to questions, etc. with the research community.

It is easy to join:

- To subscribe send a blank e-mail to irb-info-subscribe-request@lists.wayne.edu
- To unsubscribe at any time, send an e-mail to irb-info-signoff-request@lists.wayne.edu
- To send a message to all of the people currently subscribed to the list, just send an e-mail to irb-info@lists.wayne.edu

Let us know if you need help getting started (577-1628).

Wayne State University Human Research Protection Program (HRPP)

Wayne State University's HRPP is a comprehensive university-wide program that ensures the safe and ethical conduct of human participant research by all faculty, staff, and students of Wayne State University and its affiliates. This program includes review of proposed research by relevant oversight committees; continuing oversight for compliance with applicable regulations and policy; education and training for investigators, staff, and committee members; quality assurance; and continuing process improvement. The realization of the University's commitment to the highest ethical standards in the protection of human participants in research requires the dedication of all members of the WSU research community and University administration.

While the IRB forms the core of the HRPP, other regulatory committees play an important role. These include the Financial Conflict of Interest (FCOI) Committee; the Institutional Biosafety Committee (IBC); and the Radiation Safety Review Committees of our medical affiliates. The HRPP is administered mainly through WSU's Research Compliance Office in the Division of Research, but a number of other administrative units within the university and its affiliates also provide support. These include WSU's Sponsored Program Administration, WSU's Office of the General Counsel, various clinical trials offices, and several scientific review committees.

Mission Statement

Wayne State University (WSU) is committed to the safety and protection of human participants involved in biomedical and social research at our Institution and its affiliates. WSU's HRPP meets or exceeds the highest ethical standards for human research required by local, state, and federal laws and regulations. Our mission is to create an institutional culture that values

integrity in the conduct of research as well as the pursuit of knowledge and innovation that provide human benefit.

Authority

Wayne State University's IRB must review and approve all research involving human participants, both biomedical and social science/behavioral, before research commences.

WSU has established a **Federal Wide Assurance (FWA, 00002460)** through the Office for Human Research Protections (OHRP) to conduct human participant research. WSU's FWA covers all human participant research, both biomedical and behavioral, conducted at Wayne State and its affiliates, regardless of the source of funding. WSU's FWA covers faculty, employees of WSU and its affiliated institutions, students, trainees, and anyone conducting such research under the auspices of WSU or its affiliates. Investigators who wish to use an outside IRB as the IRB of record for a particular research study must apply to the IRB and/or the Research Compliance Office for authorization to do so. WSU FWA can be accessed by typing-in "Wayne State U" at this website: <http://ohrp.cit.nih.gov/search/fwasearch.aspx?styp=bsc>

All research that meets the federal definitions of human participant research (e.g. Department of Health and Human Services (DHHS), the Food and Drug Administration (FDA), Department of Defense (DoD), Veterans Administration, et al.) is subject to the policies and procedures of the HRPP and review by the IRB.

The IRB has the authority to approve, require modification in (to secure approval), or disapprove human research activities at WSU and its affiliate institutions; to suspend or terminate approval of research not being conducted in accordance with pertinent laws, IRB requirements or University policy; and to observe, or have a third party observe, the consent process and other aspects of the conduct of the research. WSU's HRPP has a **Research Subject Advocate** who is available to observe the informed consent process and/or to provide training and support for both investigators and research participants. Please call the Research Compliance Office at 577-9064 for more information about the Research Subject Advocate program.

Institutional Affiliations and Agreements

Wayne State University has a unique relationship with the Detroit Medical Center, the John D. Dingell Veterans Affairs Medical Center, and the Oakwood Healthcare System. The affiliation agreements between these organizations specifically state that all human research activities conducted by their investigators and/or within their jurisdiction will be subject to review and approval by the WSU IRB.

WSU Medical Affiliates:

- Detroit Medical Center (Contract)
- The hospitals of the Detroit Medical Center:
 - Children’s Hospital of Michigan
 - Detroit Receiving Hospital/University Health Center
 - Harper University Hospital
 - Huron Valley-Sinai Hospital
 - Hutzel Women’s Hospital
 - Kresge Eye Institute (operating rooms)
 - Michigan Surgical Hospital
 - Rehabilitation Institute of Michigan
 - Sinai Grace Hospital
- John D. Dingell Veterans Affairs Medical Center (Memo of Understanding)
- Metropolitan Detroit Research and Education Foundation
- Oakwood Healthcare System (Contract)

Use of Non-WSU IRBs

WSU has contracted with Western IRB (WIRB®) to review certain industry-sponsored clinical trials. Please refer to the IRB website or call the Research Compliance Office at 577-9064 for more information. The use of the WIRB® must receive prior authorization from the Associate Vice President for Research. No other independent or commercial IRBs are currently available for use by researchers from WSU and its affiliates.

For cooperative group oncology protocols, WSU has arranged to use the National Cancer Institute’s IRB (CIRB). Please refer to the IRB website or call the IRB Administration Office at 577-1968 for more information.

Please note that the VAMC does not permit the use of either WIRB® or CIRB at this time.

The Ethical Basis for Human Subjects Research

All human participant research at Wayne State University is conducted in compliance with the principles of the Belmont Report and other ethical codes of the conduct for research, such as the Declaration of Helsinki and the Nuremberg Code, and is consistent with Good Clinical Practice (GCP) guidelines. The Belmont Report provides three guiding ethical principles—respect for persons, beneficence, and justice—and can be found at <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html>.

Association for the Accreditation of Human Research Protection Programs (AAHRPP)

AAHRPP provides standards for the protection of human research participants that meet or exceed federal regulations and guidance. Their vision is to ensure that all human research participants are respected and are protected from unnecessary harm (www.aahrpp.org) through their worldwide network of accredited programs. WSU's HRPP is currently undergoing re-accreditation with AAHRPP; as part of this effort, the IRB's policies and procedures have been and are continuously undergoing improvement. This Investigators Handbook is the result of WSU's ongoing improvement plan for the education of the HRPP's stakeholders.

Chapter 2: **Information About WSU's IRB Committees**

Composition of the IRBs

Wayne State University has five separate committees that are constituted as IRBs, and which have oversight over all human participant research at WSU and its affiliates registered under WSU's FWA. There are four IRBs that review medical protocols involving adult participants (PH1, M1, MP2, and MP4). Three of these IRB's (MP2, MP4, and PH1) are also qualified to review research involving minors (individuals younger than 18 years of age). The PH1 Committee reviews Phase I industry-sponsored clinical trials. The Behavioral/Social Science/Education IRB (B3) is responsible for reviewing all behavioral and social science research in adults and minors. Each of these IRB's has been registered with OHRP and the FDA and this registration can be accessed by typing-in "Wayne State U" at this website: <http://ohrp.cit.nih.gov/search/fwasearch.aspx?styp=bsc>

Each IRB committee includes members as required by federal regulations:

- Appropriate scientific expertise for the research being reviewed
- At least one member who is a non-scientist;
- At least one community (unaffiliated) member;

Each committee that reviews John D. Dingell Veterans Administration Medical Center (VAMC) protocols includes members from the VAMC.

Responsibilities of the IRB

The IRBs have the authority and responsibility to approve, require modifications to, or disapprove all human subject research before it is initiated in order to comply with ethical principles and federal, state and local regulations and institutional policy. The IRBs provide continuing oversight of all human participant research, at least yearly. The IRBs have the authority to assure, on an ongoing basis, that the risks of proposed research are justified by the potential benefits to the participants and to society, that the risks do not fall disproportionately on one group and that risks are minimized to the extent possible consistent with sound research design.

The IRBs are authorized to oversee the consenting process to ensure that agreement by an individual to participate in research is voluntary and knowing. Individuals who are particularly vulnerable (pregnant women, fetuses, children, prisoners, students, employees, or those whose

capacity to consent may be in doubt) require additional protection during the consent process. In addition, there are designated members of the IRB committees to represent prisoners, handicapped and other vulnerable categories. The Research Compliance Office employs a Research Subject Advocate who is available to observe the informed consent process and/or to provide educational or advisory information pertaining to the rights of research participants.

Undue Influence

To prevent undue influence, the IRB acts independently of university officials or anyone who is not an official member of the IRB. No individual shall attempt to influence the IRB inappropriately on any matter before the IRB, or within the IRB's jurisdiction. The Associate Vice President for Research has the authority to oversee compliance issues and is charged with investigating allegations of undue influence upon the IRB and with taking corrective action if necessary.

Meeting Schedules and Deadlines

Meeting schedules and deadlines can be found: <http://irb.wayne.edu/meetings-deadlines.php>. For membership rosters call the IRB Administration Office at (313) 577-1628.

Chapter 3: **What is Human Subjects Research?**

All research involving human subjects conducted by any faculty, staff member, or student at Wayne State University and its affiliate institutions must be submitted to the WSU IRB for review and approval prior to beginning any research activities. In order for you to determine if your work involves research and more specifically, research involving human subjects, please refer to the following step-by-step guide that is provided by the Office of Human Research Protections at the U.S. Department of Health and Human Services:
<http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html#c1>.

The IRB website has a link where the definitions of human subject research can be found. This is located at Policies: <http://irb.wayne.edu/policies-human-research.php>.

Questions to ask regarding defining human subjects research*

1. Is the activity an investigation? (Investigation: a searching inquiry for facts, detailed or careful examination)
2. Is the investigation systematic? (Systematic: having or involving a system, method, or plan)
3. Is the systematic investigation designed to develop or contribute to knowledge? (Designed: evaluate behavior, non intent. Develop: to form the basis for a future contribution. Contribute: to result in. Knowledge: truths, facts, information)
4. Is the knowledge learned from the systematic investigation designed to develop or contribute in a generalizable way? (Generalizable: universally or widely applicable).

**Contributed by Scott Millis, PhD, ABPP, CStat, Pstat(r), Chair of the Behavioral IRB Committee, WSU, based on federal guidance.*

Is this Quality Improvement or Research?

Investigators often plan to conduct quality improvement or process improvement projects in their institutions. Because there are questions that usually arise about whether or not these projects fit the definition of human subjects research, a helpful chart is provided in Appendix 8 at the end of this Handbook. It is strongly suggested that you contact the IRB Administration Office prior to beginning any project involving a quality improvement or process improvement study for additional guidance on whether or not the study should be submitted for IRB review.

Chapter 4: **Principal Investigator Qualifications and Responsibilities**

The Principal Investigator (PI) who accepts responsibility for conducting research with human participants must have the experience, expertise, professional qualifications and the research facilities and resources necessary to ensure that the rights and welfare of the human participants are protected. Investigators must consider the design of the research project as it pertains to minimizing risks to participants. Although some sponsors recognize Co-Principal Investigators, WSU's IRB recognizes **only one individual** as the Principal Investigator on any given protocol. All other investigators on the protocol are considered "co-investigators" or "key personnel".

It is the PI's responsibility to ensure that the design and conduct of research involving human participants complies with institutional policies, state laws, and federal regulations. Investigators whose research is both sponsor-initiated and sponsor-funded are responsible for performing their research in accordance with Good Clinical Practice (GCP) as defined by the Food and Drug Administration. GCP applies only for clinical research and it is not applicable to non-clinical research.

The Role of Sponsors

In accordance with AAHRPP's standards, sponsors are requested to make contractual obligations related to the protection of human subjects. The appropriate language will be negotiated by the Sponsored Program Administration and the Office of General Counsel at WSU, and by their counterparts at WSU's medical affiliates. Each contract should:

- Indicate who provides care to participants for research-related injuries, and who is responsible to pay for it, when such provisions were appropriate to the type of research being conducted.
- Obligate the sponsor to promptly report to the IRB any findings of study monitors that could affect the safety of participants or influence the conduct of the study, when such provisions were appropriate to the type of research being conducted.
- Obligate the sponsor to send data and safety monitoring plans and reports to the researcher or IRB and in the time frame for providing routine and urgent data and safety monitoring reports specified in the data and safety monitoring plan approved by the IRB.
- Obligate the sponsor to notify IRB or researcher of any results from a research study after the study has ended, when those results could directly affect the safety or medical care of participants.

Definitions

The following definitions of PI are appropriate, depending on the type of human research that is being conducted:

Principal Investigator:

1. The Office of Human Research Protections (OHRP) Guidebook defines Principal Investigator as “the scientist or scholar with primary responsibility for the design and conduct of a research project.”
2. The VA defines a Principal Investigator as any individual who conducts research involving human subjects including, but not limited to, the PI, Co-PI and Local Site Investigator (LSI).” [VHA Handbook 1200.05 3.ss.].

Clinical Investigator:

1. According to the Food and Drug Administration (FDA), a clinical investigator is defined as “an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the test article is administered or dispensed or used involving a subject) or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team” [21 CFR 56.102(h)].

Responsibilities of the Principal Investigator

The Study Design

1. Develop a research plan that is:
 - a. Scientifically valid
 - b. Consistent with sound research design
 - c. Minimizes risks to human participants
 - d. Includes a data safety monitoring board when required by the National Institutes of Health, FDA, or WSU IRB
2. Ensure that all facilities and resources necessary to protect participants are present before conducting the research study.
3. Maintain oversight of the research protocols and research staff. The PI’s signature on forms submitted to the IRB certifies that he/she has reviewed all of the submitted information and affirms that it is accurate to the best of his/her knowledge.

Laws, Regulations, Ethical Standards and Internal Policies

1. Conduct the study in accordance with: (a) The protocol as approved by the WSU IRB, (b) Ethical standards (e.g., the Belmont Report, the Declaration of Helsinki), (c) Applicable federal regulations (45 CFR 46.160 and 164, 38 CFR 16, 21 CFR 50 and 56), (d) Applicable

state and local laws (45 CFR 46.102 and 116, 38 CFR 46.118, 38 CFR 16.402, 28 CFR 50 and 56), (e) Good Clinical Practice guidelines, (f) The signed agreement/contract between the study sponsor and the PI, and (g) All WSU internal IRB policies, standard operating procedures and any conditions of approval imposed by the IRB.

2. Please note, if the research is sponsored by the Department of Defense, Environmental Protection Agency, Department of Energy, Department of Education, or if is conducted by VA investigators, there are chapters in this handbook devoted to each of these Federal entities and the additional requirements and regulations for human subject research for each.

Conduct of the Study

1. Conduct the study according to the signed protocol, the investigational plan and all pertinent regulations.
2. Obtain legally effective informed consent from participants or their legally authorized representative.
3. Ensure that the currently approved version of the consent form is being used for all participants, and that it is appropriately documented.
4. Recruit participants in a fair and equitable manner, weighing the potential risks and vulnerability of the participants with the potential benefits of the research.
5. Ensure that the availability of medical care for research-related injuries is clearly defined in the contract/agreement for sponsored research. Information regarding available medical care and whom to contact for further information must be clearly stated in the informed consent document.
6. In VA studies the PI is responsible for informing Pharmacy Service that the IRB and Research and Development Committee approval has been obtained.
7. Maintain complete records and documentation appropriate to the type of research and the study population per Good Clinical Practice guidelines.
8. Ensure that response to participant complaints or requests for information are addressed in a timely manner.
9. Monitor the safety and well-being of all research participants and remain current on literature related to the research study.
10. Submit a Closure Form at completion of the study (Forms: <http://irb.wayne.edu/forms-requirements-categories.php>, policy: http://irb.wayne.edu/policies/4-8_closure_of_a_research_protocol_admin_approval.pdf);
11. For VA studies the PI must inform the Chief, Pharmacy Service, and the Research and Development Committee when a study involving investigational drugs has been terminated.
12. A qualified physician (or dentist, when appropriate), who is an investigator or co-investigator for the clinical trial, is responsible for all clinical trial-related medical (or dental) decisions.

13. During and following a participant's participation in a clinical trial, the investigator ensures that adequate medical care is provided to a participant for any adverse events, including clinically significant laboratory values, related to the clinical trial.
14. The investigators must inform participants when medical care is needed for other illnesses of which the investigator(s) become aware.
15. The investigator must follow the clinical trial's randomization procedures, if any, and ensure that the code is broken only in accordance with the protocol. If the clinical trial is blinded, the investigator must promptly document and explain to the Sponsor any premature unblinding.

