

## **Advisory Committee on Dangerous Pathogens**

### **Containment and control for work with influenza viruses**

#### **Issue**

1. Consideration of the need for guidance on the containment for work with influenza viruses.

#### **Background**

2. Members will be aware of the recent incident concerning the distribution of a panel of proficiency testing samples containing the influenza A H2N2 virus. WHO has issued a statement (Annex 1) that asks for all material associated with the distribution to be destroyed. As part of that statement, there is also a recommendation that biosafety procedures for work with similar viruses ie those that have not circulated recently, be reviewed.

3. Members may recall that they have already issued specific advice on containment on work with other influenza viruses ie avian influenza (Annex 2).

#### **Current classification and guidance**

4. The Approved List of Biological Agents currently 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 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.

5. Although there is this duty for local assessment, HSE and ACDP are being approached to provide advice on individual assessments. It would be seem preferable for a generic assessment of the risks of the different types of influenza viruses be carried out which can then be used a basis for local assessment. This will allow a more consistent, transparent and unified approach to containment, and avoid the need to provide advice on an ad-hoc basis.

6. Some work to classify the different types of viruses has already been carried out following the most recent H5N1 outbreaks, to inform the consequent research and development work being carried out in the UK.

### **Proposed classification and containment**

7. The work on suggested classification and containment conditions has been reviewed by HSE, and is shown in Annex 3. This classification identifies the containment conditions to protect both human and animal health (under COSHH and SAPO respectively). Although the remit of ACDP is to provide advice on infection risks to humans, given that the committee also advises DEFRA, and that many of the viruses in question are zoonotic, it would seem preferable that any advice issued by ACDP addresses both COSHH and SAPO containment requirements.

8. Members are invited to discuss the proposed recommended classification. In particular, members' views are sought on the most appropriate classification for the swine virus group.

### **Work with genetically modified influenza viruses**

9. Some of the work being carried out with the different groups of influenza viruses will involve genetic modification with the potential to increase virulence (eg introduction of mutations in the NS1 gene), or attenuate the virus (eg HN and N2 in a PR8 backbone). Given the potential complexity of the issue, it is recommended that this should be referred to SACGM for further consideration.

### **Actions**

10. Members are invited to discuss and agree the classification of the different influenza virus groups.

**Secretariat**

**May 2005**



# World Health Organization

## **International response to the distribution of a H2N2 influenza virus for laboratory testing: Risk considered low for laboratory workers and the public\***

**12 April 2005**

The Public Health Agency of Canada (PHAC) informed WHO on 26 March that an influenza A/H2N2 virus was identified by a local laboratory in Canada. The H2N2 virus identified was found to be similar to H2N2 viruses that circulated in humans in 1957-58 at the beginning of the so-called Asian influenza pandemic. The H2N2 virus which circulated at this time was fully transmissible among humans. It continued to circulate in humans and cause annual epidemics until 1968, when it vanished after the emergence of influenza A/H3N2 viruses that caused the next pandemic. Therefore, persons born after 1968 are expected to have no or only limited immunity to H2N2. H2N2 virus is not contained in current trivalent influenza vaccines.

Appropriate biosafety measures were immediately taken at the involved laboratory in Canada and respiratory surveillance measures initiated. Subsequent investigation by the Public Health Agency of Canada traced the source of the H2N2 virus to a panel of proficiency testing samples containing influenza A and influenza B viruses which the Canadian laboratory received from the College of American Pathologists (CAP) in February 2005. CAP routinely sends various panels of proficiency testing samples to participating laboratories every year. Normally, currently circulating influenza A viruses (H3N2; H1N1) are used for proficiency testing. The H2N2 virus was distributed by CAP for the first time in October 2004.

WHO, the Department of Health and Human Services (HHS) in the USA and its Centers for Disease Control were informed of the situation by PHAC on 8 April. Subsequent investigation revealed that similar proficiency testing samples with H2N2 virus were sent to 3747 laboratories in 18 countries. Sixty one of these laboratories are located in 16 countries outside the USA and Canada ([see list of countries and areas below](#)). HHS has recently learnt that other proficiency testing providers have sent additional H2N2 containing samples to further laboratories in the USA. HHS is taking steps to ensure the rapid destruction of this material.

On 8 April, after a request by the US government, CAP asked all laboratories which participated in the proficiency testing to immediately destroy samples containing the H2N2 virus. On 12 April, a second correspondence from CAP to these laboratories further requested that destruction of the H2N2 virus be confirmed and that any case of respiratory disease

among laboratory workers be investigated and notified to national authorities. WHO has received the list of addresses of the involved laboratories and has provided detailed contact information to the relevant Ministries of Health and requested their collaboration.

As of today, there have been no reports of H2N2 infections in laboratory workers associated with the distribution of the H2N2 samples from CAP. The proper use of biological safety cabinets, along with the use of recommended personal protective equipment, greatly reduces the risk of laboratory-acquired influenza infections. While a few H2N2 laboratory acquired infections have been documented in the past, the likelihood of laboratory-acquired influenza infection is considered low when proper biosafety precautions are followed. The risk for the general population is also considered low. As a precautionary measure, WHO is recommending that all samples of the proficiency testing panel from CAP and any other proficiency testing providers containing H2N2 and any derivatives be destroyed immediately. WHO further recommends that biosafety procedures be reviewed for use on influenza viruses that have not circulated recently in humans and against which the majority of the population would have no protective immunity.

