A REVIEW OF THE REGULATORY FRAMEWORK FOR HANDLING ANIMAL PATHOGENS

Chaired by Sir Bill Callaghan

Presented to the Secretary of State for Environment, Food and Rural Affairs

13 December 2007

A REVIEW OF THE REGULATORY FRAMEWORK FOR HANDLING ANIMAL PATHOGENS

Chaired by Sir Bill Callaghan

Presented to the Secretary of State for Environment,
Food and Rural Affairs

13 December 2007

Department for Environment, Food and Rural Affairs
Nobel House
17 Smith Square
London SW1P 3JR
Telephone 020 7238 6000
Website: www.defra.gov.uk

Further copies of this publication are available from:

Defra Publications
Admail 6000
London
SW1A 2XX
Tel: 08459 556000
Email: defra@iforcegroup.com

Contents

Foreword

1. The investigations into the outbreaks of Foot and Mouth Disease (FMD) which began in Surrey in August 2007 concluded that the most likely cause was an accidental release of virus from Pirbright – a site which houses an Institute for Animal Health (IAH) laboratory; Merial, a commercial animal vaccine manufacturer; and Stabilitech, a small company that works with FMD Virus in a small laboratory within the IAH facility. This was clearly a devastating conclusion, not just for the farmers and others who had suffered as a result of the outbreak, but also for all those working at the Pirbright site, whose reputations depended to a large degree on their maintaining the highest levels of biosecurity.

2. We recognise that the ability to handle animal pathogens is essential if we are to fully understand infectious diseases and to develop effective vaccines. We also recognise that work carried out in UK laboratories is of national and international importance.

3. In September 2007, the Secretary of State for Environment, Food and Rural Affairs asked me to lead the review of the regulatory framework for handling animal pathogens and to make recommendations to Government for changes that would strengthen the regulation of animal pathogens. Our terms of reference are set out on page viii and the membership of our team is set out in Annex 1. We were supported in this work by a Secretariat composed of Defra civil servants, whose names also appear in Annex 1.

4. We were asked to carry out an urgent review and to make recommendations by 14 December for further consideration and implementation. We began our work early in October and I am grateful for the hard work and support of Review Team colleagues and officials to enable us to meet our deadline. In the limited time available we have gathered evidence and views from a wide range of sources and identified a number of areas where we think that significant improvements can be made to the current regulatory regime. We have made a number of recommendations outlining the changes that are needed. These changes will contribute to enhancing the safety of laboratories working with animal pathogens. But it is important to remember that no regulatory system can alone deliver zero risk. The responsibility for managing risk lies clearly with those who manage laboratories and associated facilities. They must have sound management systems and well-trained and competent staff and also a strong safety culture. But we consider that good regulation, sensibly applied and observed, can reduce the risk of another escape such as the one we saw from Pirbright to a level that is very close to zero.

Sir Bill Callaghan

Executive summary and key recommendations

1. In September this year, we were asked by Government to urgently review the regulatory framework for animal pathogens. This was in the light of the findings of two earlier reviews commissioned by the Government in the immediate aftermath of the accidental release of FMD virus from Pirbright. We were also asked to review Defra's role as regulator, licensor and inspector of SAPO 4 regulation and as a major customer of animal pathogens research and diagnostics.

2. The ability to handle animal pathogens in laboratories is essential if we are to fully understand infectious diseases and to develop effective vaccines against them. Without this research, there would be a significant adverse impact on the well being of both people and animals around the world. However, the general public rightly expects that laboratories which keep dangerous pathogens are managed in a way that does not expose them to biorisks.

3. In our view, the primary responsibility for managing the risks must lie with the top managers of any facility where work on dangerous pathogens is carried out. The senior management must also be held accountable for biosecurity. There can be no ambiguity in this. Within any facility handling dangerous pathogens, it is vitally important that senior managers provide the necessary **leadership** to establish and maintain management systems that ensure staff are properly trained and have a thorough understanding of the risks. We think that it should be a top management priority to instil a **strong safety culture** in the all the staff at the facility (and contractors who come onto a site for short periods of time). In our view, there needs to be **visible** commitment from the top to this priority.

4. The role of the regulatory framework should then be to provide the necessary assurance that the management systems and standard operating procedures are effective. **In our view, the regulatory outcome we are seeking to achieve must be that the system provides an assurance that the risk of accidental release is close to zero**. The consequences of failure are just too great to permit anything else.

5. Where there are several separate organisations operating from the same site, there must, in our view, be complete clarity as to who is responsible for the site infrastructure and how biosecurity for the site as a whole is managed. At Pirbright, it was not at all clear who was ultimately responsible for the biosecurity of the site overall. This is not a satisfactory state of affairs. We believe that it is essential to identify the **'controlling mind'** in respect of biosecurity, be it a governing body or an individual, i.e. someone who is ultimately responsible for the whole site.

6. *The Management of Health and Safety at Work Regulations 1999* (MHSWR) place clear duties on employers sharing a site to co-operate with each other in managing health and safety. The MHSWR apply to laboratories handling human pathogens. It seems to us that an equivalent duty should exist for those in charge of facilities handling pathogens which though not harmful to humans, can cause immense harm to animals if released into the environment. **We recommend that consideration is**

given to extending the duty to co-operate in any new regulatory framework for handling dangerous pathogens.

7. The principal consideration in respect of handling dangerous pathogens is that of 'containment' i.e. the way in which dangerous pathogens are managed in a laboratory environment to prevent exposure of laboratory workers, other workers and people and animals in the outside environment to the pathogen. This is usually achieved by a combination of:

   Primary containment i.e. use of good microbiological techniques, personal protective equipment and devices such as safety cabinets etc., and

   Secondary containment i.e. laboratory design and operating procedures e.g. access restriction, air handling, autoclaving and safe disposal of waste.

8. In our review, we have focused on what we believe are the three key pieces of legislation that have a bearing on 'containment' levels for dangerous pathogens. These are:

   - *The Control of Substances Hazardous to Health Regulations 2002* – general and biological agents provisions;
   - the *Genetically Modified Organisms (Contained Use) Regulations 2000*; and
   - the *Specified Animal Pathogens Order 1998*.

9. We found that the regulatory landscape that applies to laboratories carrying out work with animal and/or human pathogens is complex and disjointed, with differing regulatory philosophies and practices, and different levels and types of inspection, enforcement and sanctions. This is an example where, *pace* Hampton, the complexity of the regulatory system leads to:

   - laboratories being subject to unnecessary inspections;
   - overlapping areas of responsibility by regulators;
   - regulators devoting scarce resources to activity being replicated in other regulators, especially in the collation of information
   - risk assessment not being comprehensive

10. Given that all of the regulations share the common goal of preventing the release of harmful pathogens, we think there is a compelling argument that the current differing approaches for regulating animal and human pathogens should be replaced by a single framework. **We therefore recommend that Defra, DH, HSE and other interested parties work together to develop a single regulatory framework to govern work with human and animal pathogens**.

11. We note that it is Government policy to recover costs of services wherever possible. We think this is the right way forward. **We therefore recommend that Defra, DH, HSE and other interested parties work towards the introduction of cost recovery in any new regulatory framework. We further recommend that work on this issue commence immediately**.

