

Fact Sheet:
Protocol for Approval to use
Vaccinia Virus in Research

I. Protocol for Approval to use Vaccinia Virus in Research

The Principal Investigator (PI) must submit the following to EHRS BIOSAFETY@LISTS.UPENN.EDU:

1. A brief abstract of the research project and a brief description of the PI's experience overseeing research with vaccinia virus.
2. Recombinant DNA registration document for experiments involving the generation of recombinant vaccinia virus.
3. A copy of the completed CDC "Request for Vaccinia (Smallpox) Vaccine" form. (See *II: Counseling and Vaccination Procedures*)
4. If work with vaccinia includes the use of animals, the lab must provide an Animal Hazard Briefing with ULAR staff, prior to purchasing animals and starting the work. ULAR is responsible for sending animal husbandry staff to Occupational Medicine for vaccine counseling if direct contact with infected animals and bedding will occur. For more information on the Animal Hazard Briefing program and to request a briefing with your ULAR facility, please visit: <https://ehrs.upenn.edu/health-safety/safety-animal-research>.

EHRS approval will be contingent on verification that the PI and all lab staff working with vaccinia virus have been counseled by Occupational Medicine and that proper biological safety procedures are in place.

II. Counseling and Vaccination Procedures

1. Principal Investigators must complete the CDC Request for Vaccinia (Smallpox) Vaccine form, starting at the section titled "Head of Laboratory Doing Research with Vaccinia." http://www.ehrs.upenn.edu/media_files/docs/pdf/sv_req_4_03.pdf. This form is also available by calling EHRS (215-898-4453) or Occupational Medicine (215-662-2354).
 - *The CDC request form must be completed to record everyone in the lab who will be working with vaccinia virus in order to receive mandatory confidential counseling. The form must be completed even if you or others in your laboratory working with vaccinia virus are not interested in receiving the vaccine.*
 - *Please note that everyone in your lab should NOT be listed on this form. List only those who will work directly with and handle vaccinia virus.*
 - *If your work includes the use of animal facilities, ULAR will be responsible for sending animal husbandry staff to Occupational Medicine for counseling if direct contact with infected animals and bedding will occur.*
2. PI's must return the completed CDC request form with a brief abstract of the research project which must include the PI's prior experience, if any, in working with poxviruses, by mail, email, or FAX to :
 - Occupational Medicine
 - HUP/4283
 - FAX: 215-614-0666
 - Email: Marilyn Watkins CRNP
 - Marilyn.Watkins@uphs.upenn.edu
 - Phone: 215-662-2442
3. Occupational Medicine will complete the remainder of the vaccinia (Smallpox) vaccine request form.
4. After the vaccine request form is sent to Occupational Medicine, each person listed on the form must call or email Marilyn Watkins in Occupational Medicine to set up an appointment for

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mandatory confidential vaccine counseling, which should occur within 15 days of the vaccine request date.

- Occupational Medicine will counsel personnel in conjunction with reviewing the CDC document about the ACAM2000 vaccine, "Important Information About Vaccinia (Smallpox) Vaccine For Laboratory Workers and Medication Guide ACAM2000". This document may also be obtained from Occupational Medicine.

Each person that has received the vaccination will be required to return to Occupational Medicine on the following days after immunization: 3 days, 5-7 days, 14 days, and 17 days.

It is the responsibility of the PI to ensure that individuals attend these follow-up visits.

Individuals who decline immunization will be asked by Occupational Medicine to sign the vaccinia declination form.

- If Occupational Medicine determines, during counseling, that the vaccine is medically contraindicated, that person will be advised to avoid contact with infectious vaccinia viruses in the workplace.
- Occupational Medicine will notify the PI/supervisor and EHRS in writing about each person that has been counseled and immunized or counseled and not immunized, and whether or not anyone is restricted from working directly with vaccinia.
No confidential medical information will be included in this notification.
- Individuals who cannot be vaccinated because of medical contra-indications or who decline vaccination because of risk to their household contacts per CDC guidelines, or for other reasons will not be vaccinated.
EHRS will contact the PI and the individual(s) to discuss additional safety precautions that should be followed when immunization is declined or is contraindicated. Vaccinia

III. Laboratory Practices and Procedures for work with Vaccinia

A. Vaccinia virus

Vaccinia virus is the prototype of the genus Orthopoxvirus which contain poxviruses that infect humans: variola virus (causes smallpox in humans only), monkeypox virus and cowpox virus.

There are multiple strains of vaccinia virus that have different levels of virulence for humans and animals. "Standard" vaccinia virus was used historically to immunize humans against smallpox, and it is this virus that is still used to immunize humans. This virus can replicate in human cells which presents a risk for serious human infection. A commonly used laboratory strain of vaccinia virus is the New York City Board of Health (NYCBOH) strain that was passaged in mouse brains. The resulting virus is neurovirulent in mice and is called the Western Reserve (WR) strain. Other nonattenuated parental vaccinia viruses like Copenhagen and Lister vaccinia strains are also pathogenic in animals.

