Immunization Recommendations & Requirements for Laboratory Personnel and Others Working with Vaccinia Virus (November, 2007)

Summary: As accidental exposure to some strains of vaccinia virus can lead to infection and complications not only in the exposed research personnel but also their contacts and to the public health, the University of Kentucky's Institutional Biosafety Committee is instituting the following policy:

- Vaccination **IS NOT RECOMMENDED** for researchers working with **highly attenuated** strains of vaccinia virus (MVA, NYVAC, TROVAC, ALVA), with limited exceptions.
- Vaccination **IS REQIRED** for researchers working directly with **non-highly attenuated** strains of vaccinia virus (WR, NYCBOH, Copenhagen, Temple of Heaven, Lister) or Cowpox or Monkeypox OR animals infected with those strains.
- An unvaccinated worker **shall not** work directly with non-highly attenuated vaccinia virus OR animals infected with those strains. .
- **Other factors**, such as research parameters, also influence vaccination recommendations.
- Documented confidential medical counseling by University Health Service **is REQUIRED** for anyone who will be working in a laboratory where vaccinia virus (highly attenuated or non-highly attenuated) is manipulated.

I. Introduction:

Recombinant vaccinia and other pox viruses are useful microbiological research tools for expression of exogenous proteins in a variety of cultured cell types. However, their use is not without risk to laboratory personnel. As stated in the Centers for Disease Control (CDC) and National Institutes of Health's Biosafety in Microbiological and Biomedical Laboratories 5th edition (http://www.cdc.gov/od/ohs/biosfty/bmbl5/bmbl5toc.htm, Section VIII-E) and the Vaccinia (Smallpox) Vaccine Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001 (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5010a1.htm):

- Naturally or experimentally infected laboratory animals are a potential source of infection to exposed unvaccinated laboratory personnel.
- Genetically engineered recombinant vaccinia viruses pose an additional potential risk to laboratory personnel, through direct contact or contact with clinical materials from infected volunteers or animals.
- The agents may be present in lesion fluids or crusts, respiratory secretions, or tissues of infected hosts.
- Ingestion, parenteral inoculation, and droplet or aerosol exposure of mucous membranes or broken skin with infectious fluids or tissues, are the primary hazards to laboratory and animal care personnel.
- All manipulations of vaccinia strains BSL-2 and above should be conducted in a biosafety cabinet. When work must be performed outside of a biosafety cabinet (e.g.

animal surgery, microscopy), the following personal protective equipment must be used:

- disposable gloves
- disposable lab coat or gown
- eye and mucous membrane protection [goggles which are ANSI certified and surgical mask or face shield]. Serious ocular infections can occur even in vaccinated individuals.

Multiple strains of vaccinia virus exist with varying levels of virulence for humans and animals. Depending on the strain used, vaccinia virus presents varying levels of health risk to laboratory personnel. Strains that are highly attenuated are typically unable to replicate or replicate poorly in human cells. On the other hand, nonhighly attenuated strains of vaccinia have the ability to replicate in human cells and thus pose a risk to to the public health. Risks include localized skin infections and more severe, disseminated reactions to which immunocompromized individuals may be more susceptible.

Routes of transmission for occupationally acquired infections of vaccinia:

1. needlestick injury
2. contamination of non-intact skin, mucous membranes, eyes
3. unknown exposure, possibly contamination of intact skin which was not immediately washed
4. Potential routes:
    a. ingestion
    b. inhalation
    c. exposure to fomites (virus is stable at room temperature)

II. Vaccination Recommendations and Requirements:

The following information is based on national guidelines issued by the CDC in Vaccinia (Smallpox) Vaccine Recommendations of the Advisory Committee on Immunization Practices.

Vaccination is <u>not recommended</u> for those working with the following highly attenuated strains:

Highly Attenuated Strain	Biosafety Level*	Derived from:
MVA	2	Vaccinia virus (Ankara)
NYVAC	1	Vaccinia virus (Copenhagen)
TROVAC	1	Fowlpox virus
ALVAC	1	Canarypox virus

* Biosafety level may increase depending on the presence and characteristics of a foreign protein expressed by a recombinant vaccinia virus or other aspects of the proposed experiment.

- Laboratory personnel who work with highly attenuated strains of vaccinia virus (e.g., MVA and NYVAC) or who work with the Avipoxvirus strains ALVAC and TROVAC do not require routine vaccinia vaccination.

- The Occupational Safety Health Board of NIH no longer requires vaccinia vaccination for personnel manipulating MVA or NYVAC in laboratories using only those strains.

- The Recombinant DNA Advisory Committee of the NIH reduced the biosafety level of NYVAC, TROVAC and ALVAC to level 1 based on accumulated attenuation data and biological properties of these strains.

- Although there is no formal surveillance system in place, there have not been any reports of laboratory-acquired infection resulting from exposure to any of the above highly attenuated strains or recombinant vaccines derived from these strains in the literature or to the CDC.

- Appropriate biosafety guidelines and infection control procedures should always be observed when working with viral material even if vaccination is not indicated.

There some limited exceptions to this recommendation when working with highly attenuated strains, depending upon other factors which may come into the evaluation whether to vaccinate or not. Such as:

- The preparation of large volumes of high titer vaccinia virus.
- Work with recombinant vaccinia viruses that might have enhanced virulence or that express harmful proteins.
- Injection of high titer vaccinia virus into animals or other work with sharps and the vaccinia virus.
- Other potentially hazardous manipulations of the virus.

