

An Independent Review of the Highest Level Microbiological Containment Facilities in the UK

Led by

**Professor George E Griffin PhD, FRCP, FMedSci
St George's, University of London**

Presented to the Health Protection Agency, the Medical Research Council, the Biotechnology and Biological Sciences Research Council and the Department for the Environment, Food and Rural Affairs

OCTOBER 2008

REDACTED REPORT PREPARED FOR WIDER CIRCULATION.

DELETED MATERIAL IS SUBJECT TO THE FREEDOM OF INFORMATION ACT DISCLOSURE EXEMPTIONS INDICATED.

ABBREVIATIONS

ACDP	Advisory Committee for Dangerous Pathogens
ASM	American Society for Microbiology
BBSRC	Biotechnology and Biological Sciences Research Council
CDC	Centers for Disease Control (at Atlanta, USA)
CL4	Containment Level 4 for human pathogens
COSHH	Control of Substances Hazardous to Health
DA	Devolved Administration (Wales, Scotland or Northern Ireland)
DEFRA	Department for Environment, Food and Rural Affairs
DH	Department of Health
EC	European Commission
EU	European Union
GAO	Government Audit Office (of the USA)
GMO	Genetically Modified Organism
GMO(CU)	Genetically Modified Organism (Contained Use)
HPA	Health Protection Agency
HSE	Health and Safety Executive
MRC	Medical Research Council
NaCTSO	National Counter Terrorism Security Office
NEPNEI	National Expert Panel on New and Emerging Infections
NIH	National Institutes of Health
PCR	Polymerase Chain Reaction
SACGM	Scientific Advisory Committee for Genetic Modification
SAPO	Specified Animal Pathogens Order 1998
SAPO4	Containment Level 4 for animal pathogens
UK	United Kingdom
USA	United States of America

CHAIRMAN'S STATEMENT

This review was sponsored by the Health Protection Agency, the Medical Research Council, the Biotechnology and Biological Sciences Research Council and the Department for Environment, Food and Rural Affairs. Its purpose was to generate an evidence base to aid the development of policies for maintaining the UK's strategic capacity to work with human and animal pathogens at the highest level of containment.

The review confirmed that the UK public sector needs access to modern, secure and effective high level containment facilities for work with human and animal pathogens. It identified all the facilities in the UK that are currently approved to work with these pathogens and reviewed their location, capacity and infrastructure along with any plans for refurbishment or renewal. It concluded that the current demand for high containment facilities in the UK is being met but there is little spare capacity and some of the facilities are in urgent need of replacement.

It acknowledged that the cost of providing, running and maintaining high containment facilities was high and sufficient funding needs to be secured from the public sector to maintain a national strategic capability. Failure to provide this funding will result in a general decline in the physical infrastructure of high containment facilities across the UK with the loss of both diagnostic and research capacity and the associated skill base.

Information obtained during the review indicated that the number of staff trained to work in high containment environments is relatively small making it essential for employing organisations to routinely review their staffing levels and succession plans. The review found that current training programmes for staff working in high containment facilities were adequate but they lacked consistency and transferability. It concluded that benefit would be derived from a unified training strategy to facilitate the interchange of staff between different facilities.

Finally, the review concluded that there was considerable potential to improve communications between all those involved in the design, building, operation and maintenance of high containment facilities. Some networks capable of achieving this already operate but full advantage of their potential is rarely taken. Innovative thinking may be required to network those groups such as architects, design engineers and, indeed, the emergency services to share best practice. There is a significant opportunity to use these networks to increase the visibility of UK expertise in this area and so enhance the UK's reputation across Europe for the safe handling of human and animal pathogens.

November 2008

Professor George E Griffin PhD, FRCP, FMedSci
St George's, University of London

CONTENTS

Abbreviations.....	2
Chairman’s Statement.....	3
Contents.....	4
Executive Summary.....	5
1. Introduction.....	7
2. Review Procedure.....	8
3. Need for high level containment facilities.....	9
4. Legislative and regulatory framework.....	12
5. Containment requirements for working with ACDP CL4 and SAPO4 pathogens.....	15
6. Locations and funding of high containment facilities.....	17
7. The physical infrastructure of UK high containment facilities.....	20
8. Horizon scanning and international perspective.....	24
9. Staffing levels and training.....	27
10. Conclusions and ways forward.....	30

ANNEXES

1. Terms of Reference for the review.....	35
2. Steering Committee Members.....	36
3. Stakeholder consultation statistics.....	37
4. Pathogens requiring access to high containment facilities.....	38
5. Containment measures for high containment laboratories depending on COSHH, SAPO and GMO(CU) requirements.....	39
6a. UK High Containment Facilities – General information.....	41
6b. UK High Containment Facilities – Physical infrastructure.....	44
6c. UK High Containment Facilities – Animal species and holding capacity.....	45
7. Staffing and training.....	46
8. Strengths, weaknesses, opportunities and threats for the UK’s high containment facilities.....	48

EXECUTIVE SUMMARY

- The UK public sector needs modern, secure and effective high level containment facilities in which the full range of microbiological work can be done with ACDP CL4 and SAPO4 (para 3.1).
- Advances in modern technology have replaced some of the need for highest level microbiological containment facilities (particularly those used for diagnostic assessments) but even in the face of these advances there will always be the need for laboratories to perform *in vivo* experiments and to isolate micro-organisms and biological samples (para 3.6).
- The current demand for high containment facilities in the UK is being met but there is little spare capacity. It was concluded that horizon scanning for future needs is difficult and unpredictable and needs to be kept under routine review in order to accommodate new technologies, regulations or research requirements (para 8.2).
- Sufficient funding needs to be secured to support the running costs of maintaining a national strategic capacity to work with ACDP CL4/SAPO4 pathogens. Failure to provide this funding will result in a general decline in the physical infrastructure of high containment facilities across the UK with the loss of both diagnostic and research capacity and an associated skill base (para 6.12).
- Replacing the ageing high containment facilities at (details removed under FoI S24 Exemption) is essential if the UK's strategic capacity for working with ACDP CL4 and SAPO4 pathogens is to be maintained over the longer term (para 7.4).
- Decisions are urgently needed on whether additional funds will be made available for the replacement and expansion of the SAPO4 laboratory complex at (details removed under FoI S24 Exemption) and whether the original plans need to be modified (para 7.12).
- Decisions on the geographical location of high containment facilities should be based on a robust, multi-faceted risk assessment in which microbiological science and all aspects of security, safety, and public opinion are considered and on the existence of good links to academic centres of excellence (para 6.6).
- Employing organisations should routinely review their staffing levels, succession plans and training commitments to ensure that a critical mass of trained staff with the expertise necessary to work at ACDP CL4 and SAPO4 containment levels in the UK is not lost (para 9.2).
- Current training programmes are adequate but benefit would be derived from a unified training strategy to facilitate staff interchange between different facilities. Future training programmes will need to contain both theory and competency based aspects and complement local programmes based on site-specific standard operating procedures (para 9.8).

- The capacity to handle large animals, in particular non-human primates, infected with ACDP CL4 pathogens is extremely limited. This poses a potential gap in the UK's future research capability (para 7.5).
- Capital and recurrent expenditure for ACDP CL4/SAPO4 facilities is very high. There is scope to meet the UK's needs by creating a number of well resourced, modern, flexible and effectively integrated facilities which could fulfil their strategic functions and be made available to external contractors, notably the academic community and industry (para 10.15).

1. INTRODUCTION

- 1.1 The purpose of this report is to review all the facilities in the UK capable of working at the highest level of microbial containment. These facilities are those approved to work with human and zoonotic (ACDP CL4) and animal (SAPO4) pathogens as defined by the Health and Safety at Work etc Act 1974 and the Animal Health Act 1981. The Terms of Reference for the review are given in Annex 1. The report was commissioned by the Health Protection Agency (HPA), the Medical Research Council (MRC), the Biotechnology and Biological Sciences Research Council (BBSRC) and the Department for Environment, Food and Rural Affairs (DEFRA) to inform policy development for making continuing investments in high level containment facilities.
- 1.2 Access to high containment laboratories is essential to the better understanding of ACDP CL4 and SAPO4 pathogens and for maintaining the UK's capacity for early detection and intervention in the resulting human and animal diseases. Access is also needed to underpin the UK's emergency response capacity to incursions of exotic disease, whether this occurs naturally or as the result of terrorist activity. However, high containment laboratories are expensive to build and expensive to maintain. A national strategy for their continued provision that optimises opportunities for collaboration is therefore essential.
- 1.3 Providing the physical infrastructure associated with high containment laboratories is only part of the equation. Skilled staff are also needed to operate and maintain the facilities. There is a legal requirement placed upon Government sponsors and the funders of high containment laboratories not only to protect these workers from the risk of exposure to dangerous pathogens but also to protect the public and the environment from accidental releases. Suitable staff training programmes need to be available and a national strategy for coordinating and achieving this is considered advantageous.
- 1.4 This review aims to be factual and produce a context which can facilitate the development of the required national strategies. This cannot be done in isolation as it is also influenced by regulatory and managerial frameworks that operate and these, in turn, have to be seen in a wider international, and particularly European, context. These issues therefore formed a strategic part of the overall review.