12. As we see it, the risk assessment should be the basis of regulatory compliance by a duty holder and should inform decisions about regulatory activities, such as inspections. **We therefore recommend that risk assessment be a key element of the single regulatory framework for handling human and animal pathogens.**

13. As part of the single regulatory framework, we think there should be a common set of containment measures aimed at ensuring dangerous pathogens are not released such that they can cause harm. **We therefore recommend that ACDP be tasked with formulating a common set of containment measures to apply to both animal and human pathogens.**

14. We understand that there is no simple relationship between a given pathogen's danger to animals and its danger to humans. We accept that departures from the basic framework should be permitted. The approach set out in the GMO(CU) Regulations is attractive in that it gives the regulator and the operator a clear framework within which to engage in constructive dialogue about the most appropriate measures needed. **We therefore recommend that the regulator under the single regulatory framework be given discretion to agree with operators departures from the containment measures drawn up by ACDP, on the basis of risk assessments.**

15. As regards Defra's role as regulator, licensor and inspector of SAPO 4 regulation and as a major customer of animal pathogens research and diagnostics at Pirbright, we find that there was a conflict of interest. This led us to ask whether an independent regulator with all the necessary technical knowledge would have behaved differently in the face of the published correspondence from Merial about the state of the drains on the Pirbright site. We conclude that an independent regulator would at least have sought confirmation that the drains were fully functioning at the time and would have considered the possibility of regulatory action. **We therefore recommend that responsibility for inspection and enforcement functions in respect of animal pathogens should move from Defra to a body that is not subject to the same conflict of interest and which has access to the range of technical expertise needed to carry out the regulatory function fully.**

16. Having concluded that Defra should not continue as the regulator of laboratories handling animal pathogens, and having also concluded that there ought to be a single regulatory framework for both human and animal pathogens, we considered the issue of who would be best placed for this role. **We recommend that HSE become the single regulatory body for both animal and human pathogens.**

17. We recognise that these regulatory changes will take time to effect. But, given that the current SAPO framework does not, in our view, deliver the desired regulatory outcome, it is incumbent on us to propose a practical way forward that allows the key assurances to be provided to the general public urgently. **We therefore recommend a phased approach to these changes**.

18. These phases are:

Phase 1	Defra enter into immediate discussions with HSE to formalise HSE's support of SAPO inspections by 1 January 2008. ACDP is asked to begin work now on drawing up guidance on a single set of containment requirements for human and animal pathogens.	**HSE support formalised by January 2008**
Phase 2	Changes are made to SAPO to designate HSE as the inspection and enforcement body under the Order.	**Changes needed to SAPO made by April 2008**
Phase 3	Defra, DH, HSE and other interested parties begin work urgently with a view to bringing in the single regulatory framework.	**Single regulatory framework in place by end 2008**

Terms of reference for the review

1. Following confirmation of Foot and Mouth Disease (FMD) in cattle in Surrey on 3 August 2007, it quickly became evident that a release of FMD virus from the laboratory complex at Pirbright was a possible cause of the disease outbreak. The Government commissioned two reviews of biosecurity arrangements, one conducted by the Health and Safety Executive and the other by Professor Brian Spratt.[1,2] Responding to these two reviews, the Government agreed with the HSE that a review of the regulatory framework for animal pathogens should be undertaken, and with Professor Spratt that the position of Defra as regulator, licensor and inspector of SAPO 4 regulation and as a major customer of animal pathogens research and diagnostics should also be reviewed.

2. Our review accordingly looks at both of these issues. Our terms of reference, as published in the "Government Statement in response to investigations into the probable release of FMD virus from Pirbright" are:

   "The review will take forward recommendations of the HSE's report on potential breaches of biosecurity at the Pirbright site 2007 and Professor Spratt's review of safety of UK facilities handling FMD virus, by making recommendations to Government no later than 14 December 2007 on:

   Any changes needed to clarify and strengthen the regulatory framework for animal pathogens in the light of that for human pathogens;

   Any steps needed to ensure independence and clarity on the separate roles and responsibilities of funders, regulators, customers and the institutions themselves; and

   Any steps needed to provide clear lines of accountability, inspection protocols and responses to non-compliance and breaches"

3. We will seek the advice of the Advisory Committee on Dangerous Pathogens (ACDP) on technical matters with a view to the production of new guidance on managing animal pathogens in light of our findings.

4. We have also been asked to follow up the HSE recommendation on the arrangements for setting and monitoring safe operating practices where work is sub-contracted under a single operating SAPO licence and will be seeking the advice of the ACDP on this matter.

5. We were asked to undertake this review by the Secretary of State for Environment, Food and Rural Affairs. However, we have spoken to officials in the Devolved Administrations and have found them to be generally supportive of our conclusions and recommendations. We believe that it would be sensible if our recommendations were applied across the UK as a whole. Therefore, we would look to the Devolved Administrations to consider our recommendations.

[1] Professor Spratt, *Independent review of the safety of UK facilities handling foot-and-mouth disease virus* (2007).

[2] Health and Safety Executive, *Final report on potential breaches of biosecurity at the Pirbright site 2007.*

1. INTRODUCTION

1.1 The ability to handle animal pathogens in laboratories is essential if we are to fully understand infectious diseases and to develop effective vaccines against them. The UK is a world leader in veterinary microbiological sciences and the research carried out in UK laboratories plays an important role in the international fight against existing and emerging diseases.[3] Without this research, there would be a significant adverse impact on the well being of both people and animals around the world.

1.2 Recent reviews of the need for national facilities for infectious animal disease, research, surveillance and diagnostics have concluded that there is an ongoing need for *facilities operating to high standards of biological and physical security to underpin the [UK's] strategic, emergency response capability to incursions of exotic disease*.[4,5] We believe that this is right.

1.3 However, the benefits of handling these pathogens must be viewed against the significant risks of having them in UK laboratories. The accidental or deliberate release of dangerous animal pathogens from a laboratory could give rise to a serious animal or human disease outbreak. In addition, staff working in the laboratories themselves also need to be protected from the risk of exposure to dangerous pathogens.

1.4 Aside from the capacity to cause disease, a failure of biosecurity in laboratories that are handling animal pathogens can have a devastating economic impact and cause severe disruption to the food industry. Early estimates of the cost of the FMD outbreak in August and September of this year, which was to all intents and purposes a localised outbreak, are in excess of £100 million. (The widespread FMD outbreak in 2001, which, it must be stressed, was not caused a failure of laboratory biosecurity, cost the nation around £8 billion in total).[6]

1.5 The finding by Professor Spratt and the HSE that the Pirbright site was the source of the FMD virus that caused the outbreak this year has come as a great blow to the confidence of not just the scientists working there but also to those working in other laboratories handling pathogens. Just as importantly, the public's confidence in UK science and the ability of Government to regulate it has been severely dented. The World Health Organisation (WHO) in its report on biorisk management states that:

> *The general public expects laboratory personnel to act responsibility and not to expose the community to biorisks, to follow safe working practices… associated with practices that will help keep their work and materials safe and secure…, and to follow an ethical code of conduct…. Often suspicious of work taking place in laboratories, the uninformed public may even feel threatened by the presence of a biological laboratory in their neighbourhood. It is the technical and moral duty of laboratory managers and laboratory workers, with the support of national authorities, to reassure the general*

[3] The Royal Society, *Infectious disease in livestock* (2002).