Reporting Responsibilities

1. Submit all protocol modifications or amendments to the IRB. No changes can be initiated by the PI prior to receiving IRB approval **unless** immediate changes are required in order to prevent harm to the participants or others.
2. Submit a protocol amendment upon notification of a change to the protocol. If these changes involve a change in risks or benefits to participants this should be reported to the IRB as soon as possible. Examples include: (a) An interim analysis indicates that participants have a lower rate of response to treatment than initially expected, (b) Safety monitoring indicates that a particular side effect is more severe or more frequent than initially expected, (c) A breach of confidentiality, (d) A change in FDA labeling or withdrawal from marketing of a drug, device or biologic used in a research protocol, (e) Incarceration of a participant in a protocol not approved to enroll prisoners, (f) An event that requires prompt reporting to the sponsor, (g) A protocol violation (meaning an accidental or unintentional change to the IRB approved protocol) caused harm to participants or others or indicates that participants or others are at increased risk or harm, and (h) Sponsor-imposed suspension for unacceptable risk.
3. Promptly report to the IRB any unanticipated events or adverse reactions involving risks to participants or others in accordance with IRB policies and procedures (see IRB Policies "Reporting Unexpected Problems, Suspensions, and Terminations, Serious and Continuing Non-Compliance and the Institutional Official's Responsibilities" and "Unexpected Problems" for examples and reporting time frames at <http://irb.wayne.edu/policies-human-research.php>).
4. Because full board review and approval of an amendment that alters the risk/benefit ratio of a protocol involves a time lag between submission, review, and final approval, any added risks must be communicated to existing participants and to any new enrollees **prior** to IRB approval of the change. In this case, documentation must be placed in the research record that each participant was notified about the change in risk and the exact information that was given to each (see "Amendments to the Research Protocol and Informed Consent Documents" for examples of when a participant must be made aware of changes at <http://irb.wayne.edu/policies-human-research.php>).

5. Report progress of the research at intervals as determined by the IRB, **but not less than once per year.**
6. Report any financial conflict of interest (FCOI) involving the PI, co-investigators or key personnel to the Conflict of Interest Coordinator (see “Conflict of Interest Policy and Procedure” <http://irb.wayne.edu/policies-human-research.php>)

Please refer to the IRB policy on Roles and Responsibilities of the Principal Investigator at: <http://irb.wayne.edu/policies/06-01-pi-roles-and-responsibilities-03-16-11.pdf>.

Investigator Conflict of Interest

When a Principal Investigator, co-investigator, or other member of the Key Personnel has a financial conflict of interest in relation to the proposed research, he/she must disclose it to the Financial Conflict of Interest (FCOI) Committee and the IRB. FCOI refers to situations in which the researcher and/or his/her immediate family has conflicts of interest or commitment that could compromise or have the appearance of compromising, his/her professional judgment in conducting or reporting research.

Conflicts of interest may occur when a researcher (including key personnel) and/or a member of his/her immediate family:

- receives from the sponsor of the research, financial or other forms of compensation
- has a significant financial interest in the company/agency/firm that is sponsoring or otherwise supporting the research (e.g. supplying a drug or device)
- serves in a corporate or for-profit leadership position with the company sponsor, such as executive officer, board member, fundraising officer, agent, or member of a scientific review committee, or member of a data safety and monitoring committee related to the company sponsor, regardless of compensation

Conflict of Interest Disclosure

At the time that the PI completes the Protocol Summary Form, the Continuation Form, the Exempt Protocol Summary Form, or the Amendment Form, he/she will be prompted to answer whether or not they, their spouse or domestic partner or any dependent children have a conflict of interest with the sponsor of the project. All key personnel, as well as the official signing the Protocol Summary Form, will be asked to answer the same question. If the answer is “Yes”, the individual will be directed to complete the “Individual Financial Conflict of Interest Detailed Disclosure Form”. Disclosures must be made to the FCOI committee, and a management plan or other approval memo received from this committee, prior to the submission of the research protocol to the IRB, . The FCOI disclosure must be updated on an annual basis and more frequently when significant changes have occurred.

Institutional Conflict of Interest

Institutional Financial Conflict of Interest (ICOI) may occur when the institution, any of its senior management or trustees, or a department, school, or other sub-unit, or an affiliated foundation or organization, has an external relationship, or financial interest (investments, gifts, other financial interests) in a company that itself has a financial interest in a research project. Senior managers or trustees may also have conflicts when they serve on the boards of (or otherwise have an official relationship with) organizations that have significant commercial transactions with the University. The existence (or appearance) of such conflict can lead to actual bias, or suspicion about possible bias, in the conduct of research at the University and its affiliates. If they are not evaluated or managed, they may result in choices or actions that are incongruent with the missions, obligations or the values of the institution. When PI's are aware of any ICOI relevant to their proposed project, they should disclose this to the FCOI committee and, through this committee, to the IRB for consideration.

Confidentiality of Information Provided in the FCOI Disclosure

Disclosures to the FCOI Committee are confidential and all employees of WSU who have been provided information from the FCOI database must maintain a high level of confidentiality. While IRB members and IRB administrative personnel do not have access to the actual FCOI disclosures they may have access to the summary report that the level of potential FCOI that has been assigned to the disclosure by the FCOI Committee.

Additional Conditions that the IRB May Place on a Research Protocol to Manage FCOI

When the IRB is reviewing a research protocol for which the FCOI Committee has provided a management plan for the conflict, the IRB will determine if parts of the management plan should be disclosed to the research participants in the research consent and assent documents. The IRB can also add to the FCOI Committee's management plan, but cannot remove any stipulations. In rare instance, either the FCOI Committee or the IRB may determine that the integrity of the institution and the well-being of the research participants may be in question, and that the research should be conducted outside Wayne State University by independent investigators at sites that do not have a financial stake in the outcome.

Please refer to the IRB Policy and Procedure "Conflict of Interest: Principal Investigator and Key Personnel".

Mandatory On-Line Training for Investigators and Research Staff

All investigators, co-investigators, research assistants, research coordinators, and people who interact with or intervene with human participants for research purposes must take required on-line training in human research protections prior to being approved to begin any research

activities. These can be accessed at irb.wayne.edu at the following web address <https://www.citiprogram.org/Default.asp?>.

The required modules for all investigators and key personnel depend on the type of study that is being conducted, the subjects being enrolled, and the setting in which the research is taking place. The basic sets of required modules for biomedical investigators include:

- The Basic Course in Human Participant Research for biomedical investigators
- HIPS-Health Information Privacy and Security for investigators
- Responsible Conduct in Research for biomedical investigators

For social-behavioral investigators, the required sets of modules include:

- The Basic Course in Human Participant Research for social-behavioral investigators
- Responsible Conduct in Research for social behavioral investigators.

For some studies, research personnel may be required to take modules located in the Optional Modules section. For example, if the internet is being used for recruitment, the module in Internet Research would be required. If the study involves pregnant women or the fetus, the optional module on Vulnerable Subjects: Pregnant Women and Fetus would be required. When you submit a protocol, your CITI training status is checked by the IRB Administrative staff. If there are still modules that you need to complete (regular or optional) you will be informed via an e-mail. The study cannot be approved and research cannot begin until all persons listed on the submitted protocol have taken all required and necessary optional modules.

Chapter 5: **How to Prepare an Initial Protocol Submission to the IRB**

A new protocol must be submitted to the IRB as an “Initial Protocol Submission”. Depending on the level of risk to the participants and other considerations provided in the federal regulations, initial protocol submissions will require one of the following types of reviews: full-board, expedited, or concurrence with exemption from IRB review. Any modifications or changes to a previously approved research project such as changes to the inclusion/exclusion criteria, study population, study procedures, or consent process, requested by the investigator or sponsor, must be approved by the IRB before the revisions are implemented. (See the section on Amendments below).

The IRB conducts continuing review of research taking place within its jurisdiction at intervals appropriate to the degree of risk. Periodic review of research activities is necessary to determine whether approval should be continued or withdrawn. All research involving human participants must be reviewed no less frequently than once per year according to federal regulations. See the Continuing Review policy for additional information at <http://irb.wayne.edu/policies-human-research.php>

Risk Assessment

Prior to submission of any protocol for IRB review, the PI needs to assess the actual and potential risks to participants in the research. To assist in this, the following are definitions and descriptors of minimal risk and risks that should be considered in a research study.

Minimal Risk

Minimal risk as defined in § 45 CFR 46.102(i) is the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Risk

Risk is the probability of harm, injury, or loss (e.g. physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Risks can be classified in one of the following categories.

- **Physical** – Risks that may arise from the use of test agents such as chemicals or therapeutic drugs, devices, physical agents (including radiation), and clinical procedures

- **Psychological** – Risks that may arise from the utilization of behavioral questionnaires or surveys, interview interactions, the collection of sensitive data, or the emotional stress of study participation
- **Social** – Risks that may arise from actual or potential breaches of confidentiality or anonymity such as harm to interpersonal relationships, damage to reputation or social standing, or exposure to legal sanctions
- **Legal** – Risks that may lead to legal action against the participant such as investigation or arrest
- **Economic** – Risks that may affect an individual's financial status, employment status or employability, or insurability

Exemption and Expedited Categories

Exemption

Categories of human subjects research that meet the regulatory criteria for exemption from IRB review can be found at <http://iirb.wayne.edu/exemptcat.php>. The investigator must seek concurrence of exemption from the designated reviewer in the IRB Administration Office by submitting the relevant protocol summary form found on the IRB website. The investigator cannot decide whether a protocol is exempt from IRB review: an IRB Chairperson or designee makes the determination of exemption based on regulatory and institutional criteria. The proposed study cannot be initiated until the investigator receives formal concurrence from the IRB's designated reviewer. It should be noted that the reviewer may determine that the project needs to be reviewed as either an expedited or full-board submission.

Expedited Review

The categories of research that may be reviewed through an expedited review procedure include:

1. Research activities that present no more than minimal risk to human participants,
and
2. Research activities that involve only procedures listed in one or more of the specific categories listed in the regulations at Federal Register Volume 63, No 216.

The list of expedited categories is found at www.irb.wayne.edu/expeditecat.php on our forms page: <http://irb.wayne.edu/forms-requirements-categories.php>. An IRB Chairperson or designee can review and approve initial protocol submissions that meet the regulatory criteria for this type of review. It should be noted that the reviewer may determine that the protocol should receive a full-board review.

Full Board Review

Review of a research protocol by a convened meeting of an IRB is required when a study is more than minimal risk to the participants, involves the enrollment of vulnerable subjects requiring special protections, or for a variety of other reasons (see examples of types of risks above).

Forms to Use for Initial Submission

When the exempt or expedited category that best fits your study has been determined, you can then select the forms on which to submit the proposal.

Exempt Medical Research studies

- Completed the Medical Exemption Protocol Summary Form, following the directions regarding the other required documents that need to be submitted along with the form. An exempt medical study must be no more than minimal risk. This form can be accessed at the Forms link on the IRB website at: <http://irb.wayne.edu/forms-requirements-categories.php>.

Expedited Medical Research studies

- Complete the Medical Behavioral Protocol Summary Form and All Applicable Appendices, following the directions regarding the other documents required for submission and the number of copies of the documents. An expedited medical study must be no more than minimal risk. This form can be accessed at the Forms link on the IRB website at: <http://irb.wayne.edu/forms-requirements-categories.php>.

Exempt and Expedited Behavioral studies (use of surveys, interviews, historical methodology, and qualitative research methods, etc.)

- Complete the Medical Behavioral Protocol Summary Form and all applicable appendices, following the directions regarding the other documents required for submission and the number of copies of the documents. These behavioral studies must be no more than minimal risk.

Full Board Medical and/or Behavioral Research Studies

- Complete the Medical Behavioral Protocol Summary Form and Appropriate Appendices. These should be completed and submitted with the other documents specified in the directions for the form. This form can be accessed at the IRB website at the following link: <http://irb.wayne.edu/forms-requirements-categories.php>

Appendices to the Medical Behavioral Protocol Summary Form

There are several appendices to the Medical Behavioral Protocol Summary Form that should be completed if they are applicable to the study to be submitted. These can be found at the following link on the IRB website: <http://irb.wayne.edu/forms-requirements-categories.php>.

They **must** be included in the submission if the research involves any of the following:

- Children as subjects
- Pregnant Women and/or Fetuses
- International research
- The use of biological samples in the research
- Internet use
- Drugs
- Biologic agents and device research
- Department of Defense sponsored studies
- Studies conducted by the VA
- Imaging or diagnostic radiation used in research*
- Cognitively impaired subject
- Prisoners as research subjects.

If the appropriate appendix is not included in the submission, the protocol will not be approved. *Please note that approval from the relevant radiation safety committee at our medical affiliates must be obtained and submitted along with the IRB Protocol Summary Form.

Informed Consent

Informed consent is one of the primary ethical requirements when conducting research with human participants; it reflects the basic principle of respect for persons. Informed consent seeks to ensure that prospective participants will understand the nature of the research and can knowledgeably and voluntarily decide whether or not to participate. The elements of informed consent are mandated in 45 CFR 46.116, 38 CFR 16.116, 21 CFR 50.25 and must include the following:

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the participant's participation, a description of the procedures to be followed and identification of any procedures which are experimental;
2. A description of any reasonably foreseeable risks or discomforts to the participant;
3. A description of any benefits to the participant or to others which may reasonably be expected from the research;
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant;

5. A statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained;
6. For research involving more than minimal risk, an explanation as to whether any medical treatments or compensation are available if injury occurs and, if so, what they consist of or where further information may be obtained;
7. An explanation of whom to contact for answers to pertinent questions about the research and research participants' rights, and whom to contact in the event of a research-related injury to the participant; and
8. A statement that participation is voluntary and refusal to participate will not involve a penalty or loss of benefits to which the participant is otherwise entitled, that the participant may discontinue participation at any time without penalty or loss of benefits to which he/she is otherwise entitled and that the participant will receive a copy of the signed informed consent.

When appropriate, one or more of the following elements of information shall also be provided to each participant:

1. A statement that the particular treatment or procedure may involve risks to the participant (or to the embryo or fetus, if the participant is or may become pregnant) which are currently unforeseeable;
2. Anticipated circumstances under which the individual's participation may be terminated by the investigator without regard to the participant's consent;
3. Any additional costs to the individual that may result from participation in the research;
4. The consequences of a participant's decision to withdraw from the research and procedures for early and orderly termination of the participant's participation;
5. A statement that significant new findings developed during the course of the research which may relate to the participant's willingness to continue participation will be provided to the participant; and
6. The approximate number of participants involved in the study.

The consent form VA 10-1086 must be used for Veterans Administration research [VHA 1200.05 30.d.]. If the wording of the informed consent has been initially prepared by an entity other than the principal investigator (e.g. a pharmaceutical company or a cooperative study group), then the IRB should ensure that the wording of the informed consent meets all the requirements of the IRB policy and VA policy [VHA 1200.05 31].

For all other research, the required and additional elements are addressed in the IRB consent templates. It is preferred that all consent forms be developed using the WSU IRB informed consent/assent templates. When the informed consent/assent is not in the WSU template, all of the required language from the IRB informed consent/assent templates must be included. Changes proposed to the standard language of the IRB consent templates must be approved by the IRB.

If participants include subjects from vulnerable populations then the following policies/procedures should also be consulted: the IRB Policy/Procedure on the appropriate Vulnerable Subject category, e.g. prisoners, terminally ill, children, for specific consent requirements. For specific consent criteria for research involving pregnant women see IRB Policy/Procedure “the Inclusion of Pregnant Women in Research” and “Research Involving Fetuses and Neonates”.

