MCW Office of Research
Standard Operating Procedure

USE AND STORAGE OF INVESTIGATIONAL DRUGS AND BIOLOGICS

Unit: Human Research Protections Program (HRPP), Office of Research

Applies to: MCW/FH Faculty and Staff involved in human research

PURPOSE:
It is the policy of the Medical College of Wisconsin (MCW) HRPP office and Institutional Review Board (IRB) that the use and storage of investigational drugs, agents, and/or biologics be reviewed and approved in accordance with the Federal regulations.

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

Investigational Drugs/Investigational Biologics (Test Articles): A new drug or biologic that is used in a clinical investigation. The term investigational biologic also includes a biological product that is used *in vitro* for diagnostic purposes. Investigational drugs or biologics may include:

- Products that are not generally recognized as being safe and effective for any use under the conditions prescribed, recommended, or suggested by the Food and Drug Administration (FDA); or
- Products already approved by the FDA as safe and effective for specific indications that are being studied for new indications (or doses, strengths, or frequency).

Investigational New Drug (IND): Food and Drug Administration (FDA) granting of permission that a new drug, agent, or biologic may be used in humans prior to FDA review of clinical data to determine that a particular product is safe and effective for a specific use. The FDA permission is evidenced by the assignment of an IND number by the FDA or the granting of an IND exemption.

FDA regulations allow certain individuals not enrolled in clinical trials to obtain expanded access to investigational drugs, agents, or biologics through the following methods:

Compassionate Use: Although the drug arm of the FDA does not officially use the term “compassionate use,” if is often used to refer to the provision of investigational drugs outside of an ongoing clinical trial to a limited number of patients who are desperately ill and for whom no standard alternative therapies are available. Rather than use this term, it is preferable to instead use the names of the specific access programs when discussing the use of investigational articles outside of formal clinical trials.

Group C Treatment Investigational New Drug (IND): A means for the distribution of investigational drugs, agents, or biologics to oncologists for the

treatment of cancer under protocols outside controlled clinical trials. Group C drugs, agents, or biologics usually have shown evidence of relative and reproducible efficacy in a specific tumor type. Although the FDA typically grants a waiver for most drugs used in Group C Treatment IND protocols. IRB review and approval is required

Open – Label Protocol: A project designed to obtain additional safety data, typically done when the controlled trial has ended and treatment continues. The purpose of such a project is to allow subjects to continue to receive the benefits of the investigational drug, agent, or biologic until marketing approval is obtained.

Parallel Track: A method approved by the FDA that expands the availability of investigational drugs, agents, or biologics as quickly as possible to persons with AIDS and other HIV-related diseases. These drugs, agents or biologics are utilized in separate protocols that "parallel" the controlled clinical trials and are essential to establish the safety and effectiveness of these new drugs, agents, or biologics. Although the Secretary of the Department of Health and Human Services may, on a protocol-by-protocol basis, waive the provisions of 45 CFR Part 46 where adequate protections are provided through other mechanisms, IRB review and approval is required.

Treatment IND or Biologics: A mechanism for providing eligible subjects with investigational drugs (as early in the drug development process as possible) for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. The FDA defines an immediately life-threatening disease as a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment. The FDA will permit an investigational drug to be used under a treatment IND after sufficient data have been collected to show that the drug "may be effective" and does not have unreasonable risks. Refer to *IRB SOP: Expanded Access Use of An Investigational Drug, Device or Biologic* for more information.

Single-Patient Use: The use of an investigational drug outside of a controlled clinical trial for one patient, usually in a desperate situation, who is unresponsive to other therapies or in a situation where no approved or generally recognized treatment is available. There is usually little evidence that the proposed therapy is useful, but may be plausible on theoretical grounds or anecdotes of success. Access to investigational drugs for use by a single, identified patient may be gained either through the sponsor under a treatment protocol, or through the FDA, by first obtaining the drug from the sponsor and then submitting a treatment IND to the FDA requesting authorization to use the investigational drug for treatment use. Refer to *IRB SOP: Expanded Access Use of An Investigational Drug, Device or Biologic* for more information**.**

Emergency IND: The emergency use of an unapproved investigational drug, agent, or biologic requires an emergency IND. The FDA has established mechanisms and guidance for obtaining an Emergency IND for the use of investigational drugs, agents, or biologics. Additional MCW/FH IRB guidance regarding emergency IND is provided in the *IRB SOP: Emergency Use of Investigational Drugs, Devices or Biologics.*

PROCEDURE:

1. When an Investigator wishes to conduct a project which may utilize an Investigational Drug (IND) or Investigational Biologic; the Investigator must complete and submit an initial eBridge submission for IRB review. Refer to *IRB SOP: Submitting New Projects* for further information. The MCW IRB is responsible to conduct initial reviews, grant approvals and maintain ongoing monitoring of all investigational drugs, and biologics used in human subjects under its jurisdiction.
2. The Investigator must include the following information in the eBridge submission:
    a. IND number or its approval status and;
    b. IND acknowledgement letter from the FDA. Please note this is not required for NCI-Cooperative Group sponsored projects.
    c. Plan for maintaining records that document adequately that the participants are provided doses specified by the protocol and reconcile all investigational products received from the sponsor.
3. IRB staff will confirm that there is an IND and the IND number is valid. Final IRB approval will not be granted until this has been confirmed.
4. For projects which involve Investigational Drugs or Biologics, the Investigator should make sure all advertising or recruitment documents follow federal guidelines and are in accordance with *IRB SOP: Advertisements*
5. Investigators should ensure the Informed Consent document includes the following items in accordance with federal regulations, be in accordance with *IRB SOP: Informed Consent for Human Subject Research* and to use the appropriate MCW Consent Form templates.
    a. No claims are to made which state or imply, directly or indirectly, that the investigational drug, agent, or biologic is safe or effective for the purposes under investigation or that the drug is in any way superior to another drug;
    b. The informed consent document must contain a statement that the drug, agent, or biologic is “experimental”, meaning non-FDA approved;
    c. The informed consent document must contain a statement that the FDA may have access to the subject's medical records as they pertain to the project; and
6. Investigators must notify and work with Froedtert Investigational Drug Services (IDS) Pharmacy regarding the intended handling and use of an IND or Investigational Biologic for a project. Investigators should refer to *FH Corporate: Clinical Research & Investigational Drugs (CPM.0152)*
    a. Where allowed or required, the investigator may assign some or all duties for investigational articles accountability at the trial site to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator.
    b. The investigator, pharmacist, or other designated individual will maintain records of the product’s delivery to the trial site, the inventory at the site, the use by each participant, and the return to the sponsor or alternative disposition of unused products. These records will include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational products and trial participants as described in the *FH Corporate: Clinical Research & Investigational Drugs (CPM.0152)*

7. Prospective IRB review and approval is required even if a waiver from IRB regulations has been granted by the FDA for use of the investigational drug, or biologic, unless the use meets the criteria of emergency use as described in federal regulations and *IRB SOP: Emergency Use of Investigational Drugs, Devices or Biologics.*

8. Investigators must dispense and store Investigational Drugs or Biologics in accordance with *FH Corporate: Clinical Research & Investigational Drugs (CPM.0152).* Failure to dispense or store investigational drugs, biologics in this manner will be reported to FH IDS pharmacy along with the MCW/FH IRB as noncompliance.

Determining if an IND is required

1. All drugs, biologics and/or agents as defined above are regulated by the FDA. Investigators should determine if a drug, biologic or agent to be used in a project requires an IND. INDs must be filed by Sponsor of a project, or the Sponsor must be able to demonstrate the use of the drug, biologic or agent is exempt from IND requirements. The IRB will make a formal determination regarding the exemption from IND requirements.
2. Investigators may encounter projects with the use of a drug, or biologic that is lawfully marketed in the United States. In some cases, the drug or biologic may be exempt from the requirements of an IND, *if all of the following conditions are met* as outlined in the federal regulations:
    a. Use of the investigational drug, or biologic is not intended to be reported to the FDA in support of a new indication for use nor support any significant change in labeling for the product;
    b. The use of the investigational drug, or biologic is not intended to support a significant change in the advertising of the product;
    c. The use of the product does not involve a route of administration, dosage level, and/or use in a subpopulation, or other factors that significantly increase the risks, or decrease the acceptability of the risks associated with the use of the drug, agent, or biologic;
    d. The use will be conducted in compliance with the IRB approval and informed consent procedures;
    e. The use will be conducted in compliance with the requirements concerning the promotion and sale of the drug, agent, or biologic as described in FDA regulations 21 CFR 312.7; and
    f. The use does not intend to invoke exception from informed consent requirements for emergency use.
3. For Investigators who investigate the use, efficacy, or safety of an in-vitro diagnostic biological product, the following may apply:
    a. A clinical investigation involving an in vitro diagnostic biological product (as listed below) is exempt if the diagnostic test was intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established diagnostic product or procedure and the diagnostic test was shipped in compliance with 21 CFR 312.60.
    b. Clinical investigations of an in vitro diagnostic biologic product that involves one or more of the following are exempt from the requirements of an IND: blood grouping serum; reagent red blood cells; anti-human globulin.
4. For some projects or clinical investigation involving the use of placebo may be considered exempt if it does not otherwise require IND submission.
5. If the project involves combinations of FDA approved drugs, agents, or biologics that are currently approved as single use, the combination may not require an IND. However, use of these drugs, agents, or biologics in research must still be prospectively reviewed and approved by the IRB.

Investigator-Sponsor responsibilities

1. When an Investigator serves as the sponsor for a project, the investigator- sponsor assures that research will not begin until a valid IND is in effect. This includes

recruiting, obtaining consent, and screening subjects for a specific project subject to the IND.
2. The investigator-sponsor assures that manufacturing, handling, and storage is conducted in accordance with applicable good manufacturing practice.
3. The IND goes into effect 30 days after the FDA receives the IND, unless the investigator-sponsor receives earlier notice from the FDA.

REFERENCES:
45 CFR 46
21 CFR 312.60
21 CFR 312.7

SUPPORTING DOCUMENTS:
IRB SOP: Expanded Access Use of An Investigational Drug, Device or Biologic
IRB SOP: Emergency Use of Investigational Drugs, Devices or Biologics
IRB SOP: Submitting New Projects
IRB SOP: Advertisements
IRB SOP: Informed Consent for Human Subject Research
FH Corporate: Clinical Research & Investigational Drugs (CPM.0152)

Effective Date:	06/15/2018
Version number:	5.0
Previous Version/date:	4.0, 10/21/2013
Responsible Office:	HRPP Office
Approval Date:	06/07/2018

Approved By
HRPP Authorized Official: David Clark, PhD, Director, HRPP
Human Research Protections Program (HRPP)
Office of Research
Medical College of Wisconsin