[4] Dr Richard Cawthorne, *Review of the UK's national facilities for infectious animal disease research, surveillance and diagnosis – A report for the Defra and the BBSRC* (2003).

[5] Professor Keith Gull, *Review of the Institute for Animal Health – Pirbright Laboratory – A report for BBSRC Council* (2002).

[6] National Audit Office, *The 2001 Outbreak of Foot and Mouth Disease* (2002).

public, to persuade them that the activities being conducted are beneficial and necessary, and to prove that the biorisks inherent to laboratory work are controlled with appropriate safeguards to meet their expectations.[7]

1.6 We fully concur with the view expressed in the WHO report and our review will seek to address how this can be fully implemented in all UK laboratories.

1.7 However, although they are rare, accidental releases of FMD virus have occurred on a number of occasions in the past. In 1960, an outbreak of FMD on a farm in Surrey close to the Pirbright site was believed to have arisen from an accidental release from the laboratory. Accidental release of FMD virus from laboratories has also occurred in other countries. The FMD outbreaks in Denmark in 1982 and 1983 were attributed to release and subsequent airborne transmission from a laboratory on the Baltic island of Riems.[8]

1.8 Clearly the duty lies with those who are working with hazards to prevent the accidental release of pathogens. It is incumbent on those who control work with dangerous pathogens to have in place effective management systems that embed regulatory requirements in working practices and standard operating procedures. It is essential that a strong safety culture be deeply ingrained in those organisations and facilities that handle dangerous pathogens. Without this, the best regulatory framework in the world will not deliver its objective. We return to this point later in the report.

1.9 The role of the regulatory framework should then be to provide the necessary assurance that the management systems and standard operating procedures are effective. **In our view, the regulatory outcome we are seeking to achieve must be that the system provides an assurance that the risk of accidental release is close to zero**. The consequences of failure are just too great to permit anything else. This sector is not alone in being an area where there are major risks that need to be effectively regulated and where the cost of failure can be catastrophic; the chemical, petroleum and nuclear industries are other notable examples.

1.10 Considerable attention has been given in recent years to better regulation. Most recently Philip Hampton in his report on *Reducing Administrative Burdens: Effective Inspection and Enforcement*, made a number of recommendations that we believe have a direct bearing on the regulation of laboratories working on dangerous pathogens.[9] In addition, Professor Richard Macrory in his report on *Regulatory Justice: Making Sanctions Effective* made a number of points about providing regulators with a flexible and proportionate sanctioning *toolkit* to ensure protection of workers, consumers and the environment that we believe are also salient to our review.[10] We have, therefore, made a number of direct references to these reports in our review.

---

7 WHO, *Biorisk management – Laboratory biosecurity guidance* (2006).

8 T. Hugh Pennington, *Biosecurity 101: Pirbright's lessons in laboratory security*, Biosciences (2007) 2, 449-453. At page 452, he says that *"As a biosecurity problem FMD is special. Its ability to leave the confines of a laboratory is unmatched by any other microbe."*

9 Philip Hampton, Reducing administrative burdens: effective inspection and enforcement, HM Treasury (2005).

10 Professor Richard B Macrory, *Regulatory Justice: Making Sanctions Effective*, Better Regulation Executive, Cabinet Office (2006).

2. OUR APPROACH

2.1 We were asked by the Secretary of State for the Environment, Food and Rural Affairs to carry out an urgent review and to make recommendations for further consideration and implementation. In the limited time available we have gathered evidence from a wide variety of sources. We were granted access to all relevant Defra files concerning laboratories and sites permitted to handle animal pathogens under SAPO regulations, and we have considered publicly available material, including published reports and material on websites.[11] We have also spoken to a number of key individuals. A list of individuals whom we spoke to can be found at Annex 2. We have also undertaken visits to a number of laboratories and premises where animal and human pathogens are handled. We have aimed to cover a range of the pathogen risk categories, and have looked at laboratories in the Government, commercial and academic sectors. A list of laboratories visited during the course of the review can be found at Annex 3.

2.2 We are very grateful to everyone who has assisted us in the course of this review. As our review progressed, we shared our emerging findings with those we spoke to and found general support for them. Nevertheless, the recommendations that are presented in this report are ours alone and it should not be assumed that they coincide with the specific views of any of those we spoke to in the course of our work.

2.3 In our review, we have focused on what we believe are the three key pieces of legislation that have a bearing on the containment of dangerous pathogens. These are:

The *Control of Substances Hazardous to Health Regulations 2002* – general and biological agents provisions;

the *Genetically Modified Organisms (Contained Use) Regulations 2000*; and

the *Specified Animal Pathogens Order 1998*.

2.4 In addition to these regulations, laboratories working with pathogens are usually also regulated under the *Animals (Scientific Procedures) Act 1986*. This imposes responsibilities on people with specific roles in relation to the care and use of animals in laboratories and is enforced by the Home Office. Under Part 7 of the *Anti-Terrorism, Crime and Security Act 2001* legal requirements are imposed to ensure the secure storage and use of dangerous pathogens and toxins listed in Schedule 5 of the Act. We are pleased to note that HSE and the security services work closely together in respect of these requirements. We will not be considering these particular regulations further in our review.

[11] Although, given the time constraints, we did not formally invite submissions to our review; we did receive submissions from the Biotechnology and Biological Sciences Research Council (BBSRC), Institute for Animal Health (IAH) and the Veterinary Laboratories Agency (VLA), and Professor Keith Gull, which we considered in reaching our conclusions.

2.5 For FMD virus specifically, the European Community requires (under Directive 2003/85/EC) that Member States' competent authorities strictly control laboratories and establishments in which live foot-and-mouth disease virus, its genome, antigens or vaccines produced from such antigens are handled for research, diagnosis or manufacture. Further, the handling of FMD virus is only permitted in laboratories listed in the Directive. The Directive also specifies that laboratories handling live FMD virus must meet or exceed the minimum requirements laid down in the "Minimum standards for Laboratories working with foot and mouth virus in vitro and in vivo" established by the European Commission for the control of foot-and-mouth disease, 26th Session, Rome, April 1985, as modified in 1993. For the purposes of our review, we believe that these Community requirements are implemented in GB by the *Specified Animal Pathogens Order 1998* and we will not consider them further.

2.6 For completeness, we add that although our review was not asked to look at the regulatory framework for laboratories handling fish pathogens, bee pathogens and plant pathogens, similar considerations as set out below will also apply in those areas. [12]

2.7 There is no accepted definition of the term 'biosecurity'. In this report we have used the term in the sense described in the recent HSE report on Pirbright, i.e. to cover the implementation of a combination of containment measures and work practices, supplemented by management controls, to prevent the inadvertent exposure of susceptible species to biological agents and their distribution in the wider environment.[13]

[12] Research involving some pathogens of fish is currently notifiable and controlled by Orders under the Diseases of Fish Acts 1937 and 1983, or under the Fish Health Regulations 1997 (as amended). Research involving plant pathogens and pests is regulated under the Plant Health (Great Britain) Order 1993 (as amended). Research involving bee pathogens is permitted by licence under the Bee Diseases and Pests Control (England) Order 2006.

