

Occupational Health - Disease Fact Sheet

Lentiviral Vectors

KEY FACTS:

- Lentiviral Vectors (LVVs) are derived from pathogenic viruses, including HIV-1.
- LVVs can be used in the laboratory to integrate foreign DNA into a host genome to manipulate target genes as well as gene expression.
- These viruses are attenuated, and the risk for disease in laboratory workers following exposure is currently considered low in the short term.
- However, as these vectors are designed to integrate foreign DNA into a host genome, there is oncogenic potential in the long term.

SPECIES: Lentiviruses are retrovirus that have been identified in humans, apes, cows, goats, horses, cats, sheep, monkeys, lemurs, rabbits, and ferrets [1]. Lentiviral Vectors (LVV) are modified forms of the wild types and may only be infectious to certain species, or certain cell lines. Many LVVs currently in use in laboratories are derived from HIV-1.

CAUSATIVE AGENT: Lentiviruses are retrovirus that can cause chronic as well as terminal diseases in humans and animals. LVVs are attenuated forms of wild type Lentiviruses (common example is HIV-1) and can be used for genetic modifications in hosts. Currently there are four generations of LVVs, and each has removed or modified critical genes that prevent the wild type strains from either replicating or reverting back to a pathogenic form.

TRANSMISSION: The main mode of transmission is through parenteral inoculations, contact with the mucous membranes of the eyes, nose or mouth, or through direct contact with non-intact skin [1]. Concentrations of 1×10^9 infectious units/mL or volumes greater than 100mL pose the highest risk for future health issues [2].

DISEASE IN ANIMALS: LVVs are used in genetic studies involving animals, so there may be a variety of diseases that could present over the course of a study.

DISEASE IN HUMANS: Immediate illnesses have not been observed after exposure to lentivirus vectors, however as exposure may cause integration of foreign or oncogenic genes into the host's genome long term effects may manifest. Some clinical trials in humans attempting to treat genetic disorders have resulted in cancers after the treatments were completed [2, 3]. Other trials resulted in false positives when the participants were tested for HIV [4]. There are concerns that lab worker exposures may result in negative health effects over the course of the worker's life.

DIAGNOSIS: As the risk that LVV exposure poses is long-term, diseases may manifest years after exposure and may be attributed to natural causes. It will be important for any workers exposed to LVVs to note the details of the exposure (which genes were targeted, which LVV was used, etc.) so that more accurate diagnostics and treatments may be prescribed. *Please*

review current literature before prescribing diagnostic testing as recommendations may have changed.

TREATMENT: If an exposure suspected, the supervisor should be notified immediately and a consultation with an occupational health provider at Via Christi will be needed. The occupational provider will need to be given information regarding the nature of the exposure, and the genes being targeted. As LVVs integrate foreign DNA into a host genome, early treatment will be the most effective. The current guidance is for treatment to begin preferably within 2 hours post exposure, but may still be effective up to 72 hours post exposure. The current recommendation is for a high-risk exposure is a 7 day post exposure prophylaxis which includes an integrase inhibitor (with or without NRTI) [2]. *Please consult your physician for treatment as recommendations may have changed.*

PREVENTION AND CONTROL: Universal precautions must be utilized whenever work with LVVs is required. Proper personal protective equipment, should be worn when handling potentially infectious specimens, cultures, or tissues. To prevent and control unintended infections, use uninfected animals for research, and isolate any animals used in clinical trials. Additionally, only conduct projects in laboratories with proper engineering controls and train staff members in the proper use of required personal protective equipment when they are in spaces containing live agent.

More information on LVVs can be found at the following references:

1. Safety, S.E.H.a. *Lentivirus Fact Sheet*. Available from: <https://ehs.stanford.edu/reference/lentivirus-fact-sheet>.
2. Schlimgen, R., et al., *Risks Associated With Lentiviral Vector Exposures and Prevention Strategies*. *J Occup Environ Med*, 2016. **58**(12): p. 1159-1166.
3. Persons, D.A., *Lentiviral vector gene therapy: effective and safe?* *Mol Ther*, 2010. **18**(5): p. 861-2.
4. De Ravin, S.S., et al., *False-positive HIV PCR test following ex vivo lentiviral gene transfer treatment of X-linked severe combined immunodeficiency vector*. *Mol Ther*, 2014. **22**(2): p. 244-245.