

SUMMARY OF CHANGES TO THE STANDARD OPERATING PROCEDURES – UNIVERSITY OF MICHIGAN MEDICAL SCHOOL INSTITUTIONAL REVIEW BOARD (IRBMED)

I. INTRODUCTION

The current IRBMED Standard Operating Procedures of February 2010 are organized into 12 sections and their respective subsections. A definitions appendix is also included at the end of the document.

II. FEBRUARY 2010 SOP PARTS

- Part 1 – Introduction, Purpose, and Ethical Principals
- Part 2 – Organization of the IRBMED
- Part 3 – HRPP Policy
- Part 4 – Activities Subject to the HRPP
- Part 5 – IRB Jurisdiction and Cooperative Research
- Part 6 – Roles and Responsibilities of Investigators and Research Staff
- Part 7 – Participant Protection
- Part 8 – Use of Test Articles and Humanitarian Use Devices
- Part 9 – Conflicts of Interest and Commitment
- Part 10 – Sponsored Projects
- Part 11 – Standards, Compliance, and Education
- Part 12 – Quality Assurance and Research Compliance

III. INSERTIONS

For ALL parts of the IRBMED SOPs:

Change from “federally-funded” to “federally-supported”.

Part 1 – Introduction, Purpose, and Ethical Principals

1. Part 1.III – pg. 4, page 2/4 - *deletion* of text:

“Absent an interpretation from federal funding agency to the contrary, **however** the requirements of all subparts of 45 CFR 46 are applied to University research, regardless of funding” to

2. Part 1.III.F – page 3/4 - *insertion* of section and text:

“F. Principles stated in Guideline for Good Clinical Practice (GCP) of the International Conference of Harmonization (ICH).

Refer to IRBMED SOP Part 6 – Roles and Responsibilities of Investigators and Research Staff

Refer to OM Part 6 – Roles and Responsibilities of Investigators and Research Staff

3. Part 1.III.G – page 3/4 - *insertion* of section and text:

“G. Additional Governing Laws, Regulations and Other Standards”

Refer to OM Part 2, II, A-C

Part 2 – Organization of the IRBMED

1. Part 2.II.G – page 2/2 - *insertion* of text:

“Michigan Alzheimer’s Disease Research Center (MADRC)”

Part 3 – HRPP Policy

1. Part 3.III.B.1(a) – page 3/42 – *deletion* of text:

“The Medical School Associate Dean for Regulatory Affairs then makes a recommendation to the UMHS Compliance Committee, which may adopt or reject the recommendation and in turn communicates its position to the Medical School Associate Deans for Research and Regulatory Affairs”.

“The Medical School Associate Deans for Research and Regulatory Affairs is responsible for the appointment and reappointment of Chairs”.

2. Part 3.III.B.1(b) – page 3/42 - *insertion* of text:

“Each Board member will be assigned proposals to review that fall into the appropriate scientific and/or regulatory experience. The IRBMED Regulatory team [Senior Associate Regulatory Analysts (SARAs), Junior Associate Regulatory Analysts (JARAs) and Assistant Regulatory Analysts (ARAs)] will assure that the appropriate Board members receive the proposal.”

3. Part 3.III.B.f. – page 5/42 - *insertion* of text:

“Annually, the Medical School Associate Dean for Regulatory Affairs will evaluate the Co-Chairs of the Board to ensure that their expertise adequately addresses the types of protocols reviewed and to ensure that each Chair is an active participant who is trained in current interpretations of federal regulations and other relevant ethical principles for the protection of human subjects. Vice-chairs will be similarly evaluated on an annual basis by the Co-Chairs. Feedback on the performance evaluation will be provided to the Co- or Vice-Chair.

