**Working Safely with Vaccinia Virus (VV): Biosafety Information & Procedures Note**

**Virus classification and characteristics:** Vaccinia Virus (VV) is a member of the Poxviridae family, Genus Orthopoxvirus. It is microscopic in size approx 350 by 300 nm. It is a double stranded DNA virus that unusually replicates in the cytoplasm of a cell, rather than in the nucleus (Image 1). Certain modified VV strains were (and are still) utilised as the vaccine of choice protecting against smallpox exposure.

**Disease / illness caused:** Localised epidermal lesion/s at site of entry (Image 2A) accompanied by an acute fever (temperature spike) and localised rash. Fatigue, headaches, myalgia (muscle pain) may occur to some. Eczema, encephalitis (inflammation of the brain), myopericarditis (inflammation of the heart muscle) and (localised) vaccinia necrosum (skin gangrene) can be caused in more serious infections. Entry of VV into the eye can cause ocular vaccinia lesion/s and conjunctivitis (Image 2B) and potentially affect sight.

**Host range:** Several mammalian species including humans, rabbits, cows and river buffalo. Rodents are used as experimental infection models. VV can enter most vertebrate cells although replication may be constrained depending on strain variations.

**Route/s of VV Exposure:** Close Contact with the virus and entry through broken skin (contact with VV contaminated samples, equipment, (scratching) of wound sites, bodily fluids (including those from human sexual contact; contact with contaminated catttle teats), dressings, clothing, infected animals, waste); splash of VV containing droplets into eye, mouth and other mucous membranes; inhalational exposure to aerosols released during VV manipulation or handling (e.g. centrifugation) or spils during transport; inoculation via VV contaminated needle/s and sharps.

**Infectious dose:** A (smallpox) vaccine titre is 10^6 pack-forming VV units per ml. Evidenced lesion formation by VV strains can be as small as 10^3 pack-forming VV units.

**Individuals at greater risk from VV infection:** Immunocompromised individuals, those with certain skin (e.g. eczema, psoriasis) and cardiac diseases; new and expectant mothers (including the foetus and new born child).

Serious adverse effects from the smallpox vaccine history indicate one death per million doses; 38 cases of eczema vaccinatum, 3 cases of vaccinia necrosum and 12 cases of CNS diseases per million doses. Pathogen safety data sheet, Public Health Agency of Canada: [http://www.canada.ca/en/public-health/programs/biosafety/biosafety-bacteriology/biohazard.html#safety](http://www.canada.ca/en/public-health/programs/biosafety/biosafety-bacteriology/biohazard.html#safety). In the UK, the vaccine is still in use within defence forces, however, precautions are taken (including vaccination history) to reduce the risk.

**Incubation period:** Epidermal lesions can appear 3-6 days after exposure, lesions would normally scab over and heal in about 10-15 days.

**Stability of VV:** The dried virus can survive for weeks on many surfaces / samples (up to 39 weeks at 4°C at low moisture content); virus can also survive in aqueous solutions for a few weeks.

**Inactivation:** VV is susceptible to autoclaving (121°C for 15 min holding time) and high temperature treatment (95°C for 2 hours). A number of disinfectants can inactivate the virus but efficacy data must be obtained from supplier or in house tests conducted.

**References:**


**VV strains always considered as Hazard Group 2 by ACDP / SACGM (see references opposite):**

- **Wild type / unknown strain isolates, Western Reserve:** Five strains of vaccinia virus (2018) that may be considered as Hazard Group 2 by ACDP / SACGM but with potential for derogation according to peer reviewed / approved risk assessment:
  - **Lister (E3tr)**
  - **LYV (Dryvax); Copenhagen.**
  - **ACAN2003 is a derivative of LYV.**

VV strains that are considered as Hazard Group 1 by SACGM:

- **MVA, NVVAC.**

Genetic modifications that would likely to increase the virulence / risk of a VV strain (see SACGM ref):

- Alteration of 'host range' genes that would alter / widen tissue tropism
- Insertion / expression of immune-avasion (e.g. soluble IFN α/β receptor) or immune-modulatory (e.g. IL-4) gene/s
- Homologous recombination events with other VV / pox viruses
- Expression of harmful inserts (e.g. oncogene, toxin)

The risk level assignment for a genetically modified VV strain must be peer reviewed by the QMUL BGMSC and GM Class allocated.

**Health surveillance and post exposure incident management at QMUL:**

**Health surveillance:** The QMUL pre-employment health questionnaire / supplementary health questionnaire are to be completed by the staff member / PGR student with their line manager / supervisor. It is the responsibility of the recruiting manager to complete: 'The Post Details and Potential Hazards’ section of the pre-employment health questionnaire. QMUL OH Service will then provide appropriate health surveillance advice and support for all relevant staff / PGR students working with VV.

**Vaccination** (with the designated Lister strain vaccine issued by the UK Dept of Health) is possible for the following laboratory personnel, on a case-by-case basis, utilising the information contained in a peer reviewed risk assessment for the

**References:**

- QMUL GMO topic page: [http://www.hsd.qmul.ac.uk/a/c/115genetically-modified-organisms/](http://www.hsd.qmul.ac.uk/a/c/115genetically-modified-organisms/)

[Image 1 - Vaccinia Virus Expression System and Lifecycle.](http://www.hse.gov.uk/biosafety/gms/agmcompg/part2.pdf)

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[Image 2 - (A) Localised epidermal lesion at site of VV loaded needle entry and (B) conjunctivitis and ocular lesion after eye exposure.](http://www.hse.gov.uk/biosafety/gms/agmcompg/part2.pdf)

- **(A) CDC.** Laboratory-acquired vaccinia virus infection in a recently immunized person—Massachusetts, 2013. MMWR 2015 May 1;64(16):435-8

**Image 2**

- **A** Localised epidermal lesion at site of VV loaded needle entry and (B) conjunctivitis and ocular lesion after eye exposure.
Laboratory risk control measures:

- Laboratory personnel must adhere to the QMUL procedure for contamination incidents requiring first aiders to attend so that the correct procedure is then followed before contacting OHS.
- In the event of an exposure, contact OHS Service immediately on 0207 882 7000/7207 requesting an urgent same day appointment.
- The laboratory personnel will be seen in OHS at the earliest opportunity where a strict 10 day surveillance programme will commence. A health assessment form will be completed and Public Health England (PHE), North East and North Central London Health Protection Team will be notified.
- OHS will notify the Royal London Hospital of the exposure to ensure that out of hours and weekend is provided. The designated hospital is The Royal London Hospital at Whitechapel.

See full detail in the in the ‘Occupational Health Protocol for those working with vaccinia virus’ document.

Laboratory risk control measures:

- Use of needles and sharps containing VV (e.g. experimental animal inoculations and/or preparation of syringes)
- Processes that provide energy for particle dissemination / aerosol or droplet release (e.g. centrifugation, mixing, vortexing)
- High titre or scale up cultures of VV
- Transport between rooms / buildings
- Column or other purification or concentration of the virus
- Freeze-thawing or sonication
- Removal from storage of dried virus samples

For further advice at QMUL contact –
QMUL Health & Safety Directorate
http://hr.qmul.ac.uk/about

Lead contact - Dr Mark Ariyanayagam (H&S Manager and QMUL Biosafety Adviser)
QMUL Occupational Health Service
http://hsd.qmul.ac.uk/about

Further Information (references above and)
Health & Safety Executive (HSE) Biosafety Webpages http://www.hse.gov.uk/biosafety/