Once the informed consent/assent document is approved by the IRB, all forms must have the IRB stamp of approval to be considered a valid informed consent. An IRB approved informed consent/assent document will contain the approval and expiration dates established by the IRB. The informed consent document expires when the protocol approval period expires at midnight on the date of expiration. The dates of approval and expiration are also provided to the PI on all approval memos. For VA research, if the consent document is amended during the protocol approval period, the consent document must reflect the approval date of the amendment rather than the date of the approved protocol.

Informed Consent Templates:

<http://irb.wayne.edu/informed-consent.php>

The following templates are in Microsoft Word format at the IRB website:

- [Behavioral Template \(Revised 01/09\)](#)
- [Behavioral Assent Template \(Revised 05/08\)](#)
- [Medical Template \(Revised 01/09\)](#)
- [Parental Permission Template \(Revised 02/09\)](#)
- [Parental School Permission Template \(Revised 02/09\)](#)
- [Parental School Information Sheet \(Revised 01/09\)](#)
- [Humanitarian Use Device Template \(Created 07/06\)](#)
- [Assent Template \(Revised 05/08\)](#)
- [Information Sheet \(Revised 05/08\)](#)

Short Form Consents are available in:

[Arabic](#), [Bengali](#), [Chinese](#), [French](#), [German](#), [Hindi](#), [Italian](#), [Polish](#), [Russian](#), [Spanish](#), and [Swahili](#)

[English translation of Short Form Consents](#)

All forms:

<http://irb.wayne.edu/forms-requirements-categories.php>

Informed Consent Options

Informed consent or waiver of informed consent must be obtained for every participant in a research study before that participant begins any aspect of participation in the research. Informed consent does not stop at the simple signing of a document but continues throughout the study. See IRB Policy/Procedure: “Informed Consent Process” for guidance on the complete process.

The documents for use in the informed consent process include:

1. Written Informed Consent
2. Short Form Informed Consent for Non-English Speaking Participants
3. Parental Permission
4. Assent
5. Information Sheet
6. Oral Consent
7. Waiver of Consent/Assent in Non-Emergency Research
8. Waiver of Consent in Emergency Research

Written Informed Consent

Generally, the IRB requires informed consent to be documented by a written consent form approved by the IRB. The written consent form should be written at 6th - 8th grade reading level in language that is understandable by the research participant and must be reviewed with the research participant (or the research participant’s representative) as part of the consent process. Informed consent should be obtained in person unless one of the circumstances described below occurs in which case the noted alternative method of obtaining informed consent will be permitted.

Obtaining Written Informed Consent via Fax:

Situations may arise when obtaining informed consent from participants via fax is appropriate. The following are examples of acceptable situations:

- (1) it is acceptable for the informed consent process to take place in person, allow the potential participant time to take the consent document home in order to consider participation, and then have the potential participant sign and fax the informed consent document back to the research site; or
- (2) the informed consent process takes place over the phone; or
- (3) if consent is obtained from a guardian. The person obtaining the informed consent should sign the informed consent document and make appropriate notes in the participant’s records upon completion of the informed consent discussion. The participant may then fax a signed copy of the informed consent document to the research site. Upon receipt of the faxed informed consent, the investigator or appropriate designee should again sign and date the document as acknowledgement of

its receipt and make appropriate notations to the participant's record. The participant should still return the signed original informed consent document (either at the next visit or via mail) to the research site at his/her earliest opportunity. The appropriate receipt of the signed original informed consent document should sign and date it, file it with the faxed copy, and make appropriate notes to the participant's record. The notes coinciding with the dates and signatures on the informed consent documents provide the source documentation that confirm and explain how the informed consent process occurred. All documents will be maintained in the protocol record.

Obtaining Informed Consent via Mail:

This option is used when it is not possible to complete the informed consent process in person. Generally, this option is used when the study is a minimal risk study or there has been a change to the informed consent that may affect the participant and the individual is not scheduled for a study visit. Two copies of the informed consent must be mailed so that the participant has a copy to keep and another to mail back to the site. It is strongly encouraged that a follow-up phone call be placed to ensure that the research participant understands the changes in the informed consent. A witness signature is not required for the consent process. Once the signed informed consent is received it should be signed with the date it is received. Appropriate notes to file must include the changes and if a phone call was used to answer any questions about the changes the participant may have.

Assent and Parental Permission

Permission from parents is usually obtained prior to approaching a child participant. If the IRB determines that the research involves greater than minimal risk without direct benefit to the child (45 CFR 46.407, IRB category 3), signatures from both parents are necessary. However, it is acceptable for only one parent to provide permission when the other parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. The circumstance for obtaining only one signature must be documented in the study records. In other cases, such as child abuse or sexually transmitted disease, parental permission may not be appropriate. The IRB can grant a "waiver of parental consent" if criteria in the "Review of Research Involving Children/Adequate Provision for Soliciting the Permission of Parents or Guardians" checklist are met. In most cases once parental permission has been obtained, the assent of the child participant is required. A child's assent can be waived in certain treatment studies where the study offers potentially lifesaving benefits. In the case where child assent is appropriate, however, if the parent(s) gives permission for the child to be in the study and the child doesn't assent, the child cannot be enrolled in the study. See IRB Policy/Procedures: "Vulnerable Participants: Children" for guidance on submission requirements.

Information Sheet

An investigator may submit a request to the IRB seeking waiver of the requirement to obtain written documentation of informed consent and when appropriate provide participants with a written information sheet that contains all of the required elements of informed consent. The IRB may approve this request under two circumstances described in the Criteria to Waive Requirement for Written Documentation of Informed Consent checklist.

Oral Consent

Unless otherwise approved by the IRB the informed consent process is to always be explained orally to participants. Unless the IRB waives the requirement to obtain written documentation of the informed consent process, the informed consent process **must be documented in writing**.

Waiver of Informed Consent

The IRB may approve an informed consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or the option to waive the requirement for informed consent provided the IRB finds and documents that the requirements in the “Criteria to Waive or Alter Requirement to Obtain Informed Consent” checklist are met.

Criteria for Waiver of Written Documentation of Consent

The IRB may waive the requirement of written documentation of the informed consent process provided the IRB finds and documents that the requirements in the “Criteria to Waive Requirement for Written Documentation of Informed Consent” checklist are met.

Obtaining Initial Consent

The PI does not have to obtain the informed consent personally but has the ultimate responsibility for the informed consent process. Any co-investigator listed on the Medical/Behavioral Protocol Summary Form (or added to the study by an amendment) may obtain informed consent from potential study participants. In addition, the PI may designate key personnel who are authorized to obtain informed consent. All persons designated by the PI to obtain informed consent must complete all required IRB training and be listed as key personnel on the Medical/Behavioral Protocol Summary Form via submission or added later via amendment before those designees may obtain informed consent.

The PI must confirm that he/she has trained the individuals who will obtain informed consent, and each of those trained must be knowledgeable about the study and capable of answering

study-related questions posed by the potential participant. In addition, all persons listed as investigators or key personnel on the protocol must have completed the required IRB on-line training with the CITI before they can obtain informed consent or participate in any other aspects of the study.

The PI is responsible for making sure that only the most current version of the IRB-approved informed consent document bearing the IRB approval stamp be used. The person conducting the informed consent process must sign the informed consent document as the “person obtaining consent,” as well as obtain the signature of the participant and/or their legally authorized representative. Unless informed consent is waived or altered, the authorized person obtaining informed consent must ensure that all study participants or their legal representatives sign and receive a copy of the IRB approved informed consent document. That person must also ensure that no human being is involved as a participant in a research study unless informed consent has been obtained and documented before entering the participant into a study and/or conducting any procedures required by protocol.

The person obtaining informed consent should also ensure that the participant or legally authorized representative (LAR) enters the date of signing next to their name and prints their name on the document as well. The research participant or LAR must initial each page of the consent document where required.

Consent Form Revisions

During the course of a study, it may become necessary to change some of the information in the informed consent document. This can be done by a consent form revision, an addendum, or notification to study participant or his or her legally authorized representative. Any revisions must be submitted to the IRB as an amendment for review and approval prior to use. Immediate hazards or issues of safety should be communicated to the participant upon receipt of the new information or as directed by the sponsor. The new information communicated to the participant or his or her legally authorized representative must be reported to the IRB as soon as possible. Please see IRB Policy/Procedure: “Adverse Reactions and Unexpected Events” for reporting requirements and time lines.

When there have been changes made to the informed consent, the correct revised version of the IRB informed consent document, stamped, “approved”, must be utilized when enrolling any new participants in the study. While some informed consent changes may require re-consenting with a revised consent form or an addendum for ALL participants (e.g., discovery of a previously unknown serious side effect), not all affecting the risk/benefit ratio, patients no longer receiving study treatment). In cases where participants have completed active study or follow-up procedures and new safety information is discovered that may affect a participant’s further participation or long-term risks from the treatment, the participant must be informed of

this new information. The timeliness of informing participants and re-consenting will depend on the seriousness of the new information.

Steps in the Informed Consent Process

Once a potential participant indicates an interest in joining a research study, the following must occur:

1. Details are presented by study personnel who are knowledgeable about both the study and the IRB requirements of informed consent process.
2. Adequate information is given concerning the research via the IRB approved informed consent document in a language that is as non-technical as possible.
3. Ample time and opportunity are provided for the potential participant or his/her LAR to inquire about the details of the research project and to decide whether or not to participate in the research, as well as to consider other available options, if applicable.
4. Potential participants or his/her LAR have asked questions and received answers to their satisfaction.
5. It is ensured, to the degree possible, that the potential participant has comprehended the information provided about the research.
6. The potential participant or his/her LAR voluntary consent is obtained by way of a signature on the informed consent document or as otherwise authorized.
7. Documentation is provided about the research that the participant can refer to later. This includes a signed copy of the informed consent document, calendars, instructions, etc. Note that all materials provided to participants require IRB approval.
8. Documenting that the informed consent process has occurred. This may be done in the research record, a narrative note in the medical record, or an entry onto a research worksheet kept in each participant's research file.

The IRB may at any time request that the informed consent process be observed and/or monitored [38 CFR 16.109(e), 45 CFR 46.109(e), 21 CFR 56.109(e)]. This activity may be carried out by the Sr. Research Compliance Specialist for the IRB or another individual as directed by the HIC.

The principal investigator and all research personnel are responsible for continuing the informed consent process throughout the individual's participation in the study, providing ongoing opportunities to reaffirm participation through the study, reminding the participant about important information and data collection points, and providing new information as it becomes available. All interactions with the participant are to be documented as appropriate. At each study visit, participants are encouraged to ask questions about the study and their participation, and to raise any and all concerns. Thus, informed consent becomes an ongoing, interactive process, rather than a one-time information session.

Consent of Non-English Speaking Participants

If the PI is planning to enroll non-English Speaking Participants, then ***both*** of the following must be done:

1. This requires a translated long version of the consent form, any questionnaires, or materials given to participants. This must be reviewed and approved by the IRB prior to their use according to 45 CFR 46. 116 & 117
 - Documents can be translated via a certified translation service (stamp on consent) or documentation submitted with submission; or
 - The PI can have the English version translated into language of choice, and a back translation into English done by an independent person. The PI then must make sure that the original English and back-translated version are the same and include a note with the submission that this process was completed.

And

2. This requires that a person fluent (can read and speak the language of choice) be present as a witness to the consent process to verify that the consent was understood.
 - Person obtaining consent can speak the language of choice, but a witness who is independent of the study and also is fluent in the language must be present to verify that it was informed and not coerced.
 - The person obtaining consent cannot serve as the witness.

If the PI did not plan to enroll non-English speaking participants and such a participant is eligible for the study, ***ALL*** of the following must be done:

1. Obtain the sponsor's permission to enroll, if the eligibility criteria excluded non-English speaking participants (waiver).
2. A short form that is translated into language of choice must be used (available on IRB website). If this form is available on the IRB website, then it does NOT need IRB review. If this form is not on the IRB website, then it DOES need IRB review prior to use.
3. A translator must be present to translate the long English form into language of choice.
4. A witness must be present to verify that the consent was informed and not coerced.
5. An amendment to the protocol should be submitted to the IRB reporting: 1) a protocol deviation (change in the enrollment criteria), and 2) that a non-English speaking participant was enrolled.
6. If the short forms are used 4 to 6 times in a study, the protocol should be amended changing the eligibility criteria and including a translated version of the long consent form.

7. When the protocol is being renewed, the use of the short form consent process should be documented on the Continuation Form.

Please refer to the IRB Policy 9-2 entitled “Informed Consents Involving Non-English Speaking Participants” located on the IRB website at www.irb.wayne.edu.

HIPAA

When medical records are accessed and used or disclosed for research purposes, the Protected Health Information (PHI) that is created, acquired, and maintained during the conduct of human participant research must be protected and safeguarded in accordance with the Privacy Regulations promulgated pursuant to the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Wayne State University’s IRB serves as the Privacy Board for all human subject research involving PHI for the University Practice Groups, the DMC Hospitals and Clinics, the John D. Dingell VA Medical Center, Karmanos Cancer Institute and Hospital, and Oakwood Hospital.

HIPAA Summary Form

At Wayne State University, when a research study involves the use or disclosure of medical records in any form or data from a database or registry created from medical records, a HIPAA Summary Form is required for submission. This form provides the Privacy Board and its designee information on what PHI is being used and disclosed, why it is needed, and the people and entities that may have access to the information.

HIPAA Authorization Form

In addition, when a written consent is being obtained to enroll a participant into a study, if HIPAA applies, a signed written HIPAA Authorization is required before the study begins. The language in the HIPAA Authorization is mandated in the regulations and provides the participants information about their rights and how their information will be protected.

Currently the HIPAA Authorization is attached to the end of the Informed Consent Templates (Medical, Behavioral, and Parental Permission). In the near future, the HIPAA authorization language will be included in the body of the consent templates. However, the VAMC requires a separate document and signature for the HIPAA Authorization.

Privacy and Confidentiality

Privacy interests of participants- Privacy refers to persons and to their interest in controlling the access of others to themselves.

- This definition of privacy recognizes that control and autonomy, rather than isolation, are at issue.
- Accordingly, the above definition recognizes the vital role of informed consent (properly formulated and administered) in giving participants control over whether they will allow the researcher access to themselves and to their attitudes, behavior, beliefs, and opinions(e.g., a participant's willingness or unwillingness to disclose personal details about his or her own life).

Confidentiality -Confidentiality is an extension of the concept of privacy. It refers to data (some identifiable information about a person, such as notes or a videotape of the person) and to agreements about how data are to be handled in keeping with participant's interest in controlling the access of others to information about themselves.

- The researcher must be able to assure participants that the access of others to information about themselves will be controlled in a way that is acceptable to them.
- It also reminds one that confidentiality is whatever arrangement about disclosure the researcher and participant agree upon.
- Confidentiality is more than just a promise or an intention on the part of the researcher. It is an arrangement to use certain techniques that are available for protecting information from people that should not have access to it.

Advertising and Recruitment of Research Participants

The IRB will evaluate the selection and recruitment of research participants in accordance with all relevant laws and regulations. The IRB must be particularly cognizant of the special issues or potential problems concerning research involving vulnerable populations. Also, in VAMC research, veterans must be used as participants unless no veterans are available to complete the study [38 CFR 17.45]

In order to approve research the IRB will determine:

- If the selection of human participants is equitable, taking into account the purpose of the research, the setting in which the research will be conducted and the inclusion/exclusion criteria;
- Whether potential participants are vulnerable to coercion or undue influence; and
- If the recruitment process provides participants with sufficient information and an opportunity to consider whether or not to participate.

Preparatory to Research

There are several different ways to identify potential research study participants, including recruitment by treating physicians and direct advertising. When conducting research it may be

necessary for the PI to review medical records and obtain personal health information (PHI) in order to know if there are enough potential participants who have the condition being studied. If this activity is conducted to identify whether or not potential participants are eligible for the study, it is covered under HIPAA regulations as an activity considered “preparatory to research” except at the VA. VA does not consider recruitment to be an “activity preparatory to research.” If PHI is needed for recruiting, then the IRB must have approved an appropriate waiver of authorization and waiver of informed consent before PHI may be obtained and used for recruitment. It does not matter if the PI or his/her agent is obtaining information from his/her own patients’ records or not.” If the person (PI) reviewing the records does not have a clinical relationship with the potential participant, it is necessary for the clinician or his/her personnel to introduce the initial recruitment materials.