4. Part 3.III.B.f. – page 5/42 - *revision* of text:

“If necessary, the Medical School Associate Dean for Regulatory Affairs or Co-Chairs may recommend to the Dean of the Medical School and the OVPR that board members, because of repeated non-attendance or lack of participation in continuing education, be relieved of their service on the IRBMED to “If necessary, the Medical School Associate Dean for Regulatory Affairs may relieve a Chair or Vice-Chair from IRBMED service due to repeated non-attendance, lack of participation in continuing education, or other problematic performance issues. Should this action be required, the Medical School Associate Dean for Regulatory Affairs will notify the Medical School Dean and OVPR.

5. Part 3.III.B.f. – page 6/42 - *revision* of text:

“If necessary, the Chairs may recommend to Medical School Associate Dean for Regulatory Affairs that board members be relieved of their service on the IRBMED, for example, due to repeated non-attendance. Should dismissal of a board member be required, this action will be taken by the Medical School Associate Dean for Regulatory Affairs, with notification to the Dean of the Medical School and the OVPR to “If necessary, the Chairs may recommend to the Medical School Associate Dean for Regulatory Affairs that a board member be relieved from IRBMED service due to repeated non-attendance, lack of participation in continuing education, or other problematic performance issues.

Should this action be required, the Medical School Associate Dean for Regulatory Affairs will notify the Medical School Dean and the OVPR.

6. Part 3.III.B.h. – page 6/42 - *insertion of text:*

“To ensure that the IRBMED is sufficiently diverse in experience, expertise, education, ethnicity, gender, cultural background, and sensitivity to issues as community attitudes, the Associate Dean for Regulatory Affairs and IRBMED Chairs will periodically review the membership composition.

7. Part 3.III.B.3 – page 6-7/42 – *insertion of text:*

Single IRB member reviews (expedited, Single IRB Member for AEs or ORIOs or for projects where the IRB-of-record is the NCI-CIRB or through an institutional agreement as approved by OVPR) are performed by a chair or experienced IRBMED member. Single IRB member reviewers are selected based on their knowledge of human subject regulations, and concern for human rights and ethical issues. Equivalent experience may include service on other research oversight or scientific review committees or participation in other activities that reflect consideration of issues involving human subject participation in research. Authorization to perform a qualified Single IRB Member review is based on an assessment and approval by the Chairs. In general, to become a Single IRB Member reviewer for the C1 Board, an experienced full or alternate member needs to be on the board for at least six (6) months, or fewer if designated by the Chairs as competent to conduct Single IRB Member reviews. To become a Single IRB Member reviewer for the A1, A2, B1, or B2 Boards, an experienced full or alternate member needs to be on the board for at least one (1) year, unless review competency is designated earlier by the Chairs.

IRBMED staff members who are sufficiently qualified through experience and expertise and are familiar with regulations relevant to the use of human subjects in research may be appointed to the board as alternates and review and may approve selected Single IRB member amendment changes approved by the IRBMED Chairs and Associate Dean for Regulatory Affairs.

8. Part 3.III.B.3 – page 7/42 – *insertion of text:*

The IRBMED Office includes a Regulatory Team for each of the five (5) boards. Each Regulatory Team is composed of a Senior Associate Regulatory Analyst (SARA), a Junior Associate Regulatory Analyst (JARA) and an Assistant Regulatory Analyst (ARA). Each team member has been appointed based on education and/or appropriate experience. All IRBMED staff ultimately report to the Director. The structure may change by adding additional personnel as needed.

9. Part 3.III.C.2 – page 9/42 – *insertion of text:*

In accordance with University policy, the IRBs will review payment arrangements offered to subjects. Their review will ensure the following:

The amount of payment, the proposed information collected, and the method and timing of disbursement neither is coercive nor presents undue influence or places the subject at risk.

Where appropriate, credit for payment accrues as the study progresses and may not be contingent upon the subject completing the entire study.

Any amount paid as a bonus for completion is reasonable and not so large as to unduly induce subjects to stay in the study when they would otherwise have withdrawn.

All information concerning payment, including the amount and schedule of payments, is set forth in the consent document.