[13] See reference 2, page 11 WHO make a distinction between 'biosafety' and 'biosecurity'.

3. THE REGULATORY REGIME FOR HANDLING DANGEROUS PATHOGENS

3.1 The principal consideration in respect of handling dangerous pathogens is that of 'containment' i.e. managing the laboratory environment so as to prevent exposure of laboratory workers, other workers and people and animals in the outside environment to a pathogen. This is usually achieved by a combination of:

Primary containment i.e. use of good microbiological techniques, personal protective equipment and devices such as safety cabinets etc., and

Secondary containment i.e. laboratory design and operating procedures e.g. access restriction, air handling, autoclaving and safe disposal of waste

3.2 The appropriate level of containment to be applied will depend on the hazard posed by the particular pathogen. In the UK, the Advisory Committee on Dangerous Pathogens (ACDP) categorises human pathogens into hazard groups 1 to 4 with corresponding containment levels. Defra also defines its own hazard groups 1 to 4 for specified animal pathogens and its own corresponding containment levels. The Defra specifications are based on recommendations published by the Office International des Epizooties (OIE – the World Animal Health Organisation). The Scientific Advisory Committee on Genetic Modification (SACGM) provides guidance on requirements for containment levels 1 to 4 to be applied to GMOs depending on the respective risk classification.[14,15,16]

3.3 In most other countries, World Health Organisation (WHO) (See Annex 6) and OIE classifications and guidance (See Annex 7) are followed to a greater or lesser extent. We have looked at the regulatory systems and practices which apply internationally, and at examples of regulatory regimes in some other countries (Canada, the United States, Switzerland and Norway) in Annex 12. Whilst we find general agreement over the essential principles, we also find variations in approaches and standards.

3.4 A key recommendation in HSE's final report on potential breaches of biosecurity at the Pirbright site 2007 was that there should be a review of the regulatory position for animal pathogens. In contrasting the containment requirements that applied, the HSE considered that the evident differences between the animal and human pathogens regimes required justification.[17]

[14] HSE, Biological agents – *The principles, design and operation of containment level 4 facilities* (2006).

[15] Defra SAPO Guidelines: www.defra.gov.uk/animalh/diseases/pathogens/category2.htm, , and similarly for category 3 and category 4.

[16] HSE, *SACGM Compendium of Guidance: Part 3 Containment and control of activities involving genetically modified micro-organisms* (2007).

[17] See reference 2, p 13.

3.5 The regulations

3.5.1 There are three separate but overlapping sets of regulations that bear on containment requirements for laboratories that handle human and animal pathogens.[18]

The *Control of Substances Hazardous to Health Regulations 2002* – general and biological agents provisions;

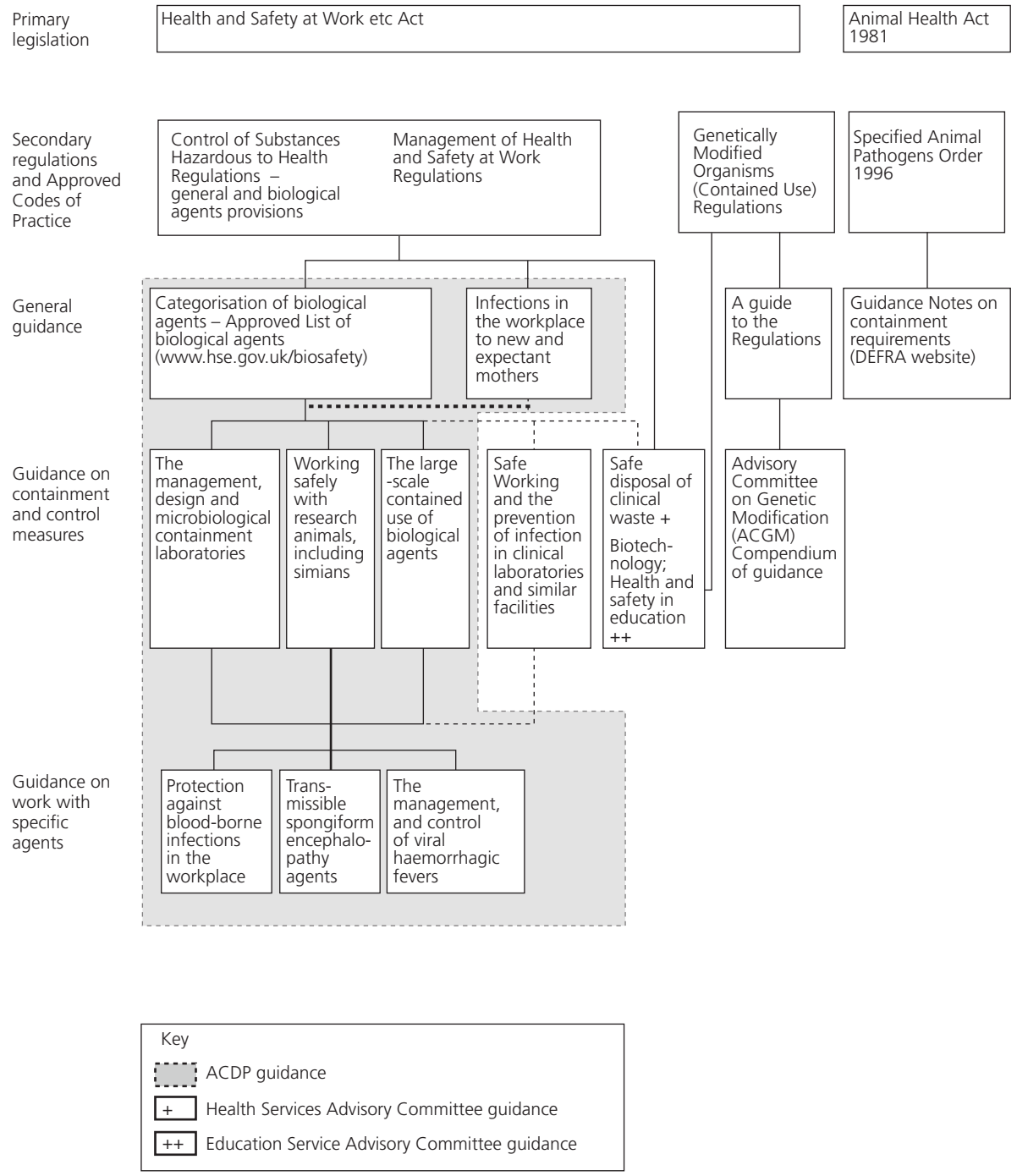
the *Genetically Modified Organisms (Contained Use) Regulations 2000*; and

the *Specified Animal Pathogens Order 1998*.

3.5.2 These regulations, and/or their accompanying guidance, specify the containment requirements proportionate to the hazard posed by individual pathogens. The overall regulatory framework is illustrated in **Figure 1**.

[18] In this report, unless otherwise stated, we refer to the legislative position in England, Scotland and Wales. However, separate but equivalent legislation has been made for Northern Ireland.

Figure 1: An overview of the relevant health and safety legislation and other guidance that should be consulted when working with biological agents in any type of microbiological containment laboratory[19]



[19] Taken from reference 14 p 3.

