

**Inspection Checklist for Biosafety Level 3 Enhanced for Research Involving
1918 Influenza Virus (BL3 Enhanced) (NIH Guidelines)**

Entity Name:
 Inspection Date:
 Street Address:
 City, State, Zip:
 RO:
 ARO(s):

Building/Room(s):
 PI(s):

Lead Inspector:
 Other Inspectors:

When information is entered in this form, the form is to be considered Sensitive Select Agent Information.

Entity Name:		Inspection Date:			
Reference	Statement	Yes	No	N/A	Comments
NIH: Section III-D-7NIH	Experiments Involving Influenza Viruses - Experiments with influenza viruses generated by recombinant or synthetic methods (e.g., generation by reverse genetics of chimeric viruses with reassorted segments, introduction of specific mutations) shall be conducted at the biosafety level containment corresponding to the Risk Group of the virus that was the source of the majority of segments in the recombinant or synthetic virus (e.g., experiments with viruses containing a majority of segments from a RG3 virus shall be conducted at BL3). Experiments with influenza viruses containing genes or segments from 1918-1919 H1N1 virus (1918 H1N1)...shall be conducted at BL3 enhanced containment (see Appendix G-II-C-5, Biosafety Level 3 Enhanced for Research Involving Risk Group 3 Influenza Viruses) unless indicated below.				
NIH: Section III-D-7-c	1918 H1N1. Experiments involving influenza viruses containing any gene or segment from 1918 H1N1 shall be conducted at BL3 enhanced containment.				

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NIH: Section III-D-7-d	Antiviral Susceptibility and Containment. The availability of antiviral drugs as preventive and therapeutic measures is an important safeguard for experiments with 1918 H1N1.... If an influenza virus containing genes from one of these viruses is resistant to both classes of current antiviral agents, adamantanes and neuraminidase inhibitors, higher containment may be required based on the risk assessment considering transmissibility to humans, virulence, pandemic potential, alternative antiviral agents if available, etc. Experiments with 1918 H1N1...that are designed to create resistance to neuraminidase inhibitors or other effective antiviral agents (including investigational antiviral agents being developed for influenza) would be subject to Section III-A-1 (Major Actions) and require RAC review and NIH Director approval. As per Section I-A-1 of the <i>NIH Guidelines</i> , if the agent is a Select Agent, the NIH will defer to the appropriate Federal agency (HHS or USDA Select Agent Divisions) on such experiments.				
NIH: Appendix G-II-C-2	Special Practices (BL3)				
NIH: Appendix G-II-C-2-n	All wastes from laboratories and animal rooms are appropriately decontaminated before disposal.				
NIH: Appendix G-II-C-2-r	Baseline serum samples for all laboratory and other at-risk personnel should be collected and stored in accordance with institutional policy and at least for the time period in which the personnel continues to work with the agent at biosafety level 3 containment....Additional serum specimens may be collected periodically depending on the agents handled or the function of the laboratory.				
NIH: Appendix G-II-C-4	Laboratory Facilities (BL3)				
NIH: Appendix G-II-C-4-i	A ducted exhaust air ventilation system is provided. This system creates directional airflow that draws air into the laboratory from uncontaminated spaces surrounding the laboratory. The exhaust air is not recirculated to any other area of the building, is discharged to the outside, and is dispersed away from occupied areas and air intakes. Personnel shall verify that the direction of the airflow (into the laboratory) is proper. The exhaust air from the laboratory room may be discharged to the outside without being filtered or otherwise treated....				

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NIH: Appendix G-II-C-5-a. Risk Group 3 Influenza Viruses (BL3 Enhanced)	Containment, Practices, and Training for Research with Risk Group 3 Influenza Viruses (BL3 Enhanced).				
NIH: Appendix G-II-C-5-a-(1) Risk Group 3 Influenza Viruses (BL3 Enhanced)	In addition to standard BL3 practices, the following additional personal protective equipment and practices shall be used:				
NIH: Appendix G-II-C-5-a-(1) (1) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Powered Air-purifying Respirators (PAPR) are worn.				
NIH: Appendix G-II-C-5-a-(1) (2) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Street clothes are changed to protective suit (e.g., wrap-back disposable gown, olefin protective suit).				
NIH: Appendix G-II-C-5-a-(1) (3) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Double gloves (disposable) are worn.				
NIH: Appendix G-II-C-5-a-(1) (4) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Appropriate shoe coverings are worn (e.g., double disposable shoe coverings, single disposable shoe coverings if worn with footwear dedicated to BL3 enhanced laboratory use, or impervious boots or shoes of rubber or other suitable material that can be decontaminated).				
NIH: Appendix G-II-C-5-a-(1) (5) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Showers prior to exiting the laboratory should be considered depending on risk assessment of research activities....				
NIH: Appendix G-II-C-5-a-(2) Risk Group 3 Influenza Viruses (BL3 Enhanced)	As proper training of laboratory workers is an essential component of biosafety, retraining and periodic reassessments (at least annually) in BL3 enhanced practices, especially the proper use of respiratory equipment, such as PAPRs, and clothing changes, are required.				