10. Part 3.III.C.2.b.(1) – page 11/42 – *insertion* of text:

a. Sound Research Design / Scientific Review

i. All eResearch and Legacy (paper) applications are reviewed by experienced IRBMED Board Member(s) or qualified IRBMED Regulatory staff to determine that the criteria in 45 CFR 46.111 are met and that the study design is adequate to protect the subjects from increased risk and yield expected knowledge. This includes:

1. 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.

2. Selection of subjects is equitable.

3. When appropriate, the research plan has an adequate data and safety monitoring plan.

4. There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

5. When appropriate, additional safeguard have been included in the study to protect the rights and welfare of vulnerable subjects.

ii. Studies that have received peer or scientific review indicate in the eResearch or Legacy (paper) application the name of the unit or person(s) who performed the review. For student applications, it is expected that the faculty advisor has reviewed the study for scientific merit before it is submitted to IRBMED. Studies that receive federal support (and thus a scientific review) must upload the grant application into the eResearch system. For studies being conducted in the Comprehensive Cancer Center, all studies are reviewed by the Protocol Review Committee (as a Core Committee of eResearch).

11. Part 3.III.C.2.b.(1) – page 12/42 – *insertion* of reference:

See also IRBMED SOPs Part 11, III.A.2.a.i.

12. Part 3.III.C.2.b.2.c) – page 15/42 – *insertion* of text:

In general, the approval period begins on the date the submission is approved by the IRBMED and expires 364 days later, which is the last date of the approval period. For example, a proposal will have an approval date of 9/30/09 and an expiration date of 9/29/10.

13. Part 3.III.C.2.h.(3) – page 18/42 – *insertion* of reference and text:

(3) "Single IRB Member" Review of Adverse Events or Other Reportable Information or Occurrences, as long as those Reports do not Constitute a Potential or Identified Unanticipated Problem Involving Subjects or Others

Refer to HRPP OM Part 3, III.C.2.a.

Refer to HRPP OM Part 12, III.B.2.a.

Prior to an expedited, Single IRB Member review of an AE or ORIO, or for a NCI-CIRB submission review, the IRBMED staff will assess the application to determine whether the Single IRB Member reviewer has a COI. IRBMED staff will not assign an application to a conflicted Single IRB Member reviewer. If a previously unreported conflict is identified in the course of reviewing an application, a different reviewer will be assigned to the application.

14. Part 3.III.C.3 – page 18-19/42 – *insertion* of text:

The IRB also may use expedited procedures to review minor changes in previously approved research during a period for which approval is authorized. For purposes of this policy, a proposed change in research is deemed "minor" if it does not significantly affect an assessment of the risks and benefits of the study and does not substantially change the aims or design of the study. Examples of minor changes to a research study include, but are not limited to: Addition or deletion of study team members other than the Principal Investigator, Co-Investigator or Sub-Investigator.

15. Part 3.III.C.3 – page 19/42 – *insertion* of text:

In conducting expedited review, the IRBMED reviewers may exercise all of the authorities of the IRBMED, except that they may not disapprove the research, in accordance with the non-expedited review procedure set forth in 45 CFR 46.108(b) and 21 CFR 56.108(c)(i). The reviewer may either approve, require modifications (to secure approval), or refer the research to the convened IRBMED for review (for example, if they determine the study has a change in risk level due to a change in the protocol).

16. Part 3.III.C.4.e) – page 22/42 – *revision* of text:

The consent process is facilitated by a person knowledgeable about the study, its enrollment criteria, and its risks and benefits, and alternatives to participating in research (usually a Principal Investigator or Co-Investigator/Sub-Investigator, though other study team members, for example, a research study coordinator or research nurse, may also be qualified and if designated by the Principal Investigator).

17. Part III.C.4.e(5)(a)(vi) – page 25/42 – *deletion* of text:

The IRBMED reviews and approves procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with paragraph (a)(7)(v) of this section.

