Advice On Working With Influenza Viruses

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Introduction

The Advisory Committee on Dangerous Pathogens (ACDP), at its meeting on 10 May 2005, discussed the need for guidance on appropriate containment for work with influenza viruses. The discussion was prompted by the incident in March 2005 concerning the distribution of a panel of proficiency testing samples containing the influenza A H2N2 virus. The Word Health Organisation (WHO) issued a statement that asked for all material associated with the distribution to be destroyed. As part of that statement, there was also a recommendation that biosafety procedures for work with similar viruses, ie those that have not circulated recently, be reviewed.

Current classification and guidance

The Approved List of Biological Agents (published in 2004) classifies influenza types A, B and C as Hazard Group 2 agents. However, there is a requirement in the Control of Substances Hazardous to Health Regulations (COSHH) (Schedule 3 para 3(1)), that where an agent with an approved ACDP classification is used, and the risk of infection is different to that expected, then a local reclassification must be carried out by the employer. Suitable containment and controls can then be selected accordingly, and in line with a local risk assessment of the activity. The local risk assessment will need to address, amongst other things, the age of those who will be undertaking the work, and the availability of prophylactic treatment.

Although there is this duty for local assessment, ACDP have produced a generic assessment of the risks of the different types of influenza viruses, which can be used as the basis for the local risk assessment. This will allow a consistent, transparent and unified approach to containment of these viruses across the UK/GB.

Some types of influenza virus will also be subject to control under animal health legislation, and different containment measures may be required in accordance with a licence issued by DEFRA under the Specified Animal Pathogens Order 1998 (SAPO) (see http://www.defra.gov.uk/animalh/diseases/pathogens/category4.htm

Any laboratory work involving the genetic modification of influenza viruses will be subject to the Genetically Modified Organisms (Contained Use) Regulations 2000. For further information on the requirements of the these regulations see http://www.hse.gov.uk/biosafety/gmo/index.htm

Recommendations for laboratories knowingly handling influenza viruses

- ACDP recommend that the following types of influenza virus should be handled at Containment Level (CL) 3:
- Highly pathogenic eg H5N1 and H7N7 and uncharacterised avian influenza viruses. These may have originated from human infections. Work with such viruses will require a licence under SAPO.
- Novel human viruses. These may have pandemic potential given that they are antigenically different from normal human viruses. If they are specified animal pathogens as defined in SAPO, a licence under this legislation will be required.
- Any animal viruses closely related to novel viruses capable of infecting humans eg H9N2 isolated from birds or H1N1 isolated from pigs. Work with these agents may also require a licence under SAPO.
- Any non-contemporary human virus eg H2N2 that caused the Asian flu pandemic in 1957 and ceased circulating in 1968

Work with all other with influenza viruses, eg with contemporary circulating human viruses, equine viruses and low pathogenicity avian influenza viruses (unrelated to those capable of causing infection in humans), can be carried out at CL2. SAPO licences are not required for work with these viruses (but see definitions in Annex 1).

Work with viruses at CL3 should be subject to review as further information becomes available. For example, further work with uncharacterised avian viruses can be carried out at CL2 if initial work indicates that the virus is non-pathogenic.

Diagnostic work

In laboratories that are not intentionally working with the viruses, Containment Level 2 should be used for clinical samples. However, CL3 is more appropriate for clinical samples, such as respiratory secretions, from patients known or suspected of being infected with the agents listed above as requiring CL3. To ascertain the risk of a patient being infected with such agents, the attending physician should determine whether the patient has recently travelled from a high risk area, and also whether there has been contact with animal species such as birds and pigs.

DEFRA advice is that SAPO licences are not required for work with human samples submitted to diagnostic laboratories for diagnosis, or for cultures of virus produced from human samples that are intended for forwarding to reference laboratories for identification purposes (for further information see Annex 1). However, a diagnostic laboratory that wishes to hold any stock a live avian influenza virus strain that is a specified animal pathogen, for diagnostic or other purposes, would need to be licensed.

Use of microbiological safety cabinets

COSHH requires that any procedures, either at CL2 or CL3, that are likely to give rise to aerosols of infectious material be carried out in a safety cabinet, or other suitable containment. Although many laboratory activities (eg centrifugation) are known to generate aerosols, other routine tasks (eg slide agglutination and even opening ampoules) may also have the potential for aerosol production. When carrying out such activities with biological agents that are infectious by the respiratory route such as influenza viruses, the assessment should reflect this risk and therefore be carried out in suitable containment.

The use of close-fronted microbiological safety cabinets (ie Class III cabinets or Class I/III cabinets in Class III mode) should be considered when handling the more virulent strains of virus eg the Indonisian strain.

Planning for pandemics

During the first stages of a human pandemic, ie before a strain is routinely circulating in the UK, then all intentional work with such viruses should be carried out at CL3. However, once the virus is the predominant circulating strain and a vaccine is available, it can be handled at CL2. However, if available information indicates that virus is still highly virulent even though it is the predominant strain, then CL3 is still appropriate.