3.5.3 **The Specified Animal Pathogens Order 1998** (SAPO) is made under the Animal Health Act 1981 (and equivalent legislation for Devolved Administrations). Its main purpose is to prevent the release of dangerous animal pathogens into the environment where they may cause a serious animal (or human) disease. Regulation 4 of the Order provides that no person shall have in his *possession* any specified animal pathogen except under licence from the appropriate Minister (Defra in England, Welsh Assembly Government in Wales and Scottish Government in Scotland).[20] A licence will have attached to it conditions which will be determined by the inspector on behalf of the Minister.

3.5.4 **The Control of Substances Hazardous to Health Regulations 2002** (COSHH) are made under the European Communities Act 1972 and the Health and Safety at Work Act 1974. Amongst other things COSHH implements EC Directive 2000/54/EC on the protection of workers from risks related to exposure to biological agents. In contrast to SAPO, COSHH is primarily aimed at preventing exposure of workers to dangerous pathogens. It places duties on *employers* (i.e. those responsible for the workers in the laboratory) to carry out risk assessments on the hazardous materials in the workplace and to ensure that exposure of employees is either prevented or adequately controlled. The Health and Safety Executive (HSE) is the regulator responsible for implementing COSHH. Although there is no formal licensing requirement, there is a *de facto* 'permissioning system' by virtue of the requirement that anyone who wants to work on a dangerous human pathogen in a laboratory environment must notify, and must receive an acknowledgement from, the HSE.

3.5.5 **The Genetically Modified Organisms (Contained Use) Regulations 2000** (GMO(CU)) are made under the European Communities Act 1972 and the Health and Safety at Work Act 1974. Amongst other things they implement EC Directives 90/219/EEC and 98/81/EC. Unlike both COSHH and SAPO, the regulations seek to both protect persons against risks to their health and protect the environment against harm from activities involving genetic modification. Specifically, the regulations place a duty on a person carrying out an *activity* involving genetic modification to carry out a *suitable and sufficient* risk assessment to human health and the environment (regulation 6). The regulations establish a 'Competent Authority' comprising Defra's Secretary of State and the Health and Safety Executive in England and Wales (and Scottish Ministers as regards Scotland). No-one may work on genetically modified organisms (GMOs) for the first time without notifying the competent authority and receiving an acknowledgement. Schedule 1 of the Regulation sets out different classes (1-4) of activity in order of increasing risk. For activity classes 3 and 4 there is a further requirement for written consent from the Competent Authority prior to the activity commencing. HSE is the focal point within the Competent Authority for notifications under GMO(CU) and consults with Defra and the Scottish Government as necessary.

[20] Before 1980, the UK had no legislative controls on holding and manipulating animal pathogens. In 1980, the Importation of Animal Pathogens Order 1980 (IAPO) was introduced to control the importation of exotic animal pathogens. IAPO requires anyone wishing to import pathogens (or their carriers) to hold a licence, attached to which are conditions aimed at preventing the release of pathogens to the environment. With the introduction of the Single Market in 1992, it was no longer possible to control the movement of animal pathogens into the UK from other members states of the European Community. As a consequence the Specified Animal Pathogen Order 1993 (SAPO) was introduced which required anyone wishing to work with animal pathogens to be licensed by MAFF (now Defra in England).

3.6 In addition to the legal instruments themselves, there is also a significant amount of guidance material associated with the three sets of regulations we have described above. The COSHH Regulations are supported by an Approved Code of Practice (ACOP) which gives practical advice on compliance and has special legal status. Additional guidance is also available for both COSHH and the GMO(CU) Regulations. HSE publish copies of the two legal instruments along with the associated guidance (and in the case of COSHH, the ACOP). Guidance on the application of SAPO requirements is published on Defra's website. These include the detailed containment measures that apply to each hazard category of pathogens.

3.7 The ACDP (see Annex 4) provides scientific advice and guidance on risks from human pathogens and mitigation measures to be applied in laboratory environments. The Scientific Advisory Committee on Genetic Modification (SACGM) advises the Competent Authority on technical issues arising from activities notified under the GMO (CU) regulations and its associated amending regulations and develops and updates guidance on all aspects of contained use of GMOs. SACGM also provides advice on risk assessments for contained use activities involving GMOs (covering >99% of GM activities in UK), including all Class 4 projects.

3.8 The regulations described above bear on *biosecurity* of laboratories handling dangerous pathogens. In addition, commercial laboratories manufacturing veterinary medicines, such as Merial at the Pirbright site, must also obtain, and work to, a Manufacturing Authorisation (Man A) from the Veterinary Medicines Directorate (VMD). There is a legal requirement for a holder of a Man A to manufacture products in accordance with the principles of Good Manufacturing Practice (GMP). The legal basis for GMP is the Veterinary Medicines Regulations which implements EC Directive 91/412/EEC.

3.9 VMD is the body with responsibility for ensuring that manufacturers of veterinary immunological products comply with the requirements of GMP. GMP inspectors from VMD inspect manufacturers every two years in accordance with the Directive and, following a satisfactory audit, will issue a GMP certificate to demonstrate that the manufacturer meets the required standard.

3.10 Similarly, commercial laboratories manufacturing human medicines (which may involve the use of animal pathogens as well as human pathogens) must also work to GMP. The Medicines and Healthcare products Regulatory Agency (MHRA) is the body responsible for ensuring that GMP is observed in those cases.

3.11 Alongside the legislation that bears directly on the handling on dangerous biological organisms, all workplaces are governed by the general provisions of health and safety legislation. In particular, there are other requirements under COSHH as well as those relating specifically to biological hazards, and HSE, as the regulator for all aspects of COSHH and other health and safety requirements, carries out inspections of all laboratories in this regard.

4. THE REGULATORY REGIMES IN ACTION: COMPARING REGULATION OF HUMAN AND ANIMAL PATHOGENS

4.1 How the regulations are implemented

4.1.1 The previous chapter set out the legislative framework as it currently stands. In this chapter we examine how the requirements of the legislation are applied in practice.

4.2 SAPO

4.2.1 There are in total 68 laboratories that have a SAPO licensee in the UK, of which 37 are in England, 28 in Scotland and 3 in Northern Ireland. There are no SAPO licensees in Wales. Of these, 10 are for work with pathogens classified as Category 4, the highest risk level, all of which are in England.

4.2.2 In England, one senior veterinary official in Defra's Food and Farming Group carries out inspections of laboratories working with pathogens in SAPO Category 4. Inspections of laboratories working with pathogens in SAPO Categories 3 and 2 (there being no pathogens listed in Category 1) are carried out on behalf of Defra by 4 members of the veterinary staff at the Veterinary Laboratories Agency (VLA). In total, Defra spends on the order of £100k per year on inspection of SAPO laboratories and issuing licences. In Scotland, where there are currently no laboratories working with SAPO Category 4 pathogens, inspections are carried out by a Veterinary Adviser working in the Scottish Government, assisted by veterinarians from Animal Health. Costs are not recovered for carrying out inspections or the issue of licences.