18. Part III.C.4.e(5)(a) – page 26/42 – *deletion* and *insertion* of text:

The IRBMED determinations required by paragraph (a) and the documentation required by paragraph (e) of this section are required to be retained by the IRBMED for at least three (3) years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by the Food and Drug Administration (FDA).

If the IRBMED determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in paragraph (a) or because of other relevant ethical concerns, the IRBMED must document its findings and provide these findings promptly in writing to the clinical PI and to the sponsor of the clinical investigation.

19. Part III.C.4.e(6)(b) – page 27/42 – *insertion* of reference and text:

See IRBMED Guidance [Emergency Use of a Test Article in Life-Threatening Circumstances](#) for additional details.

- What is the Procedure for Reporting an Emergency Use to the IRBMED?
 - Call and email the IRBMED office as soon as the decision to use an unapproved test article is made, prior to the treatment or procedure if at all possible. After hours and on weekends/holidays, in addition to emailing the office, ask the UMHS operator (734) 936-6267 to page the IRBMED Chair on call.
 - File a formal report of the emergency use in eResearch **within 5 days** of the use. Indicate in **section 1.12** whether the report is for an investigational drug/biologic or for an investigational device.
 - The Regulatory team (SARA, JARA and ARA) in conjunction with the IRBMED Board Chairs, Board Members, and Director (if required) will review the applications.
- When Must FDA Be Notified?
 - Even in an emergency where it is impossible to secure an IND or IDE in advance, the sponsor or the researcher must consult with the FDA prior to use. Contact information (24/7) for drugs/biologics and for devices is available on FDA's website. *Note: if sponsor approval is secured, the researcher is encouraged to request written assurance from the sponsor that FDA approval also has been secured.*

20. Part III.C.5 – page 30/42 – *insertion* and *deletion* of text:

The IRBMED may, at its discretion, perform monitoring or request monitoring from the OHRCR - via the OVPR - of a project in addition to ~~that accomplished~~ information received through the initial, application, any amendments, and annual continuing reviews, and analyses of interim reports, such as adverse events and audit reports.

21. Part III.C.7.d) – page 33/42 – *insertion* of text:

The Thursday board meetings are scheduled for 3-5 hours which allows adequate time for assigned applications. The Friday (C1) board meets weekly for 2-3 hours which allows adequate time for assigned applications. The Regulatory team (SARA, JARA and ARA), in consultation with Chairs and Director as needed, will determine which submissions will be reviewed at the convened board meeting.

22. Part III.C.7.e) – page 33/42 – *insertion* of new section:

(e) Board Member Reviews

The Regulatory team (SARA, JARA and ARA) will assure that Board members have adequate time to review all aspects of the applications. If a Board member feels they have been given inadequate time to review a specific application then that proposal will be

rescheduled to the next available meeting.

23. Part III.C.7.f) – page 33/42 – *change* in order of former section number:

(e) Alternate Board Meeting Format *now* **(f) Alternate Board Meeting Format**

24. Part III.C.8 – page 34-35/42 – *deletion* of text:

Documentation of all IRBMED determinations shall be available for review by the Medical School Associate Deans for **Research and** Regulatory Affairs, OVPR, IRBMED members, and authorized consultants.

25. Part III.E – page 36/42 – *insertion* of text:

E. IRBMED Members, Consultants, Staff, **Guests, Convened Board and Institutional Conflicts of Interest**

26. Part III.E.1 – page 37/42 – *deletion and insertion* of text:

The member has other conflicts that he/she, the Review Board, the **Medical School Associate Deans of Research and for Regulatory Affairs**, the Medical School COI Committee, or OVPR believe might hamper the member's ability to perform an impartial review of the application.