As with intentional work with pandemic strains, once a strain is routinely circulating in the UK and a vaccine is available, then diagnostic work previously carried out at CL3, can be carried out at CL2. If the work required the use of a cabinet at CL3, then cabinets will still be required even at CL2. Again, if information indicates that the circulating strain is still highly pathogenic, then CL3 is appropriate for work involving microbiological examination of respiratory secretions. If space to carry out a large volume of this type of work at CL3 is limited, then such work may be carried out at CL2, provided it takes place in a microbiological safety cabinet. Suitable cabinets located in other departments within pathology may need to be identified as part of the planning process.

Please note that the Health and Safety Executive must be notified of any

- first use of a biological agent (hazard group 2, 3 or 4) at a particular premises; and
- subsequent use of any agent listed in Part V of Schedule 3 of the Control of Substances Hazardous to Health Regulations 2002 (as amended).

Further information about the notification process can be found at
https://www.hse.gov.uk/forms/notification/cba1notes.htm

Queries about licensing under SAPO/DEFRA containment requirements for avian influenza viruses and the application of SAPO to genetic material derived from such viruses can be obtained from:

The Pathogens Licensing Team
Area 607
1A Page Street
London SW1P 4PQ
Tel: 020 7904 6144

For specific virological information eg about replicating the virus, contact:

HPA Enteric, Respiratory and Neurological Virus Laboratory
61 Colindale Avenue
London NW9 5DF
Tel: 020 8200 4400 ext 3016

For enquiries relating to specific legal/technical issues (such as risk assessment or containment measures or detailed interpretation of H&S legislation or guidance you should contact:

The Specialist Inspector Team
HID Specialised Industries SI4
Health and Safety Executive
Magdalen House
Stanley Precinct
Bootle
Merseyside L20 3QZ
Tel: 0151 951 3779
Fax: 0151 951 3474
Email: germs.gmos@hse.gsi.gov.uk

For advice on general government policy on safety issues relating to micro-organisms and GMOs you should contact:

Biological Agents and GMOs team
Policy Group
Health and Safety Executive
Rose Court
2 Southwark Bridge
London SE1 9HS
Tel: 020 7717 6206
Fax: 020 7717 6199
Email: BA&GMOs.Policy@hse.gov.uk

Annex 1

GUIDANCE ON THE APPLICATION OF THE SPECIFIED ANIMAL PATHOGENS ORDER 1998 (SAPO) TO WORK WITH AVIAN INFLUENZA VIRUSES

The Specified Animal Pathogens Order 1998

Animal pathogens that can cause serious diseases in farmed livestock and poultry are controlled under the Specified Animal Pathogens Order 1998 (SAPO). The purpose of the Order is to prevent the introduction and spread into Great Britain of specified animal pathogens which, if introduced, could cause serious disease and economic loss to the British livestock and poultry industries.

Avian influenza viruses that are:

(a) uncharacterised; or
(b) type A viruses which have an intravenous pathogenicity index in six week old chickens of greater than 1.2; or
(c) type A viruses H5 or H7 subtype for which nucleotide sequencing has demonstrated multiple basic amino acids at the cleavage site of haemagglutinin.

are specified animal pathogens and are controlled under SAPO.

SAPO prohibits people from having avian influenza viruses that are specified animal pathogens in their possession, or carriers (living creatures except man or materials derived from them known to contain a specified animal pathogen), unless they have a licence authorising them to do so. It also prohibits the introduction into any animal or bird of any avian influenza virus that is a specified animal pathogen, except under licence.

To be considered for licensing to hold and work with avian influenza viruses that are specified animal pathogens, laboratories must meet DEFRA's containment and operating requirements for DEFRA Group 4 specified animal pathogens (see www.defra.gov.uk/animalh/diseases/pathogens/category4.htm)

DEFRA administers SAPO in England, but the Scottish Executive Environment and Rural Affairs Department (SEERAD) and the Office of the Chief Veterinary Officer at the Welsh Assembly Government are responsible for administering the Order in Scotland and Wales respectively. Similar but separate legislation is administered in Northern Ireland by the Department of Agriculture and Rural Development Northern Ireland (DARDNI).

Additional guidance notes

- SAPO is concerned only with the control of specified animal pathogens once they are in Great Britain.
- Human diagnostic samples are not carriers under SAPO.
- Diagnostic or clinical laboratories do not need SAPO licences if they hold inactivated avian influenza viruses that are specified animal pathogens for use as control materials.
- Clinical /diagnostic laboratories do not require SAPO licences if they culture suspected avian influenza virus from human diagnostic samples for forwarding to reference laboratories for identification or confirmation of identification.
- The requirements of both COSHH and SAPO apply to the handling of avian influenza viruses that are specified animal pathogens. Neither takes precedence. COSHH requirements relate to the risk the pathogens pose to humans, while SAPO requirements relate to preventing the spread of specified animal pathogens from the laboratory to the environment, causing disease in farmed livestock and poultry.

- In the event of an outbreak of avian influenza in birds in this country, samples taken from humans for diagnosis should be submitted to HPA or other human diagnostic laboratories for testing, not to veterinary laboratories. Samples taken from birds (and any other animals) should be submitted to a veterinary laboratory.

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