SOP#: RPS-6	**Submissions to the NIH Institutional Biosafety Committee**
Version #: 2.0	**Next Review Date: 05/2019**
Approved Date: 05/2017	**Review Interval Period: Biennial**
NCI Clinical Director Signature:	William L. Dahut -S Digitally signed by William L. Dahut -S DN: c=US, o=U.S. Government, ou=HHS, ou=NIH, ou=People, 0.9.2342.19200300.100.1.1=0010106299, cn=William L. Dahut -S Date: 2017.05.22 14:38:04 -04'00'

POLICY

The initiation of any experiment at the NIH Clinical Center involving recombinant DNA (rDNA) molecules requires review by the NIH Institutional Biosafety Committee (IBC). Principal Investigators (PI) intending to work with rDNA must register their experiments through PI-Dashboard before experiments begin.

The NIH IBC, whose functions are defined under the Guidelines, reviews and approves research protocols involving the use of rDNA techniques or potentially infectious/toxic materials.

The NIH IBC may determine that:

(1) a protocol submission would significantly benefit from public Recombinant DNA Advisory Committee (RAC) review and discussion and

(2) that one or more of the following NIH RAC review criteria are met:
   (i) the protocol uses a new vector, genetic material, or delivery methodology that represents a first-in-human experience, thus presenting an unknown risk; or
   (ii) the protocol relies on preclinical safety data that were obtained using a new preclinical model system of unknown and unconfirmed value; or
   (iii) the proposed vector, gene construct, or method of delivery is associated with possible toxicities that are not widely known and that may render it difficult for oversight and federal regulatory bodies to evaluate the protocol rigorously, and is therefore requesting RAC review and public discussion.

This decision will be documented in the IBC approval document and sent to the PI to include in the submission to the Office of Science Policy. The Principal Investigator shall then submit the documentation as outlined in Appendix M-I-A of the Guidelines at least 8 weeks prior to the next scheduled meeting in order to be reviewed at that RAC meeting.

PURPOSE

To describe the process for submitting protocols to the NIH IBC.

RESOURCES

NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules

NIH Institutional Biosafety Committees

FAQs on the NIH Review Process for Human Gene Transfer Trials

NIH IBC PI Dashboard

PROCEDURES

Note: *All applicable protocols must be reviewed by the NIH IBC; however, the need for RAC review is determined by IBC and IRB.*

Step 1: Setting up the PI Dashboard — The PI must complete this action

For new PI login rights to the electronic submission system, please contact the Biological Safety Officer (BSO) Richard Baumann at baumannrg@mail.nih.gov identifying your credentials and need for access. To access PI Dashboard, please login to https://oms.ors.nih.gov. The smart card is required to access the Dashboard as it must first go through the single sign-on at the NIH. This single sign-on login site is also managed by the NIH Center for Information Technology (CIT) and may be able to help with any issues related to logging in, such as an operating system PIV Card error. You may contact the CIT NIH Helpdesk at 301 496-4357 or submit a ticket at http://itservicedesk.nih.gov/.

In addition, please use one of the latest versions of **Google Chrome (this is the preferred browser)**, Mozilla Firefox, Safari, or Internet Explorer v. 11 or higher with 'Compatibility view' turned off.

Internet Explorer may also display a blank black page if in compatibility view. To turn off compatibility mode in IE, please go to the Tools Menu -> Compatibility View Settings -> and uncheck the box for Display intranet sites in Compatibility View.

Additional configuration is necessary for Mozilla Firefox logins using PIV cards. The following link is a guide to configure Firefox:
https://myitsm.nih.gov/kb_view.do?sys_kb_id=edcee8bb19e9c500ebeb92f0c7f428e7#FAQ .

Step 2: Designate a Protocol Support person(s) as a proxy in the PI Dashboard

- Select PI-Dashboard on top left hand side (red icon).
- Click the drop down arrow by Available Options.
- Click Manage Proxies (only the PI is able to see this option).