4.2.3 Although inspections of SAPO laboratories are carried out by Defra (or its Devolved Administration equivalents) or VLA, local authorities are responsible for enforcement under SAPO (regulation 8) and we understand that in practice this would mean the Trading Standards Officers. This responsibility applies to taking prosecutions under SAPO when there is a breach of a licence conditions. Since the Local Authority does not in general fulfil any inspection role, it is therefore left to inspectors to identify failures to comply with the requirements of SAPO and to alert the Local Authority when they consider that a prosecution might be warranted. Inspectors themselves have no enforcement tools other than recommending revocation of a licence (by Defra or one of the devolved departments) or alerting the relevant local authority that a prosecution might be appropriate. As far as we are aware, no-one has ever been prosecuted for breach of a SAPO licence condition.[21]

[21] We understand that Surrey County Council Trading Standards Department are considering the evidence with a view to determining whether to bring a prosecution following the release of FMD virus from the Pirbright site in August.

4.3 COSHH and GMO(CU)

4.3.1 HSE's Biological Agents Unit (BAU), part of the Hazardous Installations Directorate, is responsible for regulating facilities and work activities where highly pathogenic micro-organisms and genetically modified organisms are intentionally handled. BAU's main aim is to ensure that the risks arising from these activities are properly controlled and to assure the public that this is so. BAU inspectors enforce the Health and Safety at Work Act 1974 (HSWA) and other relevant statutory provisions, including COSHH and GMO(CU). They use enforcement powers under HSWA to secure compliance and to prevent infection and ill-health in the work place and in respect of environmental protection.

4.3.2 BAU provides specialist advice on all aspects of micro-organisms, including to other parts of HSE which have responsibility for regulating work activities which may involve or give rise to bacteria, viruses, transmissible biological agents and genetically modified organisms.

4.3.3 BAU currently comprises 26 staff, of whom 15 are Specialist Inspectors – specialists in the fields of microbiology and biotechnology with a broad collective experience in the research, clinical and industrial biosciences sectors, and who are also competent in the regulation of occupational health and safety.

4.3.4 BAU has national primary inspection and enforcement responsibilities for all GB facilities working:

- at containment level 4 (handling the most hazardous pathogens in Hazard Group 4 e.g. Lassa fever) and High Security Infectious Disease Units (where human patients infected with such agents are treated)

- at containment level 3 (handling serious pathogens in Hazard Group 3 agents e.g. those that are responsible for diseases such as anthrax, HIV, Tuberculosis)

- at containment level 2 (handling moderate pathogens in hazard group 2 agents e.g. salmonella, E coli)

- with genetically modified micro-organisms at containment levels 4,3,2, &1 including those posing an environmental risk (e.g. GM animal and plant pathogens) and with GM plants and animals, including the environmental aspects of the contained use of transgenic organisms under agency agreement with Defra, the Scottish Government and the Welsh Assembly.

4.3.5 BAU manages the notification scheme for biological agents under COSHH and the national statutory scheme under the GMO(CU) for GMO notifications and consents on behalf of the UK Competent Authority. That Competent Authority is HSE and Defra for England and Wales (HSE liaises with the Welsh Assembly Government), HSE and the Scottish Government for Scotland, and HSE through an agency agreement for Northern Ireland. Since 1 April 2002, the HSE has received and processed 216 notifications related to COSHH and 1,117 notifications related to GMO (CU).

4.3.6 BAU specialist Inspectors are recruited directly from industry, academia and other government departments. Although they come with a wide range of scientific and technical backgrounds, they are given specific training in biosafety, regulatory framework and enforcement processes, and the behaviours HSE expects inspectors to demonstrate in the course of carrying out their duties. Specialist Inspectors undergo a programme of continuous professional development (CPD).

4.3.7 The full economic cost of the BAU was £1,536k in 2006/07. There are 8 facilities in GB operating at ACDP containment level 4 (CL4), 352 CL3 facilities in England, 21 CL3 facilities in Wales, 43 CL3 facilities in Scotland and 1 CL3 facility in N Ireland.

4.3.8 In carrying out its work, the BAU is required to follow the guidance provided in the Health and Safety Commission's "Enforcement policy statement". This document, published by HSE, sets out the general principles and approach which HSC expects the health and safety enforcing authorities (including HSE) to follow. It sets out guidance on the principles of enforcement under the headings of proportionality, targeting, consistency, transparency, and accountability, and also provides advice on determining whether a prosecution is justified. HSE has also published an Enforcement Management Model (EMM) – a framework which helps inspectors make enforcement decisions in line with the Health and HSC's Enforcement Policy Statement (EPS). Fundamental to this is the principle that enforcement action should be proportional to the health and safety risks and the seriousness of the breach.

4.3.9 HSE has also published a 'management plan' setting out how HSE will develop its internal management systems to respond to its strategic objectives. This includes measures to recruit and train staff and to build and manage expertise within the organisation.

4.4 Our Findings

4.4.1 The conflicting regulatory requirements

4.4.1.1 We spoke to a number of practitioners who work within these different regulatory frameworks on a daily basis. In most cases we found that they were sufficiently well-versed in the various requirements to steer a course between the differences and to maintain appropriate measures. However, it was also clear from our discussions that there is considerable room for uncertainty about exactly what the requirements are and how best to comply with them.

4.4.1.2 Our visits to laboratories that are inspected by the HSE showed that there was a high awareness of COSHH and the ACDP guidance about hazards and containment measures. Responsibilities under COSHH were clearly understood. In contrast, SAPO and its requirements were not always well understood even in those laboratories that had a SAPO licence.

4.4.1.3 We think it is important to note that the majority of laboratories will be working with pathogens that are a threat to both animal and human health (i.e. *zoonoses*). On our laboratory visits, we were often confronted with the explanation that a particular laboratory suite was "ACDP 3 but SAPO 4" (we have no doubt that other combinations and permutations are possible).

4.4.1.4 The HSE report on Pirbright highlighted their concern that the guidance on SAPO containment levels was likely to cause confusion because it states that the SAPO level 4 containment requirements were based on ACDP level 4 requirements, whereas in fact the SAPO requirements were quite different.22 The report noted that the culture at IAH Pirbright was quite different from that observed at ACDP 3 and 4 laboratories, with workers at IAH routinely coming into contact with virus materials. Although in that case no harm would be caused to the workers themselves from the purely animal pathogens, we consider that this could lead to an increase in risk of contamination of the environment.

4.4.1.5 We were also surprised to find that at IAH, and within the confines of a SAPO 4 facility with the most stringent containment requirements for the most dangerous animal pathogens, it was possible to walk outside the laboratory buildings with only a wire mesh fence separating the open-air area of the high-containment complex from the rest of the site.

4.4.1.6 Although there is a need to recognise the different threats posed to animal or human health by different pathogens, we do not think it is helpful to have in place two separate regulatory systems, each dealing with a different aspect of what is essentially the same thing i.e. the need to contain the pathogen and prevent its release such that it can cause harm. We have concerns that the various containment requirements are not set out in a way that encourages a clear understanding of what measures are necessary in order to achieve a given level of containment.

4.4.2 The different approaches to inspections

4.4.2.1 We were told that Defra's inspections under SAPO focused on risks to the environment whereas HSE inspections under COSHH focused on mitigating risks to people and particularly staff working with pathogens (the BAU usually carry out inspections of a facility under both COSHH and GMO(CU) at the same time).

