TITLE: UAB HIV/LENTIVIRUS EXPOSURE RESPONSE PLAN		ACTIVATION DATE:
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CROSS REFERENCE: UAB EXPOSURE RESPONSE FLOWCHART		LAST REVISED: 09/1/23

A. Purpose: Agent-specific Safety and Data Plans aim to mitigate the risks of an exposure, while Exposure Response Plans describe the procedures to follow in the event of an exposure. The purpose of this plan is to provide instructions to individuals exposed to cultures/stocks of HIV or lentiviral vectors, to communicate the risk factors to responding clinicians, and to decrease the risk of infection, insertional mutagenesis, and/or transgene-associated malignancies. **Timely reporting is the key!**

B. Scope: Researchers often work with high titer stocks and cultures of replication competent HIV, or replication-incompetent lentiviral vectors. **These concentrated research samples may pose an increased risk of infection, compared to potentially contaminated primary human tissues. In addition, replication-incompetent vector systems are often conferred with expanded host cell tropism and maintain the ability for insertional mutagenesis and/or transgene toxicities.** This plan applies to UAB faculty, staff, or students working with cultures/stocks of HIV, lentiviral vectors, or retroviral vectors.

C. Risk factors for considering post-exposure treatment recommendations:

- **Exposure level:** Estimates of titer, volume, and potential exposure routes are critical for determining the relative risk associated with an exposure. The average viral load of an untreated HIV patient is 100,000 viral copies/mL of serum. The titers of HIV or viral vectors in the lab can vary widely, from 1×10^5 to 5×10^7 infectious units/mL.
- **Viral tropism (host or cell type specificity):** The envelope gene used to package a lentiviral vector will determine the host or cell type specificity of the vector. For example, most lentivirus preparations are pseudotyped with the vesicular stomatitis virus G protein, which infects a broad range of species and cell types.
- **Generation of Packaging System:** The lentiviral vector systems used in the laboratory are generally "replication incompetent," meaning that they cannot cause an infection that will become self-perpetuating in the host (i.e., able to produce more virus). The "generation" of a lentivirus system conveys the degree of safety features engineered into the vectors to reduce the relative risk that a reversion to wild type (replication competent) virus can occur. Third and 4th generation systems are less likely to revert and considered more safe than 1st and 2nd generation systems.
- **Insertional Mutagenesis:** Replication incompetent vectors MAINTAIN the ability to insert their genetic material into the genome of exposed cells, with the potential for insertional mutagenesis of tumor suppressor genes or transcriptional activation of proto-oncogenes.
- **Transgenes expressed:** While the impact of experimental genetic material on human cells is usually unknown, there is presumed to be significant risk for vectors that express oncogenes, proto-oncogenes, cancer promoters, and toxins (e.g., proto-oncogenes used to induce pluripotent stem cells).
- **HIV rescue or amplification: UAB does not screen researchers for HIV.** The impact of a lentiviral vector exposure to a person who is already HIV positive is unclear. There is a concern that the "wild type" HIV may rescue defects engineered into vectors and allow the vector to mobilize.

D. PROCEDURES FOR THE EXPOSED INDIVIDUAL:

1. Wash the exposure site:
   - dermal/percutaneous: 15 minutes with soap and water
   - mucous membranes: 15 minutes with water only

2. While washing the exposure area, have a colleague contact and report the incident to your supervisor (Supervisor's Phone Number: _____). Based on the material you were exposed to, work with your colleague or supervisor to estimate the following parameters important in the risk assessment:

   - Agent/Material: _____
   - Titer of material: _____
   - Volume of exposure: _____
   - Route of exposure: _____
   - Transgenes expressed (are they oncogenes): _____
   - Virus/vector tropism: _____
   - Generation of LV system (if applicable): _____

3. Contact Employee Health immediately. Maximum benefit from prophylaxes for lentiviral exposures is achieved if treatment can be started within 2 hrs, but benefits from treatment can extend to 72 hrs post-exposure.

   See Attached Flowchart: Treatment for Exposures at UAB

4. If you have an injury requiring medical treatment that would cause a bill to be generated, you MUST fill out an OJI Application for Benefits form as well as a Release of Information form. The Trend Tracker Incident Report must also be completed before any bills will be paid.

5. Schedule a 1-week follow-up appointment with the appropriate provider to get a recommendation to continue or suspend treatment with antiretrovirals.

6. After the urgent response issues are addressed, the supervisor should report the exposure incident to the EH&S Biosafety Officer
   - During work hours (8 AM – 5 PM): call 205-934-2487 and ask to be connected with an Occupational Health or a Biosafety representative.
   - After hours or weekends: email biosafety@uab.edu

E. INFORMATION FOR THE HEALTHCARE PROVIDER:

THIS PATIENT HAS BEEN EXPOSED TO A LABORATORY GRADE OF HIV, OR A LENTIVIRUS/RETROVIRUS VECTOR.

