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ACDP/82/P5

Advisory Committee on Dangerous Pathogens

Animal Isolators for Small Animals Infected with Biological Agents – First Draft

Issue

1. Consideration of the overall framework proposed for the guidance document '*Animal Isolators for Small Animals Infected with Biological Agents'*.

2. Consideration of the suitability and practicability of the tests proposed at installation.

Background

3. HSE is updating and replacing the 1985 ACDP publication: '*Guidance on the Use, Testing and Maintenance of Laboratory and Animal Flexible Film Isolators*'. This is intended to be a web-based document with the ability to update and add additional sections when they become available.

4. The paper proposes a framework for the document; following recommendations made at this meeting, the next draft of the guidance will go for wider consultation (including ACDP members). Other proposed consultees are listed in Annex A.

5. The document will be subsequently revised and will be presented as a substantive item at the next meeting of ACDP.

Scope

6. The guidance will only cover negative pressure isolators practicable to be used for containing small experimental animals (predominantly rodents but up to and including rabbits) infected with biological agents.

7. The guidance will not cover:

- isolators used for human patients – these will be the subject of future Viral Haemorrhagic Fever guidance.

- other systems such as individually ventilated cages, ventilated chambers, mini-rooms, downdraught tables used for infected animals – these may be the subject of future updates when relevant information becomes available.

The Guidance

8. An outline framework for the document is presented at Annex B. This gives a general overview of the different headings planned, which will be worked up with more text.

9. Part 6 of the document contains more detailed descriptions of the proposed tests which should be undertaken when commissioning the isolators.

Action

10. Members are invited to:

a) review and discuss the scope given in paragraphs 7 and 8 above.
b) review and discuss the outline framework in Annex B and to comment in particular on the general format, structure and order'. Also to note whether there are any omissions or whether certain points should be removed
c) review and discuss the suitability and practicability of the tests proposed at installation (Section 6), including consideration of the 7 Drafting Notes in the body of the text
d) comment on the appropriateness of the consultation list in Annex A

Secretariat

January 2006

Annex A

Proposed Consultation list

Sector	Representatives
Government Committees	ACDP SACGM
Regulators	Home Office – policy & inspectorate DEFRA – policy & inspectorate
Selected Users	MRC IAH VLA Moredun HPA (Colindale) CEPR DSTL University Vet Schools
Commercial Companies	E.g. Bell Isolators, PrimaTec, pfi systems, Crowthornes, Tecniplast, ACE Caging, Harlan Isotec
UK professional bodies	Institute of Animal Technology
European/wider perspective	European Federation Of Animal Technology

Annex B

ANIMAL ISOLATORS FOR SMALL ANIMALS INFECTED WITH BIOLOGICAL AGENTS

1. BACKGROUND

2. INTRODUCTION

Will cover issues such as:

- Guidance replaces 1985 publication: 'Guidance on the Use, Testing and Maintenance of Laboratory and Animal Flexible Film Isolators'
- Guidance focuses on negative pressure isolators for containing small animals (predominantly rodents but up to and including rabbits) infected with biological agents
- Guidance will focus on use, testing and maintenance of isolators: will not cover generic 'strategies' for working with infected animals
- Guidance will not cover other systems such as individually ventilated cages, ventilated chambers, mini-rooms, downdraught tables: they may be the subject of future updates
- Guidance will not cover isolators used for human patients: these will be covered in future Viral Haemorrhagic Fever guidance

3. LEGAL REQUIREMENTS

3.1 Health & Safety Issues

3.1.1 Biological Agents

- Guidance will focus on the Control of Substances Hazardous to Health Regulations (COSHH) and the Genetically Modified Organisms (Contained Use) Regulations and the control of aerosols of biological agents using Microbiological Safety Cabinets (MSC), isolators or equivalent.

3.1.2 Other Health & Safety issues

- Guidance will explore manual handling/ergonomics/human factors issues associated with working in isolators.
- Will briefly reference other issues e.g. optical clarity, lighting, noise levels, humidity, electrical and temperature etc

3.2 Animal Welfare Issues

- Guidance will explore animal welfare requirements specified by the Animals (Scientific Procedures) Act 1986; there will be consultation with Home Office).

3.3 Environmental Issues

- Guidance will explore exotic animal containment under Specified Animal Pathogens Order; there will be consultation with the Department of Environment, Food and Rural Affairs.

4. USE OF ANIMAL ISOLATORS

- Generic introduction including diagrammatic representation of air flows, locations within labs etc

5. TYPES OF ANIMAL ISOLATORS

- Basic description of 3 main types of negative pressure isolators. Will include images:

5.1 Flexible Film Isolators

5.2 Rigid Isolators

5.3 Half suit isolators

6. TESTING ANIMAL ISOLATORS AT INSTALLATION (OR AFTER MAJOR CHANGES)

6.1 *Air Leaktightness*

6.1.1 Positive pressure hold test

- Current MSC Standard (EN BS 12469:2000[1]) for Class 3 MSC requires 500 Pa overpressure. Film isolators unlikely to be able to meet this; rigid isolators more likely to. Practicable alternative for film isolators is overpressure of between 150 Pa and 250 Pa as determined by supplier.
- [**DN1 – Do Members feel that the containment level for work within the isolator should influence the minimum overpressure? e.g. should all isolators used for HG3/4 work be able to be overpressured to 250 Pa?]**
- Test involves no more than a 10% loss of pressure when the isolator is overpressured and held for 30 minutes.

