1. POLICY

Federal regulations 45 CFR 46.108(a)(4) and 21 CFR 56.108(b)(2) require institutions to have written procedures for ensuring prompt reporting to the Institutional Review Board (IRB), appropriate institutional officials, and the department or agency head of serious or continuing noncompliance with the governing regulations or the requirements or determinations of the IRB.

When the Purdue HRPP is in pending or active accreditation status from the Association for the Accreditation of Human Research Protection Programs (AAHRPP), Purdue University must report to AAHRPP within 24 hours after the university or any researcher (if the researcher is notified rather than Purdue University) becomes aware of:

1.1 Any negative actions by a government oversight office, including, but not limited to, OHRP determination letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA restrictions placed on IRBs or ECs or researchers, and corresponding compliance actions taken under non-US authorities related to human research protections.

1.2 Any litigation, arbitration, or settlements initiated related to human research protections.

1.3 Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding Purdue University's HRPP.

These policies and procedures apply to all reviewed research activities that fall under the jurisdiction of the Purdue University Human Research Protection Program (HRPP).

2. DEFINITIONS

2.1 *Allegation* - An unconfirmed report.

2.2 *Complaint* - A report made by a party who either experienced or witnessed an event of potential noncompliance.

2.3 *Continuing Noncompliance* - Repeated noncompliance that, in the opinion of the IRB Chair or designee, suggests the likelihood that noncompliance will continue without intervention.

2.4 *Noncompliance* - Failure to comply with any of the federal or state regulations or institutional policies governing Human Subjects Research or the requirements or determinations of the IRB.

2.5 *Report* - Notification to the IRB that an incident of potential noncompliance has occurred.

2.6 *Serious Noncompliance* - Failure to comply with any of the federal or state regulations or institutional policies governing Human Subjects Research that increases risks, or decreases benefits to subjects, and/or significantly affects the subject's rights, safety or welfare and/or integrity of the data. An example of serious noncompliance includes conducting Human Subjects Research without appropriate IRB approval.

3. PROCEDURES

Investigating complaints, allegations and self-reported noncompliance is integral to the IRB's ability to protect the safety, rights and welfare of human subjects. The IRB is authorized to receive, investigate and make determinations about allegations and/or incidents of noncompliance associated with all Human Subjects Research, including both IRB-reviewed protocols and covered activities which should have been submitted to the IRB for review. The IRB is authorized to take action to protect human subjects and promote compliance with the University's Federalwide Assurance and HRPP policies.

3.1 Handling Reports of Noncompliance

3.1.1 Reports, complaints or allegations of noncompliance should be made to the HRPP. Any event meeting the definition of noncompliance should be reported to the HRPP within 48 hours after the Investigator first learns of the event. Initial reports can be made either orally or in writing; however, a written follow up may be requested by the HRPP. Specifically, reports should be sent to irb@purdue.edu or delivered in person to the office.

3.1.2 When HRPP Staff receive reports, complaints, or allegations of noncompliance, they must immediately report it to the IRB Administrator, IRB Chair, or IRB Associate Chair (or designees).

3.1.3 The IRB Administrator, IRB Chair, or IRB Associate Chair will compile the information regarding the allegation, complaint or report and will work with the IRB Chair to submit the information to the IRB for further review and processing as needed.

3.2 Initial Inquiry

3.2.1 The IRB Chair and/or IRB Associate Chair will serve as the primary designee for inquiry unless another IRB Member is specifically named by the IRB Chair or Institutional Official or a conflict of interest prevents this duty. The IRB Chair, Associate Chair, or their designee, may request additional information, as needed, in order to verify that an incident of noncompliance has occurred as well determine the degree of noncompliance. An individual with a potential conflict of interest may not

participate in the initial inquiry. All communication between the IRB and the Investigator will be documented and recorded in the IRB study file. The IRB Chair (or designee) may secure critical documents at any time during the investigation, as necessary to assure the protection of human subjects.

3.2.2 In case of emergency, the IRB Chair (or designee) may temporarily suspend approval of the investigator's research in accordance with SOP 410: Suspension or Termination of Research, until the matter can be presented to the convened IRB for further review.

3.2.3 If the IRB Chair (or designee) determines that no incident of noncompliance occurred or the investigation cannot proceed due to lack of information/evidence, the allegation or complaint will be dismissed. Such determination will be made in consultation with the IRB Associate Chair, HRPP Director or an IRB Member. This determination will be documented and filed in the IRB study file. The determination will be promptly communicated to the complainant and Investigator as appropriate.