Contacting Prospective Participants Who Were Identified From Medical Records

When the participant’s clinician is also the PI for the study, the PI may approach a patient directly about participation in any of his/her IRB approved research trials. His/her clinical personnel may approach the patient and provide information about the research study.

A clinician who is not the PI of a research study may approach his/her patient with information from the PI about the research study. If the potential participant is interested in the research study, the clinician may provide information about the research study and/or provide a contact number to the patient, for more information. Information may be released to the PI if potential participants give permission for their identifying information or contact information to be shared. The clinical personnel may also discuss the patient's Protected Health Information (PHI) with other research personnel, such as the coordinator, as long as the patient first has given his/her verbal permission for this disclosure.

When the PI is not the clinician, the prospective participant’s clinician may send a letter informing a potential participant about a study and inviting him/her to participate by contacting the investigator in charge of the study. The letter should not contain any information that may be perceived as undue influence or contain coercive information or language and must be reviewed and approved by the IRB prior to sending it to the prospective participant. These relationships are addressed in the HIPAA Summary Form. It is important to clearly define the roles of persons doing the initial introduction of the study when completing that form for submission (See “HIPAA Requirements in Research”).

Follow-up in Mail Questionnaires

An investigator may contact potential participants whose names were obtained outside of the medical record by mail and may enclose a card that the prospective participant can return indicating that he/she is interested in being contacted to participate in a study. Potential participants may be sent two to three letters, but if the person does not respond, the

investigator must remove that person from the contact list. All letters to potential participants must be approved by the IRB prior to sending.

Secondary Recruitment

An example of secondary recruitment is when an investigator wishes to obtain the names of family members of a participant for a genetic study. Secondary recruitment should be done by giving a stamped envelope containing the solicitation materials (letter, study brochures, return postcard, etc.) to the participant. In this instance, the participant is asked to address and mail the envelope to his or her relative. If the investigator does not receive a response from the secondary recruit, it is reasonable to ask the study participant to contact the individual to be sure that he or she received the materials. If the person does not respond, the investigator should remove that person from the list of potential participants.

Recruiting Students/Trainees/Employees

An underlying ethical principle in research involving human participants is the belief that a person's participation must be voluntary and based upon full and accurate information. When a student is asked to volunteer in a study being conducted by his/her teacher, the concept of "voluntariness" may be questionable. Students may volunteer to participate under the belief that doing so will place them in a favorable light with the principal investigator/faculty member (e.g., better grade, good recommendation, employment possibilities), or that failure to participate will negatively affect their relationship with the investigator or faculty (e.g., lower grade, less favorable recommendation, being perceived as "uncooperative" and not part of the scientific community). Similar perceptions may apply to an employee/employer relationship. . Whenever the potential participant is a student, trainee or employee of the institution then the IRB Policy for "Vulnerable Participants: Students, Trainees and Employees" should be followed.

Recruitment Materials

Direct advertising for study participants begins the informed consent and participant selection process. IRB review and approval is required for all recruitment materials that are intended to solicit participation for a research study. This approval must be given prior to the use of any recruitment materials. For other specific guidance see IRB Policy: "Advertising for Research Participants" and "Compensation for Research Participants".

Finders' Fees

The WSU IRB does not allow the use of finders' fee in research (See IRB Policy: "Finders' Fee").

Submission Deadlines

Research submitted for **exempt** and **expedited** review can be submitted to the IRB at any time. There is no deadline attached to these types of studies.

Full board protocols must be submitted to the IRB Administration Office two weeks prior to the convened meeting of the committee at which the study will be reviewed. The PH1 committee has separate deadlines that are consistent with its scheduled weekly meetings. See the schedule of meetings and submission deadlines for each at our website.

How To Submit

The IRB administration process is transitioning to electronic submissions of protocols. However, not all of the committees are ready to accept electronic submissions at this time. When paper submissions are required, all documents for submission should be hand delivered, mailed, or sent by Fed Ex to the IRB Administration Office. Make sure you have the **correct number of copies** and documents in your packets. The directions on the forms are quite clear.

Original signatures on all signature pages are required on at least one of the sets of documents, regardless of the method of submission.

Approvals that are Pre-Requisite to IRB Submissions

Scientific Review

Before the IRB can review a protocol involving the use of human participants in research, the protocol must be reviewed for scientific merit by the Principal Investigator's (PI) department. The scientific review must address the following:

- Appropriate support will be provided for the research project including adequate facilities and staff
- Appropriate scientific and ethical oversight has been and will be provided
- The research uses procedures consistent with sound research design
- The research design is sound enough to yield the expected knowledge

Any comments or feedback related to this certification should be in writing and accompany the research proposal submission. Various departments conduct this scientific review in different ways and the IRB will accept any of these methods as long as the Chair and/or his/her designee certifies by signing the Protocol Summary Form that the scientific review has been completed and is satisfactory. Research initiated by an investigator without a designated department must

obtain certification from a department with the expertise to determine the scientific merit of the study.

Other Mandatory Pre-Reviews

Scientific Reviews

Some of the WSU affiliate institutions or Departments require some type of pre-review of research prior to the protocols being submitted to the IRB for review. These are listed below:

- All research involving **cancer** and human participants or their tissues or data must be reviewed and approved by the Protocol Review Committee of the Karmanos Cancer Institute (PRMC). The approval letter must accompany the protocol submission.
- All research involving human participants at the **John D. Dingell VA Medical Center (JDD VAMC)** must be reviewed and approved by the JDD VAMC Clinical Investigation Committee (CIC) before the protocol can be reviewed by the IRB . If the VA research involves cancer, an approval letter from the PRMC (see above) should be obtained before submission for review by the CIC. The approval letter(s) must accompany the protocol submission.
- All research involving human participants whose PI is a faculty member in the **Department of Psychiatry and Behavioral Neuroscience** must first be reviewed and approved by the Department Review Board. That approval must accompany the protocol submission.
- Clinical Trials conducted at **Oakwood Hospital** must be reviewed by the Clinical Trials Office prior to submission to the WSU IRB Administration Office. Contact Diane Powers at Diane.powers@oakwood.org. If you are a resident physician, contact researchreview@oakwood.org for information on how those protocols are to be submitted and the pre-review required.
- The **Detroit Medical Center** requires that all studies being conducted in any of their settings receive a research review prior to the study receiving final approval by an IRB. This review can be submitted to the DMC at the same time as an IRB submission, but the IRB cannot give final approval until the DMC has provided documentation of DMC review to the IRB Administration Office. The link to this application process is: <http://content.dmc.org/researchreviewprocess/dmc.org>.

Documentation of scientific review by a specially designated committee (currently required by Psychiatry, Karmanos Cancer Institute, and VAMC), or by the signatory official who signs the IRB submission forms (e.g. Chair, Director). These signatory authorities have been briefed on what questions they are required to answer, either on the Protocol Submission form or in a separate approval memo. Please be sure to provide the relevant information in your submission materials to assist the committee or signatory official with answering these questions:

- Is the research design sound enough to yield the expected knowledge?

- Are the aims/objectives likely to be achievable within the given time period?
- Is the rationale for the proposed number of participants reasonable?
- Is the scientific design described and adequately justified?
- For biomedical research: Is there a clear differentiation between research procedures and standard care and evaluation?

The Institutional Biosafety Committee (IBC)

- **What type of research requires the Institutional Biosafety Committee (IBC) approval?**
 - Research at Wayne State University involving the use of biological materials, including; recombinant DNA, agents infectious to humans, animals or plants, CDC/USDA Select Agents (including listed biotoxins), and other genetically altered organisms and agents are reviewed by the IBC. The use of transgenic animals (knock-out, knock-in) or plants is also reviewed.
- **When and where must projects be submitted?**
 - You must submit a completed “IBC Biological Agent User Application Form” and laboratory specific biosafety Standard Operating Procedures (SOPs) to the IBC via the Office Environmental Health and Safety, 5425 Woodward Ave, Suite 300, for review and approval before beginning the project. The IBC meets every month. Meeting dates are posted here:
<http://oehs.wayne.edu/biosafety/index.php#biosafetycommittee>. Applications and SOPs must be submitted at least one week prior to the meeting date.

Radiation Safety

- Radiation safety review and approval by a designated committee at the clinical institution(s) where any research procedures involving radiation will occur is now mandatory. Specifically, radiation safety reviews will be conducted by the hospitals in the Detroit Medical Center; the VAMC; and Oakwood Health System. Appendix G has been revised to include electronic drop boxes for each entity’s review committee.
- If only standard-of-care procedures are involved in the proposed research, the protocol does not require separate radiation safety review (beyond that which the IRB provides). For protocols involving procedures used only for research purposes, the PI will submit Appendix G and other required documents to the relevant radiation safety committee(s) for review and approval, and must include the approval memo with the submission to the IRB.

Financial Conflict of Interest (FCOI) Committee Reviews

- Financial Conflict of Interest (FCOI) disclosures must be made to the FCOI committee and the resulting memo (describing management plan, if any) must be included with the submission to the IRB.

What to Include in a Research Protocol

A common question concerning the IRB submissions involves the definition of a “protocol”. The IRB directions specify that in addition to all of the required forms, consent templates, etc., a formal protocol be submitted as well. This document should describe the science of the study. Common elements that are found in a protocol include:

- Background and Significance (including a literature review that justifies the study)
- Hypotheses or Research Questions
- Inclusion/Exclusion Criteria
- Methodology (including data collection and proposed analyses)

Retrospective/Prospective Chart Review Submission

When medical record data (paper, electronic, or databases created from a medical record) are being used for research, one of two review processes are used by WSU’s IRB.

Exemption

When the proposed research fits exemption category 4 (45 CFR 46.101(b)(4)), the following steps should be used to prepare the submission. For a chart review to receive concurrence of exemption from the IRB, it means that a master list with a code number and identifiers cannot be kept. Exemption categories can be found on the IRB website.

1. Complete a Medical Exemption Protocol Form
2. Complete a HIPAA Summary Form (and request a waiver of authorization)
3. Submit a Protocol (background, significance, research questions, inclusion/exclusion, methodology, including a few literature references to support your design)
4. Submit a list of variables to be collected from the record (data collection sheet)
5. Follow directions on the back page of the form

Expedited Review

When the proposed research fits expedited category 5 (45 CFR 46.110), the following steps should be used to prepare the submission. Please note that when a chart review is appropriate for expedited review, a master list can be kept with identifiers and a code number throughout data collection and analysis. Expedited categories can be found on the IRB website.

1. Submit a Medical Behavioral Protocol Summary Form
 - a. Most of the questions about recruitment and consent are N/A, except for the request for a waiver of consent (see Section C).
 - b. Protecting confidentiality is the most important issue for a chart review – usually the only potential risk. You must request a request for a waiver of consent to conduct this retrospective review of records. Be sure to justify your request carefully.
2. Submit a HIPAA Summary Form requesting a waiver of authorization – provide justification
3. Submit a Protocol – Background, significance, research questions, inclusion/exclusion, methodology, including literature references to support your design
4. Submit a list of variables to be collected from the record (data collection sheet)
5. Follow the directions on the front of the form

Things to Remember

1. Risk of a chart review is a breach of confidentiality and the socio-legal consequences that may result. When you describe your confidentiality plan, make sure to include how you will be keeping the coded data separate from the master list that contains identifiable information.
2. There are no deadline dates for either of these submissions.
3. Give yourself enough time if you are on a deadline – our turnaround time is 3-4 weeks at present for exempt and expedited submissions.

If you want to have your submission pre-reviewed prior to submitting for formal IRB review, please call the main office number at 313-577-1628 and ask to speak to the Education Coordinator. Please refer to the following policies and procedures at www.irb.wayne.edu for more information on submissions.

All Forms:

<http://irb.wayne.edu/forms-requirements-categories.php>

Submission Requirements:

<http://irb.wayne.edu/policies/4-2-initial-protocol-submission-requirements.pdf>

Exempt Review:

<http://irb.wayne.edu/policies/4-4-exempt-review.pdf>

Expedited Review:

<http://irb.wayne.edu/policies/4-5-expedited-review-procedures.pdf>

Common Problems Found in Submissions

Full Board Submission

- Relying on an assistant to prepare the submission. Review before submitting.
- Protocol, consent form, and answers on Protocol Summary Form do not agree on key elements such as procedures, risks, sample characteristics, etc. Make sure the content is consistent across documents.
- The lay summary on the Protocol Summary Form is too technical and cannot be understood by non-scientific members of the board. Use simple, non-technical language.
- Missing Data Safety and Monitoring Plan or description of the board.
- Missing letters from the FDA regarding IND and IDE notifications.
- Very complex, technical consent forms that the normal participant cannot understand.

Expedited/Exempt Protocols

- Choosing wrong category or not selecting one at all.
- Cutting and pasting language from the formal protocol into the narrative summary.
- Forgetting to submit a protocol.
- Missing survey instruments, interview schedules, data collection sheets.
- Insufficient description of the methods.
- Missing literature citations.

All Submissions

- Missing signatures on forms.
- Boxes on forms that are not checked.
- Missing materials (appropriate appendices, consents and assents, Investigator's Brochure, Package Inserts, educational materials for the participants, surveys, interview questions, diaries, etc.).
- Unclear recruitment information.
- Non-specific descriptions of confidentiality/privacy protections.
- Confusing and technical consent documents.
- Missing justification for the inclusion of vulnerable groups.
- Inadequate justification for requesting a Waiver of Consent, Waiver of the Requirement for Documentation of the Consent, and Waiver of HIPAA Authorization.
- Lack of consideration for risks to participants, other than physical risks.
- Missing pre-reviews required for DMC, VA, Oakwood, Karmanos, and Psychiatry protocols.
- Letters of support from settings where research will take place (if out of the institutions or department).

Assistance with Preparation and Pre-Review of Submissions

A PI may request that a pre-review be done on the protocol submission materials prior to formal review. This involves assistance with completion of the proper forms and inclusion of necessary information. It does not substitute for IRB review, nor does a pre-review guarantee that the IRB will approve the submission without further requirements. An appointment should be made with the Education Coordinator at least a week in advance in order to schedule a meeting after the pre-review has been completed (577-1628).

Helpful tip: The IRB website provides the **checklist that IRB members use for their reviews** of protocols: PIs are encouraged to “review” their own protocols with this tool before submission to the IRB.

Chapter 6: **IRB Initial Review and Criteria for Approval**

Criteria for IRB Approval of Research

All research projects that fit the definition of human subjects research must be reviewed and approved by the WSU IRB before study-related procedures can be initiated. The IRB reviews each protocol on its merit and is required to ensure that the study meets all of the following criteria before it can be approved and research activities start. These criteria have been codified at § 45 CFR 46.111 and are described below.

In order to approve research covered by this policy, the IRB shall determine that all of the following requirements are met:

- Risks to subjects are minimized.
- By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk.
- Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
- Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.
- Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by §46.116.
- Informed consent will be appropriately documented, in accordance with, and to the extent required by §46.117.
- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

When some or all of the subjects are likely to be vulnerable to coercion or undue influence (such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons) additional safeguards have been included in the study to protect the rights and welfare of these subjects.

If an IRB Committee or reviewer is not provided with enough documentation in the research submission that can be used to judge whether or not any of these criteria have been met, the study cannot receive approval until these deficiencies are addressed by the PI.

IRB Decisions for New Submission

Approval

When this decision is made, no changes are required in the submission. The protocol has been fully approved and research activities can begin.

Scientific Minor Revisions Required

This type of decision means that minor changes are required to the protocol submission, but none that would affect the 8 criteria needed for approval. These types of changes are usually limited to clarifications, minor grammatical changes, and a rewording or reorganizing of the content.