Note: *Designating protocol support staff as a proxy is completed the first time the PI logs in. This will allow the access to the PI's IBC registrations for completion and maintenance. Please also note that as staff leave and are replaced, the PI will need to update/add the proxies in the system.*

Step 3: Create a New Registration in Dashboard (PI or Proxy can complete)

- PI or proxy logs into the PI Dashboard at: https://oms.ors.nih.gov
- **To create a brand-new registration** – Go to Available options on the top and click on the option "Create New."
- Select "Principal Investigator" then select registration type "Blank registration" then click "create."
- Proxy should review with the PI all sections including the last section, called Principal Investigator Attestations.
- Then you will be on the start page of the registration that applies to research click on "I am proposing a gene transfer experiment in humans" then click "save" and continue to next page "project team and lab selection."
- You will need to complete the next page "project team and lab selection" with the following details:
    - Title of the study.
    - List Associated Investigators (AI) and /or Support staff. Any personnel working in the lab (as opposed to animal technicians) must be listed. You will not need to include all the AIs listed on the title page. Only investigators who are involved in the handling of the gene therapy product including the lab personnel.
    - Point of contact other than PI who should receive notices and questions about this registration with contact information.
    - List Laboratory locations, not including animal facilities.
    - Then click on "registration form" button at the bottom of the screen.
- You will need to complete the following details in the registration form:
    - Synopsis (Which includes purpose, Description, start date of project and Duration of Project) then click "save" and "next" at the bottom of the screen.
    - Recombinant Nucleic Acids (Which includes Source of Nucleic Acids), Recombinant or Synthetic Molecules, question regarding whether IRB/OSP has approved this registration, upload study and consent, Phase etc. Then click "save" and "next" at the bottom of the screen.

- Research product questions that will generally require assistance from the PI (Expression, Expression product, Nature of Expression, Product Exposed to, Exposure details, Vector use, and proposed NIH guidelines would be **Section III-C**). Then click "save" and "next" at the bottom of the screen.
- Dual use questionnaire regarding intermediate or final product of experiments (Which includes "Yes", "No" and "N/A" option). Most likely will be "N/A" to all of these questions but please double check with PI. Then click "save" and "next" at the bottom of the screen.
- PI Attestations questions requires the PI to answer all questions.

- If the PI did not complete the form, the proxy will notify the PI that registration is complete and ready for review/submission.

Step 4: Submitting a New Registration in Dashboard (PI must complete)

- PI logs into PI-Dashboard.
- Select the desired protocol by right clicking on the completed draft registration and selecting "Edit." From the start page, proceed to the "registration form" pages by clicking button at center bottom of page to review registration details.
- Click "**PI-E-Signature"** at bottom right side of page to submit for review when completed.
- Enter Password as electronic signature (same as NIH password).
- Click "Save" and "Close."

Note: Once PI has signed off this registration then you will find this new registration under "Completed- awaiting e-sign." You may verify this registration by date of the submission and PI's name. A system generated e-mail will be sent to research personnel requesting signoff. Instructions are included in the email. <u>The submission will not be received by the IBC until all investigators have signed off</u>. At any time, you can review the status of personnel sign-off by reviewing personnel shown on the right side of the screen. Individuals with a red 'x' icon have not completed e-sign, individuals with a green check icon have completed e-sign.

- Once all investigators have signed off, the PI and designated proxies will get the confirmation email from Health RX Support that registration has been submitted by PI for approval and can be found under "Submitted- Awaiting Review" folder under My Research tab.
- Once the registration has been approved, an email from IBC Safety Officer is sent to the PI and designated proxies that approval has been given for the type of action with assigned IBC number (e.g., RD-15-X-07).

- The approval document itself can be obtained within PI Dashboard under the "Active" folder by the assigned IBC number. To view a PDF of the registration, click the assigned IBC number then click "Preview" button on the top right hand side. Then click the "Download" button on the bottom of right hand side and then select "Full form" (This form has signature).
- Save this full approval document in the regulatory folder.