3.2.4 If the IRB Chair or designee determines that the reported events is neither Serious Noncompliance nor Continuing Noncompliance and did/does not have a significant impact on subjects' rights, safety or welfare, and/or the integrity of the data, the incident will be reviewed via expedited procedures. The IRB Chair (or designated expedited reviewer) will determine and implement appropriate corrective action(s). If such corrective action includes more than a minor modification to previously approved research, the modifications must be reviewed via the convened IRB. See SOP 305: Amendment Requests. The determination will be filed in the IRB study file and will be reported to the full IRB at its next convened meeting. After the matter is reported at the convened meeting, the Investigator will be promptly notified of the outcome.

3.2.5 If the IRB Chair or designee determines that the reported event requires additional fact finding, the IRB Chair can refer the matter to an Investigative Subcommittee or the Institution (e.g. Post-Approval Monitor), to further investigate the matter in order to make a recommendation to the full IRB.

3.2.6 If the IRB Chair (or designee) determines that the reported event is Serious Noncompliance or Continuing Noncompliance, or determines that the incident cannot be adequately resolved via the expedited review process, she or he can refer the matter either to an Investigative Subcommittee or to the convened IRB for review. A summary report of the investigation including the initial incident report and the information reviewed by the IRB Chair (or designee) will be provided to the members of the Investigative Subcommittee. The status will be promptly reported to the Investigator and,

if appropriate, to the department head, the complainant, and applicable federal agencies.

3.2.7 The HRPP Director and IO must be notified within 48 hours of all reports that include any of the following conditions:

(a) Any substantiated reports of Serious Noncompliance or Continuing Noncompliance;

(b) Any action that results in the constitution of an Investigative Subcommittee;

(c) Any act by the IRB to secure critical documents.

(d) Any suspensions or terminations resulting from the report and/or investigation.

3.3 Assignment to Investigative Subcommittee or Post-Approval Monitor

3.3.1 Assignments to the Post-Approval Monitor are conducted utilizing procedures detailed in SOP 306. If the initial inquiry of the incidence requires additional fact finding, the IRB Chair can assign the matter to an Investigative Subcommittee, consisting of, at a minimum: the IRB Chair or Associate Chair, the IRB Administrator, and 2 IRB Members (regular or alternate). At least one Investigative Subcommittee member should possess expertise appropriate for review of the allegation. Any individual with a potential conflict of interest shall not participate in the investigation. The IRB Chair or Associate Chair, or designee, will lead the investigation. The IRB Administrator will act as secretary to the Investigative Subcommittee. The Investigative Subcommittee will meet as necessary to ensure timely review of pending allegations.

3.3.2 The Investigator, and if appropriate the complainant, will be informed in writing of the allegation and investigation. If additional information is required to facilitate review of the investigation, the Investigator will be asked to respond in writing within ten (10) days. The Investigator, other research team members, and/or others may be interviewed and/or an audit of the Investigator's research may be conducted, as necessary.

3.3.3 On behalf of the IRB, the Investigative Subcommittee may suspend IRB approval of the Investigator's research in accordance with SOP 410: Suspension or Termination of Research, until the matter can be reviewed by the convened IRB. The Investigative Subcommittee may also secure critical documents at any time during the investigation, as necessary to assure the protection of human subjects. A written report of the investigation including the initial incident report, information reviewed by the Investigative

Subcommittee, determination of whether the incident constitutes Serious Noncompliance and/or Continuing Noncompliance, and its conclusions and recommendations will be submitted to the IRB Chair (if not a member of the Investigative Subcommittee) and the IRB responsible for reviewing the research.

3.4 IRB Convened Meeting

3.4.1 At a convened meeting, the IRB responsible for reviewing the research will review the summary report and all relevant materials submitted by either the IRB Chair or designee or the Investigative Subcommittee.

3.4.2 After consideration of the report, the IRB can move take the following actions:

(a) Request additional information.

(b) Accept the recommendation(s) of the report.

(c) Accept the recommendation(s) of the report with modifications.

(d) Refer the event to the appropriate University process (e.g., misconduct).

3.4.3 The IRB will make its final determination(s) by majority vote of a quorum of the IRB Members at the convened meeting.