Tabled

A tabled protocol means that one of the 8 criteria for approval was not met and the protocol will need to be reviewed at the next convened meeting of the committee. This decision can only be rendered for full board protocols.

Disapproved

Disapprovals are given if the protocol lacks scientific merit, has multiple problems, and the committee did not feel that it should go forward in its current state. A new protocol should be developed and submitted.

Notifying the PI of the IRB Decision

The PI will be notified of all review decisions in writing by an e-mail and a signed hard copy of the memo. **Please note** - the IRB usually does not copy study coordinators or other research personnel on these memos. This means that when you receive your memo, you need to make sure that the research team receives it as well if they are responsible for regulatory functions for your study. Please keep all copies of any submission documents and the IRB memos that are sent after the protocol has been reviewed. The memos contain important information about your approval dates and when your study is due to expire, as well as the findings from the IRB reviews.

Chapter 7: **Submitting Amendments to the IRB**

Under federal regulations § 45 CFR 46.109, § 38 CFR 16.109, and § 21 CFR 56.109, the Institutional Review Board (IRB) is responsible for review of all revisions to an IRB-approved research protocol. Revisions range from a request to correct a simple typographical error in the consent form to a significant change in the study design. Researchers must be aware that all revisions **must be approved by the IRB before implementation of the changes**. The only exception to this is when a change must be made in the protocol to prevent or alleviate an immediate harm to research participants.

Revisions can be divided into two types: Minor revisions (involving no more than minimal risk) and substantive revisions (any modification that affects one or more of the regulatory criteria for the approval of research). The IRB Policy and Procedure “Amendments to Research Protocols and Informed Consent” can be found at the IRB website.

Minor Modifications

An amendment with minor modifications would include a change that would not materially affect an assessment of the risks and benefits of the study, does not substantially change the specific aims or the design of the study, and all added procedures do not change any of the regulatory criteria necessary to approve the protocol.

Amendments with minor modifications can be submitted for expedited review (by one designated IRB member).

Substantive Modifications (revisions that are more than minor)

An amendment with substantive modifications would include changes that would materially change any of the regulatory criteria necessary to approve a protocol. Amendments with substantive modifications must be reviewed by a convened meeting of the IRB. At WSU, the amendment is almost always sent back to the committee that originally approved the protocol. If, in the opinion of the IRB reviewer(s), an amendment changes the protocol design appreciably, it may need to be re-submitted as a new protocol to the IRB.

Pre-Review of Amendments

For all research conducted at the John D. Dingell VA Medical Center (JDD VAMC), the amendments must first be approved by the JDD VAMC Clinical Investigation Committee (CIC) before the amendment can be reviewed by the IRB. The CIC approval letter must accompany the amendment submission.

For research sponsored by the Department of Defense, substantive changes to approved research must undergo scientific review prior to IRB review. For further information, please see the IRB Policy, “Department of Defense Regulations” at the IRB website.

Amendment Forms

The form to use for submission of all amendments is available at: <http://irb.wayne.edu/forms-requirements-categories.php/>

Common Problems with Amendments

- Missing the old approved version newly revised versions of what is changing
- The changes are not highlighted in the revised versions
- Insufficient number of copies of documents per the amendment directions
- When adding key personnel, the Conflict of Interest box is not always checked

Chapter 8: **Submitting Continuations to the IRB**

Under federal regulations the Institutional Review Board (IRB) is responsible for a continuing review of research at intervals appropriate to the degree of risk, but at least once each year §45 CFR 46.109(e). A protocol must be reviewed for continuation as long as the collection of private identifiable information of human participants is being conducted through interaction or intervention with those participants or as long as there is analysis of private identifiable information.

If the protocol received full board review initially and enrollment of participants continues, the renewal application must be submitted to the full board for continuation review and approval. If the study was initially reviewed by the full board and there has been no enrollment or accrual and no full board amendments submitted in the past year, that renewal can be given expedited review.

A protocol that was originally approved under an expedited review process usually receives expedited review for the renewal/continuation.

Issues That Delay Approvals of Continuations

- Accruing more than the approved number of subjects than was originally approved without submission of an amendment to do so
- The table of subjects does not match the number approved initially
- PI's and research staff do not adequately track the expiration dates on approval memos
- Failure to submit documents to the IRB Administration Office in a timely manner (2 months prior to expiration date) often resulting in a lapse of approval
- Inconsistencies in the number of previously submitted amendments, unexpected problems, and adverse events between what is reported on the continuation form and the documents housed in the official IRB records
- Failure to submit a progress report with the continuation form
- Submission of the wrong consent documents (the most recently approved consent form is required)
- Failure to submit abstracts or publications with the continuation form

Chapter 9: **Submission of Clinical Trial Protocols involving Drugs, Biologics, and Devices**

Investigational Drug Research

Faculty and physicians at Wayne State University (WSU) and their affiliates may be involved in doing research on investigational drugs in one of two situations:

1. A multi-center clinical trial where the sponsor and medical director for the study have secured Food and Drug Administration (FDA) approval for such research; or
2. A local principal investigator has initiated such research and applied and received both FDA approval and licensure for conducting the research at WSU. In both cases, WSU Institutional Review Board (IRB) review and approval of the protocol must occur before the research begins.

Investigational Drug

An investigational drug is one that:

- is in clinical evaluation, for which a sponsor or PI has filed an Investigational new Drug (IND) Application with the FDA, has not been released by the FDA for general use, and is not available through regular channels of interstate commerce, but has been granted approval to use for research or humanitarian purposes by the FDA;
- FDA approved drugs which are used in a non-FDA approved manner under a study protocol (i.e., change in therapeutic indication, dosage, route of administration, use with a different age group); and
- is any drug that is deemed “investigational” by the FDA

For all John D. Dingell Veterans Administration Medical Center (JDD VAMC) research, any approved drug that is being studied in a controlled, randomized, or blinded clinical trial is also considered an “investigational drug” VHA Handbook 1200.5 14(b) & JDD VAMC Appendix A – Procedures for Utilizing Investigational Drugs-1.1(1), (2).

An investigational new drug is a new drug or biological drug that is used in a clinical investigation. The term also includes a biological agent that is used in vitro for diagnostic purposes. The term investigational drug and investigational new drug are deemed to be synonymous for purposes of this part [see §21 CFR 312.3(b)].

Investigational New Drug (IND) An **IND** refers to an Investigational New Drug application. An IND is a request for authorization from the Food and Drug Administration (FDA) to administer an investigational drug or biological product to humans. Such authorization must be secured

prior to interstate shipment and administration of any new drug or biological product that is not the subject of an approved New Drug Application or Biologics/Product License Application.

Submission of a Study Involving Investigational Drugs

When IND is needed:

- As the PI, prior to submitting the study, the FDA must be contacted to determine if the drug would require an investigational new drug exemption. If approval for investigational use is obtained, the FDA usually provides the PI with a letter that has the date of issue and the IND number. This letter **MUST** be included with the IRB submission in order for the protocol to be approved by the IRB.
- It is the responsibility of the IRB to confirm that the IND is current.
- If the IND is not required, the FDA must confirm that the IND is not needed and that confirmation provided to the IRB.
- The submission materials must contain justification for why the study would not require an IND. Appendix F must be submitted with the protocol materials and must provide the following:
 1. IND number
 2. Date of initial IND
 3. Whether current study is being done under the original IND or as part of an
 4. amendment to the original IND
 5. A letter from the FDA is generated when an original IND is received. It will either state that the investigation can go forward or it will specify changes that it wants the PI to make. This letter should be provided to the IRB Committee to verify that an IND number has been generated for this drug or study and the date that it was written. Whenever the holder of the IND submits an amendment to the FDA, a letter is usually provided by the FDA acknowledging the receipt of that amendment.

Waiver of requirement for IND

If the PI indicates in the submission that the requirement for an IND can be waived, justification from the PI must be provided to the committee. The IRB will then conduct its own assessment to determine if it concurs that an IND is not required for a particular study. The IRB must make its own determination of whether or not an IND can be waived for the protocol that was submitted. The requirement for an IND can be waived if the study meets all of the following criteria, according to the FDA Regulation § 312.2(b):

- If the study is not intended to support FDA approval of a new indication or a significant change in the product labeling

- If the study is not intended to support a significant change in the advertising for the product
- If the study does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product
- If the study is compliant with institutional review board (IRB) and informed consent regulations set forth in parts 56 and 50 (21 CFR parts 56 and 50); and
- If the study is compliant with § 312.7 (promotion and charging for Investigational drugs)

Investigational Use of Biologics

Biological products include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. The Center for Biologics Evaluation and Research (CBER) is responsible for ensuring the safety and efficacy of the biological products. For investigational biologics, the PI must submit an application for an Investigational New Drug Exemption (IND) to the FDA.

Submission of a study involving biological products

When an IND is needed

When an IND is required for a biologic, the same application process for drugs is required for biologics. The IND notice from the FDA with a current IND date must be submitted to the IRB before the study will be approved.

Waiver of requirement for IND for a biological product

If the PI indicates in the submission that the requirement for an IND can be waived, **justification from the PI must be provided to the committee**. The IRB will then conduct its own assessment to determine if it concurs that an IND is not required for a particular study. The IRB must make its own determination of whether or not an IND can be waived for the protocol that was submitted.

The PI should complete Appendix F and submit it with the protocol materials for research involving in-vitro diagnostic biologic products.

An IND is not required for a clinical investigation involving an in-vitro diagnostic biologic product if it is:

- Intended to be used in a diagnostic procedure that confirms diagnosis made by a medically established diagnostic product or procedure
- Shipped in compliance with §312.16

- Blood grouping serum, reagent red blood cells, and/or anti-human globulin
- Intended solely for tests in-vitro in laboratory research with animals

Investigational Device Research

For all investigational device research an application for an Investigational Device Exemption (IDE) must be submitted to the FDA according to the regulations under §21 CFR 812. An approved IDE means that the IRB (and FDA for significant risk devices) has approved the sponsor's study application and all the requirements under 21 CFR 812 are met. An investigational device is a device, including a transitional device that is the object of a clinical investigation.

All clinical investigations of devices must have an approved IDE or determine that the clinical investigation can be waived from the IDE regulations. Device studies that may be waived from the requirements for an IDE, found at the FDA regulation §21 CFR 812.2(c) include:

- a legally marketed device when used in accordance with its labeling
- a diagnostic device if it complies with the labeling requirements in §809.10(c) and if the testing
- devices that are noninvasive;
- a device that does not use an invasive sampling procedure that presents significant risk
- the device does not by design or intention introduce energy into a participant;
- those that are not used as a diagnostic procedure without confirmation by another medically established diagnostic product or procedure; and
- a device that has not been determined to be a significant risk device (SRD)

A significant risk device (SRD) presents a potential for serious risk to the health, safety, or welfare of a participant. It may include an implant, devices that support or sustain human life, and devices that are substantially important in diagnosing, curing, mitigating or treating disease or in preventing impairment to human health. **A SRD does require an IDE.**

A non-significant risk (NSRD) device is one that does not pose a significant risk to the human participants and therefore does not meet the criteria described above. A NSRD study requires only IRB approval prior to initiation of study. **IDE applications are not required.**

Appendix F should be submitted with all other protocol documents and should include:

- The IDE number and date it was assigned by the FDA
- A description of why the device meets the criteria for significant risk device (SRD) or justification of why it does not meet the definition of a SRD

In addition to Appendix F, a letter from the FDA should be submitted with the IRB application including the following:

- IDE application was received by the FDA
- The date the application was received
- The IDE number assigned to the protocol by FDA; and
- Whether or not the IDE is original or part of an amendment to the original IDE

The IRB committee will verify that the number provided by the PI is current and compare the number to the one in the letter. In addition, the IRB will then conduct its own assessment to determine if it concurs that an IDE is not required for a particular study.

Abbreviated Review for IDE

When the IRB agrees with the non-significant risk determination, the sponsor must also comply with the abbreviated IDE requirements under §812.2(b) and the IRB must verify these:

- **Labeling**-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 law to investigational use”
- **IRB Approval**-The sponsor must obtain and maintain IRB approval throughout the investigation as a non-significant risk device study
- **Informed Consent**-the sponsor must assure that investigators obtain and document consent from each participant according to 21 CFR 50, unless documentation is waived by an IRB according to §56.109(c)
- **Monitoring**-all investigations must be properly monitored to protect human participants and assure compliance with approved protocols
- **Records and Reports**-sponsors are required to maintain specific records and make certain reports as required by the IDE regulation
- **Commercialization**, promotion, test marketing, misrepresentation of an investigational device, and prolongation of the study are prohibited

“Compassionate Use” of Drugs and Devices

Investigational drugs and devices may be used for the treatment of serious or debilitating conditions either for a single subject or for a small group of subjects. The United States Food and Drug Administration (FDA) recognizes that there are circumstances in which patients with a serious, and potentially debilitating or life-threatening condition have no other treatment options other than to receive an investigational drug or device for treatment of those conditions.

Sponsors will frequently refer to this type of treatment use as “compassionate use”. However, the use of this term “compassionate” is not recognized by the Food and Drug Administration (FDA) or the Office for Human Research Protections (OHRP) for investigational drugs or biologics and must not be confused with an emergency single time use of a test article.

However, compassionate use of an investigational device can be approved under an existing Investigational Device Exemption, according to the FDA.

The use of investigational drugs and devices for expanded treatment **will always** require the submission of a prospective research protocol to the Wayne State University Institutional Review Board for review and approval prior to the use.

Humanitarian Use Devices (HUD)

A Humanitarian Use Device (HUD) is a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the US per year. It is allowed by the FDA when a device manufacturer's research and development costs could exceed its market returns for diseases or conditions affecting small patient populations. The HUD provision of the regulation provides an incentive for the development of devices for use in the treatment or diagnosis of diseases affecting these populations.

FDA regulations §21 CFR 814.124 provide for the submission of a Humanitarian Device Exemption (HDE) which the manufacturer is not required to provide the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose prior to marketing.

- A Humanitarian Device Exemption (HDE) is an application similar to a premarket approval application but is exempt from effectiveness requirements
- To obtain approval for an HUD, a humanitarian device exemption (HDE) application is submitted to FDA
- The FDA needs to determine if a device is eligible for designation as an HUD
- An HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose. The application, however, must contain sufficient information for FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. Additionally, the applicant must demonstrate that no comparable devices are available to treat or diagnose the disease or condition, and that they could not otherwise bring the device to market.
- An IRB must review the HUD submission before it can be used in an institution.
- If an HUD is used in a "clinical trial", it must be reviewed under all appropriate regulations for an IDE protocol and a regular submission and review by the IRB Committee would be required
- An approved HDE authorizes marketing of the HUD. However, an HUD may only be used in facilities that have established a local institutional review board (IRB) to supervise

clinical testing of devices and after an IRB has approved the use of the device to treat or diagnose the specific disease. The labeling for an HUD must state that the device is a humanitarian use device and that, although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated.

Emergency Single Time Use of a Test Article

An exemption under Food & Drug Administration (FDA) regulations at § 21CFR 56.104(c) allows for the emergency use of an investigational drug, device, or biologic on a one-time basis per institution without IRB review and approval when all of the following conditions are met:

- A participant is in a life-threatening situation
- No standard acceptable treatment is available
- There is insufficient time to obtain IRB approval
- The emergency use is reported to the IRB within five (5) working days (this is not to be construed as an IRB approval for the emergency use).
- The PI obtains informed consent from the participant or legally authorized representative for such emergency use, except when there are circumstances that prevent obtaining consent.
- The patient is not eligible for enrollment in a local clinical trial or no such trial is available

This is not considered a research protocol. If the person requesting emergency use for a patient wishes to establish a protocol for the drug or device, an IRB submission and full review by the committee is required.