2. REVIEW PROCEDURE

- 2.1 This review was overseen by a Steering Committee composed of representatives from the HPA, MRC, BBSRC, the Department of Health (DH) and DEFRA. The Steering Committee was chaired by Professor Griffin (St George's, University of London) who, with Professor Rowlands (University of Leeds), formed a small independent Review Team that visited sites in the UK, France and the USA; Dr Greenaway (Horus Research Management Ltd) provided secretariat functions. The Review Team had freedom to operate independently of the Steering Committee and was responsible for producing the final report.
- 2.2 The Steering Committee was advised by experts from the HPA, the Defence Science and Technology Laboratories (DSTL), the Health and Safety Executive (HSE) and the National Counter Terrorism Security Office (NaCTSO). A full listing of the Steering Committee members, their advisers and their affiliations is given in Annex 2.
- 2.3 The remit of the Steering Committee was to agree the review terms of reference and to facilitate the review process. Steering Committee members were given the opportunity to seek clarification of the issues raised and to comment on the accuracy of the review findings and the conclusions it contained. The Steering Committee received and approved the final review report on behalf of the sponsor organisations, after receiving advice from NaCTSO.
- 2.4 A total of 92 organisations or individuals were contacted and comments requested on issues associated with the provision of the highest level microbiological containment facilities for handling ACDP CL4/SAPO4 pathogens in the UK. The overall response rate was approximately 67% and a total of 28 written responses were obtained (Annex 3).
- 2.5 The Review Team also visited nine of the highest level containment facilities in the UK. In addition, and in order to get a wider strategic assessment, visits were also made to the facility at Lyon, France and to the Government Audit Office, the American Society for Microbiology and the National Institutes of Health, all in Washington DC, USA.

3. NEED FOR HIGH LEVEL CONTAINMENT FACILITIES

- 3.1 **The UK public sector needs modern, secure and effective high level containment facilities in which the full range of microbiological work can be done with ACDP CL4 and SAPO4 pathogens.** This is essential for diagnostic work, research and development and for national security, particularly with respect to bioterrorist threats. These needs apply to both the human medical and veterinary sectors.
- 3.2 Diseases caused by ACDP CL4 and SAPO4 pathogens, those needing the highest level of containment for handling, are generally rare in the UK but with modern travel infected individuals and legally or illegally imported infected susceptible animals or animal products can arrive from anywhere in the world well within the associated disease incubation period. The risk to humans is managed by the existence of robust public health policies which are routinely reviewed. It is managed in relation to animal disease, by regulatory controls on the import of animals/animal products which reflect the Government's knowledge of diseases present in their country of origin. Nonetheless, incursions of exotic animal disease can occur through import of animals from countries with undisclosed disease, via wild birds and other migratory species, or through illegal imports. It is essential for the UK to maintain a robust and rapidly mobilised diagnostic capability for both human and animal disease to enable appropriate interventions and identification of infected human or animal contacts to be made quickly.
- 3.3 Diagnostic laboratories capable of handling ACDP CL4 pathogens are likely to experience high levels of demand early following the diagnosis of the index case and until the infection has been contained and/or eradicated. High level containment laboratories for ACDP CL4 pathogens therefore have to be maintained and ready for use at all times. They must also be capable of accommodating surge capacity in the event of an emergency.
- 3.4 In the case of incursions of exotic animal disease, the level of demand for diagnostic testing depends on the number and size of the infected premises. However, the largest demand on diagnostic capacity occurs during post-outbreak surveillance work, which is undertaken on all susceptible stock deemed to be 'at risk'. This provides evidence of disease freedom in the animal population as a whole and is necessary to secure the re-opening of markets for International Trade.
- 3.5 It is important to recognise that the diagnostic, and hence containment, requirements for human and animal pathogens offer quite different challenges and the laboratories capable of providing the required diagnostic capability can not always be seen as interchangeable except under very specific and emergency situations.

- 3.6 **Advances in modern technology have replaced some of the need for highest level microbiological containment facilities (particularly those used for diagnostic assessments). However, even in the face of these advances there will always be the need for laboratories to perform *in vivo* experiments and to isolate micro-organisms and biological samples** for definitive identification, to determine antimicrobial sensitivity, to produce some of the diagnostic reagents (antigens, antibodies or nucleic acids) required in specific tests and provide new vaccines in epidemic situations.
- 3.7 There are already a substantial number of pathogens that need to be handled under the highest level of containment (Annex 4). These pathogens are constantly evolving, changing their behaviour and potential to cause serious disease. Climate change, demographics and changes in human behaviour are all likely to exacerbate this problem and could also result in the emergence of new, previously unrecognised organisms. Robust data collected over the past 30 years suggest that, on average, at least one new infectious agent emerges every year; most of these (77%) are zoonoses. The Chief Medical Officer established a specific committee in 2003 (the National Expert Panel on New and Emerging Infections – NEPNEI) to monitor new and emerging infections and to report its findings to the relevant authorities.
- 3.8 Diverse strategies are needed to cope with such threats and one of these has to involve expanded research on the structure and biological properties of the pathogens themselves in order to obtain a better understanding of disease pathogenesis. New vaccines and antiviral compounds will also need to be developed and assessed both *in vitro* and *in vivo* in suitable animal models.
- 3.9 These research programmes will require access to high containment facilities as growth of the pathogen, sometimes in large quantities, will be necessary. In addition, there will be an increasing number of *in vivo* studies that move beyond the need for small animals, particularly for vaccine challenge and pathophysiological experiments. This presents considerable challenges for the design and provision of appropriately equipped high containment facilities that include provision for adequate and safe removal of contaminated bedding and other animal waste. Lack of these facilities would leave the UK vulnerable to the impact of new and emerging disease threats. More specifically, the protection of public and animal health and the maintenance of a world class research capability will both become more difficult.
- 3.10 Associated with this is the on-going need for the UK to maintain a vaccine manufacturing capacity for ACDP CL4 and SAPO4 pathogens. This will necessitate having access to manufacturing plant capable of operating under high containment conditions. Responsibility for the provision of such facilities traditionally rests with the private sector however *Government and the funding organisations need to maintain a strategic oversight so*

that they can take steps, if necessary, to ensure that the UK capability in this area is strengthened.

- 3.11 Finally, it is clear that the UK needs to maintain clinical facilities that are able to provide clinical care to individuals infected with ACDP CL4 pathogens, whether this occurs naturally or through accidental exposure. Two such units exist, one at the Royal Free Hospital and the other at Newcastle General Hospital. Both units are supported by consultants trained in infectious diseases, tropical medicine and general internal medicine, and by nurses able to provide appropriate clinical care. Samples from infected patients that require laboratory manipulation for further investigation are generally referred to the HPA.
- 3.12 The Review Team was informed that the clinical facilities at the Royal Free Hospital had been renovated and that it is planned to relocate those in Newcastle to the Royal Victoria Infirmary in mid 2010. It did not consider these clinical facilities any further save to note that the ways in which clinical care is provided to patients infected with dangerous pathogens is being reviewed by the ACDP which will report shortly.
- 3.13 Corresponding clinical facilities are generally not needed for animals naturally infected with SAPO4 pathogens as, during disease outbreaks, animal movement restrictions are imposed in defined areas according to the level of risk and the modes of spread of the pathogens concerned. If animals die or are slaughtered for disease control, then their carcasses are made safe by incineration or heat treatment. However, containment facilities capable of holding experimentally infected animals, usually rodents or domesticated farm animals and poultry, are essential. These form part of this review.