In some instances, an IRBMED member may have involvement in a research study that solely involves the provision of a service to a study (e.g., a Pharmacist from Investigational Drug Service who prepares and dispenses study medication, or a Radiologist who performs a diagnostic imaging study that is part of the research). The IRBMED does not consider this to be a conflict of interest with regard to reviewing an IRBMED submission, provided the member's role in the study is limited to providing a service to the PI and they are not otherwise engaged in the research study. For example, a board member is not permitted to be listed on the FDA Form-1572. If additional clarification is needed, contact IRBMED. This is consistent with the examples of non-engagement in research provided in OHRP's Guidance on Engagement of Institutions in Human Subject's Research, October 16, 2008, Section III.B.1.

27. Part III.I – page 41-42/42 – *insertion of text*:

As part of the Proposal Review Process, all proposals may be reviewed by IRBMED **Core or Ancillary Committees**. These could include: Michigan Clinical Research Unit (formerly General Clinical Research Center), Comprehensive Cancer Center - Protocol Review Committee, Institutional Biosafety Committee, etc. These reviews are communicated to the IRBMED Regulatory teams via eResearch.

28. Part III.I – page 41/41 – *insertion of new section and text*:

J. International Research

Generally, the IRBMED reviews all international human subject research projects conducted by UM investigators under its jurisdiction, rather than deferring review to a collaborating international institution. When an international site is engaged in the conduct of a UM research project and the research is supported by a Common Rule agency, the regulatory requirements of 45 CFR 46 are applied and local IRB or ethics committee review is required. Supporting agencies may require a FWA. For international research that is not federally supported, the IRB may apply the same or equivalent protections as those described in the Common Rule and UM institutional policy. IRBMED

may require local IRB review, particularly for studies involving more than minimal risk to participants. Where the international research site is not engaged in the conduct of the research, IRBMED may request a letter of collaboration from an appropriate official agreeing to the conduct of the research.

IRBMED will consider local research context when reviewing research conducted in international settings. Elements of consideration include laws and regulations, local customs and cultural norms, political and socio-economic conditions, and language and literacy issues. The eResearch application elicits information from the study team regarding their experience with and knowledge of the community and culture in which the research will take place. When IRBMED members do not possess the appropriate cultural knowledge to review research in a particular country or region, IRBMED will seek guidance from consultants with cultural expertise to assist with the review. IRBMED may also request that the investigator seek cultural review by an IRB or ethics committee review or from a government agency in the region. For exempt research, IRBMED does not require documentation of IRB review or other approvals from international sites.

Projects conducted in international settings are subject to the same IRB requirements for review and approval of initial applications, scheduled continuing review and review of modifications as projects conducted domestically. A key element of the review process is the assessment of the informed consent process and documents. IRBMED evaluates the consent process to ensure that it is culturally sensitive and in a local language that is understandable to the subject, and that the complexity of the information is appropriate for the research population. Consent documents and other study materials must be provided to IRBMED in the languages in which they will be offered, as well as in English.

Post approval monitoring, such as project reports to IRBMED by the PI, may be imposed when necessary. As with domestic projects, investigators are obligated to report subject complaints, unanticipated problems involving risk to subjects or others and other reports of potential non-compliance to IRBMED. Research subjects are provided with the IRBMED email address and international phone number as part of the consent process.

Part 4 – Activities Subject to the HRPP

1. Part 4.V.A – page 1-2/4 – *insertion* of text:

As part of the administrative review process the IRBMED Regulatory teams [Senior Associate Regulatory Analysts (SARAs), Junior Associate Regulatory Analysts (JARAs) and Assistant Regulatory Analysts (ARAs)], in consultation with IRBMED Chairs or Director, as necessary, assesses whether the project meets the definition of human subjects research.

The IRBMED Regulatory teams review all submitted eResearch and Legacy applications that meet the regulatory definition of research to assess whether the proposed study involves human subjects using [Decision Trees](#) posted on the HRPP Website, the [OHRP Decision Charts](#), guidance found in [HRPP OM Part 4 Table 3](#), as well as the eResearch or Legacy applications. The IRBMED Chairs or Director may be consulted as necessary to determine if the study involves human subjects.