When a PI chooses to use this process, the usual practice is to:

- Notify the IRB Chair of planned use via phone, e-mail, fax, etc.
- Notify the manufacturer of the drug or device for permission to use the test article
- Obtain permission from FDA to use test article for Emergency Use
- Develop a consent form for use in this circumstance
- Submit a signed Single Time Emergency Use of a Test Article Form to the IRB within 5 days of the use, if not before
- A copy of the signed consent must be submitted to the IRB as well

Each use of an emergency test article must be reported to the IRB Committee.

Off-Label Use of Drugs and Devices

Good medical practice and the best of interest of patients require physicians to use commercially available drugs, biologics, and devices according to their best knowledge and judgment. If, in the treatment of individual patients, physicians use a product for an indication

not in the approved labeling, they have the responsibility to be well-informed about the product, to base their use of the product on firm scientific rationale and on sound medical evidence, and to maintain records of the product's use and effects. (FDA Information Sheets: Guidance for Institutional Review Boards and Clinical Investigators 1998 Update. Off Label" and Investigational Use of Marketed Drugs, Biologics, and Medical Devices").

The use of a product in this manner as part of the practice of medicine does not require the submission of a research protocol with an Investigational New Drug Application (IND) or an Investigational Device Exemption (IDE) for review by the WSU IRB.

The investigational use of approved marketed products differs from the situation described above. "Investigational Use" means the use of an approved product in the context of a clinical study protocol. When the intent of the investigational use of a drug is to develop information about the product's safety or efficacy, submission of a protocol to the IRB for review and approval is required unless the criteria for exemptions are met.

Chapter 10: **Planned Emergency Research**

The Food and Drug Administration (FDA) and the Department of Health and Human Services (HHS) permit “planned emergency research” as long as Institutional Review Board (IRB) approval and extensive community consultation §21 CFR 50.24; VHA Handbook 1200.5 14(h)] (OHRP Guidance 97-01) has occurred. This exception under FDA regulations permits planned research in an emergency setting when human subjects (participants) who are in need of emergency medical intervention cannot provide legally effective informed consent and their legally authorized representatives (LARs) are unable to give informed consent as well. The Secretary of Health and Human Services (DHHS) has implemented an Emergency Research Consent Waiver under §45 CFR 46.101(i) with provisions identical to those of the FDA except that there is no IND/ IDE requirement and the definition of family member includes spouses of brother/sisters. The waiver is not applicable to research involving prisoners because of the limitation at §45 CFR 46.101(i) & 46.306(b).

The WSU IRB adheres to the FDA Planned Emergency Use requirements and the requirements for HHS Emergency Research Consent Waiver for studies where the FDA does not apply. Most planned emergency research involves the use of a FDA regulated test article and therefore is subject to FDA regulations §21 CFR 50.24§

Principal Investigators who are planning emergency research should contact the IRB Administration Office for assistance at least 6 months before the desired start date. The requirements are very complex and include consultation within the institution, in the community in which the research is to be conducted, and with the FDA or the Department of Health and Human Services (DHHS). **Planned emergency research cannot be conducted at the VAMC.**

The FDA website has guidance for planning and conducting this type of research:
<http://www.fda.gov/RegulatoryInformation/Guidances/ucm126482.htm>

Chapter 11: **Enrolling Vulnerable Subjects in Research**

Certain categories of research participants are considered vulnerable and will receive specific considerations during the IRB's review of the proposed research. These considerations include the use of appropriate methods of recruitment, informed consent, and other protections. These vulnerable groups and requirements for their protection are described in the following IRB policies found at <http://www.irb.wayne.edu/policies-human-research.php>:

[8-1 Research Involving Fetuses and Neonates](#)

[8-2 Vulnerable Participants: Children](#)

[8-3 Vulnerable Participants: Cognitively Impaired and Mentally Disabled](#)

[8-4 Vulnerable Participants: Prisoners](#)

[8-5 Vulnerable Participants: Terminally Ill](#)

[8-6 Vulnerable Participants: Normal Volunteers](#)

[8-7 Vulnerable Participants: Students, Trainees and Employees](#)

Justification for the Inclusion of Vulnerable Groups

The protocol submission form requests that the PI provide justification for including vulnerable groups in the research study. Some sample **examples** of appropriate justifications include:

Inclusion of Children (45 CFR 46 Subpart D)

- "Use of this drug has been tested in adults, but has promise for use in children"
- "There have been limited toxic effects in a previous study using children of this age"
- "The FDA is requesting studies of test article in pediatric populations"
- "The PI has very close monitoring and controls in place to identify problems early and treat them"

Inclusion of Participants with a Cognitive Impairment

- "Use of this group is necessary to test a drug that may improve memory and cognition"
- "The PI has an adequate assessment of cognitive function in place and plans to use it frequently during the trial."

- “The LAR status will be verified with court documents and/or follow the proxy consent hierarchy.”
- “The research question cannot be answered without studying persons with cognitive impairments.”

Inclusion of Prisoners (45 CFR 46 Subpart C)

- “The study involves the effect of altering prison environments to reduce episodes of violence.”
- “Results of the study may improve facility’s handling of this type of prisoner behavior.”
- “The study may improve methods to prevent the spread of influenza viruses among inmates.”

Inclusion of Pregnant Women/Fetuses/Neonates (45 CFR 46 Subpart B)

- “The research procedures do not harm fetus”
- “The study involves an intervention with premature infants that may prevent the development of GI complications”
- “Previous studies with animal models indicate rare side-effects for the fetus”
- “The PI will be closely monitoring the neonate during the study”
- “The study involves administration of questionnaires and observation of maternal behaviors during the post-partum period”
- “The drug has potential for limiting development of pre-clampsia during pregnancy”

Research with Children or College Students

The Family Education Rights and Privacy Act (FERPA) of 1974 is a federal law that protects the privacy of student education records. All schools that receive funds under an applicable program of the U.S. Department of Education are under this law’s jurisdiction. This law applies to student records in elementary, secondary, and post-secondary educational settings. Up to the age of 18 the law gives parents certain rights with respect to their children’s records. The rights transfer to the student when he or she reaches the age of 18 or attends school beyond the high school level. Please see the WSU site for information:

<http://reg.wayne.edu/faculty/privacy.php>.

Consent of Non-English Speaking Participants

If the PI is planning to enroll non-English speaking participants or if the PI did not plan to enroll non-English speaking participants and such a participant is eligible for the study, please see Chapter 5: How to prepare an initial protocol submission to the IRB in this Handbook.

Chapter 12: **Research Involving Use of Biological Specimens & Tissue Banking**

With the increased use of human biological samples from tissue banks and repositories for research purposes, ethical and regulatory dilemmas exist regarding the distribution and use of these materials in research projects. The implications that this has on individuals and families when these samples are used for genetic research increase the regulatory and ethical burdens.

There are three distinct areas of concern in biological specimen research. The first involves genetic studies where the findings might involve risks that could harm an individual, a family, a group or community. These risks could include psychological, social, or economic harm. Examples of this might include an employer or insurance company learning of a genetic predisposition for a particular disorder and refusing employment or coverage. For this type of genetic research, the issues of confidentiality become paramount and the Principal Investigator (PI) should detail the steps that will be taken to prevent the misuse or unauthorized disclosure of the participants' records. Full Board review by the WSU IRB may be required for this type of genetic research protocol.

The second area of biological specimen research involves genetic research where there is very little perceived risk for psychological, social or economic harm to individuals or groups from whom the specimens are derived. In this type of research, the specimens are usually rendered anonymous and the results cannot be linked in any way to individuals or groups from whom they are obtained. An example of this type of research would be anonymous samples of tumor cells being analyzed for specific genetic information. In this case, the PI should detail the steps that will be taken or have been taken to de-identify and render the samples in question anonymous. The method that the IRB would use to evaluate this type of research would vary depending upon the protocol.

The third type of biological specimen research involves non-genetic studies. Although there may be less effect on perceived risk, to the groups, families, individuals and communities, the method that the IRB would use to review this protocol and the type of consent process required would vary depending on the protocol.

Tissue Banks

Tissue banks and specimen repositories are established for a variety of purposes, ranging from clinical evaluation and diagnosis, to the use of discarded materials, or the use of samples collected specifically for research purposes. All of the implications for use of these samples and materials may not have been addressed at the time that the sample was collected and added to the bank or repository. However, it is important to anticipate potential future use of the database and/or repository in order not to limit how that data may be used in research in the

future. The prudent step is to submit a protocol for the tissue bank and/or specimen repository to the IRB for review and approval, even if future use of such banks or repositories is not initially known.

Prior to HIPAA, the creation and maintenance of a specimen repository did not require IRB review and approval unless the repository or specimen database was specifically created for research purposes. However, with the advent of HIPAA, the creation and maintenance of a specimen repository or database that may subsequently be used for research must have review and approval from the organization's Privacy Board before that data may be deposited in the repository and/or database. Because of this, the WSU IRB must review and approve all repositories and specimen databases used or created at WSU and its affiliate institutions that may subsequently be used for research purposes.

IRB Form Appendix H

Appendix H is required for submission with other protocol materials for any research that is being conducted on biological specimens. In order to determine what level of review the protocol involving specimens will require, it is recommended that the PI call the IRB Administration Office to discuss the protocol.

Consent

When prospective biological samples are collected from humans for research purposes, informed consent is required. If the specimens will be kept in a specimen bank, used to develop a cell line, or other future use, the consent template section "**Future Use of Biological Specimens**" must be completed and included in the consent document. This allows the participant to be informed about the planned future use of their tissues or samples, whether or not they will be able to have results of any testing on those samples, and allows them the choice of whether or not they want their samples saved.

The development of written guidance on biological samples and a revision of the WSU Policy and Procedure on the use of biological samples and tissues in research are underway. When the revisions and new documents are available, they will be available on the IRB website.

Chapter 13: **International Research**

Research conducted outside of the United States may be subject to additional ethical and regulatory requirements that have been established by the country where the study will take place. The WSU IRB requires submission of all international research for review and approval prior to any research activity taking place. Some of the specific requirements for international research include:

- Adherence to the DHHS regulations and FDA regulations governing human subject protections in research;
- Adherence to the laws, regulations, and local customs in the country where the research will take place;
- Adherence to travel advisories and safety requirements;
- Adherence to US Export Control Policies and Procedures

In addition, other issues a PI would need to consider when planning the research in another country would include:

- The political climate in that country;
- The languages you would need to use;
- How informed consent would be done and which process would be appropriate
- The differences between the official procedures in that country and usual practice.

Things to do when preparing for the submissions:

- Call the IRB Administration Office in the beginning of the process. It may take several months to get all of the documents needed and approvals completed prior to the study being initiated. Administrative review is usually required for all out of US studies.
- Get your documents translated, if needed, into the languages of the persons you will be enrolling, if applicable. (See Consenting Non-English Speaking Participants for guidance).
- Obtain written approval from a sponsor in the country, a government official, if necessary, and if available, an IRB or ethics committee. This must be submitted with all other documents.
- You may be asked to submit information to the Export Control Office in the Office of Research Compliance regarding your research and the country and people with whom you will be working. See <http://research.wayne.edu/export-control/index.php>
- Familiarize yourself with the cultural context in the country where the research will take place.
- Know the monetary exchange for goods and services if you plan to compensate your participants.

- Develop a safety plan for research participants and members of the research team, if applicable.
- Prepare and submit Appendix A with your documents.
- Provide the IRB with evidence that you are sensitive to the cultural belief, norms, and practices in the country and have designed your study with these in mind.

Chapter 14: **Reportable Unanticipated Problems, Protocol Deviations and Violations, Suspensions and Terminations of IRB Approval, Non-Compliance, and Participant Complaints**

Unanticipated Problems Involving Risks to Participants and Others

Investigators are required to promptly report any unanticipated problem that involves risks to participants or others. These incidents involve problems that were unforeseen at the time of occurrence, and that place participants (either research participants or research staff) at increased risk of harm. This would include actual harm to participants or staff.

Protocol Deviations and Violations

Protocol Deviations

A protocol deviation is any change, divergence, or departure from the study design or procedures of a research protocol that is under the investigator's control and that has not been approved by the IRB. Investigators must promptly report protocol deviations. Examples include improper or unapproved procedures used during recruitment, enrollment, consenting, study visits, etc. Protocol deviations may or may not place participants at risk, but they must be reported to the IRB.

Minor Protocol Deviations

Changes or alterations in the conduct of the trial which do not have a major impact on the subject's rights, safety or well-being, or the completeness, accuracy and reliability of the study data. Examples of minor deviations include but are not limited to:

- a missed visit window for follow-up with no procedures required at that visit;
- initials missing from one page of consent;
- Parent or participant forgets to print name on consent form.

Submission of these types of protocol deviations is not required.... **unless they become a part of a continuing trend of minor deviations.**

Protocol Violations

A protocol violation is any change, divergence, or departure from the study design or

procedures of a research protocol that affects the subject's rights, safety, or well-being, and/or the completeness, accuracy and reliability of the study data. Examples include but are not limited to:

- Incorrect intervention given
- enrollment of ineligible participant
- key safety procedure/lab not done or done outside window
- Problem with consent or recruitment process
- significant complaint or concern
- lapse in study approval
- loss of adequate resources
- breach of confidentiality.

Submit reportable violations to the IRB within 5 days of becoming aware of the problem using the Unexpected Problem Report Form.

All forms: <http://irb.wayne.edu/forms-requirements-categories.php>

Reportable Unexpected Problems

A reportable Unexpected Problem is unforeseen and unexpected and may indicate that participants or others are at increased risk of harm, if the problem is related or possibly related to the research. An IRB is required to promptly report unexpected problems involving risks to participants and others to appropriate institutional officials, and departmental or agency heads. The types of events that will be sent to the IRB for review and adjudication are those that are unexpected, related to the study activity, and cause actual or potential harm to human participants or others.

Examples:

- **Adverse Event:** Any harm experienced by a participant, regardless of whether the event was internal (on-site) or external (off-site), and regardless of whether the event meets the FDA definition of “serious adverse event”, which in the opinion of the principal investigator is **unexpected, related to the study (definitely, probably, more likely than not, or unable to determine), and suggests that participants are at greater risk than was previously known or recognized.**
 - An adverse event is “unexpected” when its specificity and severity are not accurately reflected in the informed consent document, the protocol or the investigator’s brochure.
 - An adverse event is “related to the research procedures” if, in the opinion of the principal investigator, it was more likely than not to be caused by the research

- procedures, or if it is more likely than not that the event affects the rights and welfare of current participants.
- In general, an adverse event observed during the conduct of a study should be considered an unanticipated problem involving risk to human participants, and reported to the IRB, only if it were unexpected, serious, and would have implications for the conduct of the study (e.g., requiring a significant, and usually safety related, change in the protocol such as revising inclusion/exclusion criteria or including a new monitoring requirement, informed consent, or investigator's brochure).
 - An individual adverse event occurrence ordinarily does not meet these criteria because, as an isolated event, its implications for the study cannot be understood.
- Any harm experienced by a participant or others as a result of involvement in research activities (internal or external, **excluding** adverse events).
 - Information that indicates a change to the risks or potential benefits of the research. For example:
 - An interim analysis or safety monitoring report indicates that frequency or magnitude of harm or benefit may be different than initially presented to the IRB.
 - A paper is published from another study that shows the risks or potential benefits to your research may be different than initially presented to the IRB.
 - Study put on hold by the PI, FDA, or the Sponsor for reasons that may include safety, toxicity and/or efficacy.
 - A change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
 - Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant.
 - Research conducted without prior WSU IRB approval or conducted during a lapse of approval.
 - Event that requires prompt reporting to the sponsor.

Submitting a UP Report

A PI must submit a written report to the IRB on all of the above types of unexpected problems within 5 working days of becoming aware of it. The report should be submitted on the "Unexpected Problem Report Form" located at: <http://irb.wayne.edu/forms-requirements-categories.php>. The report will be reviewed by an IRB member and taken to the convened meeting of the IRB, if warranted. A written response will be sent to the PI after the review has been completed.