4. LEGISLATIVE AND REGULATORY FRAMEWORK

- 4.1 Maintaining a UK capability to work with ACDP CL4 and SAPO4 pathogens can be fully justified but work with such pathogens is not without some risk. Accidental release of pathogens from high containment facilities is extremely rare but unfortunately does occur.
- 4.2 Those working with ACDP CL4/SAPO4 pathogens and their employing organisations have a legal responsibility for ensuring that all work is carried out responsibly and safely. There is also a heavy associated obligation on all those involved to reassure the general public that any work involving dangerous pathogens is necessary and that all risks are adequately controlled. This obligation is reinforced by a legislative framework under which all work with ACDP CL4 and SAPO4 pathogens is undertaken.
- 4.3 There are five main pieces of primary legislation currently used to regulate and provide guidelines for all work associated with ACDP CL4 and SAPO4 pathogens. These are the European Communities Act 1972, the Health and Safety at Work etc Act 1974, the Animal Health Act 1981, the Animals (Scientific Procedures) Act 1986 and the Anti-terrorism, Crime and Security Act 2001. These provide the legal instruments through which specific regulations, guidelines and approved codes of practice have been introduced.
- 4.4 The Health and Safety at Work etc Act 1974 and the European Communities Act 1972 were used to create the Control of Substances Hazardous to Health (COSHH) Regulations 2002. These regulations place obligations on employers to prevent or adequately control (minimise) exposure of their workers to pathogens. The regulations also provide information on the categorisation of biological agents and on their containment and control.
- 4.5 The Government has created an Advisory Committee on Dangerous Pathogens (ACDP) as a non-statutory advisory Non-Departmental Public Body. The Committee comprises a Chairman (currently Professor George Griffin) and 17 members. The membership is tripartite, with scientific experts, employer and employee representatives. The work of the ACDP involves a number of Government Departments, and the Committee is supported by a Secretariat with representatives from the Health and Safety Executive (HSE), the Health Protection Agency (HPA) and the Department for Environment, Food and Rural Affairs (DEFRA). The remit of ACDP is to provide advice to the HSE and Ministers for the Department of Health (DH) and DEFRA and their counterparts under devolution in Scotland, Wales and Northern Ireland, on the risks to workers and others, including members of the public, from exposure to pathogens (also known as biological agents and infectious agents).

- 4.6 The Specified Animal Pathogens Order (SAPO), which categorises animal pathogens according to the threat posed to the environment and animals, but not to the worker, was made under the auspices of the Animal Health Act 1981. This order defines the containment conditions under which animal pathogens must be handled; it also requires all individuals having any specified animal pathogen in their possession to be licensed by DEFRA or its Devolved Administration (DA) equivalents.
- 4.7 Also impacting on this review are the Genetically Modified Organisms (Contained Use) Regulations 2000 (as amended 2005) that have been created using both the European Communities Act 1972 and the Health and Safety at Work etc Act 1974. These regulations set out the requirements for risk assessment, containment and classification of work involving genetically modified organisms (including human and animal pathogens). They ensure that both the worker and the environment are protected from any harmful effects of genetically modified organisms (GMOs). A Scientific Advisory Committee on Genetic Modification (Contained Use) (SACGM) has been established to provide technical and scientific advice on all aspects of the human and environmental risks associated with the contained use of GMOs.
- 4.8 The two remaining legal instruments affect how high level containment facilities are used. The Animals (Scientific Procedures) Act 1986 regulates all laboratories working with both human and animal pathogens where designated scientific procedures are conducted on animals. It identifies responsibilities for individuals and organisations involved in both the use and husbandry of animals in laboratory environments. The provision of suitable animal holding and care facilities must be taken into account in the design of high containment laboratories.
- 4.9 Finally, the Anti-Terrorism, Crime and Security Act 2001 imposes legal requirements that cover the secure storage and use of the pathogens defined in Schedule 5 of the Act. These requirements are superimposed on, and augment, those specified through the COSHH, GMO(CU) or SAPO regulations and also provide a level of control on the possession of selected pathogens. Permission for organisations or individuals to hold or work with pathogens can be withdrawn under the auspices of this Act.
- 4.10 *The Review Team are aware that there will be fundamental changes to the regulations governing deliberate use of human & animal pathogens by the introduction in 2010 of a single regulatory framework.* It is anticipated that these new regulations will replace existing COSHH, GMO(CU) and SAPO regulations to form a single regulatory framework for those deliberately working with human and animal pathogens.
- 4.11 However, continuous improvement in the way that bio-containment is managed is likely to be required, as and when technological and

scientific advances permit. For example, security at sites containing high containment facilities may have to be improved and better staff vetting procedures introduced to enhance current public safety and anti-terrorism procedures. This possibility was highlighted in the recent report from the House of Commons Innovation, Universities and Skills Select Committee on Biosecurity in UK research laboratories. It was noted that the Government, in its response on 9 October, agreed to review the arrangements in place for staff employed in high containment facilities.

- 4.12 *Whilst possible changes in the interpretation of existing legislation may have no bearing on either the need for or availability of high containment facilities in the UK, they do underline a major issue for all funders and sponsors to consider. Namely, investments in the physical infrastructure of high containment facilities represent both a very considerable initial capital expenditure and an ongoing commitment to maintain these facilities, to accommodate new technology to improve safety and security and to introduce improved management and working practices. The provision and operation of high containment facilities therefore requires a full appreciation and understanding of the considerable long-term cost and manpower implications involved. It also requires regular independent and internal assessment of the status of all such facilities.*

5. CONTAINMENT REQUIREMENTS FOR WORKING WITH ACDP CL4 and SAPO4 PATHOGENS

- 5.1 In general terms human pathogens are categorised into four hazard groups depending on the severity of human disease caused by exposure, the hazard to workers using these pathogens, their capability of spread into the community and the availability of effective treatment and prophylaxis. These categories are recognised universally and formulated through European directives which are implemented as an Approved List within the UK. The ACDP provides advice and regularly reviews the UK categorisation list. *This review is concerned only with the agents in the highest risk category (ACDP Hazard Group 4; see Annex 4). There are currently three laboratories in the UK that have been approved to handle these agents.*
- 5.2 A similar categorisation exists for animal pathogens but the risk level is determined by the threat to animals and the environment rather than any danger to humans. DEFRA defines these hazard groups using the Specified Animal Pathogens Order. This review is again concerned only with agents in the highest risk category (SAPO category 4; see Annex 4). *There are currently seven laboratories in the UK that are licensed to work with SAPO4 agents.*
- 5.3 There is a limited overlap between the lists of ACDP CL4 and SAPO4 pathogens. This overlap involves agents that are able to be transmitted from animal to man (zoonotic organisms) to cause severe disease. In general terms, the fail-safe handling requirements for these organisms relate to the conditions imposed by COSHH however, where particular control or containment measures are not required or alternative equally effective measures are available, derogations may be sought from the regulator.
- 5.4 A similar risk categorisation system is in place for GMOs but this is determined by the potential risks posed to both human and animal health and also the wider environment. This review is concerned only with genetic modification projects that are within the highest risk category all of which must be undertaken in one of the laboratories approved for handling ACDP CL4 or SAPO 4 pathogens. The GMO(CU) regulations also specify additional control measures for work with genetically modified micro-organisms in animal units, plant growth facilities and large-scale work. As before, derogations may be sought from the regulator to accommodate specific circumstances or containment requirements.
- 5.5 Work with the highest hazard groups of human and animal pathogens (and GMOs) cannot commence without notification to the regulatory authority and subsequent receipt of consent or licence. In all cases, the safe handling of ACDP CL4 and SAPO4 pathogens requires the use of standard operating procedures and personal protective equipment

(primary containment). Access to an approved and suitable physical laboratory infrastructure with negative pressure filtered air environments, autoclaves and other waste disposal systems (secondary containment) is also necessary. There are some differences between the infrastructure requirements for working with ACDP CL4 or SAPO4 pathogens in the corresponding ACDP or SAPO high containment laboratories (Annex 5).

- 5.6 These differences were referred to in the 'Review of the Regulatory Framework for Handling Animal Pathogens' conducted by Sir Bill Callaghan and resulted in the recommendation, accepted by the Secretary of State for Environment, that the ACDP should be tasked with formulating a common set of containment measures to apply to both animal and human pathogens including GMOs. The Review Team understand that this work is in progress but acknowledge that the outcome will not influence the strategic need for high containment facilities in the UK. However a new regulatory framework may have design consequences for renovations to existing SAPO4 laboratories and for any planned new building works.
- 5.7 Guidance on the design and operation of the highest containment laboratories has been developed by the ACDP and published by the HSE. It is not within the remit of this review to comment on this guidance however, there does seem to be some confusion in the field regarding the designation of high containment laboratories; *the new regulatory framework should greatly facilitate the clarification required.*
- 5.8 Some basic requirements for high containment laboratories may change as new technologies are developed and introduced. It is difficult to predict how this will influence the operation of high containment laboratories. For example, the introduction of remotely operated robotic systems will clearly have cost and safety implications. Likewise, the introduction of improved diagnostic procedures using nucleic acid amplification techniques could reduce the need for access to high containment facilities. It is important that any planning for new facilities should accommodate some of the more likely advances and incorporate these into the design concepts.