Principal Investigators (PI) may consult informally with an IRBMED Regulatory team to determine if their research project involves human subjects. To obtain a formal, documented regulated/not OHRP or FDA-Supported determination, an eResearch “Projects Not Regulated as Human Subjects Research” application must be prepared.

This application allows the Principal Investigator to self-generate a determination letter that may be used for funding or publication purposes or to request an IRBMED review to confirm the project is not regulated.

Applications submitted in eResearch as “Projects Not Regulated as Human Subjects Research” may also be reviewed by the Privacy Board Coordinator. The Privacy Board Coordinator will then determine applicability. They may contact the IRBMED Privacy Board Members, IRBMED Chairs or Director for consultation.

Part 5 – IRB Jurisdiction and Cooperative Research

1. Part 5.C.A – page 2/3 – *deletion* and *insertion* of text:

The University maintains an Institutional Authorization Agreement (IAA) with the National Cancer Institute - Central Institutional Review Boards (NCI-CIRBs).

2. Part 5.C.B – page 3/3 – *insertion* of text:

Applications submitted to the IRBMED involving multi-site research projects are reviewed by the board. The IRBMED will consider:

- (1) Whether UM is the Lead or Operating Coordinating Center; or Data or Statistical Coordinating Center for purposes of determining oversight responsibilities. For example, assessing whether the participating site is providing appropriate subject safety management, maintaining the required regulatory documentation and reporting adverse events and unanticipated events as required.
- (2) Depending on the type of project whether the IRBMED has the capability to provide appropriate ethical and scientific review.
- (3) The level of risk for the project.
- (4) Whether there is an IAA or IIA among the participating sites, if the IRBMED is being asked to serve as the IRB-of-record for any of the participating sites.

Whether the IRBMED has ceded responsibility to an outside IRB with respect to determining appropriate research subject protections and adequacy of the facility/site to perform the procedures.

Part 6 – Roles and Responsibilities of Investigators and Research Staff

1. Part 6.II.A.7. – page 1-2/3 – *insertion* of new section and text:

7. Guidelines for Good Clinical Practice (GCP) of the International Conference of Harmonization (ICH)

From time to time, especially in multi-site clinical research where UM is a proposed performance site, a Sponsor may represent that the FDA-approved protocol and any Principal Investigator SOPs associated with that protocol, if followed, assure ICH-GCP compliance. In those instances, IRBMED will make the determinations required by institutional policy and will also review the research plan submitted to identify aspects that may be inconsistent with ICH-GCP. Such review will include evaluation of the adequacy of the available nonclinical and clinical information on an investigational product to support the proposed clinical research project, and a review that proposed clinical research is

scientifically sound and described in a clear, detailed protocol. IRBMED will bring any area of concern to the attention of the Principal Investigator, who may in turn ask for clarification from the Sponsor.

Principal Investigators who agree to perform research represented to be ICH-GCP compliant are required to follow the protocol as written and will be advised by IRBMED to review all Principal Investigator Obligations in the ICH-GCP as well as any aspects of ICH-GCP incompletely captured or not captured in the research protocol and investigator SOPs.

If a Principal Investigator in the research contract agrees to conduct an investigation in full compliance with the Principal Investigator Obligations under ICH-GCP, any compliance review conducted by OHRCR will be done against the complete set of ICH-GCP requirements.

The complete ICH-GCP Guidance can be found at:
<http://www.ich.org/LOB/media/MEDIA482.pdf>.

Part 7 – Participant Protection

1. Part 7.IV – page 1-10/11 – *deletion* and *insertion* of text:

[See attachment for prior Part 7 (IRBMED SOPs/Approved 2/1/10)]

Current Operations Manual text inserted in place of previous language for Section 7.IV. This was done to ensure consistency between the IRBMED SOPs and the Operations Manual.

