Procedures for Continuing Review by the CWRU IBC:

Continuing Review Process:
Research approved by the Case Western Reserve University (CWRU) IBC may continue only for the time frame established by the IBC. In accordance to the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (*NIH Guidelines*), investigators are required to submit a continuation application for review by the CWRU IBC on a yearly basis from the date of approval for recombinant DNA (rDNA) or synthetic nucleic acid molecule experiments that involve Human Gene Therapy or experiments conducted under Biosafety Level Three (3) or Biosafety Level Four (4). Investigators that conduct experiments at Biosafety Level One (1) or Biosafety Level Two (2) are required to submit a continuation application for review by the IBC every three years from the date of approval. The expiration date will be determined by the CWRU IBC. Due to the nature of some experiments, the CWRU IBC may request a shorter duration between continuing review periods to ensure safe conduct of research covered by the *NIH Guidelines*.

Therefore, it is the responsibility of the Principal Investigator to complete and submit a "Continuing Review/Termination Submission Form" application no less than six weeks prior to the expiration of the protocol to be compliant with the *NIH Guidelines* for rDNA or synthetic nucleic acid experiments. The investigator will need to access the application through the iRIS submission system: https://cwru-iris.case.edu/

At sixty (60) days and thirty (30) days prior to a protocol's expiration date, the Principal Investigator and key study personnel will receive a continuing review courtesy reminder that includes the IBC protocol number, title of protocol, and the definitive expiration date. On the date of expiration, the Principal Investigator(s), Responsible Investigator, Co-Investigator(s) and key study personnel will receive a notification of study expiration. The notification will include the IBC protocol number, title of the protocol, and the definitive expiration date. The notification will also clearly indicate that the protocol is in administrative hold (see below) and that all work must discontinue immediately.

Late Continuing Review:
Investigators should allow adequate time for the CWRU IBC review process. If the protocol expires before the CWRU IBC's continuing approval, all rDNA and synthetic nucleic acid experiments are to be discontinued. The following are the CWRU IBC actions regarding late continuing review:

Administrative Hold:
If the continuing review materials or required revisions are not approved by the expiration date determined by the CWRU IBC, the protocol will be placed on administrative hold. The protocol is considered to be on administrative hold effective immediately on the expiration date. Therefore, the Principal Investigator must discontinue his/her work on the protocol until he/she is in compliance with this policy. The CWRU IBC will issue a notice to the Responsible Investigator and Co-Investigator(s) with regard to the administrative hold status of an IBC protocol (see above).

Administrative Termination:
If the appropriate continuing review materials or required revisions are not approved by the CWRU IBC within two months past the expiration date, then a summary of the protocol, including relevant information for consideration and review, may be forwarded to the full board. The expired protocol will be reviewed and discussed by the committee prior to formal administrative termination. Once a study is administratively terminated, a new initial review request will need to be submitted to continue any work on the protocol. Please note that administrative termination is not routinely considered a reportable "for cause" termination (see below).

"For Cause" Terminations
The CWRU IBC has the authority to halt, suspend, or terminate approval of research which is not being conducted in accordance with the *NIH Guidelines* and/or CWRU IBC policy and procedure. In addition, research that has been associated with unexpected harm to participants or others directly involved with the research can be subject to temporary or permanent termination. There are additional circumstances that might result in "for cause" termination, including research or Investigators involved on-going review for allegations of non-compliance. Please note that administrative termination is not routinely considered a reportable "for cause" termination.

Where appropriate, reviews for non-compliance will conducted with the assistance of the CWRU Biosafety Officer and his/her colleagues in the Department of Environmental Health and Safety (EHS). Sources of allegations of non-compliance can include findings during EHS audits and/or safety inspections.

Completed and Discontinued Research:
When Principal Investigators have completed or discontinued their recombinant DNA or synthetic nucleic acid experiments, they must formally close-out the research protocol. This requirement ensures that the CWRU IBC is informed about the study up until the point of completion or discontinuation. To formally close-out a research protocol, investigators are required to complete and submit a "Continuing Review/Termination Submission Form" application to the CWRU IBC office. Upon request from the investigator, this form will be forwarded by the CWRU IBC office. Failure to formally close-out a study before the expiration date will initiate the Late Continuing Review procedures, which are noted above.

Notifications of the CWRU IBC Decisions:

Notification of Terminations:
The CWRU IBC Director or his/her staff drafts a letter to the Principal Investigator on behalf of the IBC Chair and committee. The letter includes, as appropriate, the following information:

- The activities to be discontinued (i.e. title of protocol).
- A list of actions that need to be taken by the investigator.
- An explanation of the reasons for the decision.
- A request to immediately notify the CWRU IBC Chairperson if any human subjects would be harmed by stopping research procedures and a rationale why they might be harmed.

- The date and time of the CWRU IBC meeting at which the termination was or will be reviewed by the convened CWUR IBC.
- A proposal for the Principal Investigator to respond to the convened CWRU IBC in writing.
- A statement that the CWRU IBC office is required to report the termination to the CWRU IBC, organizational officials, and the Chairperson of the Principal Investigator's primary department.

Notification to the Institutional Officials and Federal Agencies:
The CWRU IBC office will provide written notification of all "for cause" terminations of CWRU IBC approval to the Institutional Research Compliance Officer and appropriate officials (i.e., the Associate Vice President for Research, the appropriate Research Administration Officials, Grants and Contracts Office and any relevant federal or funding agencies).