6. LOCATIONS AND FUNDING OF HIGH CONTAINMENT FACILITIES

6.1 The first term of reference for this review instructed the Review Team to obtain, validate and keep secure, a definitive list of all ACDP CL4 and SAPO4 facilities currently in operation across the UK, their location, capacity and capability in terms of the type of work they support. This information is summarised in Annexes 6a – 6c (Deleted subjected to FoI S24 and S38 exemptions).

6.2 *Three facilities -* (details removed subject to FoI S24 and S38 exemptions)

– are approved to operate at an ACDP CL4 level.

6.3 *Seven facilities –* (details removed subject to FoI S24 and S38 exemptions)

– are licensed to operate at a SAPO4 level.

6.4 The Review Team visited eight of these high containment facilities. It also visited the (details removed subject to FoI S24 and S38 exemptions). Finally, the Review Team was informed of plans to convert a SAPO3 facility to a SAPO4 facility at (details removed subject to FoI S24 and S38 exemptions) and of plans to build a new ACDP CL4 laboratory at (details removed subject to FoI S24 and S38 exemptions).

6.5 The Review Team noted that there are no ACDP CL4 or SAPO4 high containment facilities in Wales, Scotland or Northern Ireland and that those currently approved are located exclusively in the South East of England. The facilities visited were located in environments that ranged from rural settings well away from major population centres to suburban areas adjacent to high density housing. Each location presented different challenges for the safe operation of high containment facilities. Maintaining the physical security of each site was generally not a problem.

6.6 The geographical locations of the existing high containment facilities have arisen for historic operational reasons and few opportunities exist to alter this situation. When such opportunities do arise then **decisions on their location should be based on a robust, multi-faceted risk assessment in which microbiological science and all aspects of security, safety, and public opinion are considered and on the existence of good links to academic centres of excellence.** The Review Team concluded that great emphasis should be placed on the benefits to be gained from taking account of local public opinion when locating or renovating high containment facilities; it was made aware of several international examples where serious operational and planning

difficulties were encountered when the broader economic, social and political issues were not given due regard.

- 6.7 *The UK's high containment facilities are largely funded by grants from government.* This was considered entirely appropriate given the considerable capital investment needed to provide a robust physical infrastructure. Furthermore, continuity of funding is arguably the single most critical issue in terms of maintenance and high running costs. The only exception to this generality was *(details removed subject to FoI S24 and S38 exemptions)*.
- 6.8 The Review Team explored the possibility of obtaining a breakdown of the annual operating costs of high containment facilities but quickly recognised that the parameters involved were too diverse to make comparisons across different sites. However, it was estimated that costs were large and likely to exceed £750k per annum even for a modest facility with a single laboratory.
- 6.9 The Review Team considered it essential for the government agencies responsible for operating high containment facilities to be reminded of their on-going commitments to make adequate funds available to maintain a national strategic capacity in this area. It was concerned to find that some of the publicly funded facilities need additional support from external, sometimes international, sources to maintain a strategic capability. Such a situation poses considerable pressure on these facilities and could divert human resource from research and maintaining essential national functions. It could also compromise the maintenance of a 'critical mass' of staff.
- 6.10 The Review Team were informed of several instances across the world where the withdrawal of operational funding has left state of the art high containment facilities non-functional (Italy, Japan). Whilst these were extreme examples they accentuate the need to put in place long term funding commitments to support the operation of high containment facilities. Such commitments extend beyond the normal funding cycles that operate in government and so some ring-fencing of the operational and maintenance budgets involved is essential.
- 6.11 High running costs are a major contributory factor to the lack of high containment facilities within the UK's university sector. Whilst the academic sector is fully capable of operating high containment facilities, maintaining the ongoing funding commitment could be difficult if it is to be sustained by recurrent short-term grant based funding. The Review Team strongly urges those university authorities who are thinking of developing high containment facilities to reflect on these high ongoing running costs before making their investment decisions.
- 6.12 The Review Team concluded that there is a major issue associated with **securing sufficient funding to support the running costs of maintaining a national strategic capacity in this area. Failure to do**

this will result, in a general decline in the physical infrastructure of high containment facilities across the UK with the loss of both diagnostic and research capacity and an associated skill base.

7. THE PHYSICAL INFRASTRUCTURE OF UK HIGH CONTAINMENT FACILITIES

7.1 The second term of reference for this review requested the Review Team to obtain information on the life expectancy and plans for refurbishment/new build of existing high containment facilities, to identify organisations which have an interest in using or providing ACDP CL4/SAPO4 facilities in the future and which may be planning their construction. This information is summarised in Annex 6b *(details removed subject to FoI S24 and S38 exemptions)*.

7.2 The high containment facilities at *(details removed subject to FoI S24 and S38 exemptions)*

This drew the Review Team's attention to the vital importance of ongoing effective surveillance and maintenance programmes, irrespective of the age of the facilities, to ensure that the operational safety of high containment facilities is not compromised.

7.3 The remaining two facilities approved to operate at the ACDP CL4 level *(details removed subject to FoI S24 and S38 exemptions)* They conduct complementary functions and together maintain the national diagnostic capacity for ACDP CL4 pathogens. Strategic agreements are in place to ensure that when one facility is out of action for maintenance or refurbishment the other remains fully functional.

7.4 The high containment facility at *(details removed subject to FoI S24 and S38 exemptions)* In contrast, the corresponding facilities at *(details removed subject to FoI S24 and S38 exemptions)* Design plans are being developed and funds are being sought to support the major building programme needed to replace this aging stock. The Review Team consider **this replacement programme essential if the UK's strategic capacity for working with ACDP CL4 and SAPO4 at high containment levels is to be maintained over the longer term.**

7.5 *(details removed subject to FoI S24 and S38 exemptions)* are the only two approved ACDP CL4 facilities able to undertake a variety of experimental protocols involving infected animals (Annex 6c) *(details removed subject to FoI S24 and S38 exemptions)*. There is adequate capacity to handle rodents and other small mammals but **the capacity to handle larger animals, in particular non-human primates, is extremely limited. This poses a potential gap in the UK's future research capability.**

- 7.6 The seven SAPO4 licensed facilities vary considerably in sophistication and capacity. *(details removed subject to FoI S24 and S38 exemptions)* is the only facility able to work with both ACDP CL4 and SAPO 4 organisms. These organisms are zoonotic in nature and the work relates to applied research and development for vaccine assessments, diagnosis and for diagnostic reagent production. The observation that most emerging infections are zoonoses emphasises the importance of this work. Such work could become compromised in a relatively short period if the plans for *(details removed subject to FoI S24 and S38 exemptions)* are not rapidly developed and adopted.
- 7.7 The SAPO4 facilities at *(details removed subject to FoI S24 and S38 exemptions)*
- Both have only limited capacity to work with animals infected with SAPO4 pathogens (Annex 6c) *(details removed subject to FoI S24 and S38 exemptions)*.
- 7.8 The high containment facility at *(details removed subject to FoI S24 and S38 exemptions)*.
- The Review Team was informed that this facility had been built to ACDP CL4 standards but work at this level was not currently being carried out. The animal holding capacity of this facility is currently restricted to infected mice and ferrets; there are no plans to use other species. The *(details removed subject to FoI S24 and S38 exemptions)* and provides an associated research capacity.
- 7.9 The remaining three SAPO4 licensed facilities at the *(details removed subject to FoI S24 and S38 exemptions)* complement each other and provide both laboratory accommodation and holding areas for infected farm animals and poultry. These facilities all provide essential national and international reference functions for animal diseases. The Review Team was informed by staff at these sites that the current animal holding capacity is likely to match the UK's short and long term requirements. Under-provision of holding areas for large animals infected with SAPO4 agents was not an issue raised during the consultation exercise with stakeholders. However, some stakeholders did comment that access to the high containment animal holding facilities by external personnel to support specific research projects that are not part of the core research activity of the organisation concerned can be difficult to arrange.
- 7.10 The infrastructure at *(details removed subject to FoI S24 and S38 exemptions)*. In particular, surge capacity is very well provided for foot-and-mouth disease serology in the foreseeable future. *(details removed subject to FoI S24 and S38 exemptions)*