2. Part V. – page 10/11 – *insertion* of reference:

V. Compensation for Injuries

Refer to HRPP OM Part 7, V., OHRP "Exculpatory Language" in Informed Consent and UM Clinical Research Calendar Review & Analysis Office (CR²AO)

3. Part 7.VI – page 11/11 – *insertion* of new section and reference:

VI. Advertising Materials

Refer to HRPP OM Part 7, VI.

Refer to <http://med.umich.edu/irbmed/guidance/advertising.htm>

Refer to http://med.umich.edu/irbmed/guidance/general_studies_ads.htm

The IRBMED reviews advertising materials intended to recruit prospective subjects. Recruitment materials are submitted as part of the eResearch application and are reviewed as part of the initial review or submitted as part of an amendment and must be approved prior to implementation. As part of its review, the IRBMED considers:

- The information contained in the advertisement
- The mode of its communication
- The final copy of printed advertisements
- The final audio or video taped advertisements.

In its review of advertising materials, the IRBMED considers that the materials:

- Do not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent and the protocol.
- Do not include exculpatory language.
- Do not emphasize the payment or the amount to be paid, by such means as larger or bold type.
- Do not promise “free treatment” when the intent is only to say subjects will not be charged for taking part in the investigation.

Advertisements should be limited to the information prospective subjects need to determine their eligibility and interest, such as:

- The name and address of the Investigator or research facility.
- The purpose of the research or the condition under study.
- In summary form, the criteria that will be used to determine eligibility for the study.
- A brief list of benefits to subjects, if any.
- The time or other commitment required of the subjects.
- The location of the research and the person or office to contact for further information.

When following FDA regulations the IRBMED considers the materials:

- Do not make claims, either explicitly or implicitly, about the drug, biologic, or device under investigation that are inconsistent with FDA labeling.
- Do not use terms, such as “new treatment,” “new medication,” or “new drug,” without explaining that the test article is investigational.
- Do not allow compensation for participation in a trial offered by a sponsor to include a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

Part 8 – Use of Test Articles and Humanitarian Use Devices

1. Part 8.II – page 1/4 - *insertion of text:*

As part of the eResearch or Legacy (paper) applications, the study team is required to upload all documentation submitted to and received from the FDA regarding IND/IDE information. This information is available to the IRBMED Regulatory team as well as IRBMED Chairs and Board Members via eResearch for review. The Regulatory team [Senior Associate Regulatory Analysts (SARA), Junior Associate Regulatory Analysts (JARA) and Assistant Regulatory Analysts (ARA)] will verify that this documentation is included in the eResearch or Legacy application and check the validity of the IND or IDE number.

Part 9 – Conflicts of Interest and Commitment

1. Part 9.III – page 1/2 – insertion of text

Additional language in the header – IRBMED Members, Consultants, Staff, **Guests, and Convened Board**

Part 10 – Sponsored Projects – NO CHANGE

Part 11 – Standards, Compliance, and Education

1. Part 11.A and B. – page 1/7 - *insertion* of text:

2. Genetic Information Nondiscrimination Act of 2008 (GINA)

GINA is a Federal law that prohibits discrimination in health coverage and employment based on genetic information. GINA, together with already existing nondiscrimination provisions of the Health Insurance Portability and Accountability Act (HIPAA), generally prohibits health insurers or health plan administrators from requesting or requiring genetic information of an individual or an individual's family members, or using such information for decisions regarding coverage, rates, or preexisting conditions. GINA also prohibits employers from using genetic information for hiring, firing, or promotion decisions, and for any decisions regarding terms of employment.