3.4.4 If there is a finding of Serious Noncompliance or Continuing Noncompliance or a suspension or termination of IRB approval, the Investigator will be notified in writing within five (5) business days of the IRB's final determination and a due date for corrective actions to be implemented. If appropriate, the Investigator will be instructed to notify the funding agency upon receipt of the IRB's final determination. If appropriate, the complainant will also be notified of the determination.

3.5 IRB Determinations

3.5.1 In the event of a determination of Serious Noncompliance and/or Continuing Noncompliance or any suspension or termination of IRB approval, the IRB will report the event to the IO. The IO is then responsible for reporting the event to the Office for Human Research Protections and/or the Food and Drug Administration, as appropriate.

3.5.2 The IRB may take additional actions as it deems necessary and appropriate. Possible actions include, but are not limited to, the following:

(a) Require corrective actions such as modifications to the research protocol and/or informed consent documents.

(b) Restrict use of research data.

(c) Require past and/or current subjects to be informed of the incident and/or be re-consented.

(d) Modify the continuing review cycle.

(e) Require increased reporting by the Investigator and/or increased monitoring of the research and/or informed consent process.

(f) Suspend or terminate the protocol's approval or suspend specific research activities in accordance with SOP 410: Suspension or Termination of Research.

(g) Require mentoring and/or educational measures.

(h) Recommend sanctions to the IO.

(i) Referral to other appropriate University processes.

3.5.3 Determinations will be documented in the IRB study file as well as in the minutes of the convened IRB meeting.

3.6 Further Actions

3.6.1 If the Investigator does not comply with the IRB determination(s) by the time specified in the notification to the Investigator, the IRB Chair or the Investigative Subcommittee may recommend additional action, including suspension or termination of IRB approval(s) for ongoing Human Subjects Research activities. The need for additional action(s) will be considered by the full IRB at a convened meeting.

3.6.2 The Investigator will be promptly notified in writing of any further IRB review and will be given an opportunity to respond in writing.

3.6.3 The Investigator will be notified in writing within five (5) business days of the final decision of the IRB.

3.7 Appeals

Although the determinations of the IRB are final, the convened IRB may consider an Investigator's response or appeal to the IRB's determination if new information or unusual circumstances are presented. All appeals must be made no more than thirty (30) days after the receipt by an Investigator of the IRB's determination, with

the exact number of days determined by the IRB based on determined severity of Noncompliance. The IRB will review an Investigator's appeal within thirty (30) days of receipt of the appeal, and the Investigator will be notified in writing of the IRB's response to the appeal within five (5) business days.

4. RESPONSIBILITY

4.1 HRPP Staff members are responsible for receiving reports and forwarding them immediately to the IRB Administrator (or designee).

4.2 The IRB Administrator or designee is responsible for pre-reviewing reports, compiling related information, and forwarding to the IRB Chair and/or Associate Chair.

4.3 The IRB Chair (or designee) is responsible for reviewing reports, conducting investigations, making determinations regarding the nature of the event, requiring corrective actions for deviations, constituting Investigative Subcommittees, and, if appropriate, making recommendations to the full IRB.

4.4 IRB Members are responsible for reviewing reports, making determinations, requiring corrective actions, when appropriate, serving on Investigative Subcommittees to conduct investigations and make recommendations to the IO.

4.5 The IRB Administrator administratively supports and participates in investigations into Serious Noncompliance and Continuing Noncompliance. The IRB Administrator is responsible for communicating with appropriate federal agencies and sponsors as needed and ensuring that other parties are informed of IRB actions (e.g. suspensions or terminations) on an as needed basis.

4.6 The IO is responsible for evaluating the IRB's report and considering its recommendations. The IO is responsible for submitting reports to the Office for Human Research Protections or the Food and Drug Administration as appropriate.

4.7 Investigators are responsible for self reporting noncompliance to the IRB. Additionally, they are responsible for training research team members in the recognition and reporting of noncompliance.

4.8 Purdue University Office of Legal Counsel is responsible for reporting Any litigation, arbitration, or settlements initiated related to human research protections to the IO and/or the HRPP Director (who will report to AAHRPP) or to AAHRPP directly, as appropriate.

5. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 50.25(b)(5), 21 CFR 56.108(b)(2)

45 CFR 46.108(a)(4), 45 CFR 46.116(c)(5)

6. REFERENCES TO OTHER APPLICABLE SOPs

306 Post-Approval Monitoring

410 Suspension or Termination of Research