Recombinant variants from these non-attenuated parental viruses created for experimental purposes present a similar risk to laboratory personnel.

In addition, there are highly attenuated, host-restricted, non or poorly replicating poxvirus strains that are used for recombinant vaccine development. These strains include the modified vaccinia Ankara (MVA) and NYVAC (derived from the Copenhagen vaccinia strain) and the Avipoxviruses, ALVAC and TROVAC (derived from canarypox and fowlpox viruses).

Animal studies indicate that recombinant viruses are usually less pathogenic than the parent strain of vaccinia virus. However, laboratory-acquired infections with non-attenuated vaccinia and recombinant viruses derived from non-attenuated vaccinia strains have been reported. The highly attenuated poxvirus

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strains (MVA, NYVAC, ALVAC and TROVAC) are unable to replicate (MVA, ALVAC, and TROVAC) or replicate poorly (NYVAC) in mammalian host cells; therefore, highly attenuated poxvirus strains do not generate productive infections.

B. Procedures for Laboratory Use of Vaccinia Viruses

1. All laboratory personnel who directly handle cultures or animals contaminated with standard non-attenuated vaccinia virus, recombinant vaccinia viruses or other similar orthopoxviruses that infect humans, must follow Biosafety Level 2 (BSL-2) and Animal Biosafety Level 2 (ABSL-2) practices and procedures.
Appropriate PPE required for handling vaccinia:
 - a. Lab coat
 - b. Gloves
 - c. Eye protection
2. Biosafety Level 1 (BSL-1) practices and procedures may be followed for work with highly attenuated vaccinia strains (NYVAC, ALVAC, MVA and TROVAC) in areas where no other human orthopoxviruses are being used.

For complete descriptions of Biosafety Level 1 and 2 and animal Biosafety level 1 and 2 please see the Biosafety in Biomedical and Microbiological Laboratories (BMBL, 6th edition).
https://www.cdc.gov/labs/pdf/SF_19_308133-A_BMBL6_00-BOOK-WEB-final-3.pdf

Strain	Parent virus strain	Biosafety level
Western Reserve (WR)	NYCBOH	2
MVA	Vaccinia virus (Ankara)	1
NYVAC	Vaccinia virus (Copenhagen)	1
TROVAC	Fowlpox virus	1
ALVAC	Canarypox virus	1

IV. Exposure Protocol

Each person that will be working with vaccinia viruses will be given a yellow wallet sized card explaining the procedures to follow in case of a known or unknown exposure to vaccinia virus. These procedures are to be followed for occupational exposures.

Protocol for Occupational Exposure
Vaccinia Card (Yellow)

Medical Alert Information

If the person carrying this card has had an accidental exposure to vaccinia virus, immediately do the following:

- *If eye exposure, irrigate with water from an eyewash for 15 minutes*
- *If skin exposure, wash thoroughly with soap and water*
- *Seek medical help:*
 - o *All faculty, employees, post docs, undergraduate and graduate students report to Occupational Medicine 215-662-6110 or 215-662-4047.*
 - o *After normal work hours, report to HUP emergency room 215-662-3920.*

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When seeking medical advice for any illness, it is important for the treating physician to be aware of the fact that potential occupational exposure to vaccinia virus may have occurred.

- *During normal work hours please contact University of Pennsylvania the department of Occupational Medicine at 215-662-6110 or 215-662-4047.*
- *After hours please call the Emergency Department at the Hospital of the University of Pennsylvania at 215-662-3920 and request that Occupational Medicine is notified.*
- *CDC website for information and pictures of reactions and adverse events from vaccinia virus exposures: <http://www.bt.cdc.gov/training/smallpoxvaccine/>*

V. References

(1) Vaccinia (Smallpox): **Vaccine Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001.** MMWR, June 21, 2001.
<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5010a1.htm>

(2) Notice to Readers: **Newly Licensed Smallpox Vaccine to Replace Old Smallpox Vaccine.** MMWR, February 29, 2008.
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5708a6.htm>

(3) Biosafety in Microbiological and Biomedical Laboratories, 6th edition
https://www.cdc.gov/labs/pdf/SF_19_308133-A_BMBL6_00-BOOK-WEB-final-3.pdf

(4) **Accidental Infection of Laboratory Worker with Vaccinia Virus.** Emerging Infectious Diseases, Vol.9, No.6, June 2003.
<http://www.cdc.gov/ncidod/EID/vol9no6/02-0732.htm>

(5) MMWR, July 31, 2009: **Laboratory-Acquired Vaccinia Virus Infection—Virginia, 2008.**
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5829a1.htm>