Boston Public Health Commission

Biological Laboratory Safety Permit Application

SECTION 13: BSL-3/BSL-4 STRAIN VERIFICATION

Boston University

National Emerging Infectious Diseases Laboratories

~~May 2013~~~~July~~ September 2014

CONTENTS

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1.0 VERIFICATION OF THE IDENTITY OF ATTENUATED PATHOGENS

This policy covers attenuated pathogens ~~which~~that meet all of the following criteria:

i. ~~the~~The attenuated pathogen is derived from a known, virulent pathogen that requires BSL-3 or BSL-4 biosafety containment;

ii. ~~attenuation~~Attenuation results in decreased virulence of the organism;

iii. ~~attenuation~~Attenuation results in a reduction in the level of biosafety containment in which the attenuated pathogen can be handled, compared with the biosafety level required for the safe handling of the non-attenuated counterpart.

~~This~~Although no specific attenuated BSL-4 pathogen has been used in the NEIDL facility and verification of such a strain has not yet been necessary, the same policy would be in effect should there be any use of attenuated BSL-4 pathogen. However, this policy does not apply to pathogens that have been inactivated by a process established and accepted as scientific and safety standard and approved by the ~~IBC.~~ Institutional Biosafety Committee (IBC). The necessary requirements to work with inactivated pathogens derived from BSL-3 or BSL-4 containment facilities are covered in the ~~"Validation of Inactivated pathogens" policy.~~Validation of Inactivated Pathogens policy.

As is the case with all proposed studies at Boston University and Boston Medical Center~~,~~ (BU/BMC), work with any pathogen, including attenuated and inactivated pathogens, cannot be initiated (and the pathogens cannot be brought into BU) without prior approval from the ~~Institutional Biosafety Committee (IBC).~~IBC.

2.0 POLICY

The identity of any attenuated BSL-3 or BSL-4 pathogen must be verified before it can be handled at the lower biosafety containment level ~~of~~ designated for the attenuated pathogen. Verification ~~should~~ must be conducted at the biosafety level designated for the virulent wild-type strain. In the case of an attenuated BSL-4 agent, it will be initially received in the BSL-4 where it will be tested to verify for its attenuation to ensure that it can be handled at a lower laboratory containment level. Th~~H~~e same will be performed for attenuated BSL-3 agents where it will be received and tested in the BSL-3 laboratory facility prior to being handled in a lower laboratory containment level. The testing will be ~~and be~~ by DNA restriction analysis ~~or another method that has been proven to~~, polymerase chain reaction (PCR) amplification and subsequent DNA sequence analysis of a genomic region that rigorously distinguish the wild-type and attenuated ~~pathogens.~~variety of a BSL3/BSL4 pathogen. The verification method may also include individualized verification protocol that experimentally distinguish the two variety. Each verification protocols must include DNA samples from inactivated wild-type and attenuated strain or plasmid DNA containing original and attenuated virulence factor (obtained from other investigator/s). . Verification ~~should~~must be conducted on the received stock which is designated the Master Stock and, whenever possible, verification should be carried out on an individual clone (colony- or plaque-purified, for example) of the incoming attenuated pathogen~~.~~ that has been isolated from the Master Stock. Only material from the verified clone ~~(or stock~~which has been used to prepare the Seed or Stock) can be studied at the lower biosafety level.

Verification should be carried out ~~by the receiving BU laboratory~~ pursuant to an IBC-approved protocol for verification~~. The attenuated pathogen must not be received at BU until after the~~ by the receiving BU laboratory. IBC~~-~~ approval of the protocol for verification, including how and where the specimen will be stored upon receipt~~.~~, must precede receipt of the pathogen at BU. Upon receipt of the specimen, the pathogen must be handled at the higher biosafety level of the non-attenuated, wild-type pathogen until the specimen has been verified to contain only the attenuated pathogen that can be safely handled at the lower biosafety level. Verification result must be submitted to the IBC, or ~~their~~its designee, for review and approval prior to transferring the attenuated pathogen to the lower containment level.

If the identity of an attenuated pathogen cannot be verified, it must be handled at the higher biosafety level ~~of~~designated for the non-attenuated wild-type pathogen.

Food and Drug Administration (FDA)-approved ~~human~~ vaccines that contain attenuated BSL-2 agents derived from BSL-3 or BSL-4 agents may be excluded from the BU ~~strain~~ verification ~~policy~~of attenuated pathogenspolicy if the formulated vaccines are obtained directly from the

vaccine manufacturer. ~~EHS and IBC offices will review the~~However, ~~T~~the manufacturer's documentation will always be reviewed by the Environmental Health & Safety (EHS), and full IBC committee to determine whether exclusion from the BU policy is ~~warranted and can request further review by the full IBC committee.~~allowable.~~.~~

The IBC will not directly approve verification of attenuated pathogens based on documentation provided by off-campus producers of attenuated BSL-2 strains derived from BSL-3 or BSL-4 pathogens. These attenuated strains must undergo similar verification protocol as stated in paragraph 1 of this section, especially verification from a single colony or plaque and preparation of master stock from the verified colony/plaque will be strictly enforced. Also, as stated earlier, until strain verification is successfully completed, unverified strains must be handled in the same BSL level as of the wild-type pathogen.

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~~The IBC may consider and approve strain verification of attenuated pathogens documentation provided by off campus producers of attenuated BSL-2 strains derived from a BSL-3 or BSL-4 pathogen if name and contact numberinformation of the facility that verifies the sample is provided together with a copy of the verification result. Strain verification document documentation must come together withaccompany the shipment of the sample and providenceprovenance must be evident, documenting the strain handling from verification through shipment to Boston University and Boston Medical Center.BU/BMC. This documentation will always be reviewed by EHS and full IBC offices which can request further review by the IBC committee. .~~

3.0 RELATED DOCUMENTS

Policy: -Laboratory Safety Training

~~Policy: Disease Surveillance Reporting~~

~~Policy: Strain Verification Procedure~~

Policy: Disease Surveillance Reporting

Policy: Strain Verification Procedure (under revision)