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APPENDIX A

Instructions for Medical Care of Lentivirus Vector (LVV) Exposures

To: Hospital ER Staff (*Preferred provider is St. David's Medical Center ER or St. David's affiliated ERs*)

From: University of Texas *HealthPoint* Occupational Health Program, 512-471-4OHP(4647)

The employee named here _____ works with lentiviruses and has experienced an exposure incident.

The University of Texas' consulting physician is the Director of St. David's Occupational Health Services (OHS). The Medical Director may be contacted for any questions regarding the testing and disposition of this university employee. You may also contact the *HealthPoint* Occupational Health Program to obtain additional information about the exposure risk.

St. David's Occupational Health Services Medical Director:

Office: 512-544-8195

After hours: 512-699-7022

External Emergency Room/Clinic Treatment Guidance:

- Should an employee have LVV **contact to intact skin**, wash the area with soap and water immediately. If the only contact involved intact skin, no exposure incident occurred and no additional post-exposure follow-up care is indicated.
- Should an employee have a LVV exposure, i.e., exposure to the eye, mucous membrane, non-intact skin, or parenteral exposure to lentivirus containing material in the research laboratory they should immediately perform the following steps:
 - Wash the area of exposure with soap and water for 15 minutes.
 - If eye or mucous membrane exposure, rinse with copious amounts of water for 15 minutes. If contacts are worn, remove contacts to fully irrigate the eye.
 - Perform any necessary first aid, such as applying pressure to a bleeding wound, etc.
 - The employee should obtain a baseline HIV test and repeat HIV test in 6 weeks.

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- The employee should advise the treating provider of the type of lentiviral vector (e.g., HIV backbone) and its generation, replication incompetent or competent, transgenes of concern, knockdown or knockout of tumor-suppressor genes, or toxins carried by the vector.
- The employee should advise the treating provider of what type of animal, cells, or tissues are being manipulated, as these may present additional hazards, including bloodborne pathogens (for human cells or tissues), zoonoses, chemicals, or drugs.
 **Macaque cells/tissues may harbor macacine herpes B virus.
- For **replication incompetent** lentiviral vector exposures: There are no studies or national public guidelines on the benefits or risks of post-exposure prophylaxis for insertional risks. The treating provider should consider offering PEP consisting of Isentress (raltegravir) 400 mg twice daily for 7 days with or without Truvada (emtricitabine/tenofovir) 1 po daily unless the employee is pregnant or is otherwise contraindicated. **If possible, begin treatment as soon as possible; ideally within 2 hours of exposure since the primary goal of therapy is to prevent a LVV integration event.** After 72 hours, there is likely no benefit to PEP treatment, as any LVVs present will have either entered the cell or have been cleared. If pregnant, the employee should be offered Combivir (zidovudine/lamivudine) 1 po twice daily for 7 days unless contraindicated. Protease inhibitors, such as Kaletra, have no effect on transduction or integration of the lentiviral vector and therefore should not be used for insertional hazards. Exposure to cells or animal tissues that have been transduced with a lentiviral vector presents minimal risk and there is no likely benefit to post exposure prophylaxis, especially if the transduction occurred more than 72 hours prior. Expert consultation can be made by calling the National Clinicians' Post-Exposure Prophylaxis Hotline (PEpline) at 888-448-4911.
- For **replication competent** lentiviral vector exposures: These should be treated similarly to a wild-type HIV BBP exposure. For this, the treating provider should follow the normal HIV exposure protocol for 28 days.
- LVV PEP represents off label use of FDA approved medications. These recommendations are based upon hypothetical exposures to experimental viruses including retroviruses. According to an article in the Journal of Occupational & Environmental Medicine, Dec.2016, *Risks Associated with Lentiviral Vector Exposures and Prevention Strategies*, **the consideration of PEP is recommended given the potential risks of LVVs versus the generally favorable safety profiles of newer anti-HIV drugs.**

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- The treating provider may wish to consult with an infectious disease specialist. In any event, the employee should be advised that there have been no definitive case reports of harm from LVV occupational exposures. The conversation between the provider and employee should note that the proposed PEP treatment is based on accepted HIV PEP and demonstrated to reduce the risk of HIV infection (the parent virus) after exposure, but has not been clinically proven to prevent insertional mutagenesis from an integrated LVV.