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NIH: Appendix G-II-C-5-a-(3) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Reporting of all spills and accidents, even if relatively minor, is required as described in Appendix G-II-C-2-q: [Spills and accidents which result in overt or potential exposures to organisms containing recombinant or synthetic nucleic acid molecules are immediately reported to the Biological Safety Officer, Institutional Biosafety Committee, and NIH/OBA. Reports to NIH/OBA shall be sent to the Office of Biotechnology Activities, National Institutes of Health, 6705 Rockledge Drive, Suite 750, MSC 7985, Bethesda, MD 20892-7985 (20817 for non-USPS mail), 301-496-9838, 301-496-9839 (fax). Appropriate medical evaluation, surveillance, and treatment are provided and written records are maintained.]				
NIH: Appendix G-II-C-5-a-(4) Risk Group 3 Influenza Viruses (BL3 Enhanced)	To avoid inadvertent cross contamination of 1918 H1N1, HPAI H5N1 or human H2N2 (1957-1968):				
NIH: Appendix G-II-C-5-a-(4) (1) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Containment facilities and practices appropriate for highest Risk Group virus shall be used at all times with lower Risk Group viruses, when studied in the same laboratory room.				
NIH: Appendix G-II-C-5-a-(4) (2) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Tissue cultures with these viruses shall be conducted at separate times (temporal spacing) in the same room.				
NIH: Appendix G-II-C-5-a-(4) (3) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Separate reagents shall be used to minimize risk of cross contamination.				
NIH: Appendix G-II-C-5-a-(4) (4) Risk Group 3 Influenza Viruses (BL3 Enhanced)	A laboratory worker shall not perform concurrent influenza virus experiments that carry the risk of unintended reassortment among 1918 H1N1, human H2N2 (1957-1968), HPAI H5N1 and other human influenza viruses.				
NIH: Appendix G-II-C-5-a-(4) (5) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Two or more laboratory workers shall not perform within the same work area simultaneous influenza virus experiments that carry the risk of unintended segment reassortment between 1918 H1N1, or HPAI H5N1, or human H2N2 (1957-1968) and other human influenza viruses.				

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NIH: Appendix G-II-C-5-a-(4) (6) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Between experiments good biosafety decontamination practices (e.g., surface and biosafety cabinet surface decontamination according to standard BL3 procedures) shall be used and there shall be a thirty minute wait period after decontamination before equipment is used for experiments with any other influenza A viruses.				
NIH: Appendix G-II-C-5-a-(4) (7) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Between experiments, in addition to decontamination of the work area, clothing changes and PAPR disinfection shall be performed prior to handling a different influenza virus in the same work area.				
NIH: Appendix G-II-C-5-a-(5) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Continued susceptibility of the reassortant influenza viruses containing genes and/or segments from 1918 H1N1...to antiviral agents shall be established by sequence analysis or suitable biological assays. After manipulation of genes that influence sensitivity to antiviral agents, susceptibility to these agents shall be reconfirmed.				
NIH: Appendix G-II-C-5-b Risk Group 3 Influenza Viruses (BL3 Enhanced)	Containment for Animal Research. Guidance provided in Appendix G-II-C and Appendix Q-II-C is applicable with the following emphasis on standard BL3 or BL3-N containment or additional enhancements.				
NIH: Appendix G-II-C-5-b-(1) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Research with small animals shall be conducted in a class II biosafety cabinet. Small animals such as rodents (e.g. mice, hamsters, rats, guinea pigs) can be housed within a negative pressure BL3 animal suite using high-density individually vented caging (IVC) systems that independently supply high efficiency particulate air/HEPA-filtered and directional air circulation. Other animals (e.g. rabbits, ferrets) that are of a size or have growth or caging requirements that preclude the use of high-density IVC systems are to be housed in negative pressure bioisolators				
NIH: Appendix G-II-C-5-b-(2) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Large animals such as non-human primates shall be housed in primary barrier environments according to BL3-N containment requirements (see Appendix Q-II-C).				
NIH: Appendix G-II-C-5-b-(3) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Specialized training and proven competency in all assigned practices and procedures shall be required for laboratory staff, including staff involved in animal care.				