4.4.2.2 The predominant view expressed by people working at laboratories we visited and which are regulated under SAPO was that Defra followed a 'tick box' and not a risk-based approach to the regulation. This is not surprising given that, unlike the COSHH or GMO(CU) regulations, there is no formal requirement for those handling animal pathogens to carry out a risk assessment. In the absence of any such requirement, a 'tick box' approach by the regulator might have seemed appropriate. On the other hand, HSE inspections were generally felt to be risk-based.

[22] See reference 2, p13.

4.4.3 The effectiveness of SAPO inspections

4.4.3.1 The effectiveness of Defra inspections was also questioned. This was understandable in the light of comments made by the Defra inspector, who told us that inspection work had been under-resourced for a number of years. It was explained to us that for both Defra and the VLA this was one responsibility amongst many others and as a result there had been insufficient time for training. Inspectors were basically required to learn on the job and essentially get on with it. In contrast we found that the HSE BAU was well trained and resourced to perform an inspection function efficiently and effectively. The problems perceived by the regulated parties were not, in our view, a reflection of failings on the part of the individuals who carried out the SAPO inspections for Defra. Instead we think they reflected more systemic failings as a result of the fact that Defra's regulatory enforcement function is a relatively small task, tacked on to a large organisation with other strategic goals.

4.4.3.2 We have found a significant difference between the resources allocated by HSE to laboratory inspections under COSHH and GMO(CU) and those allocated to inspections under SAPO by Defra (and the Devolved Administrations). We consider that the resources allocated to inspections and licensing under SAPO are less than we would expect for a regulatory task of this importance and should be increased.

4.4.3.3 It seems to us that Defra is not well placed to carry out this regulatory function. It lacks the depth of expertise needed and has not, in the past, allocated sufficient resource to the task. In this respect, that part of Defra responsible for SAPO regulation is effectively behaving like a "small regulator" in the terms described by Philip Hampton in his report. As a result, this function lacked the *political and institutional prominence* to be properly resourced.[23]

4.4.3.4 We understand that this problem had been recognised in Defra and some work has been done in the past to identify a delivery agent to carry out inspection functions. As far as we are aware, this work did not come to fruition.

4.4.4 Sanctions available to the regulator

4.4.4.1 We noted in Section 4 that under the SAPO regime the only sanction available to the regulator is the withdrawal of a licence. We also noted that local authorities were formally responsible for enforcement of breaches of licence conditions. This does not seem sensible to us because we do not believe that the local authorities would ever have the necessary expertise to fulfil this responsibility. As far as we are aware no one has ever been prosecuted for a breach of a SAPO licence term.

4.4.4.2 We believe that this does not constitute an effective sanctioning system. Richard Macrory in his review on regulatory sanctions recommended that regulators have a flexible and proportionate sanctioning toolkit. Evidence submitted to his review suggested that regulators reliant on one tool as the main sanction may

[23] See reference 9, p 60.

be unwilling to use it.[24] We found that this was also the case in applying the SAPO to IAH Pirbright. Defra had concerns about biosecurity at the IAH Pirbright facility but did not terminate the licence, instead continuing to issue licences for shorter periods than the normal 5 years.

4.4.5 Good Manufacturing Practice and Biocontainment

4.4.5.1 We heard from the top management team at Merial that the key driver for their systems and processes for manufacturing animal vaccines was the GMP requirements under the Veterinary Medicines Regulations. These GMP requirements (colloquially known as the "Orange Book") were designed to ensure that a product is safe for use and free from contamination from live virus. Failure would produce a severe reputational damage from which it would be difficult to recover. The Merial team gave an impressive account of the measures that had to be taken to meet the GMP requirements. However, we conclude from the most recent (November) release of virus from the Merial facility into the Pirbright drainage system that following GMP is not a substitute for effective regulatory measures to prevent accidental release of pathogens.

4.4.6 Biosafety officers

4.4.6.1 All laboratories now appear to have designated biological safety officers as part of their safety management systems. These individuals have a very important role to play in ensuring that a safety culture is maintained and enhanced. We heard that the role of biosafety officers is in the process of being given a professional status and we welcome this development and encourage regulatory authorities to actively engage in this process.

[24] See reference 10, p16.

5. ROLES AND RESPONSIBILITIES

5.1 In our terms of reference we were asked to look at:

> *Any steps needed to provide clear lines of accountability, inspection protocols and responses to non-compliance and breaches*

5.2 We want to emphasise the point that, in our view, the primary responsibility for biosecurity must lie with the top managers of any facility where work on dangerous pathogens is carried out. The senior management must also be held accountable for biosecurity. There can be no ambiguity in this. We are aware of the view held by some that, because the work carried out at some facilities is of national importance, the national regulator should accept a share of the risk involved in the handling of dangerous pathogens in those laboratories. We do not agree with this view. We do, however, agree that there should be constructive dialogue between the operators of facilities that are being regulated and the regulator, but this should not extend to acceptance of part of the risk on the part of the regulator. To do so would, in our view, compromise the independence of the regulator.

5.3 Within any facility handling dangerous pathogens, it is vitally important that senior managers provide the necessary leadership to maintain management systems that ensure staff are properly trained and have a thorough understanding of the risks. We think that it should be a top management priority to instil a **strong safety culture** in the all the staff at the facility (and contractors who come onto a site for short periods of time). In our view, there needs to be visible commitment from the top to this priority.

5.4 As our review was prompted by the investigations carried out by HSE and Professor Spratt into the release of FMD virus from the Pirbright site, we visited both IAH and Merial to gain a better appreciation of the facts on the ground for ourselves. At Pirbright, there are three different organisations (Merial, IAH and Stabilitech) working on the same site. We understand that the site is owned by BBSRC (which is the landlord for Merial and the sponsor for IAH).

5.5 We share concerns contained in Professor Spratt's report about the apparent lack of communication between IAH and Merial over issues of crucial importance to the overall biosecurity of the site. There is evidence of a continued lack of communication even after the August outbreak; and after it had been established that the release of virus was via the drainage system. We find this very surprising given what has happened.[25]

5.6 Where there are several separate organisations operating from the same site, there must, in our view, be complete clarity as to who is responsible for the site infrastructure and how biosecurity for the site as whole is managed. At Pirbright, it was not at all clear who was ultimately responsible for biosecurity of the site overall.

[25] We found the analysis in Rhodes, Catherine (2007) on the comparison between international guidelines on biosecurity and the situation in Pirbright compelling (Rhodes, Catherine, Genomics Monitor Issue No. 5, November 2007. Part II. *'Laboratory Biosafety and Biosecurity – A Case Study: The August 2007 Foot and Mouth Disease Outbreak in the UK')*.

This is not a satisfactory state of affairs. We believe that it is essential to identify what is sometimes termed the **'controlling mind'** in respect of biosecurity, be it a governing body or an individual, i.e. someone who is ultimately responsible for the whole site. The complexity of the relationships between the various parties on the Pirbright site left us somewhat baffled. We understand that there is a review looking into the funding, governance and risk management at Pirbright led by BBSRC. We await with interest the findings of this review and hope our review will contribute to its deliberations.

5.7 At the Moredun Research Institute in Edinburgh, where facilities are shared between a number of organisations, commendable efforts are being made to identify clear responsibilities and lines of communication – despite the complexity of the current regulatory framework. We also note that the use of shared facilities and sites is likely to increase (a pertinent example of which being the proposed move of the VLA's virology team to the Pirbright site. All concerned will have to be quite clear about responsibility for shared facilities and overall management).

