# Information to Assist with the Risk Assessment for Lentiviral Use

Please complete the following information in order to assist the CLEB with the Risk Assessment for lentiviral vector use. Check all items that are applicable to your research utilizing lentiviral vectors.

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|  | Column 1 | Column 2 |
| What is the transgene function? | [ ]  Low risk, such as Protein-based fluorescence (eg, GFP) | [ ]  High risk, such as silence a tumor-suppressor or express an oncogene (ie, Ras, Myc, etc.) |
| What number of plasmids are used to generate virions? | [ ]  3–4 plasmids | [ ]  2 or fewer plasmids |
| What type of mutations are within the lentiviral vector? | [ ]  Vectors that use self-inactivating long terminal repeats (LTRs) and other deleterious mutations | [ ]  Wild-Type LTRs |
| Will viruses be concentrated? | [ ]  No | [ ]  Yes |
| What percentage of the viral genome is deleted or substituted? | [ ]  >2/3 | [ ]  <2/3 |
| If endonuclease technology is used with lentiviral vectors, how will this be accomplished? | [ ]  Endonuclease or derivative will be stably integrated into the cell lines in a separate step | [ ]  Lentivirus will deliver a complete genome editing system |

If any boxes are checked in Column 2, please complete the Lab-specific Lentivirus Exposure Response Plan 2. If boxes are only checked in Column 1, please complete the Lab-specific Lentivirus Exposure Response Plan 1.

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| **Lab Information** |
| **Name of PI** |       | **Date** |       |
| **PI Email** |       | **Emergency Phone Number** |       |
| **Department** |       | **BUA Number** |       |

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| **Lentivirus Exposure Response Plan** |
| **Biological Agent Information** | Lentiviral vectors are single-stranded RNA viral vectors derived from the human immunodeficiency virus (HIV) that retain the ability to integrate into the genome of infected cells.  |
| Please fill out as completely as possible. |
| **Vector System**(See examples. Fill in lab-specific information.) |  |
| **Transgene Information**(See examples. Fill in lab-specific information.) |  |
| **Risks of Exposure** | * **Insertional mutagenesis**: The lentiviral vector can disrupt the normal regulation of cell development and proliferation leading to oncogenesis.
* **Generation of replication-competent retrovirus:** The lentiviral vector may undergo a series of low probability events to revert to a replication-competent retrovirus.
* **Transgene oncogenesis** (*if oncogenes are used*): The transgene is an oncogene and may induce oncogenesis in infected cells.
 |
| **Routes of Transmission** | * Direct parenteral inoculation.
* Contact with mucous membranes or non-intact skin.
* Direct contact at a close range to droplets from an aerosol-generating procedure outside of primary containment.
 |
| **Response** | * **Intact Skin Exposure**: Immediately wash off the affected area with copious amounts of running water to dilute, cleanse, and flush (do not scrub) the LVVs from intact skin.
* **Non-intact Skin Exposure**: Immediately wash the exposed area with copious amounts of soap and water to dilute, cleanse, and flush the LVVs from the area.
* **Mucous Membrane Exposure (Eyes, Nose, or Mouth)**: Immediately flush the area with running water for at least 15 minutes.
* **Droplet Exposure**: See above based upon the area exposed.
 |
| **First Aid Treatment** | * Call emergency personnel for injuries if immediate medical care is needed (911 or 510-642-3333 from a cell phone)
* Stabilize the individual and provide first aid for injuries that require immediate medical care (e.g., deep cuts, bleeding, etc.).
* Seek immediate **(within 2 hours)** medical attention (Alta Bates for after-hours care) for decontamination and possible Post-Exposure Prophylaxis (PEP).
	+ Based on the evaluation and information provided by your lab, the following treatments may be offered:
	+ An integrase inhibitor such as raltegravir
	+ 7-day course
	+ This is best administered ASAP, but within 72 hours of exposure
	+ Observation and treatment of overt effects of the exposure incident.
 |
| **Reporting Incident** | All exposure incidents should immediately be reported to the principal investigator, and the Office of Environment, Health & Safety (510-642-3073) or Occupational Health (510-642-6891).  |

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| **Instructions for Clinicians** |
| Decontamination | * Assure that adequate decontamination occurred at the time of exposure. If not, follow instructions above for First Aid.
 |
| Exposure Assessment | * OFFER PEP if:
	+ Exposure to LVV was via injection, non-intact skin, via mucous membrane or droplet aerosol outside primary containment.

AND* + There are no contraindications
* PEP is not recommended for exposure to intact skin that has been appropriately decontaminated. (If skin was inadvertently broken, due to vigorous scrubbing, consider PEP).
* Chemoprophylaxis should begin ASAP. Integration of the transgene can occur as early as 2 hours and most likely within 10-12 hours after the exposure. Note that there is no likely benefit from PEP 72 hours after exposure.
* Assess other consequences of exposure: trauma, bleeding, tetanus vaccine status, HIV/AIDs history
* Consider risk/benefit of use of these antivirals. Generally considered safe, but consider nephrotoxicity, drug resistance, etc.
* If concerned about drug toxicity, use single drug regimen.
* Assess pre-existing HIV and HBV infection status.
 |
| **RECOMMENDED****PEP Regimen:**  | * Single Drug Regimen
	+ Raltegravir – 400 mg pg twice daily x 7 days.
 |
| **Notes on PEP** | * This is an off-label use of these anti-retrovirals, but routinely used in HIV PEP. They have very good safety profiles, and further made safe by short regimen (7 days)
* Documented in the Journal of Occupational and Environmental Medicine
* NNRTIs, protease inhibitors, entry inhibitors and fusion inhibitors would NOT be effective in this type of exposure
 |

**RESOURCES**

UC Berkeley Biosafety Officer

Phone #: (510) 849-7142

email: bso@berkeley.edu

Sutter Alta Bates Summit MC - Emergency Department

2450 Ashby Avenue, Berkeley CA

510-204-4444

Open 24 hours

Reference:

Schlimgen R, Howard J, Wooley D, Thompson M, Baden L, Yang O, Christiani D, Mostoslavski G, Diamond D, Duane E, Byers K, Winters T, Gelfand J, Fujimoto G, Hudson TW, Vyas J. 2016. Risks Associated with Lentiviral Vector Exposures and Prevention Strategies. J Occup Environ Med Dec; 58(12): 1159-1166.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5152689/

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	+ Based on the evaluation and information provided by your lab, the following treatments may be offered:
	+ An integrase inhibitor such as raltegravir
	+ An NRTI (nucleoside reverse transcriptase inhibitor) such as tenofovir
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* If concerned about drug toxicity, use single drug regimen.
* Assess pre-existing HIV and HBV infection status.
 |
| **RECOMMENDED****PEP Regimen:**  | * Two Drug Regimen
	+ Raltegravir – 400 mg po twice daily x 7 days
	+ Tenofovir – 300 mg po once daily x 7 days.( may substitute Descovy, tenofovir/emtracitabine 1 pill daily x 7 days.)
 |
| **Notes on PEP** | * This is an off-label use of these anti-retrovirals, but routinely used in HIV PEP. They have very good safety profiles, and further made safe by short regimen (7 days)
* Recommended by the Eagleson Institute on lentiviral vector exposures.
* NNRTIs, protease inhibitors, entry inhibitors and fusion inhibitors would NOT be effective in this type of exposure
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