3. Genome-Wide Association Studies (GWAS)

GWAS is defined as any study of genetic variation across the entire human genome that is designed to identify genetic associations with observable traits (such as blood pressure or weight), or the presence or absence of a disease or condition. Whole genome information, when combined with clinical and other phenotype data, offers the potential for increased understanding of basic biological processes affecting human health, improvement in the prediction of disease and patient care, and ultimately the realization of the promise of personalized medicine. In addition, rapid advances in understanding the patterns of human genetic variation and maturing high-throughput, cost-effective methods for genotyping are providing powerful research tools for identifying genetic variants that contribute to health and disease.

Part 12 – Quality Assurance and Research Compliance

1. Part 12.III.B.2.a – page 7-8/9 - *insertion* of text:

IRBMED Board Members consider the following when reviewing an UaP/UPIRSO. Is the event:

- Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research);
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

The list of problems that require reporting in accordance with the above definition.

Include:

- Internal AEs that are unexpected, involve new or increased risks, and are related to the research.
- External AEs that are UaPs/UPIRSOs.
- Changes made to the research without prior IRB approval in order to eliminate apparent immediate harm.
- Other unanticipated information that is related to the research and indicates that subjects or others might be at increased risk of harm. For example:
 - 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 harms or benefits may be different than initially presented to IRBMED.
 - A paper is published from another study that shows that the risks or potential benefits of your research may be different than initially presented to IRBMED.
 - A breach of confidentiality.
 - 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 IRBMED review to eliminate an apparent immediate hazard to a research subject.
 - Incarceration of a subject in a protocol not approved to enroll prisoners.
 - Event that requires prompt reporting to the sponsor.
 - Sponsor imposed suspension for risk.
 - Complaint of a subject when the complaint indicates unexpected risks or cannot be resolved by the research team.
 - Protocol violation (meaning an accidental or unintentional change to the IRB approved protocol) that harmed subjects or others or that indicates subjects or others may be at increased risk of harm.

The review of problems reported by investigators. In this description, specify the following:

- The individual or individuals (by position or title) who are responsible for making an initial determination about whether a reported event is an UaP/UPIRSO.
- The information that reviewers receive to determine whether a reported event is an UaP/UPIRSO

2. Part 12.III.B.2.b – page 7-8/9 - *insertion* and *deletion* of text:

Unanticipated UaP/UPIRSO problems will be reported to OVPR in a timely manner, meaning no later than from the date of the IRBMED's determination as soon as possible, but not later than seven (7) days from IRBMED's Board determination.

All AEs and ORIOs review decisions for Legacy and eResearch projects are documented electronically.

Definitions Appendix

1. *Insertion of additional definitions applicable to the Human Research Protection Program (HRPP):*
 - a. *CareWeb*
 - b. *CDC*
 - c. *Co-Investigator*
 - d. *eRRM – eResearch Regulatory Management*
 - e. *eRPM – eResearch Proposal Management*
 - f. *eThORITY*
 - g. *GINA – Genetic Information Nondiscrimination Act*
 - h. *GWAS – Genome-Wide Association Studies*
 - i. *HITECH – Health Information Technology for Economic & Clinical Health*
 - j. *IAA – Institutional Authorization Agreement*
 - k. *ICD – Informed Consent Document*
 - l. *IIA – Individual Investigator Agreement*
 - m. *ITS – Information and Technology Services*
 - n. *MCIT – Medical Center Information Technology*
 - o. *MSIS – Medical School Information Services*
 - p. *NCRC – North Campus Research Complex*
 - q. *NIAAA – National Institute on Alcohol Abuse and Alcoholism*
 - r. *NIDA – National Institute on Drug Abuse*
 - s. *NIMH – National Institute on Drug Abuse*
 - t. *NSR – Non-significant Risk Device*
 - u. *Nonaffiliated Member*
 - v. *PHS – Public Health Service*
 - w. *SR – Significant Risk Device*
 - x. *STARS – Speak To A Regulatory Analyst*
 - y. *Sub-Investigator*
 - z. *UAP/UPIRSO – Unanticipated Problem Involving Risks to Subjects or Others*