**\*List of countries and areas**

Bermuda  
Belgium  
Brazil  
Chile  
France  
Germany  
Hong Kong Special Administrative Region of China  
Israel  
Italy  
Japan  
Lebanon  
Mexico  
The Republic of Korea  
Saudi Arabia  
Singapore  
Taiwan, China

## **Advice on Assessing the Risks of Working with Highly Pathogenic Avian Influenza Virus**

The Advisory Committee on Dangerous Pathogens (ACDP), at its meeting on 19 March 2003, discussed the reports of influenza A virus subtype H5N1 (a highly pathogenic avian influenza [HPAI] strain) in Hong Kong and considered the implications for laboratory workers in the UK. Since the meeting an outbreak of influenza A subtype H7N7 was recognised in the Netherlands, which also extended to Belgium and Germany.

There are several strains of HPAI, including subtypes H5N1 and H7N7; the importation and holding of these viruses falls under the responsibility of the Department for Environment, Food and Rural Affairs (Defra). Laboratories who wish to import and work with these strains will need to meet the appropriate legal requirements<sup>1</sup>. At the present time, the HPAI strains are being handled in only a few designated laboratories in the UK for investigative purposes.

However, there is the possibility that other laboratories may receive specimens from patients returning from Hong Kong, the Netherlands, Belgium and Germany, who have conjunctivitis and/or febrile respiratory illness, and workers in these laboratories may be concerned about the containment measures required. [Note: if there is any indication that a patient has returned from a SARS-affected area, there is specific advice for handling such specimens provided by the Health Protection Agency, the World Health Organisation and the Health and Safety Executive.]

- [Click here for more information on SARS](#)

A risk assessment must be performed, and the results of this assessment communicated to laboratory staff, before work starts with the agent. All staff potentially handling specimens containing such viruses should be given detailed information and instructions on the hazard and the measures needed to reduce the risk of exposure to the agent.

**The ACDP makes the following recommendations:**

### **Laboratories knowingly handling influenza A virus subtypes H5N1 and H7N7**

For deliberate work with these agents laboratories are required to meet the requirements of Defra. These requirements are primarily to prevent environmental spread of a biological agent.

In addition, in order to protect workers from potential exposure, the appropriate containment level (CL) for working with these agents must be selected after performing a full risk assessment that takes into account the risks presented by the strain of virus and the type of work that will be carried out in the laboratory.

ACDP recommends that CL3 is appropriate for work involving this virus. The use of close-fronted microbiological safety cabinets should be considered (ie Class III cabinets or Class I/III cabinets in Class III mode).

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.


Further information about the notification process can be found in the [sixth edition of the Biological Agents Bulletin](#).

#### **Other clinical laboratories**

In laboratories that are not intentionally working with the virus, 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 these agents. To ascertain the risk of a patient being infected with influenza A strains H5N1 or H7N7, the attending physician should determine whether the patient has recently travelled from a high risk area. [Note: the physician should also have considered the risk of a patient having been exposed to SARS; see previous paragraph for links to relevant advice.] Again, the use of close-fronted microbiological safety cabinets should be considered (ie Class III cabinets or Class I/III cabinets in Class III mode). However, if Class I/III or III cabinets are not available a standard Class I cabinet should be sufficient for initial diagnostic work.

If there is an intention to replicate the virus, specific advice should be sought from the Health Protection Agency (HPA) Enteric, Respiratory and Neurological Virus Laboratory.

## Description and classification of Influenza viruses

Group	Description	ACDP	SAPO
1	Highly pathogenic (HP) and uncharacterised avian influenza viruses. These viruses may be from human infections (e.g. human H5N1 and H7N7 viruses). If the uncharacterised viruses are subsequently found non-pathogenic (NP), derogation to Group 6 should be evaluated	3	4
2	Newly isolated human pandemic virus. This will be a novel human virus (ie susceptible populations) and may be either highly pathogenic or non-pathogenic.	3	4 
3	Novel human influenza viruses. These viruses (eg human H9N2 viruses) will be antigenically different from normal human viruses and may be considered to have pandemic potential. There may be limited or no evidence of person to person transmission. It is expected that the viruses will be of avian origin, so DEFRA approval will be required.	3	3
4	Animal viruses closely related to novel viruses capable of infecting man (eg H9N2 viruses isolated from birds or pigs).	3	3
5	Human H2N2 viruses. These viruses caused the 'Asian flu' pandemic of 1957 and ceased to circulate in 1968. People born after 1968 may be susceptible to infection	3	n/a
6	Non-pathogenic avian viruses, unrelated to viruses capable of infecting man.	2	n/a
7	Swine viruses. Some of these are related to older human viruses (eg H1N1 of 1930's), some are related to newer human viruses and others are related to avian viruses. As humans are known to be susceptible to swine viruses, there is a greater hazard than that associated with most avian viruses	? 2 or 3	n/a
8	Equine viruses.	2	n/a
9	Normal human influenza viruses, including clinical specimens.	2	n/a