1. **Integration can occur within 2 hrs. Timely access to antivirals may be crucial.**

2. **An OJI Form is not a prerequisite for treatment in this situation.**

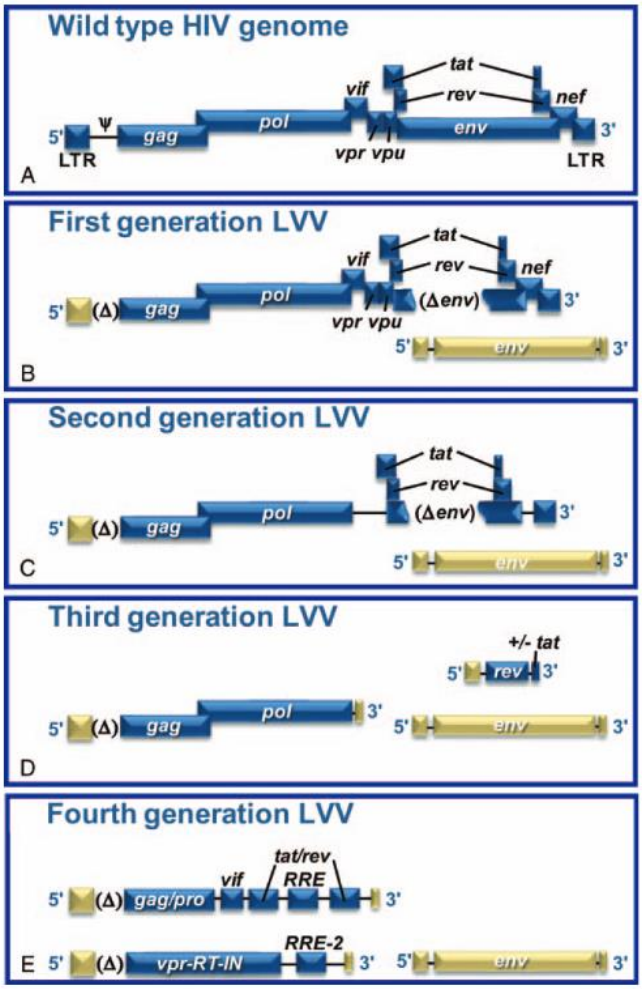
3. Verify exposure area has been washed/irrigated. Consider factors listed in D.2. in your risk assessment.

   - Lentiviral vectors are replication defective, so prophylaxes should be limited to those acting on pre-integration pathways (integrase, reverse transcriptase).
   - If treatment is deemed necessary, have the patient take the initial doses immediately

4. If there are questions concerning the exposure risk, medical staff may contact EH&S Biosafety

   - During work hours (8 AM – 5 PM): call 205-934-2487 and ask to speak with a biosafety team member
   - After hours or weekends: call EH&S Directors on Call at 205-917-4766 and ask to speak with a Biosafety representative.

5. Advise the patient to schedule a 1-week follow-up with their appropriate provider



The development of LVV packaging systems from HIV. **A**, Wild-type HIV genome with all of its genes and regulatory elements provides the backbone for LVVs. **B**, First-generation LVVs removed the envelope protein and the psi packaging signal and incorporated a heterologous promoter to reduce recombination potential. **C,** Second generation of LVV removed accessory genes (vif, vpr, vpu, and nef) to reduce the virulence of any potential replication-competent lentivirus. **D,** Third-generation LVV eliminated the transactivator gene, tat, and split the vector into three plasmids to reduce further recombination potential, retaining only the three genes necessary for transgene expression (gag, pol, rev). **E,** Fourth-generation LVV split the gag and pol onto separate plasmids to reduce even further recombination potential. This generation added back some HIV genes toenhance transduction efficiency and transgene expression. From: JOEM. **58** (12). pg 160. Dec. 2016

F. REFERENCES:

1. R. Schlimgen *et. al.* **Risks Associated With Lentiviral Vector Exposures and Prevention Strategies**. JOEM Med. 58(12):1159-1166. Dec. 2016

2. **Biosafety in Microbiological and Biomedical Laboratories (BMBL).** 6th Ed., June, 2020.

Treatment for Exposures at UAB

I was exposed to
human blood, fluid, or tissue, biologic agent, chemical agent, radiation lasers, animal

CALL 911 IN AN EMERGENCY
unconscious, seizures, difficulty breathing, significant bleeding, chemical spills of 500mL or more, or other life threatening injuries

Activate agent-specific safety plan, initiate decontamination procedures

205-934-3411
Ask for the "needlestick and exposure team"

Campus Employees and Students
Complete OJI Incident Report

Supervisor should also complete "Initial Medical Evaluation Form" and send it with the employee; paperwork MUST BE COMPLETED within 48 hours

OJI form located at:
https://www.uab.edu/humanresources/home/relations/oji

Hospital/Medicine Employees and Students
Complete Trend Tracker

Trend Tracker information located at:
https://www.uab.edu/humanresources/home/relations/oji

You will be triaged to care depending on exposure

UAB EMPLOYEE HEALTH
The University of Alabama at Birmingham