- 7.11 The SAPO4 *(details removed subject to FoI S24 and S38 exemptions)* ; some facilities are new whereas others have been decommissioned and are awaiting refurbishment or replacement to meet regulatory requirements. *(details removed subject to FoI S24 and S38 exemptions)*.
- 7.12 In contrast, the laboratory accommodation at *(details removed subject to FoI S24 and S38 exemptions)*. Funds have been assigned to the proposed programme and there is an anticipated completion date of 2012/2013. However, estimates of the true building costs have escalated due to delay, inflationary and other pressures and now greatly exceed the original approved budget. This has resulted in a planning blight that has serious implications for the UK's capability to conduct essential research and development on SAPO4 pathogens. **Decisions are urgently needed on whether additional funds will be made available for the project and whether the original plans need to be modified.** The Review Team urges the relevant funding organisations to make their intentions known with all possible speed.
- 7.13 This review and analysis of the UK's high containment facilities drew attention to three significant and related areas where highly desirable improvements can be made.
- 7.14 First, designing, engineering and fabricating high containment facilities involves many categories of players including architects, designers, manufacturers of specialist plant and equipment, ventilation engineers, building contractors etc. The availability of those with direct experience of working on projects associated with the building or renovation of high containment facilities is extremely limited. Many of the design and build specialist contractors have developed their expertise from building clean or remote operation rooms in the pharmaceutical, semi-conductor or nuclear industries. This expertise needs to be identified and harnessed to ensure that the UK retains access to relevant specialists that are capable of working together as a project team to service the needs of high containment facilities.
- 7.15 Second, and related to the above, the Review Team were shown several different designs of Class III safety cabinets. Some designs represented incremental improvements, some were to allow specific procedures to be undertaken safely. Specialist manufacture was always involved and the number of companies able to do this is extremely limited. There is a potential UK vulnerability in this area through the loss of essential expertise by retirement and because lack of business opportunity may prevent sharing of best-practice design solutions.
- 7.16 Last, staff employed in the organisations with high containment facilities need to communicate more effectively across sites, especially when it comes to the design of new facilities, so that lessons can be learnt and mistakes prevented. This will not only ensure that new facilities can be commissioned without delay but will also ensure that they provide sufficient flexibility to accommodate future technological improvements

and so remain state of the art for a considerable period. The Review Team was disappointed by the insular nature of some of the organisations involved.

8. HORIZON SCANNING AND INTERNATIONAL PERSPECTIVE

- 8.1 The third and fourth terms of reference for the review requested that a strategic horizon scanning programme be undertaken to identify scientific and technology drivers that will define future needs and access requirements, in terms of capacity, technologies, safety, security and regulation, over a 10-20 year period and that this should consider possible exemplars in Europe and North America particularly with respect to trends in likely physical infrastructure (suited versus cabinet line laboratories), location (urban versus remote sites) and security requirements.
- 8.2 The Review Team developed a consensus view following discussions with staff on the various site visits and from responses to the general consultation exercise that **the current demand for high containment facilities in the UK is being met but there is little spare capacity** (see below). It was not possible, within the time constraints of this review, to make a more comprehensive assessment of the future requirements for high containment facilities or to conduct a comprehensive horizon scanning programme to identify scientific and technological drivers that might significantly modify these demands. It was clear that some new technologies for example, remotely operated robotic systems or improved diagnostic procedures using nucleic acid amplification techniques, could reduce the need for access to high containment facilities. Equally, an increased interest in emerging exotic diseases could promote a demand for limited expansion. **It was concluded that horizon scanning for future needs is difficult and unpredictable and needs to be kept under routine review.**
- 8.3 In order to place the review in an international context the Review Team interviewed staff from the USA Government Audit Office (GAO), American Society of Microbiology (ASM) and the European Commission (EC) and staff with experience of operating high containment facilities in National Institutes of Health (NIH) and in France.
- 8.4 The Review Team was informed that outside of the USA and Europe there were at least seven other countries in possession of high containment facilities (Canada, Russia, China, Japan, Australia, India, and Africa). Some of these facilities are well established (South Africa, Russia), others are relatively new with state of the art designs (Canada, Australia) whereas others are still under construction (China). This is not intended to be a comprehensive list but merely an indication of the level of global capacity.
- 8.5 Discussion with the Board of Scientific Affairs at the American Society for Microbiology (ASM) indicated that there was no accurate information on the number of high containment facilities in the USA. However, it was

noted whilst that the number of these facilities had proliferated significantly since the introduction of Project Bioshield, there was no defined national strategy for their provision either in terms of capacity or preferred locations. The Centers for Disease Control (CDC) oversees the registration and inspection of containment facilities which is done on the basis of the pathogen being handled.

- 8.6 Two main issues relevant to the current review were raised. First, planning for new facilities had sometimes resulted in difficulties with planning authorities and with objections from local communities; this had delayed or prevented the necessary construction work. Second, the rapid expansion of high containment facilities across the USA had not been matched by the availability of trained staff, the implication being that many of the facilities will either remain idle or will operate at a lower level of containment. The impression given was that there is currently an over-capacity for high containment in the USA.
- 8.7 In Europe, apart from the UK, there are active high containment laboratories in Germany, France, Italy, Sweden, Switzerland and Spain (animals only). Additional capacity is being planned or built in Austria, Germany and the Netherlands. As with the UK, their operation is governed by Directives from the EU as transposed into national law. There is therefore a generic legal framework for the design and maintenance of high containment facilities and for the designation of human and animal pathogens across Europe with some variations at local level.
- 8.8 There is no over-arching European strategy for the provision of high containment facilities, this being totally driven by the strategic requirements determined by each Member State. Memoranda of Understanding exist between some Member States on the provision of essential back-up capacity during maintenance of their high containment facilities and to accommodate surge requirements during epidemic situations. It is unknown how robust these agreements would be in times of a national emergency.
- 8.9 The funding of high containment facilities across Europe is viewed largely as a Government or corresponding Agency or Research Council responsibility. However, it was noted that the initial infrastructure cost of at least one of the European facilities (Lyon) had been provided from private sources. The EC does not directly contribute to the construction or maintenance costs of Europe's high containment facilities but it does provide funding to support a number of networks that facilitate communication between scientists engaged in disease diagnosis and control and between high containment laboratories.
- 8.10 A relevant network for ACDP CL4 pathogens is the European Network of P4 Laboratories (EURONET-P4) which was created in 2005 with the aim of enhancing and maintaining cooperation, communication and exchange of information between the European Bio-safety Level 4 laboratories. It also aims to promote harmonisation and standardisation of biosafety

practices and diagnostic procedures and offers assistance to countries where new BSL-4 laboratories are under construction or planned. The HPA leads for the UK on this network.

- 8.11 There appears to be no direct equivalent network on the SAPO4 pathogens however a Network of Excellence for Epizootic Disease Diagnosis and Control (EPIZONE) has been established. EPIZONE aims to develop a network of scientists to improve research on preparedness, prevention, detection and control of epizootic diseases within Europe. IAH and VLA represent the UK on this network but there is no focus on high containment facilities.
- 8.12 Whilst the existence of these networks can only be viewed as beneficial, their operation does not receive high priority in the UK. They were mentioned only in passing in discussion with UK scientists during site visits and there appears little communication outside of the network membership. This lack of communication is accentuated by the fact that the two networks are funded by different Directorates General from within the EC. The Review Team views this as a significant weakness for the UK (and the EU) and another missed opportunity for the UK to showcase its expertise and develop collaborative partnerships with like-minded European organisations and scientists.
- 8.13 There is no preferred geographical location of the high containment facilities across Europe and many are integral to, or closely associated with, academic centres of excellence. The majority of the facilities available appear small and offer limited capacity to handle infected animals. The preferred model of containment, as elsewhere in the world, involves the use of positive pressure personal protection suits.
- 8.14 Discussions with scientists working in high level containment laboratories indicated that this form of personal protection was essential when dealing with infected animals and that it offered considerable freedom of movement. However, working within cabinet lines was itself seen to be advantageous for some operations, offering considerable economies of time. The Review Team was given to understand that some of the new facilities in the US are being built to operate using both suits and cabinet lines however, this is an expensive option. The Review Team therefore made no definitive conclusion regarding the preferred provision of either suits or cabinet lines. In so doing, the Review Team recognised that advances in the design of protective suits make their prolonged continuous use much easier than previously and that this is likely to represent a major way forward for the future.