Duplicating from an existing Registration in Dashboard:

To base a new registration off a current registration:

- Go to Available options on the top and click on the option "Create New" and select "Principal Investigator" by drop down arrow.
- Then select registration type "Copy registration."
- Use the drop down arrow to select an assigned IBC registration number for the study that you would like to use to copy for this study (e.g., RD-15-X-07).
- Then click "Create" button.
- Proxy should review with the PI ALL SECTIONS including the "Principal Investigator Attestation"' to insure all information is correct.
- You will need to revise the following details based on the study:
    - Title of the study.
    - List Associated Researchers and /or Support staff. Any personnel working in the lab (as opposed to animal technicians) must be listed.
    - Point of contact other than PI who should receive notices and questions about this registration with contact information.
    - List Laboratory locations, not including animal facilities.
    - Recombinant Nucleic Acids (Which includes Source of Nucleic Acids, Recombinant or Synthetic Molecules, question regarding IRB/OSP has approved this registration, upload study and consent, Phase etc. Then click "save" and "next" at the bottom of the screen.
- Notify the PI that registration is complete and ready for review/submission
- PI logs into PI-Dashboard, selects the protocol and applies signature as described.

Step 5: Creating and Submitting Amendments to Approved Clinical Trials

NOTE: Amendments that are only administrative in nature do not need to be submitted to the IBC. Substantive amendments, such as those related to risk or safety, or are otherwise significant changes to procedure, or study parameters need to be submitted to the IBC, including if the PI of the study has been changed. If the amendment is to change the PI of the study, please send an email directly to Richard Baumann at: baumannrg@od.nih.gov and notify him that you are submitting the amendment changing the PI.

- Log in using the same credentials used to access NIH at https://oms.ors.nih.gov .
- Select the protocol's original registration by IBC assign number (e.g., RD-15-X-07), click "Available Options" or right click.
- Choose "Amendment" option.
- You will be led to a new window where you describe how you wish to amend the registration.
- Then upload the following documents:
    - Cover memo detailing the purpose of the amendment request.
    - Clean and track copy of the protocol.
    - Clean consent documents (if applicable).
    - Investigator brochure (only if applicable and pertinent to the proposed change).
    - IRB review findings (if available).
- Select/click "Save" at bottom of screen and move to next page "Dual-Use Questionnaire."
- Dual use questionnaire regarding intermediate or final product of experiments (Which includes "Yes", "No" and "N/A" option). You will answer this based on your original registration. Then click "save" button at the bottom of the screen.
- If submitting at a later date, save all work and then click "**Close."** Registration will show under "**Drafts"** section.
- Notify the PI that registration is complete and ready for review/submission.
- PI logs into PI-Dashboard.
- Select the desired protocol by right clicking on the completed draft registration and selecting "Edit/Review Registration Document." From initial page, select "registration" to review.
- Click "**PI-E-Signature"** at bottom right side of page to submit for review when completed.
- Enter Password as electronic signature (same as NIH password).

- Then click 'Save' and 'Close'

Note: The amendment review and approval process mirrors that for new registrations. The PI or designated proxy should never attempt to amend an existing amendment file. Rather, amendments are only to be submitted against the existing original clinical trial/registration.

Step 6: Submitting the Annual Report or Safety reports including SAEs to the IBC

Note: *Following the Appendix M-I-C-4 guidelines, the PI must submit a written report on:*
(1) any serious adverse event that is both unexpected and associated with the use of the gene transfer product and
(2) *any finding from tests in laboratory animals that suggests significant risk for human research participants including mutagenicity, teratogenicity, or carcinogenicity.*

Annual reports, and any serious adverse event that is fatal or life-threatening, unexpected, and associated with the use of the gene transfer product must be reported to the NIH IBC as soon as possible, but not later than 7 calendar days after the Principal Investigator's initial receipt of the information (i.e., at the same time the event must be reported to the IRB). These reports are submitted in the PI Dashboard in a manner analogous to the amendment submission procedure previously described.

Serious adverse events that are unexpected and associated with the use of the gene transfer product, but are not fatal or life-threatening, must be reported to the NIH IBC as soon as possible, but not later than 15 calendar days after the Principal Investigator's initial receipt of the information. Provide a purpose for the report submission and a brief description, a letter from the PI on Institute letterhead may suffice, or write in in the amendment request.