Vaccination <u>is required</u> for laboratory workers who directly handle a) cultures or b) animals infected with:

- Non-highly attenuated Vaccinia virus strains
- Recombinant Vaccinia viruses derived from nonhighly attenuated vaccinia strains
- Other orthopox viruses that can infect humans

Non-highly attenuated strains	WR (Western Reserve,mouse neuroadapted derivative) NYCBOH (strain used in vaccinia vaccine) Copenhagen Temple of Heaven Lister
Other orthopox viruses	Cowpox, Monkeypox

III. Advantages and Disadvantages of Vaccination

Post-vaccination complications are possible. The risks and benefits of the vaccine have to be weighed against the exact duties of the worker. Therefore, a mandatory counseling session is required before any worker accepts or declines the vaccinia vaccination. The Principal Investigator is required to make arrangements with the University Health Service/Employee Health Service (323-5823x228) for all laboratory workers who would work with the vaccinia virus to receive this counseling. All medical information is deemed confidential and cannot be disclosed by UHS/EHS to supervisors, etc. without the employee's written permission.

Some of the arguments for the **advantages** of vaccination:

1. It confers some protection in the event of an accident. (Vaccinia immune globulin (VIG) is also available through the CDC as an Investigational New Drug (IND)).
2. It may reduce the risk of seroconversion to genetically inserted material such as protein products of inserted gene material.
3. It may reduce the risk of serious eye infections following an accidental splash (this risk could also be mitigated by wearing proper personal protective equipment).

Some of the arguments for the **disadvantage**s of vaccination:

1. Risk of side-effects, which may be greater for primary rather than secondary vaccinees and for adults rather than children.
2. It does not always offer full protection
3. Strict personal hygiene precautions must be followed for at least two weeks after vaccination. The vaccinia virus **can** be spread to close contacts which is especially dangerous for certain populations:
    a. infants, children
    b. elderly
    c. people who are immunocompromised
    d. people with a history of eczema or atopic dermatitis
    e. people who are pregnant or breastfeeding
    f. people with allergies to components of the vaccine (which may be trace amounts of polymyxin B, streptomycin, tetracycline, neomycin, glycerin, phenol)

IV. Additional Considerations for Vaccination

- Revaccination every 10 years is recommended by the CDC for people working with nonhighly attenuated vaccinia strains; more frequent revaccination may be required for more virulent orthopox viruses.

- Laboratory personnel not directly handling cultures of vaccinia or animals infected with vaccinia, but working in the same lab where nonhighly attenuated strains are being used should be offered medical screening for potential contraindications to vaccinia exposure.

- Other health-care workers (such as physicians and nurses) working with vaccinia virus and whose contact with these viruses is limited to contaminated materials (for example, dressings), but who adhere to appropriate infection control measures, are probably at lower risk for inadvertent infection than laboratory workers. However, because a theoretical risk of infection exists, vaccination may be considered for this group.

- A summary of published case reports of laboratory-acquired vaccinia virus infections is available in the Journal of the American Biological Safety Association, *Applied Biosafety*, 10(2) 2005, p.118-122 by Karen Byers.

V. University of Kentucky Policy Statement:

In the interest of providing a safe workplace, to comply with federal regulations, and to protect the public health, the Institutional Biosafety Committee (IBC) has formulated a policy regarding immunization for workers in laboratories using vaccinia and other pox viruses. Recommendations and requirements for vaccination will be dependent upon the strain used and procedures in the proposed research. The IBC policy incorporates national guidelines set forth by the CDC as described above and as instituted by the CDC and NIH at their own facilities.

Based on these guidelines, laboratory personnel for whom vaccination is recommended or required must receive mandatory confidential medical counseling before beginning work with the virus. These individuals must be counseled on the risks and benefits of the vaccine and medically screened for contraindications to vaccinia exposure or vaccination.

VI. Instructions to Principal Investigators for obtaining IBC approval to use vaccinia virus and receiving vaccination:

1. Principal Investigators (PI) must register research involving vaccinia virus work with the IBC.
2. PIs who have proposed research activities involving vaccinia must contact University Health/Employee Health Service (UHS) to arrange for counseling of all laboratory workers who would be in a laboratory where the virus (highly attenuated or non-highly attenuated) will be manipulated or where animals infected with vaccinia are held or manipulated.
3. If research will involve non-highly attenuated vaccinia virus, the PI must also contact UHS to arrange for acquisition of the vaccine and vaccination of all laboratory workers who would be working directly with the virus or with animals infected with the virus, even if they think they do not want to be vaccinated.

Following medical consultation, the individual will decide whether to receive the vaccination or not.

a. If they decide to receive the vaccination, they will sign a vaccinia vaccination consent form and receive the vaccine (This will require follow-up visits to monitor the vaccination site.), OR
b. If they decide not to receive the vaccine, or if UHS determines that vaccination is contraindicated, they must sign a declination form, the PI will be contacted by UHS and alterations in the individual's lab or clinical duties and responsibilities will be made such that they will not directly handle vaccinia or animals infected with vaccinia, in order to protect the health and safety of that person, their contacts, and the public health.

4. If the individual does not take the vaccination, for whatever reason, and other duties cannot be found in the laboratory such as to prevent potential contact with non-highly attenuated vaccinia, the employee must resign from his/her position. UK Human Resources will attempt to help the individual find another comparable position at the University, however a position is not guaranteed.
5. IBC approval may occur before all personnel listed on the IBC registration form have been counseled and vaccinated. It is the Principal Investigator's responsibility to ensure that all personnel working directly with vaccinia have received counseling and vaccination. Documentation of medical counseling of all laboratory workers, whether they will work directly with the vaccinia virus or simply work in the laboratory, must also be present in the PI's laboratory biosafety manual. Copies of this documentation must be sent to the Biological Safety Officer.

Approved by unanimous vote of the University of Kentucky Institutional Biosafety Committee

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