9. STAFFING LEVELS AND TRAINING

- 9.1 The fifth term of reference for the review requested that manpower, skills and training requirements for specialist personnel employed in ACDP CL4/SAPO4 facilities should be considered along with all aspects (including costs) of the re-accreditation of both staff and facilities. Relevant information obtained by the Review Team is given in Annex 7 *(details removed subject to Fol S24 and S38 exemptions)*.
- 9.2 It was observed that the number of staff trained to work in ACDP CL4 laboratory environments was small; whilst this currently does not compromise safety it was considered that these levels would make it difficult for the UK to maintain a sustainable workforce with expertise to work at this containment level. The Review Team was informed that some of the trained staff are now approaching retirement age thus presenting their employing organisation with succession problems. Similar arguments do not apply to staff working with animals infected with SAPO4 pathogens as this represents a much larger workforce. However some recruitment problems were noted, largely due to the local nature of the employment creating a non-mobile workforce. Retention was generally not an issue as it was clear that there were high levels of job satisfaction amongst this staff group. Taking these issues into consideration, the Review Team consider **it essential for employing organisations to routinely review their staffing levels, succession plans and training commitments to ensure that a critical mass of trained staff with the expertise necessary to work at ACDP CL4 and SAPO4 containment levels in the UK is not lost**
- 9.3 The Review Team observed that all facilities offered similar generic training programmes to staff in accordance with the training guidance contained within the ACDP's document 'Biological Agents – The Principles, Design and Operation of Containment Level 4'. These training programmes always involve a general induction to the site with briefings on laboratory procedures, biosafety, staff health, waste treatment, health and safety etc and are followed by on-site competency based training to acquire general laboratory skills including working under low containment conditions. Individuals selected to work under higher levels of containment then generally undergo an apprenticeship involving close supervision and monitoring by senior staff, with competency being assessed locally.
- 9.4 The Review Team found that training programmes tend to be both bespoke to the individual and bespoke to the facility. The Review Team fully appreciated that training requirements were somewhat different depending on whether staff were graduates or non-graduates and whether they were to operate in laboratory or animal handling (both large and small species) environments. Nevertheless, it observed that there is no standardised curriculum.

- 9.5 Whilst there is a willingness to cross-accredit training programmes between facilities this does not happen often in practice. The Review Team recognised that this problem is due partly to operational differences imposed by the varied physical infrastructures at each site and partly because of the necessity of having trust and confidence in the competence of a colleague working in the same high containment area, this being best gained by observation rather than the acquisition of formal training certificates.
- 9.6 The Review Team noted that one UK organisation has assigned staff to receive training at a high containment laboratory in the United States. The Review Team felt that this was an innovative way of gaining exposure to a broader perspective of containment working and a practice that may be worth adopting more widely, if only to bring fresh ideas into UK ways of working. The Review Team also noted that at one site at least, the overall Director of the establishment was responsible for 'signing off' an individual's competency assessment and thereby gave approval to work in the high containment suites. This was considered a good practice that could be usefully adopted across all high containment facilities.
- 9.7 Like the UK, there are no formal training courses operating in European countries that specifically give competency based training for working under high containment conditions. Officials from DG-SANCO in the EC indicated that they would be sympathetic to receiving proposals for the creation of such courses particularly where this facilitated the exchange of scientists. It was recognised that this could result in problems associated with the security vetting of potential trainees. There is significant scope for the UK to increase the visibility of its expertise in this area and so greatly enhance the UK's reputation for the safe handling of dangerous human and animal pathogens.
- 9.8 Regardless, the Review Team supported the introduction of greater consistency to the training programmes available to staff working in, or being associated with, high containment facilities. The Review Team felt that this consistency should also be extended into re-accrediting the competency of trained staff, particularly where there had been no working at high containment levels for some time. It concluded that whilst **current training programmes are adequate, benefit would be derived from a unified training strategy to facilitate staff interchange between different facilities. Future training programmes will need to contain both theory and competency based aspects and complement local programmes based on site-specific standard operating procedures.** The costs involved in developing the proposed national strategy and the constituent training programmes were not explored by the Review Team.
- 9.9 The Review Team made two other observations. First, it understood that some facilities provided limited training to engineers and other support staff to enable them to enter operational containment facilities and effect minor repairs to equipment. Other facilities also held routine briefing sessions on appropriate procedures and practices with

representatives from the external emergency services. These were considered good and expedient practices that optimised the use of the facilities available and something that most organisations should consider.

- 9.10 Second, the Review Team was informed that organisations in Europe and the United States routinely undertake medical and psychological assessments of staff selected to work in positive pressure personal protection suits. This drew attention to the variety of challenges and pressures facing staff working under high containment conditions and it exposed a gap in UK practices. The Review Team considered that more attention should be given to medical and psychological parameters when selecting staff to work at high levels of containment. It felt that this would become more vital if or when working in positive pressure suits was introduced into UK facilities. This should be considered at the design stage of these facilities.

10. CONCLUSIONS AND WAYS FORWARD

- 10.1 The final relevant term of reference requested that opportunities for collaboration and synergy should be identified in order to optimise effective and efficient provision, and value for money, in delivering UK high level containment needs for research and public health protection. An analysis of the strengths, weaknesses, opportunities and threats for the UK's high containment facilities was undertaken to partly fulfil this requirement. This analysis is given in Annex 8.
- 10.2 The major strengths are centred on the UK's robust and internationally recognised expertise for all aspects of work involved with the handling of ACDP CL4 and SAPO4 pathogens. These are balanced by the major weakness of only having access to ageing high containment facilities at some sites. There is also a lack of standardised training programmes with which the competency of the future generation of high containment workers can be developed.
- 10.3 In their responses to the consultation exercise, several stakeholders drew attention to a further potential weakness namely, whether the UK had access to sufficient ACDP CL4 and SAPO4 facilities. However, the general consensus was that the current level of demand could be sustained over the short term and that only limited expansion should be anticipated. This expansion would be mitigated to some extent by the introduction of new technologies that either reduce the access requirements for high containment (for example, by the introduction of remote monitoring and handling devices) or reduce the risks involved (for example, genetic modification to reduce pathogenicity). That said, concerns were raised over the general state of preparedness for an outbreak or epidemic and, in the light of government financial cutbacks, where high containment work can in fact be done and with what facilities.
- 10.4 The Review Team carefully considered these views and concluded that the current demands for high containment facilities were indeed being met but that there was little spare capacity. This conclusion was made partly because those operating high containment facilities did not report a high level of demand for access from either internal or external academic sources and partly because significant operational down-time of existing facilities had been experienced over the past few years and there had been no significant adverse consequence to any of the essential national diagnostic or surveillance programmes.
- 10.5 It was recognised however that lack of funding for research on ACDP CL4 and SAPO4 pathogens organisms, which are not currently a threat to the UK, has depressed academic interest in this area. This situation is slowly changing and interest in new and emerging threats has increased significantly in recent years and it can be expected that there will be increased requests from academic groups for access to high-containment facilities. In the past such requests have proved difficult to fulfil due to operational difficulties and mechanisms to overcome these difficulties may

now need to be sought. Finally, the Review Team *(details removed subject to FoI S24 and S38 exemptions)* has resulted in a lack of suitable SAPO4 laboratory accommodation and that this has curtailed research on foot-and-mouth disease virus; diagnostic capacity is however considered adequate.

- 10.6 Lack of access to high containment facilities was considered a significant threat to the UK's future capability in this area, particularly given the age of the existing building. The major imponderable in any consideration of future requirements is the need to accommodate significant surge capacity in the event of a future disease outbreak or epidemic where the demand could not be quantified. The Review Team concluded that if this surge demand ever did exceed the high containment capacity available then it was likely that a national emergency would exist and that other containment facilities would be pressed into use with suitable derogations from the regulatory authorities. This was certainly the experience during the previous large foot and mouth disease outbreak in the UK (in 2001) and the lessons learnt resulted in significant investment in veterinary laboratory space to increase capacity for handling large numbers of serological samples.
- 10.7 These conclusions are all predicated on the assumption that adequate funds will be made available for the planned renovation and building programmes to replace the UK's existing ageing facilities. The Review Team felt that an opportunity existed for reducing uncertainty and for developing a co-ordinated national strategy to sustain capacity and achieve a balance between over and under provision if the necessary capital investment funds were clearly and unequivocally identified and made quickly available.
- 10.8 The Review Team was made aware of six building/renovation programmes that were either in planning or were being considered.
- 10.9 Two of these are in major universities, one involving the up-grading of a yet to be licensed SAPO3 facility to a SAPO4 level the other, the construction of a completely new ACDP CL4 laboratory. It is beyond the remit of the Review Team to recommend whether or not these projects should go ahead however, the Review Team would urge the relevant university authorities to reflect on the necessity of either facility, the capital costs involved and how the long term maintenance and running costs will be provided.
- 10.10 One of the potential building programmes involves the further development of the *(details removed subject to FoI S24 and S38 exemptions)* which currently only has access to SAPO3 facilities and which is developing a business case to extend its capability to handle SAPO4 pathogens (excluding foot-and-mouth disease virus). Such a development will enhance the capacity for research in the expanding veterinary facilities in this location.