6.2 Leak detection

[1]Biotechnology – Performance criteria for microbiological safety cabinets

- The positive pressure hold test described above can be challenging to achieve as well as being somewhat crude; because it relates to leak rates, the larger the isolator volume, the greater the possible leak rate before failure. As such direct testing of the system by leak detection should be undertaken in addition to the pressure hold test.

6.2.1 Particle Tracer test

- This is the recommended method for leak testing. Method using dispersed oil particles (DOP – particles of Ondina food oil) very sensitive and relatively easy to perform (uses standard equipment for testing HEPA filters). Use photometer to scan all seals, filter housings etc.
- Can be done at the same time as the positive pressure hold test

[**DN2 – The NaCl method described in the 1985 guidance is no longer considered appropriate. Whilst tracer gas (helium) is used in pharmaceutical isolator applications, this involves additional equipment of varying cost. Do Members agree that the DOP test be the recommended method for animal isolators?]**

- The following non-exhaustive list of test may be used in addition to the DOP test.

6.2.2 Soft soap

- Overpressurise and monitor all welds, gaskets etc. A simple and effective test, but not as sensitive as tracer testing and is also messy.

6.2.3 Smoke pencil

- Overpressurise and monitor all welds, gaskets, joints filter housings etc. Only likely to identify gross leaks - may not give the sensitivity required for smaller leaks.

[DN3 - Leak testing with biological tracers is not considered practical for most people. Do Members agree that this should not be listed in the range of tests?]

[DN4 – The MSC BS specifies an apf of $1x10^5$ for open fronted cabinets. No equivalent for Class 3 MSC nor enclosed isolators. May be difficult to test (specialist knowledge and equipment). Do Members agree that this should not be listed in the range of tests, even for high containment work?]

6.3 *Filters*

- H14 HEPA filters, meeting the relevant standard (BS EN 1822:2000) must be in place for both the supply and extract air; double HEPA

filters are required if the exhaust air is to be re-circulated into the laboratory.

- The filters must be seated appropriately and all must be fitted with access ports to allow independent, full face scan testing. The test should meet the standard.

6.4 *Negative pressure*

- A working pressure of at least 30 Pa below the air pressure of the laboratory should be maintained within flexible isolators. For rigid isolators, particularly those with half-suits, this differential may need to be higher to compensate against potential pressure fluctuations during use, particularly when operatives enter the gloves/suits.
- As a minimum, positive pressurisation must not occur during normal working practices.

6.5 *Air flows rates*

- In the event of a major breach in the isolator envelope, an inward air velocity needs to be maintained. The BS for a Class 3 MSC identifies a major breach as analogous to the removal of an entire glove/gauntlet where a minimum inward air velocity of 0.7 m/s is required to be maintained. This can be replicated in an isolator.

[**DN5 – The 1985 guidance had no equivalent; do Members feel that this is a valid test?]**

6.6 *Air change rates*

- The rapid removal of potentially contaminated air through the exhaust filters reduces the likelihood of accidental exposure. Higher air change rates (e.g. 40 air changes per hour – ach) may be required for specific procedures where aerosols are generated, but are unlikely to be appropriate long term from an animal welfare perspective.
- For routine activities, a minimum of 20 ach should be in place.

[DN6 – 1985 guidance recommended minimum of 13 ach whereas BS EN 12741:1999[2] recommends 20 ach. Do Members agree that 20 ach should be set for newer systems whereas 13 ach may need to be retained for older systems?]

[**DN7 – the following sections 7&8 are to be completed. Members are asked to advise on whether anything is missing or should not be listed]**

7. MAINTENANCE TESTING OF ANIMAL ISOLATORS

[2] Biotechnology – Laboratories for research, development and analysis – Guidance for biotechnology laboratory operations

- LEV regularly examined & tested at intervals of not more than 14 months. At containment levels 3 & 4 recommend that this be done every 6 months
- Calibration of manometer
- Testing of alarms
- All surfaces examined for defects, cracks & other damage
- Check anti blowback valve functioning
- Filter & seal integrity
- Airflow through each open glove port – at least 0.7 m/s
- Airflow at face of inlet filter – indication of filter blockages over time

8. IN-USE TESTING OF ANIMAL ISOLATORS

- Continuous monitoring of alarms
- Regular observations of wear and tear
- Should be kept clean and free of unnecessary equipment
- Should be easy to clean/sterilise
- Entry filter checked with anemometer each week if in daily use or monthly if used less frequently; indication of blockages over time

9. REFERENCES