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NIH: Appendix G-II-C-5-c Risk Group 3 Influenza Viruses (BL3 Enhanced)	Occupational Health. A detailed occupational health plan shall be developed in advance of working with these agents in consultation, as needed, with individuals with the appropriate clinical expertise. In addition, the appropriate public health authority shall be consulted (e.g. local public health officials) on the plan and a mock drill of this plan shall be undertaken periodically. The plan shall include a description of the incident reporting system in place for incidents, which include any loss of containment, spills, accidents, or potential exposures. The plan must specify that all incidents must be reported immediately to the appropriate institutional authorities, and no later than 24 hours to the appropriate public health authorities (e.g., the USDA, the CDC, NIH, local and state health authorities).				
NIH: Appendix G-II-C-5-c-(1) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Laboratory workers shall be provided with medical cards which include, at a minimum, the following information: characterization of the influenza virus to which they have been potentially exposed, and 24-hour contact numbers for the Principal Investigator and institution's occupational health care provider(s).				
NIH: Appendix G-II-C-5-c-(2) Risk Group 3 Influenza Viruses (BL3 Enhanced)	A detailed occupational health plan shall include:				
NIH: Appendix G-II-C-5-c-(2) (1) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Unless there is a medical contraindication to vaccination (e.g. severe egg allergy) annual seasonal influenza vaccination as prerequisite for research to reduce risk of influenza like illness that would require isolation and testing to rule out infection with experimental viruses and raise the risk for possible co-infection with circulating influenza strains.				
NIH: Appendix G-II-C-5-c-(2) (2) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Virus specific vaccination, if available, should be offered....				
NIH: Appendix G-II-C-5-c-(2) (3) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Reporting of all respiratory symptoms and/or fever (i.e. influenza-like illnesses).				

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NIH: Appendix G-II-C-5-c-(2) (4) Risk Group 3 Influenza Viruses (BL3 Enhanced)	24-hour access to a medical facility that is prepared to implement appropriate respiratory isolation to prevent transmission and is able to provide appropriate antiviral agents. Real-time reverse transcription-polymerase chain reaction (RT-PCR) assays should be used for virus detection and to discriminate these viruses from currently circulating human influenza viruses. For exposures to viruses containing genes from 1918 H1N1...specimens shall be sent to the CDC for testing (RT-PCR and confirmatory sequencing).				
NIH: Appendix G-II-C-5-c-(3) Risk Group 3 Influenza Viruses (BL3 Enhanced)	In preparing to perform research with 1918 H1N1...Principal Investigators should develop a clear plan specifying who will be contacted in the event of a potential exposure (during and after work hours) to conduct a risk assessment and make decisions as to the required response, including the need for and extent of isolation of the exposed worker. After any kind of potential exposure, a rapid risk assessment shall be performed by the Principal Investigator, health and biosafety officials, and subsequent actions should depend on the appraised level of risk of respiratory infection for the individual and potential for transmission to others. A laboratory worker performing research with...an influenza virus containing genes and/or segments from 1918 H1N1...shall be informed in advance that, in the case of a known laboratory exposure with a high risk for infection, e.g., involving the upper or lower respiratory tract or mucous membranes, the laboratory worker will need to be isolated in a predetermined facility, rather than home isolation, until infection can be ruled out by testing (e.g., negative RT-PCR for 1918 H1N1...) of appropriately timed specimens.... The action taken for other types of exposures should be based on the risk assessment. In addition, based on the risk assessment:				
NIH: Appendix G-II-C-5-c-(3) (1) Risk Group 3 Influenza Viruses (BL3 Enhanced)	treatment with appropriate antiviral agents shall be initiated, and				
NIH: Appendix G-II-C-5-c-(3) (2) Risk Group 3 Influenza Viruses (BL3 Enhanced)	the appropriate public health authorities shall be notified.				

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NIH: Appendix G-II-C-5-c-(4) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Influenza-like illness. If an individual has entered (within ten days) a laboratory conducting research with influenza viruses containing any gene from the 1918 H1N1 virus...or housing animals exposed to such virus...and the individual demonstrates symptoms and/or signs of influenza infection (e.g., fever/chills, cough, myalgias, headache), then he/she shall report by phone to the supervisor/Principal Investigator and other individuals identified in the occupational health plan. If needed, the person with influenza-like illness shall be transported, under the appropriate isolation conditions, to a healthcare facility that can provide adequate respiratory isolation, appropriate medical therapy, and testing to determine whether the infection is due to a recombinant or synthetic influenza virus. The appropriate public health authorities shall be informed whenever a suspected case is isolated.				
NIH: Appendix G-II-C-5-c-(5) Risk Group 3 Influenza Viruses (BL3 Enhanced)	For 1918 H1N1 research, the use of antiviral agents (e.g., oseltamivir) for pre-exposure prophylaxis shall be discussed with laboratory workers in advance including a discussion of the data on the safety of long term exposure to these agents and their ability to reduce the risk of clinical disease and the limits of the data regarding protection of close contacts and the community.				
NIH: Appendix G-II-C-5-c-(6) Risk Group 3 Influenza Viruses (BL3 Enhanced)	Antiviral agents for post exposure prophylaxis shall be provided only after medical evaluation. Home supplies shall not be provided in advance for research with 1918 H1N1....				

Comments continued:

Inspector summary and comments:

Lead inspector:

Date:

Other inspectors present:

Date:

Lead inspector signature: _____

Date: _____