- 10.11 One further building project is part of a wider long term development plan *(details removed subject to FoI S24 and S38 exemptions)*. The detailed plans have yet to be developed but if there is considered to be a case for providing high containment capability it will be essential to take account of the views raised by both local planning authorities and the local community during this process. Failure to accommodate these views could, as experienced in France, Japan, Australia and America, lead to the delay or cancellation of parts of the relocation programme.
- 10.12 The remaining two proposed building projects are concerned with the replacement of *(details removed subject to FoI S24 and S38 exemptions)*. As indicated previously, a fully costed business plan for one of these projects has yet to be submitted whereas the building programme for the other has been compromised because of cost escalations. The Review Team consider the completion of these projects to be essential if the UK's strategic capacity to handle dangerous human and animal pathogens is to be maintained in the future. These projects also provide a great opportunity to create state of the art facilities that help the UK to retain its competitive and leading global position. The Review Team wishes the potential government sponsors and funders of high containment facilities to urgently consider these opportunities in three main ways and make relevant funding decisions with the greatest possible speed.
- 10.13 First, plans for new high containment facilities should be developed with sufficient flexibility to accommodate future technological improvements. At the very least this will mean the creation of containment facilities that can accommodate the use of both positive pressure personal protection suits and class III cabinet lines, and the creation of containment facilities that can hold a range of infected experimental animal species, in particular non-human primates, with remote monitoring. The objective should be to build laboratories that can accommodate new technologies and new regulations and so remain operational for at least 20 to 50 years. The planners of these laboratories would do well to consult widely across Europe and the America to identify examples of best and innovative practice.
- 10.14 Second, new containment facilities should be developed as multi-functional and multi-use units. A review of future service and research requirements that involves all major potential stakeholders is considered essential if adequate provision is to be generated. Any new facilities should be created not only with some expansion of capacity in mind but also with a view to their routine use at lower containment levels with ready conversion to high containment operation to cope with surge demands during national emergencies. The Review Team saw examples of this already in operation at one of the UK sites visited.
- 10.15 Last, the Review Team would wish the sponsors and funders of high containment facilities to think creatively about how newly built facilities might be used. A major question to answer is whether the perceived use of high containment facilities could be met by providing greater

access to an already established and centralised resource. In short, the Review Team believe that, **as capital and recurrent expenditure for ACDP CL4/SAPO4 facilities is very high, there is scope to meet the UK's needs by creating a number of well resourced, modern, flexible and effectively integrated facilities which could fulfil their strategic functions and made available to external contractors, notably the academic community and industry.**

- 10.16 The Review Team noted that this concept had worked successfully in the UK during the early 1980's and that it was currently working very well at the high containment facility in France. It also noted that the multi-national use of highly specialised facilities was working well in other scientific disciplines. A key factor for success appears to be having direct and ready access to a strong academic research base.
- 10.17 For this concept to work well in the UK there would have to be legally robust and long term agreements between the agencies involved on how work was prioritised, conducted and funded. The management structures at the high containment facilities would need to be strong but sufficiently flexible to accommodate the demands of external workers. There would need to be good working relationships and communications between all those involved. Finally, the governance arrangements would need to be acceptable to the regulatory authorities.
- 10.18 The Review Team acknowledged that this concept would not be universally welcomed but on balance felt that if trust and confidence could be built up between the operators of high containment facilities and potential contractors then there would be additional benefits. The increased variety of work undertaken by the facilities would expand the interests and expertise of the workers involved. It would help to maintain their expertise and increase job satisfaction. It would also make better and more economic use of an extremely limited resource.
- 10.19 The Review Team viewed the lack of standardised training programmes for staff in high containment facilities to be a weakness that could eventually compromise the overall UK capability. The development of suitable training programmes and making them widely accessible across Europe was viewed as an opportunity to increase the visibility of UK expertise and greatly enhance the UK's reputation in this area.
- 10.20 The Review Team was informed of several national and international networks that existed for workers and organisations involved with working with ACDP CL4 and SAPO4 pathogens. Whilst it was encouraged by the existence of these networks it was also concerned that they are not being used as effectively as possible by all those working in this area. This could account for some of the poor communications that exist between ACDP CL4 and SAPO4 workers and the apparent reluctance to share best practice, particularly around

the design of high containment facilities. Networking between architects, design engineers etc with expertise in high containment was generally lacking and the Review Team considered this a UK weakness that should be addressed either by the funders of high containment facilities or the regulatory authorities, although it recognised that commercial market pressures were also a factor.

ANNEX 1

TERMS OF REFERENCE FOR THE REVIEW

1. To obtain, and keep secure, a definitive list of all ACDP CL4 and SAPO4 facilities currently in operation across the UK, their location, capacity and capability in terms of the type of work they support;
2. To obtain information on the life expectancy and plans for refurbishment/new build of these existing facilities, to identify organisations which have an interest in using or providing ACDP CL4/SAPO4 facilities in the future and which may be planning their construction;
3. To undertake a strategic horizon scanning programme in order to identify scientific and technology drivers that will define future needs and access requirements, in terms of capacity, technologies, safety, security and regulation, over a 10-20 year period. This will also consider the scope and constraints for introducing flexibility and sharing of the facilities available;
4. To consider possible exemplars in Europe and North America particularly with respect to trends in likely physical infrastructure (suited versus cabinet line laboratories), location (urban versus remote sites) and security requirements;
5. To identify the manpower, skills and training requirements for specialist personnel employed in ACDP CL4/SAPO4 facilities and all aspects (including costs) of the re-accreditation of both staff and facilities;
6. To identify opportunities for collaboration and synergy to optimise effective and efficient provision, and value for money, in delivering UK high level containment needs for research and public health protection; and
7. To submit a confidential review report to the sponsors by October 2008.

ANNEX 2

MEMBERSHIP OF THE REVIEW STEERING COMMITTEE

Professor George Griffin, St George's, University of London (Chair)

Ms Lis Birrane, Director of Communications, Health Protection Agency

Dr Steve Chatfield, Centre for Emergency Preparedness and Response,
Health Protection Agency

Mr Brian Harris, Biotechnology and Biological Sciences Research Council

Dr Ruth Lysons, Department for Environment, Food & Rural Affairs

Dr Kevin Moreton, Medical Research Council

Professor David Rowlands, University of Leeds

Dr John Stephenson, Director of Research and Development, Health
Protection Agency

Ms Maggie Tomlinson, Department of Health

ADVISORS

Dr Tim Brooks, Centre for Emergency Preparedness and Response, Health
Protection Agency

Mr Guy P Collyer, National Counter Terrorism Security Office

Dr Steve Lever, Defence Science and Technology Laboratories

Dr Mandy Gates, Defence Science and Technology Laboratories

Ms Liz Morgan-Lewis, Health Protection Agency

Dr John Newbold, Health and Safety Executive

Dr Mike Paton, Health and Safety Executive

Ms Karen Reid, National Counter Terrorism Security Office

SECRETARIAT

Dr Peter Greenaway, Horus Research Management Ltd (Secretariat)

ANNEX 3

STAKEHOLDER CONSULTATION STATISTICS

Number of individuals/organisations contacted	92
Number of individuals/organisations responding	62
Nil returns or making no significant comment	30
Those commenting orally or via site visits	35
Written comments	28

WRITTEN COMMENTS FROM:

1. Faye Stokes, Society for General Microbiology
2. Heather Sheeley, European Biosafety Association
3. Tracy Hussell, Imperial College
4. Paul Wiles, Home Office
5. David Lynn, Wellcome Trust
6. Mike Dennis, Centre for Emergency Preparedness and Response
7. Wendy Barclay, Imperial College
8. Brian Duerden, Inspector of Microbiology and Infection Control
9. Vanessa Mayatt, Mayatt Risk Consulting Ltd
10. Chris Thorns, Veterinary Laboratories Agency
11. Scientific Advisory Committee for Genetic Modification
12. Don Jeffries, Queen Mary's School of Medicine and Dentistry
13. John McLuckie, Belfast City Hospital
14. Ed Ong, Newcastle General Hospital
15. Julie Fitzpatrick, Moredun Research Institute
16. David Brown and Robin Gopal, Centre for Infections
17. David Hume, Roslin Institute
18. Robin Weiss, University College London
19. Barbara Bannister, Royal Free Hospital
20. Simon Denegri, Association of Medical Research Charities
21. Andre Rycroft, Royal Veterinary College
22. John Keddie, GlaxoSmithKline
23. Stewart Gray, NPHS Wales
24. Mike Simmons, Welsh Assembly
25. Mike Francis, Schering Plough
26. Jonathan Heeney, University of Cambridge
27. Gary Burns, AstraZeneca
28. Colin Howard, Royal Veterinary College

ANNEX 4

PATHOGENS REQUIRING ACCESS TO HIGH CONTAINMENT FACILITIES ^{1,2}

HUMAN CATEGORY 4 ORGANISMS

Lassa fever virus
Guaranito virus
Junin virus
Machupo virus
Sabia virus
Crimean/Congo Haemorrhagic Fever virus
Ebola virus (all subtypes)
Marburg virus
Omsk haemorrhagic fever virus
Kyasanur Forest disease virus
Russian spring-summer encephalitis virus
Herpesvirus simiae (B-virus)
Hendra virus
Nipah virus
Variola (major and minor)