OHRP has *Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events*:

<http://www.hhs.gov/ohrp/policy/advevtguid.html>

The FDA guidance for reporting unexpected problems and adverse events can be found at:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079753.pdf>

Suspensions and Terminations of IRB Approval

Suspension – A suspension of a research protocol or selected research activities means that those activities as delineated are placed on hold as soon as the PI has been officially notified by the IRB, the sponsor, or a regulatory authority. This can be permanent or temporary. A suspension can occur as a result of an unexpected problem resulting in actual or potential harm to participants or others; continuing or serious non-compliance, scientific misconduct, or temporary suspension of a portion or all of the research until interim analyses are completed and amendments are completed by the sponsor. The IRB at WSU has the authority to suspend **all research activities** or one or more research activities such as:

1. No new participants can be accrued,
2. No research interventions may occur unless necessary for the safety and well-being of the enrolled participants,
3. And no follow-up can be conducted unless it is in the best interest of the participant and approved by the IRB.

If a Quality Assurance audit or IRB for-cause audit is conducted on a research protocol and yields multiple protocol violations and issues of non-compliance, this may result in suspension of all or some of the research activities until the problems have been resolved. If a unit conducts its own review and places a study on temporary hold, this should be reported to the IRB on an Unexpected Problem Report Form.

If a sponsor suspends research activity for reasons of harm or toxicity, this should be reported to the IRB within **5 working days of the PI becoming aware**. The suspension should be reported on an Unexpected Problem Report Form.

If a sponsor suspends research activities to temporarily stop enrollment until such time as protocol or consent changes can be made, if it is not related to harm or risk, this may be reported via an amendment form.

The IRB may request a for-cause audit, mandatory remedial education, and review of the protocol at intervals less than 1 year, corrective actions submitted by the PI at intervals, and other requirements to be set by the IRB Committee.

The IRB has the authority to terminate a suspended study where failure to comply with required corrections occurs. All suspensions for cause must be reported to federal authorities.

Termination of a previously approved protocol – Termination of a previously approved protocol means that all research activities that have been approved by the IRB are stopped permanently. It means that IRB approval has been withdrawn. No new participants may be enrolled and no additional research interventions can occur. However, future follow-up may be conducted with the approval of the IRB to monitor the subject's well-being and any for potential risk to participants.

Termination of activities that have never received prior review and approval – On the occasion when research activities have occurred that did not receive prior review and approval from the IRB, the IRB shall stop all such activities permanently. None of the data collected during this activity can be used in any future publication or presentation. Some examples include:

1. Collecting data prior to IRB approval
2. Obtaining consent prior to IRB approval;
3. Distributing survey materials and information sheets prior to IRB approval;
4. Phoning participants for recruitment prior to IRB approval;
5. 5. Reviewing a medical record to collect data in order to contact and recruit participants into the research before IRB approval.

The IRB may require the submission of a plan for safe withdrawal of subjects by the PI in order to prevent harm.

The IRB has the authority to terminate a research protocol due to an unexpected problem causing risk or harm to participants or others, serious and/or continuing non-compliance, and when required corrective actions after a suspension do not result in an improvement or solutions to the original problems. All terminations of research protocols must be promptly reported by the IRB to appropriate institutional officials and departmental or agency heads (OHRP, FDA, VA ORO, OCR, etc.)

Participant Complaints

When a participant has a concern or questions about participating in a research study or about the treatment they have received from research personnel, these concerns are often reported to an IRB Chair, the IRB Administration Office or the Research Compliance Office. If the participant has not shared their concern with the PI or research team members, the IRB contact will encourage the participant to contact the PI. If the participant declines to do this, or has made an unsatisfactory attempt to contact the research team or PI, then the IRB contact will direct the issue to the appropriate authority for resolution.

When a PI is aware of a complaint that cannot be resolved by the PI or research team, it

must be reported to the IRB on the Unexpected Problem Report Form. The issue will be reviewed by an IRB member and if warranted, it will be discussed and adjudicated at a convened meeting of the Committee.

Corrective actions taken after a participant complaint, if solved by the research team, should be documented in the research record. Corrective actions that are taken after the IRB has reviewed the complaint and issued remedial requirements should be reported to the IRB when the issue is resolved.

If you receive a participant complaint, please direct it to the Associate Director, IRB Administration; the Director, Responsible Conduct of Research; or the appropriate Chair.

Non-Compliance

Non-Compliance is a failure (intentional or unintentional) to comply with applicable federal regulations, state or local law, the requirements and determinations of the IRB or University Policy regarding research involving human subjects. Non-compliance may be minor, serious and/or continuing.

It is the responsibility of the PI to report any event that can be categorized as non-compliance, continuing non-compliance, and/or serious non-compliance to the IRB within 5 days of an occurrence. The IRB is required to promptly report to agencies, sponsors, and/or relevant officials:

- (1) unexpected problems involving risks to subjects and others;
- (2) serious or continuing noncompliance; and
- (3) suspensions and/or terminations of previously approved research.

See 45 CFR 46.103(a), 38 CFR 16.103(a) and 21 CFR 56.103(a).

Minor/Non-Serious Non-Compliance does not increase risk to research participants, compromise participant's rights or welfare, or affect the integrity of the research or data. Some examples may include but are not limited to:

1. A one-time lapse in IRB approval, (unless it becomes a continuing and recurring problem),
2. Minor changes in or deviations from an approved protocol, or administrative errors that do not impact the welfare or rights of the participant.
3. Some protocol deviations or violations may be considered minor non-compliance.

Serious Non-Compliance is non-compliance that has the potential to increase risk to research participants, compromise participant's rights or welfare, or affect the integrity of the research/or data. Some Examples may include but are not limited to:

1. Conducting or continuing research without IRB approval;
2. Lack of legally effective informed consent from research participants;
3. Failure to report or review serious reportable adverse events, unanticipated events or substantive changes in research;
4. Inappropriate or inadequate oversight of the research to insure the safety of human subjects and the integrity of the data.
5. Some protocol deviations or violations may be considered serious non-compliance.

Continuing Non-Compliance (serious or non-serious) is non-compliance that has been previously reported, or where there is a pattern of ongoing activities that indicate a lack of understanding of human subjects protection requirements that may affect research participants or the validity of the research and suggest the potential for future non-compliance without intervention. Some examples may include, but are not limited to:

1. Repeated failures to provide or review progress reports resulting in lapses of IRB approval;
2. Inadequate oversight of ongoing research;
3. Failure to respond to or resolve previous allegations or findings of noncompliance;
4. Some protocol deviations or violations may be considered continuing non-compliance.

IRB Actions: Submit an "Unexpected Problem Report" to the IRB to report non-compliance. The IRB will review the report and collect information to verify the facts of the case, and take actions that might include: require a full audit, suspend the study, terminate the study, require mandatory remedial education for all research staff, require a written and detailed corrective action plan, observe the consent process, require changes to the protocol and/or consent form, require continuing renewal more frequently than once per year, require notification of all past and current participants, and require re-consenting currently enrolled participants.

Chapter 15: **Closing your Study**

When you are ready to close your protocol, there are administrative details to attend to and a form to submit.

Criteria for Study Closure

A study may be closed when all of the following apply:

1. All collection of data involving interventions and interactions has been completed for all participants. No further contact with participants is necessary.
2. All collection of private identifiable information has been completed for all study participants. No further collection of data/information from or about the individuals will be obtained.
3. If the study involves the testing of a medical device with tissue specimens where the data will be submitted to or held for inspection by the FDA, the study may be closed when all collection and use of the specimens for the research protocol has ended.
4. If the study is funded and the sponsor agrees to or recommends closure.

Retention of Identifiers after Study Closure

If a Principal Investigator conducting human participant research is analyzing identifiable private information but is not obtaining any new information, the study does not meet all criteria for human participant research and may be closed. The identifiable information may be retained in the database so that on-going analysis can proceed. If the database containing identifiers is transferred or shared with another investigator, IRB review and approval must be obtained.

Retention of Specimens after Study Closure

If a PI conducted a study on specimens that constituted human subject research, those specimens may be retained for future use in research if the participant, at the time of consent for the study, permitted the retention for this purpose. If the specimens are identified, this information may be retained in the database and on-going analysis can proceed after study closure as long as no new specimens are obtained and added to the database. If the specimen bank containing identifiers is transferred or shared with another PI, IRB review and approval of the new research study must be obtained. If specimens are unidentifiable, these can be kept as

well. If the participant requested that they be contacted for permission to use specimens in a future protocol, the PI must do so prior to using the specimens in a new research project.

The PI is responsible for providing the IRB with any changes to the protocol. Once it has been determined that the protocol can be closed, the following actions are required:

1. Complete and submit a **Protocol Closure Form** to the IRB Administration Office at any time during the period of research approval, but BEFORE the study expires.
2. Attach any documentation received from the sponsor regarding the closure of the study.
3. If available, attach any other new findings/publications that relate to the study.

Appendices to
Handbook for Investigators

Appendix A: **Radiation or Radioactive Drug Use**

Appendix G has recently been revised to collect more specific information about procedures involving radiation: imaging, therapeutic and/or diagnostic use. These include standard of care procedures using radiation as well as those being done for research purposes only. The PI is directed to complete this appendix and submit it with the Protocol Summary Form to the appropriate Radiation Safety Review Committee(s) at the affiliated hospital(s) where these procedures will be done.

The PI must submit the radiation safety approval memo to the IRB along with his/her submission packet.

Protocols Requiring Review by a Radioactive Drug Research Committee (RDRC)

- Human research protocols involving *radioactive drug research* require either an Investigational New Drug (IND) application or exemption, or review by an FDA-approved Radioactive Drug Research Committee (RDRC).
- Radioactive drug research involving an IND is covered by the federal regulations found in 21 CFR § 312, while research that may be conducted under an RDRC is covered by 21 CFR § 361.1.
- Under § 361.1, human research using a radioactive drug or biological product may be conducted with approval from an RDRC under specific circumstances. The purpose of such research must be to obtain “basic information regarding the metabolism (including kinetics, distribution, and localization) of a radioactively labeled drug or regarding human physiology, pathophysiology, or biochemistry”. These protocols involve basic science research that does not have immediate therapeutic, diagnostic, or similar uses; that is, they do not constitute clinical trial protocols for the drug or biological product.
- All protocols conducted under the purview of the WSU IRB and which meet the criteria found in 21 CFR § 361.1 must:
 - First be reviewed and approved by the RDRC of Children’s Hospital of Michigan (CHM).
 - This committee’s approval must be included in the protocol submission packet for IRB review.

Appendix B: **Veterans Administration Research**

When research involves the Veterans Administration, there are special rules to follow and special requirements that must be met.

General Information

- Wayne State University has 3 IRB Committees (MP4, M1, and B3) that have 2 members representing the John D. Dingell Veterans Administration Medical Center (VAMC). MP2 and PH1 do not review VA studies.
- All VAMC protocols including initial submissions, amendments and continuations must receive review and approval by the Clinical Investigation Committee (CIC) at the VA prior to being sent to the IRB for review.
- A memo from the CIC must accompany the protocol documents submitted to the IRB.
- The VA uses the social security number as the medical record number; this is acceptable to the WSU IRB.
- No research can be conducted at a VA setting that involves in-vitro fertilization or fetuses.
- When the research involves prisoners as participants or children as participants, a waiver must be granted by the Chief Research and Development Officer.
- If the study involves non-veterans, the PI must indicate that there are insufficient veterans available to complete the study on Appendix J.

VA Consent Form

- The consent template (Form 10-1086) for the VA must be submitted for review.
- The participant's social security number must be included on all pages of the consent form document.
- The consent must have a statement in it that states in the event of a research-related injury, the Veterans Administration has to provide necessary medical treatment to a participant injured by participation.
- The consent form must disclose that a veteran-participant will not be required to pay for care received as a participant in a Veterans Administration research project except in accordance with federal law and that certain veterans are required to pay co-payments for medical care and services provided by the VA.
- The consent form includes language explaining the VA's authority to provide medical treatment to research participants injured by participation in a VA research project.

- Although the VA no longer mandates a witness to the consenting process in addition to the participant's signature, the IRB or sponsor may require this be added to the consent form.

The VA and HIPAA

- The WSU IRB's serve as the Privacy Board for research at the VAMC.
- The HIPAA Authorization for the VA is a separate document (as of 3/31/11) and not included in the body of the consent.
- A HIPAA Summary Form should be submitted with every VA protocol if medical records are being used for the study.

Payments to VA Participants

Payment to participants may be permitted, with IRB approval, in the following circumstances:

- No Direct Participant Benefit. When the study to be performed is not directly intended to enhance the diagnosis or treatment of the condition for which the volunteer participant is being treated, and when the standard of practice in affiliated non-VA institutions is to pay participants in this situation.
- Others Being Paid. In multi-institutional studies, when human participants at a collaborating VA or non-VA institution are to be paid for the same participation in the same study, participants may be paid at a rate comparable to that proposed at the other sites, if deemed reasonable by the local IRB.
- Comparable Situations. In other comparable situations in which, in the opinion of the IRB, payment of participants is appropriate.
- Transportation Expenses. When transportation expenses are incurred by the participant that would not be incurred in the normal course of receiving treatment and that are not reimbursed by any other mechanism.

Investigators must not pay human participants to participate in research when the research is integrated with a patient's medical care and when it makes no special demands on the patient beyond those of usual care.

Flagging the VAMC Medical Record

For full board studies, the IRB must agree or not agree with the VA decision to flag the electronic medical record. This is applicable if:

- The research involves any invasive procedure.
- Interventions or clinical services that are used in the medical care of the participant, or that could interfere with other care the participant is receiving or may receive (e.g.,

administration of a medication, treatment, use of an investigational device, orders for labs or x-rays for the study).

- The use of a survey or questionnaire may provoke undue stress or anxiety unless the IRB determines that mandatory flagging is not in the best interests of the participant (e.g., an interview study of victims of sexual assault).
- In other situations, the IRB determines that the patient health record must be flagged to protect the participant's safety by indicating the participant's participation in the study.

The medical record does not need to be flagged if:

- 1) The participation in the study involves only one encounter.
- 2) Participation involves the use of a questionnaire or previously collected biological specimens,
and
- 3) Identification of the participant in a particular study would place the participant at greater than minimal risk.

Note: If the decision involves the last item, the ICF must have language advising the participant to review the risks of usual care with the health care providers and must define the research risks clearly.

VA Studies Involving Pregnant Women

In order for the VA to conduct research involving pregnant women, the following criteria must be met:

- Appropriate studies on animals and non-pregnant women have been completed and data for assessing potential risks to pregnant women and fetuses is provided.
- The purpose of the activity is to meet the health needs of the mother or the particular fetus, the risk to the fetus is minimal, and in all cases, is the least possible risk for achieving the objectives of the study.
- Individuals engaged in the research activity will have no involvement in:
 - Any decisions as to the timing, method or procedures used to terminate the pregnancy.
 - Determination of the viability of the fetus at the termination of the pregnancy.
 - Introducing any procedural changes, for research purposes, into the procedures for terminating the pregnancy.
- No inducements, monetary or otherwise, may be offered to terminate pregnancy for purposes of research activity.
- The mother and father are legally competent and have given their informed consent after having been fully informed regarding possible impact on the fetus, except that the father's informed consent need not be secured if the purpose of the activity is to meet the health

needs of the mother, his identity or whereabouts cannot be reasonably ascertained, he is not reasonably available, or the pregnancy resulted from rape.

Unanticipated Problems and the VA

The VA Investigator must report all unanticipated internal or local Serious Adverse Event (SAE's), whether related or unrelated to the research, to the IRB as specified under local SOPS and VHA Handbook 1058.01.

A qualified IRB voting member reviewer or the convened IRB must review the reports of internal or local SAE's and must determine and document whether the event is serious, whether it is anticipated or unanticipated, and whether it is related, possibly related, or probably related to the research in accordance with VHA Handbook 1058.01.

After determining whether or not the study still meets IRB approval in light of the information provided in the report (whether or not risk to benefit ratio has changed; and whether or not this constitutes new information that should be given to participants) the qualified IRB voting member-reviewer or convened IRB must document whether or not one of the following applies:

- Immediate action is warranted to prevent an immediate hazard to a study participant.
- No immediate action is warranted but IRB review is needed.