- Use the FDA MedWatch form for safety reports.
- Verify that the report does not include PII (Personal Identifiable information). Confidential information, if included, should be indicated as such.
- The report should include, in addition to what is required in a standard MedWatch report:
    - the vector type, e.g., adenovirus;
    - vector subtype, e.g., type 5, relevant deletions;
    - gene delivery method, e.g., *in vivo, ex vivo* transduction;
    - route of administration, e.g., intratumoral, intravenous;
    - dosing schedule; and
    - reports from laboratory animal studies as delineated in Appendix M-I-C-4.
- For annual reports, use the continuing review report that was most recently submitted to the IRB.
- Verify that the report does not mention that the information is confidential.

- Save the continuing review report or safety report in regulatory folder – IBC subfolder.
    - Save as: "IBC Annual Report (and date)" or "IBC Safety Report (and date)"

Process for submitting the Annual Report:

- Log in using the same credentials used to access NIH at https://oms.ors.nih.gov
- Select the protocol's original registration by IBC assign number (e.g. RD-15-X-07), click "Available Options" or right click.
- Choose "Create new" option.
- Use the drop down arrow to select the "Principal Investigator" then select registration type "Amendment to Registration."
- Use the drop down arrow to select an assigned initial IBC registration number for the study (e.g., RD-15-X-07).
- Then click "create."
- After you select the registration to amend, you will be led to a new window where you describe how you wish to amend the registration.
- Then upload the most recent final IRB approved CR Approval Packet.
- Then click "save" and move to next screen "Dual Questionnaire."
- Dual use questionnaire regarding intermediate or final product of experiments (which includes "Yes", "No" and "N/A" option). You will answer this based on your original registration. Then click "save" button at the bottom.
- If submitting at a later date, save all work and then click "**Close."** Registration will show under "**Drafts"** section.
- Notify the PI that registration is complete and ready for submission.
- PI logs into PI-Dashboard.
- Select the desired protocol by right clicking on the completed draft registration and selecting "Edit/Review Registration Document."
- Click "**PI-E-Signature"** to submit for review when completed.
- Enter Password as electronic signature (same as NIH password).
- Then click "Save" and "Close."
- Then PI and designated proxies will get the confirmation email from Health RX Support that amended registration has been submitted by PI for approval and can be found under Submitted- Awaiting Review folder under my Research tab.

- Once the registration has been approved then an email from IBC Safety Officer is sent to the PI and designated proxies that approval has been given for the type of action with assigned IBC registration number (e.g., RD-15-X-07-SAE X- for Safety report and RD-15-X-07-AnnRev X- for annual report).
- The approval document itself can be obtained within PI Dashboard under the "Active Research Registrations" by the assigned above IBC registration number – then click the approved registration then click "Preview" button on the top right hand side. Then click the "download button" on the bottom of right hand side and then select "Full form" (This form has signature).
- File the annual report and the receipt from IBC in the regulatory folder

Step 7: Completing registration Annual Review and requesting inactivation

New registrations will be assigned an expiration date 5 years after their approval date. Annual review is still required as a vital mechanism to keep registration information accurate. If a registration has not been amended within the last year, it will be "due for annual review." The annual review process can be initiated under "Available options" and insures appropriate administrative (labs and personnel) and substantive details pertaining to a registration are kept up-t- date. It involves the PI addressing 5 questions about the registration on the first page, and readdressing the dual-use questions on the second page. The process can be initiated and saved by proxies; however, the PI will need to apply their signature at the bottom of the second page as usual. On the registration expiration date, the PI will be given a simple option to automatically "RENEW" their registration during the Annual Review Process and reset the 5-year expiration period.

The registration's expiration date is visible under the "Review Comments" tab on the right side of the page in the PI Dashboard module, and will appear during the annual review process. A "Request inactivation" option is available under the "Proxy/PI Options" section. If this action is selected, it will be followed up with direct e-mail correspondence asking the PI to attest that he/she no longer possess the described agent, and that no individuals in their laboratory are working on the described project. Biological material accountability should preface all laboratory and personnel transitions. In addition to the button under "Available options," PIs will also be given the option to request registration inactivation during the annual review process.

For clinical trials, the PI can request inactivation once all subjects have been removed from the protocol. (If new safety data is received after the study has been inactivated, it is possible to reactivate the study in the system).