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Revised Animal Tissue Sample Request Workflow to Address NHP-related Risks

Looi Wenjie, SEMC
Edgar Macabe Pena, SEMC
Inria Kurniawan Then, SEMC
Zheng Lin, SEMC

Introduction

The Ministry of Health (MOH) has issued an advisory on handling of samples derived from non-human primates (NHP). The advisory contained several guidelines and requirements on the part of the facilities providing the NHP samples, as well as on institutions of requestors receiving and handling the samples. NHPs are a potential host to a number of zoonotic pathogens, including the Herpes B virus, that can cause serious and life-threatening conditions in humans. Exposure can occur during direct contact and or injury involving NHP tissues and body fluids. Hence, utmost care must be given while handling such samples.

SingHealth Experimental Medicine Centre (SEMC) and National Large Animal Research Facility (NLARF) already have an established animal tissue and request procedure which include obtaining signed Letter of Undertaking (LOU) from Principal Investigators prior to collection of samples. However, the workflow has to be revised in line with the guidelines indicated in MOH Advisory. The aim was to:

- ❖ Improve communication of the MOH requirements to requestors and,
- ❖ Improve requestors' awareness on their responsibilities and the relevant safety procedures.

The LOU summarizes responsibilities of investigators and their institutions related to the collection and use of animal samples from SEMC and NLARF.



Methodology

Amendment of LOU

Update existing Tissue Request workflow by incorporating an amended LOU.

Develop Info Sheet

Prepare an Info Sheet to raise awareness of NHP-related risks to be provided to all researchers working with NHPs.

Email Communication

Prompt communication sent to all relevant users on the new MOH advisory and the updated Tissue Request workflow.

Results

LOU amended to include the requirements for:

- Personnel having undergone appropriate training
- Sufficient risk management measures in place
- Security of samples
- System for maintaining sample's accountability
- Having read and understood the MOH Advisory.

Assistance from Legal was sought to fine tune the LOU.

Additionally, the LOU is extended for use to all NHP projects. The revised LOU fulfils the facility's role and duties in the supply of such samples, while at the same time ensuring that requestors are aware of the hazards and their responsibilities in order to comply with the MOH requirements.

A single paged Info Sheet was prepared, which contained:

- Important information on the possible hazards when dealing with NHPs and samples.
- Safety precautions to be taken when transporting and handling NHP tissues and fluids.
- Emergency response steps during accidental exposure
- Useful contact information.



An email communication was sent out to all researchers working with NHPs and samples in SEMC/NLARF facilities. The MOH Advisory and the Info Sheet was attached in the email, for their information and reference.



Conclusion

Revising the Animal Tissue Request workflow was a necessary process to comply with new requirements. The updated LOU and new workflow also helped to raise awareness on the risks associated with handling NHP-related samples which improves safety practices. The Info Sheet also serves as a reference for existing and new researchers who wish to embark on NHP-related work.

EXPOSURES TO NONHUMAN PRIMATE TISSUES AND FLUIDS HAZARDS, PRECAUTIONS AND POST-EXPOSURE PROCEDURES

HAZARDS

All fresh or frozen samples of tissues or fluids from non-human primates (NHPs) are potentially contaminated with pathogens that may be infectious to humans (zoonotic agents). Tissues from macaques (*Macaca spp.*) in particular may be contaminated with zoonotic viruses, with Macaque Herpesvirus 1 (aka: Herpes B virus) being of greatest concern, since it has caused death in humans. Exposure can occur from cuts, scratches, needle sticks or mucous membrane splashes. Herpes B virus can survive for only a few hours on exposed dry surfaces and formalin fixation will kill the virus.

There are no vaccines available to prevent the onset of disease in humans exposed to Herpes B. However, post-exposure procedures of **immediately** cleansing or flushing the exposure site (wound or mucous membrane) for 15 minutes have been 100% effective in preventing disease (See URL: <https://www.cdc.gov/herpesvirus/firstaid-treatment.html>)

SAFETY PRECAUTIONS IN TRANSPORT AND HANDLING OF NHP TISSUES AND FLUIDS

1. Ensure that you understand completely the risks mentioned above and you have reviewed the health record of the animal that was the source of the tissues. You can obtain or request the health record from the source facility or provider of the tissues.
2. When receiving the tissues, ensure that they are packed securely in containers with proper labels and identification, including, but not limited to date of collection, species and investigator name or research project number. When transporting tissues from one facility to another, they should be placed in a secured/sealed and leak-proof box with proper labels. The tissue handler should prevent any chances of spills and leakage from tissues/fluids while in transit.
3. Wear appropriate PPE (i.e. double gloves, face mask, face shields, gowns, shoe covers) and cover your body parts that may be exposed to accidental spills or splashes.
4. Perform the tissue manipulation in a downdraft table, laboratory fume hood or biosafety cabinet using Universal Precautions.
5. If storing the tissues for future use, secure the container, label properly and create tracking and inventory files for reference.
6. Use tissue digester (if available) or use double biohazard bag to dispose the unwanted tissues for collection by a licensed biohazardous waste disposal service company.

WHAT TO DO WHEN ACCIDENTALLY EXPOSED WITH ANIMAL TISSUES AND FLUIDS?

Accidental exposures to NHP tissues/fluids may include spills or splashes on mucous membranes or direct inoculation via wounds or needle-stick. Follow your institution's SOP on Management of spills or contaminated splash if any. If no SOP is in place, please do the following to manage the exposure.

A.

For mucous membrane exposure i.e. eye splash, immediately flush the eye with water or saline and continue for 15 minutes.

B.

For wound or needle-stick exposure, immediately cleanse or scrub the wound with water and a disinfectant soap or detergent (e.g. Betadine or Chlorhexidine) and continue for 15 minutes. If needle-stick injury, massage the site to express blood out of the puncture wound while scrubbing. Dry the wound and apply plaster.

C.

Report the incident to your Supervisor and/or your units' Occupational Health and Safety Officer immediately after cleansing the wound. Initial assessment and follow up should be performed by a physician knowledgeable in Occupational Health and Safety related to work with macaques (e.g. Dr. Gregory Chan, Chinatown Medical Centre).

CONTACT INFORMATION

SingHealth Experimental Medicine Centre (SEMC) and National Large Animal Research Facility (NLARF) conduct training sessions on Herpes B and proper handling of NHP tissues FREE of charge for our investigators. For information on this training, please contact us at 6576 7041 or email us at sbs.semc@singhealth.com.sg.

* Animal Tissue Health Checklist issued by SEMC and NLARF prior to releasing the tissues to requestors specifies the possible hazards. In addition, the attached MOH Advisory Notice provides important information on handling tissues derived from NHPs. The SEMC/NLARF Letter of Undertaking, which requires the signature of the Principal Investigator of the relevant projects, seeks to ensure his/her team's understanding on the relevant hazards.