If the previous determinations have been made by an IRB voting member, the report must be taken to the next IRB convened meeting.

If the IRB member reviewer or convened IRB determines that the AE is serious, unanticipated, and related, or possibly related to the research, the IRB Chair must report the event to the VA facility Director as soon as possible, but no later than 5 business days after the determination.

If informed consent modifications are warranted, the convened IRB must determine and document in its records whether or not previously enrolled participants must be notified of the change and if so, when and how.

Appendix C: **Department of Defense**

When research is sponsored by the Department of Defense, additional special requirements must be met. Wayne State University has signed an addendum with the DoD; this is recognized by all branches: Navy, Army, and Air Force. Each branch of the DoD may have their own specific requirements for reviewing research protocols that they support and these requirements must be followed.

What Qualifies as DoD Research

- Research that is funded by a component of the DoD-Army, Navy, Air Force.
- Research that involves cooperation, collaboration, or other type of agreement with a component of the DoD.
- The participant population will intentionally include personnel from a component of the DoD.

Note: DoD policies do not apply when DoD personnel incidentally participate in studies that are not supported by the DoD and DoD personnel are not an intended population of the research.

Note: The research must not involve prisoners of war as participants [any person captured, detained, held, or otherwise under the control of Department of Defense personnel (military and civilian, or contractor employee)].

Required Training

- Completion of all required CITI modules as specified by the WSU IRB.
- For Department of Navy: CITI modules plus 4 additional modules are required.

Additional Requirements for DoD Studies at Wayne State University

- If the research involves interventions or interactions with participants, the research cannot involve a waiver of consent or parental permission unless permission has been obtained from the Secretary of Defense.
- If the research involves cognitively impaired adults, there must be an anticipated direct benefit to the participant.
- If the research involves more than minimal risk to participants:

- An independent medical monitor must be appointed by name.
- The medical monitor is a physician, dentist, psychologist, nurse, or other healthcare provider capable of overseeing the progress of the research protocol, especially issues of the individual participant/patient management and safety.
- The medical monitor is independent of the investigative team.
- The medical monitor possesses sufficient educational and professional experience to serve as the participant advocate.
- The medical monitor has the authority to stop a research study in progress, remove individual participants from a study, and take whatever steps are necessary to protect the safety and well-being of research participants until the IRB can assess the medical monitor's report.
- Research involving the use of human participants for the testing of chemical or biological agents is generally prohibited, with the possible exception for research done for prophylactic, protective, or other peaceful purposes.
- Evidence of review of scientific merit must be submitted to the IRB.
- When survey research is being conducted, DoD personnel may require DoD approval of the surveys or interview questions.
- For research involving more than minimal risk to participants and involving military personnel:
 - Unit officers and noncommissioned officers will not influence the decisions of their subordinates to participate or not to participate as research participants.
 - Unit officers and senior non-commissioned officers in the chain of command will not be present during the time that research participant are solicited and/or consented when the research participants are members of units under their command.
 - When applicable, officers and non-commissioned officers so excluded will be afforded the opportunity to participate as research participants in a separate recruitment session.
 - During recruitment briefings to a unit where a percentage of the unit is being recruited to participate as a group, an ombudsman (not connected in any way with the proposed research or the unit) will be present to monitor that the voluntary nature of individual participants is adequately stressed and that the information provided about the research is adequate and accurate.
- The disclosure regarding provisions for research-related injury follows the requirements of the Department of Defense component.
- Issues related to non-compliance with these requirements shall be referred initially to the next higher management echelon to manage. All findings of serious non-compliance shall be reported to the Director, Defense Research and Engineering.

Additional Criteria for Department of the Navy

- For research involving more than minimal risk to participants, the protocol must include an arrangement for emergency treatment and necessary follow-up of any research.
- If research involves any of the following, the Secretary of the Navy must approve the research:
 - Waiver or alteration of the consent process.
 - Exceptions to the requirement for the consent process under 21 CFR 50.24.
 - Request for waiver of requirements of Department of Navy Policy regarding research protections.
 - Research involving severe or unusual intrusions, either physical or psychological, on human participants such as consciousness-altering drugs or mind control techniques.
 - Prisoners.
 - Potentially or inherently controversial topics (such as those likely to attract significant media coverage or that might invite challenge by interest groups).
- If the research involves human participants who are not US citizens or Department of Defense personnel, and is conducted outside the US, and its territories and possessions:
 - The permission of host company has been obtained.
 - The law, customs and practices of the host country and the US will be followed.
 - An ethics review by the host country, or local Navy IRB with host country representation will take place.

To access the Department of Defense Directive for human research protections, visit:

<http://www.dtic.mil/whs/directives/corres/pdf/321602p.pdf>

Appendix D: **Department of Education**

If research involving human participants is funded by the Department of Education, there are special regulations that must be followed. In addition to the Common Rule requirements set forth in Subpart A, B, & D, the following are additional criteria that must be followed when research is sponsored by the Department of Education:

- If the research requires the inclusion of children with disabilities or individuals with mental illness as research participants, the IRB must have at least one person primarily concerned with the welfare of these research participants.
- If consent or written documentation of consent or parental permission is waived, the research **may not involve** gathering information about any of the following:
 - Political affiliations or beliefs of the student or the student's parent.
 - Mental or psychological problems of the student or student's family.
 - Sex behavior or attitudes.
 - Illegal, anti-social, self-incriminating, or demeaning behavior.
 - Critical appraisals of other individuals with whom respondents have close family relationships.
 - Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers.
 - Religious practices, affiliations, or beliefs of the student or student's parent.
 - Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program).
- Alleged unanticipated problems involving risks to participants or others in research funded or sponsored by the US Department of Education, or of serious or continuing noncompliance with the Common Rule for the Protection of Human Participants, and/or protection of children in research must be reported to the US Department of Education.
- Visit the Department of Education website to learn more about human subject research regulations at: <http://www.ed.gov/>.

Appendix E: **Department of Energy**

If research involving human participants is funded by the Department of Energy, there are special requirements that must be met. The Department of Energy has adopted the Common Rule and these additional requirements must be met:

1. The Department of Energy requires that all human participants research adhere to the Department of Energy's "*Checklist For Use by Researchers Conducting Human Participants Research that Utilizes Personally Identifiable Information*" (PII).
2. The PI is required to submit this checklist with the protocol submission requirements.
3. The IRB must verify that the protocol complies with these protections.

To access the Department of Energy website, please visit: <http://www.energy.gov/>

Appendix F: **Department of Justice**

If research involving human participants is funded by the Department of Justice, there are special requirements that must be met. In addition to adherence to the Common Rule to protect the rights and welfare of human research participants, the Department of Justice requires the following:

- If the research involves Federal Bureau of Prisons, the IRB's approval will be submitted to the Bureau Research Review Board for final approval before the research can begin.
- The research must have a Privacy Certificate approved by the National Institute of Justice Human Participants Protection Officer.
- The consent document must disclose that:
 1. Confidentiality can be broken if the participant reports immediate harm to participants or others.
 2. The research staff does not have to report child abuse unless the participant agrees in writing to allow such reporting.
- A copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys, or other relevant research materials.
- To find out the specific criteria for human participant research funded by the Department of Justice, visit: <http://www.justice.gov/>.

Appendix G: **Environmental Protection Agency**

If research involving human participants is funded by the Environmental Protection Agency, the following additional criteria must be met:

- The research cannot involve the intentional exposure of pregnant or nursing women to any substance.
- If the results of the research involving an intentional exposure of human participants are intended to be submitted to or held for inspection by the EPA, the IRB determinations and approval will be submitted to EPA Human Participants Research Review official for final review and approval before the research can begin.
- If research involves children, the research must meet the criteria for either risk category 1 (no more than minimal risk) or category 2 (more than minimal risk but with potential benefit). No category 3 research is allowed.
- Please visit the EPA Home Page and search for human research protections at:
<http://www.epa.gov/>.

Appendix H: **Research versus Quality Improvement**

Distinctions Between Research and Quality Improvement or Quality Assurance

| | Research | Quality Improvement or Quality Assurance |
|----------------------------------|--|--|
| Purpose | Test a formal hypothesis or research question and advance science/discipline | Assess a process, program, or system |
| Starting Point | A prospectively designed, formal, written research hypothesis | An established set of standards |
| Benefits | Knowledge sought may not benefit participants involved in study | Knowledge sought directly benefits process/ program/system/and may benefit patients |
| Risks/Benefits | May put participants at risk | No risk, with exception of possibly privacy/confidentiality concerns |
| Data Collection | Systematic data collection | Systematic data collection |
| End Point | Answer research question | Improve program/ process/ system |
| Testing/Analysis | Involves an in-depth review of relevant literature. Determine validity of hypothesis. | Compare the program/process/system to established set of standards. |
| Intended Result | Share findings with individuals associated with investigation and individuals not associated with investigation. | Share findings with only those individuals associated with the process/ program/system. If findings are shared with individuals unassociated with the process/program/system, then activities are considered research. |
| IRB Review & Approval | Required | Not Required |

**Modified from guidance used by George Washington University Committee on Human Research IRB & Cambridge Health Alliance. Permission granted for use on 3/2/2011 by George Washington University.*

Appendix I:

What to Include in a Research Protocol that is Submitted to the IRB

1. Background and rationale, including a literature review that justifies the study.
2. The primary objective of the study.
3. Secondary objective of the study, if any.
4. Inclusion and exclusion criteria.
5. Methodology, including:
 - a. Conduct of the trial
 - b. Data collection
 - c. Plan for data analysis, including:
 - i. Number of subjects based on a statistical rationale for the effect size (e.g., power calculation)
 - ii. Intended statistical plan based on the primary and secondary objectives of the study
 - iii. Data and Safety Monitoring Plan
 - iv. Appropriate literature citations supporting the methodology
6. Literature cited (Reference List).
7. Appropriate appendices, including IDE, IND, etc.

Appendix J:

Contact Information and Resources

Contact Information

The IRB Administration Office main line.....577-1628Fax 993-7122
Associate Director, IRB Administration993-7155
Education Coordinator577-9534
Program Project Assistant.....577-1628
Director, Responsible Conduct of Research577-0646
Associate Vice President for Research577-9064

Resources

WSU IRB Website

www.irb.wayne.edu. This website contains all policies and procedures, reviewer forms, submission forms, consent/assent forms, and other information. Soon there will be a sign-up for a listserv on the website and other new resources.

Federal Regulations and Guidance

OHRP

- [Office for Human Research Protections](http://www.hhs.gov/ohrp/)
<http://www.hhs.gov/ohrp/>
- [Human Participants Regulations Decision Charts](http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html)
<http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html>
- [Institutional Review Board Guidebook](http://www.hhs.gov/ohrp/archive/irb/irb_guidebook.htm)
http://www.hhs.gov/ohrp/archive/irb/irb_guidebook.htm
- [Protection of Human Participants: 45 CFR 46](http://www.hhs.gov/ohrp/humanparticipants/guidance/45cfr46.html)
<http://www.hhs.gov/ohrp/humanparticipants/guidance/45cfr46.html>

FDA

- [Food and Drug Administration](http://www.fda.gov/)
<http://www.fda.gov/>
- [Human Participant Protection \(Informed Consent\): 21 CFR Part 50](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRsearch.cfm)
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRsearch.cfm>
- [IRB Regulations: 21 CFR 56](#)

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm>

- [Information Sheets: Guidance for IRBs, Clinical Investigators, and Sponsors](http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/ucm113709.htm)
<http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/ucm113709.htm>
- [Investigational New Drug Application: 21 CFR Part 312](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRsearch.cfm)
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRsearch.cfm>
- [Investigational Device Exemptions: 21 CFR Part 812](http://www.access.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRsearch.cfm)
<http://www.access.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRsearch.cfm>

Ethical Principles & Codes

- [American Society for Bioethics & Humanities \(ASBH\)](http://www.asbh.org/)
<http://www.asbh.org/>
- [Belmont Report](http://www.ohsr.od.nih.gov/guidelines/belmont.html)
<http://www.ohsr.od.nih.gov/guidelines/belmont.html>
- [Declaration of Helsinki \(World Medical Association\)](http://www.wma.net/en/30Publications/10policies/b3/index.html)
<http://www.wma.net/en/30Publications/10policies/b3/index.html>
- [NIH Bioethics Resources on the Web](http://www.nih.gov/sigs.bioethics/)
<http://www.nih.gov/sigs.bioethics/>
- [Nuremberg Code](http://ohsr.od.nih.gov/guidelines/nuremberg.html)
<http://ohsr.od.nih.gov/guidelines/nuremberg.html>
- [National Bioethics Advisory Commission \(NBAC\)](http://bioethics.georgetown.edu/nbac/)
<http://bioethics.georgetown.edu/nbac/>
- [Public Responsibility in Medicine and Research \(PRIM&R\)](http://www.primr.org)
<http://www.primr.org>
- [The President's Council on Bioethics](http://bioethics.gov/)
<http://bioethics.gov/>

Good Clinical Practices

- [Good Clinical Practice in FDA-Regulated Clinical Trials](http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm)
<http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm>
- [Good Clinical Practice Contacts](http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm134476.htm)
<http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm134476.htm>
- [ICH E6: Good Clinical Practice: Consolidated Guidance](http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073122.pdf)
<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073122.pdf>
- [Medical Devices \(Device Advice\)](http://www.fda.gov/cdrh/devadvice/)
<http://www.fda.gov/cdrh/devadvice/>

HIPAA

- [IRBs and the HIPAA Privacy Rule \(NIH\)](http://privacyruleandresearch.nih.gov/irbandprivacyrule.asp)
<http://privacyruleandresearch.nih.gov/irbandprivacyrule.asp>

- [NIH Guidance on Protecting Personal Health Information in Research](http://privacyruleandresearch.nih.gov/pr_02.asp) (NIH)
- [NIH Guidance on Research Repositories, Databases, and the Privacy Rule](http://privacyruleandresearch.nih.gov/research_repositories.asp) (NIH)
- [NIH Guidance on Clinical Research and the HIPAA Privacy Rule](http://privacyruleandresearch.nih.gov/clin_research.asp)

Veteran Affairs Administration

- <http://www.va.gov/ORPM/index.asp>

Department of Defense

- <http://www.dtic.mil/whs/directives/corres/pdf/321602p.pdf>

Department of Energy

- <http://www.energy.gov/>

Department of Education

- <http://www.ed.gov/>

Department of Justice

- <http://www.justice.gov/>

Environmental Protection Agency

- <http://www.epa.gov/>

Radiation

- <http://www.safety.duke.edu/RadSafety/consents/default.asp>

Appendix K: **Website Resources**

Resources

WSU IRB Website

www.irb.wayne.edu. This website contains all policies and procedures, reviewer forms, submission forms, consent/assent forms, and other information.

Join the IRB Info Listserv:

Please join the WSU IRB Info listserv that has been created for all researchers and research staff who are using the WSU IRB. This listserv provides a means for us to occasionally share information, make announcements, advertise the training calendar, share answers to questions, etc. with the research community.

It is easy to join:

- To subscribe send a blank e-mail to irb-info-subscribe-request@lists.wayne.edu
- To unsubscribe at any time, send an e-mail to irb-info-signoff-request@lists.wayne.edu
- To send a message to all of the people currently subscribed to the list, just send an e-mail to irb-info@lists.wayne.edu

Meeting Schedules and Deadlines

Meeting schedules and deadlines can be found: <http://irb.wayne.edu/meetings-deadlines.php>. For membership rosters call the IRB Administration Office at (313) 577-1628.

Institutional Review Board Forms

Access the IRB forms page at <http://irb.wayne.edu/forms-requirements-categories.php>).

Collaborative Institutional Training Initiative (CITI)

Collaborative Institutional Training Initiative at <https://www.citiprogram.org/Default.asp>.