ANIMAL SAPO 4 ORGANISMS

African swine fever virus
Avian influenza viruses (pathogenic)
Avian influenza viruses (uncharacterised)
Foot and mouth disease virus
Hendra virus
Newcastle disease virus (pathogenic)
Newcastle disease virus (uncharacterised)
Nipah virus
Peste des petits ruminants virus
Rinderpest virus
Swine vesicular disease virus
Teschen disease virus
Rabies virus and all viruses under the Lyssavirus family

¹ www.hse.gov.uk/pubns/misc208.pdf

² www.defra.gov.uk/animalh/diseases/pathogens/classification.htm

ANNEX 5

CONTAINMENT MEASURES FOR HIGH CONTAINMENT LABORATORIES DEPENDING ON COSHH, SAPO AND GMO(CU) REQUIREMENTS ^{1,2}

Containment measures	COSHH	SAPO	GMO(CU)
The workplace is to be separated from any other activities in the same building	Yes	Yes	Yes
Input air and extract air to the workplace are to be filtered using HEPA or equivalent	Yes, on input and double on extract air	Yes, single on input and double on extract air	Yes, extra requirements for viruses
Access is to be restricted to authorised people only	Yes, via airlock key procedure	Yes, restricted and entry through an airlock, clean/dirty area. Shower on exit	Yes, via airlock key
The workplace is to be sealable to permit disinfection	Yes	Yes	Yes, sealable for fumigation
Specified disinfection procedure	Yes	Yes	Yes
The workplace is to be maintained at air pressure negative to atmosphere	Yes	Yes, pressure to be maintained at not less than -75 Pa	Yes
Efficient vector control, eg rodents and insects	Yes	Yes, and proofed against entry or exit of animals and insects	Yes
Surfaces impervious to water and easy to clean	Yes, for bench, floor, walls and ceiling	Yes, for working surfaces, walls and ceiling	Yes, for bench, floor, walls and ceiling
Surfaces resistant to acids, alkalis, solvents, disinfectants	Yes, for bench, floor, walls and ceiling	Yes, for working surfaces, floor, walls and ceiling	Yes, for bench, floor, walls and ceiling

Containment measures	COSHH	SAPO	GMO(CU)
Safe storage of a biological agent	Yes, secure storage	Yes, secure storage in the laboratory suite, inventory to be maintained	Yes, secure storage
An observation window, or alternative, is to be present, so that occupants can be seen	Yes	Yes	Yes
A laboratory is to contain its own equipment	Yes	Yes	Yes
Infected material, including any animal, is to be handled in a safety cabinet or isolator or other suitable containment	Yes	Yes	Class III cabinet required
Incinerator for the disposal of animal carcasses	Yes, on site	Yes, or some other validated means of pathogen inactivation and safe carcass disposal	Yes, on site
Treatment of liquid and solid wastes	All waste should be made safe or safe to handle before leaving the laboratory	All wastes to be sterilised by a procedure known to inactivate the pathogen(s). For solids this requires autoclaving followed by incineration	Inactivation by validated means
Laboratory security		Laboratory and animal rooms to be kept secure and locked. Intruder alarm system to be fitted	

¹ From the Health and Safety Executive's guidance on 'Biological Agents – The principles, design and operation of containment level 4 laboratories' first published in 05/06.

² Anti-Terrorism, Crime and Security Act 2001 Part 7, Schedule 5 as amended in 2002 and 2007

ANNEX 6A

UK HIGH CONTAINMENT FACILITIES – GENERAL INFORMATION

SITE, AND LOCATION	CONTAINMENT LEVEL AND PHYSICAL SECURITY	FUNDING	MAIN FUNCTION
	SAPO4.		Animal vaccine production.
	SAPO4.		Research and development, diagnosis and animal vaccine testing, National and International Reference Laboratories for epizootic viral diseases of animals
	SAPO4.		Research and development
	SAPO4.		Research, surveillance, diagnostic testing, emergency response to exotic diseases, International reference centre for animal diseases
	SAPO4 & ACDP CL4.		Applied research and development and diagnosis of human

			and zoonotic infections
	ACDP CL4.		Diagnosis and associated applied research and development for human infections (limited by mandate); some diagnostic reagent production
	SAPO4.		Applied research, development of biological standards and control of biological products
	ACDP CL4.		Applied research; speciality in aerosol challenge
	SAPO4.		Research, diagnosis and production of diagnostic reagents; WHO influenza surveillance and reference centre
	SAPO 3.		Applied research and development on prevention and control of endemic animal infectious diseases; epidemiology and

			surveillance; contract research
--	--	--	------------------------------------

ANNEX 6B UK HIGH CONTAINMENT FACILITIES – PHYSICAL INFRASTRUCTURE

SITE	STATUS	EXPECTED LIFETIME	SIZE AND NUMBER OF LABORATORIES	TYPE OF LABORATORIES

ANNEX 6C UK HIGH CONTAINMENT FACILITIES – ANIMAL SPECIES AND HOLDING CAPACITY

SITE	CONTAINED ANIMAL FACILITIES	SPECIES AND HOLDING CAPACITY
------	-----------------------------	------------------------------

ANNEX 7 STAFFING AND TRAINING

SITE	STAFFING	TRAINING PROCESS
		Generic induction on site requirements, biosecurity, health and safety. Facility specific training for manufacturing procedures (SAPO4 and non-containment areas) with effective apprenticeship process
		Series of induction modules covering microbiological safety and 1 to 1 tuition through a competent mentor during the training period. Training given in clean units before proceeding to work in high containment areas
		Staff provided with internal bespoke theory and competency based training programmes; refresher courses on a regular basis for all staff
		Apprenticeship first at ACDP CL3 level and then mentoring at ACDP CL4/SAPO4 level; visiting staff can be accommodated subject to security vetting, safety training and close supervision with in house staff; some cross accreditation of competence with staff in other high containment facilities
		Documented history of substantive work at containment levels 2 and 3 prior to commencing training for containment level 4. Full training including all emergency procedures relating to both the specific work being undertaken by the individual and all the risks associated with other viruses and procedures being undertaken in the laboratory must be undertaken before commencing work. Only visiting workers that have been previously trained to work under containment level 4 can be accommodated
		Prior to selection to work at SAPO4, staff must demonstrate

		competence in relevant procedures at CL2 and CL3. All procedures and practices are performed according to SOPs. Institute Director approves competency training of high containment staff
		Training involves apprenticeship and progression through containment levels but has only been in operation for 2 years; external workers can use facilities but competency assessed on an individual basis and they are subject to supervision by known trained staff; some cross accreditation of competence with staff in other high containment facilities (HPA CEPR)
		Training is through an apprenticeship system via ACDP CL3 containment; CCTV monitoring of staff during training; competence is assessed internally
		Training is informal and largely in-house, especially for animal technicians; some staff trained by HPA; training provided to external workers for HO licences for large animals

ANNEX 8 STRENGTHS, WEAKNESSES, OPPORTUNITIES AND THREATS FOR THE UK'S HIGH CONTAINMENT FACILITIES

STRENGTHS	WEAKNESSES	OPPORTUNITIES	THREATS
<ul style="list-style-type: none"> • Good international reputation for working with dangerous pathogens • Strong academic base • Good legislative and regulatory framework • Sound physical and biosecurity systems in place; some new facilities • Expertise in diagnostic testing disease, surveillance systems and epidemiology • Emergency response plans to accommodate disease emergence and surge capacity • Current demands for high containment facilities being met • Strong ethical position on animal handling 	<ul style="list-style-type: none"> • Some ageing facilities • Significant 'down' times for maintenance • Low level of communication between ACDP CL4 and SAPO4 workers • Restricted access to academic workers • Little networking between architects, design engineers etc with expertise in high containment • No standardised training programmes • Staff security vetting • Limited capacity to accommodate improved technologies • Limited capacity to handle non-human primates 	<ul style="list-style-type: none"> • Development of a co-ordinated national strategy to sustain capacity and achieve balance between under and over provision • Centralisation of facilities and development of 'research hotel' concept • Creation of state-of-the-art facilities over medium time scale • Development of accredited training programmes • Improved visibility and presence across European network of high containment facilities • Development of good governance arrangements between collaborative partners 	<ul style="list-style-type: none"> • Lack of capital investment for new building programmes • Adverse judgements from local planning authorities for new building projects • Lack of on-going ring-fenced support for running costs and routine maintenance • Staff turnover and marginal succession planning • Insufficient capacity to cope with surge demands • UK becoming uncompetitive in this area • Poor public perception of the facilities and needs for high containment work

