DEPARTMENT: Clinical Operations Group – Research	**POLICY DESCRIPTION:** IRB Review and Reporting of Unanticipated Problems Involving Risks to Subjects or Others
PAGE: 1 of 3	**REPLACES POLICY DATED:** 3/1/12, 9/1/13
EFFECTIVE DATE: February 22, 2019	**REFERENCE NUMBER:** COG.IRB.011 (formerly CSG.IRB.011)
APPROVED BY: Ethics and Compliance Policy Committee	

SCOPE: This policy applies to all Company-affiliated facility-run Institutional Review Boards (IRBs).

PURPOSE: To provide guidance regarding the IRB's review of meaningful new events that affect human subject protection and provides all required internal, external and governmental reporting of these events. The events the IRB must review are often not routine and thus require prompt review and reporting, sometimes to federal regulators.

POLICY:

IRB Review of Unanticipated Problems Involving Risks To Subjects or Others

1. A facility run IRB must review Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs) pertaining to the research it oversees. Note that UPIRSOs may include serious adverse events but, in fact, most serious adverse events do not meet the full definition of UPIRSOs and thus do not need IRB review or actions. Additionally, many problems can occur that are not adverse events but are UPIRSOs (e.g., the loss of a study laptop with unencrypted protected health information on it, protocol deviations that potentially caused serious harm to subjects). More information and examples of what meets the legal requirement of reporting are in the OHRP and FDA guidance documents which overall define UPIRSOs as meeting all three of the following criteria:
    a. **Unexpected.** *Unexpected* means not otherwise previously known to the IRB (in terms of nature, severity, or frequency) given: (a) the research procedures that are described in the protocol-related documents, such as the already IRB-approved research protocol and informed consent document, the Investigator's Brochure if applicable (or other information supplied to the IRB about the drug/device/biologic etc); and (b) the characteristics of the subject population being studied;
    b. **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. Adverse events, even serious adverse events, that are caused by an underlying disease, disorder, or condition of the subject or caused by other circumstances unrelated to either the research or any underlying disease, disorder, or condition of the subject are not related. Protocol deviations or mishaps are usually related as they would not have been done absent a protocol; and
    c. 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**. Note, if the problem was a Serious Adverse Event, this third criteria is automatically deemed to be met. A Serious Adverse Event, according to federal regulations, results in any one of the following:
        i. death;
        ii. life-threatening condition (places the subject at immediate risk of death from the event as it occurred);
        iii. an inpatient hospitalization or prolongation of an existing hospitalization;

iv. a persistent or significant disability/incapacity;
v. a congenital anomaly/birth defect; or
vi. intervention to prevent one of the above.

2. Problems not meeting all three above criteria are not UPIRSOs and need not be reported to nor be reviewed by the IRB. Recall, the IRB previously approved the known risk/benefit analysis as well as the adequacy of the monitoring plan as part of its approval criteria thus only UPIRSOs (i.e., meeting all three criteria) demonstrate additional risks to be promptly considered by the IRB.
3. Investigators should be educated (i.e., through manuals and/or approval letters) of their regulatory obligation that UPIRSOs are to be reported promptly (as defined by the IRB in accordance with the IRB Development of Local Standard Operating Procedures Policy, COG.IRB.005) after their obtaining knowledge of them.

Review Process

1. When the IRB staff receive reports of problems (i.e., adverse events, protocol deviations, study mishaps etc.), the IRB staff should verify that the problem met the criteria for an UPIRSO. They may seek consultation from the Chair or the Chair's designee if needed. Reported events that are not UPIRSOs should not be submitted to the IRB or be reviewed by the IRB.

2. If the event is an UPIRSO, the IRB Chair or their designee shall determine if the action needed meets the criteria for expedited review or, if not meeting such criteria, shall call an ad-hoc meeting of the convened board if the next scheduled meeting is not proximal. Promptness of review should depend on the severity and circumstances of the event.

3. Examples of possible actions resulting from the UPIRSO include but are not limited to the following:

   a. Modification of Informed Consent documents to include a description of newly recognized risks
   b. Provision of additional information about newly recognized risks to previously enrolled subjects
   c. Modification of inclusion or exclusion criteria to mitigate the newly identified risks;
   d. Implementation of additional procedures for monitoring subjects;
   e. Corrective and preventative action plans to prevent protocol/regulatory deviations;
   f. Suspension of enrollment of new subjects (if not voluntarily done by the Investigator);
   g. Suspension of the specific risk-inducing research procedure(s) in currently enrolled subjects (if not voluntarily done by the Investigator);

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h. Modification of informed consent documents to include a description of newly recognized risks; and

i. Provision of additional information about newly recognized risks to previously enrolled subjects.

4. Legally required reporting the IRB must perform includes the following:

   a. Report to Investigator any changes to the IRB approval (i.e., consent forms, additional conditions of approval, etc.)

   b. Report the UPIRSO to Facility's Institutional Official (or their designee) if (1) the Institutional Official is not part of the IRB reviewing personnel, OR (2) the Institutional Official will not receive a copy of such event from the IRB (i.e. in the minutes) and if the Investigator did not make such report themselves.

   c. If the research was suspended or terminated because of the UPIRSO, the IRB must follow its procedures for reporting suspensions and terminations as well as, if applicable, report the suspension or termination to the governing agency(ies) (i.e., OHRP or FDA).

   d. If it has been delegated to the IRB to fulfill the Institution's obligation to report the UPIRSO to any federal agency, then (unless otherwise reported in a suspension or termination) the IRB shall make the report to the governing agency(ies):

      i. Report to OHRP and/or FDA if the activity is governed by them.

      ii. Report to DHHS Agency Head (if the activity is part of a federal grant).

   To meet these deadlines for the above (see Policy COG.IRB.005 pertaining to the required timeframes of such reporting), it may be necessary to provide staged reporting, such as an initial report within these timeframes and follow-up reports as new information is gathered.

REFERENCES:

1. Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events (January 15, 2007) http://www.hhs.gov/ohrp/policy/advevntguid.html
2. FDA Guidance: Adverse Event Reporting to IRBs- Improving Human Subject Protection (January 2009) http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126572.pdf
3. IRB Related Definition and Common Acronyms Policy, COG.IRB.001
4. Clinical Operations Group Research Policies in the COG.IRB series (COG.IRB.001 through COG.IRB.011)