5.8 For the moment, we note that *The Management of Health and Safety at Work Regulations 1999* (MHSWR) places clear duties on employers sharing a site to co-operate with each other in managing health and safety. The MHSW regulations apply to laboratories handling human pathogens. It seems to us that an equivalent duty should exist for those in charge of facilities handling pathogens which though not harmful to humans, can cause immense harm to animals if released into the environment. **We recommend that consideration is given to extending the duty to co-operate in any new regulatory framework for handling dangerous pathogens.**

6. DEFRA AS REGULATOR

6.1 In the final part of Professor Spratt's report, he noted that there is:

> *… a potential conflict of interest between the role of Defra as regulator, licensor and inspector of SAPO4 regulation and as a major customer of research and diagnostics related to exotic animal pathogens.*[26]

6.2 We have been asked specifically to consider "any steps needed to ensure independence and clarity on the separate roles and responsibilities of funders, regulators, customers and institutions themselves".

6.3 Professor Spratt's comments arose in relation to his consideration of the arrangements at the Pirbright site, specifically the Institute for Animal Health (IAH). IAH is a company limited by guarantee with charitable status. It is one of seven Research Institutes sponsored by the Biotechnology and Biological Sciences Research Council (BBSRC), a non-departmental public body which is itself supported by the Department for Innovation, Universities and Skills (DIUS). IAH receives core funding from BBSRC, the rest of its income coming from competitive grants won from BBSRC and Defra, and from research contracts, most of which are with Defra.[27]

6.4 The Governing Body of IAH is appointed by IAH, although the appointment to the Chair is approved by BBSRC. Defra's then Chief Veterinary Officer, Debby Reynolds, was appointed, albeit in a personal capacity, to the Governing Body. As IAH is a company limited by guarantee, the Governing Body is the body recognised in law as being responsible for control and direction of the organisation, irrespective of who provides the funding. IAH plays a pivotal role in Defra's emergency response to exotic animal diseases and it also is a World Reference Laboratory for FMD.

6.5 Given these facts, we find that there is, on the face of it, a conflict of interest for Defra, clearly illustrated by the specific case of IAH. It is the regulator, inspector and issuer of licenses under SAPO, yet at the same time it has a compelling interest in ensuring that the IAH facility and any others doing similar work continue to operate, notwithstanding any problems that may arise in respect of conditions attached to licences.

6.6 We do not doubt the integrity of the individual Defra officials involved, nor do we doubt their awareness of the need to avoid such conflicts as far as possible. However, we do not think that Defra as an organisation can distance itself sufficiently from the compelling interest we referred to above to be able to guarantee the independence of regulatory decisions.

6.7 Defra has published correspondence with Merial from 2004 about plans to replace part of the drainage system on the Pirbright site. In response to Merial's request for views on their proposal, Defra's correspondent replied that it was *"outwith my*

[26] See reference 1 p 58.

[27] Defra's investment in R&D projects with IAH in 2006/7 was £6.24 million, and this is planned to rise to £6.76 million in 2007/8. Defra has also committed £67 million capital to the £121 million programme to redevelop the IAH Pirbright site, the balance coming from BBSRC and DIUS.

competence to be able to comment on the specification". We are concerned that this is an indication that Defra as regulator lacks the technical expertise to judge the effectiveness of a proposed modification to the containment facilities on the site.

6.8 This also leads us to ask whether an independent regulator with all the necessary technical knowledge would have behaved differently in the face of the correspondence from Merial about the state of the drains on the Pirbright site. **We conclude that an independent regulator would at least have sought confirmation that the drains were fully functioning at the time and would have considered the possibility of regulatory action.**

6.9 Taking together the potential conflict of interest and our concerns about Defra's technical expertise, and noting the low level of resource Defra has committed to an area that clearly demands a high level of expertise across a range of technical areas, we conclude that Defra is not in a position to act as an independent regulator of laboratories handling animal pathogens.

6.10 **We recommend that responsibility for inspection and enforcement functions in respect of animal pathogens should move from Defra to a body that is not subject to the same conflict of interest and which has access to the range of technical expertise needed to carry out the regulatory function fully.**

7. THE WAY FORWARD

7.1 Our fundamental aim is to encourage the development of a regulatory framework that is consistent, transparent, proportionate, and targeted on where the greatest risks are, and that includes a high level of accountability. Above all, we seek a regime that encourages compliance, and which emphasises that primary responsibility for the safe operation of laboratories rests with the laboratory operators, not with the regulator. We consider that an effective regulatory framework should require duty holders to take all reasonably practicable measures to protect others from harm and demonstrate this by preparing a thorough risk assessment identifying the measures needed to contain hazards. In turn, we think that the regulator's role should be to consider the risk assessment and to take action as appropriate.

7.2 One of the first things we noted looking at all the regulatory measures that apply to laboratories carrying out work with animal and/or human pathogens, is that the landscape is complex and disjointed, with differing regulatory philosophies and practices, and different levels and types of inspection, enforcement and sanctions. This is an example where, *pace* Hampton, the complexity of the regulatory system leads to:

- laboratories being subject to unnecessary inspections;
- overlapping areas of responsibility by regulators;
- regulators devoting scarce resources to activity being replicated in other regulators, especially in the collation of information
- risk assessment not being comprehensive

7.3 We consider that this represents a considerable regulatory burden on the activities of laboratories. It is of course quite right that there should be comprehensive regulation of their activities, given the seriousness of the harm that could result from poor practices. Nevertheless, we consider that it is vital that this regulation be as clear and simple as possible if we are to be confident that laboratories are able to comply with it. We consider that this is a fertile area to apply the Hampton principles of inspection and enforcement. These are reproduced in Box 1 below.

Box 1: Hampton principles of inspection and enforcement[27]

- Regulators and the regulatory system as a whole, should use comprehensive risk assessment to concentrate resources on the areas that need them most
- Regulators should be accountable for the efficiency and effectiveness of their activities, while remaining independent in the decisions they take
- All regulations should be written so that they are easily understood, easily implemented and easily enforced, and all interested parties should be consulted when they are being drafted
- No inspection should take place without a reason
- Businesses should not have to give unnecessary information, nor give the same piece of information twice
- The few businesses that persistently break regulations should be identified
- quickly, and face proportionate and meaningful sanctions
- Regulators should provide authoritative, accessible advice easily and cheaply
- When new policies are being developed, explicit consideration should be given to how they can be enforced using existing systems and data to minimise the administrative burden imposed
- Regulators should be of the right size and scope, and no new regulator should be created where an existing one can do the work; and
- Regulators should recognise that a key element of their activity will be to allow, or even encourage, economic progress and only intervene when there is a clear case for protection

7.4 In the introduction we said that the regulatory outcome must be that the system provides an assurance that the risk of accidental release of pathogens is close to zero. For the reasons given in the preceding sections, we conclude that the SAPO framework as it is currently administered has not delivered a satisfactory regulatory outcome. There is therefore a pressing need for change. In this section we present the changes we think are needed, and our thoughts on how they might be introduced.

[28] See reference 8, p7.

7.5 A single regulatory framework for both animal and human pathogens

7.5.1 The current situation, with quite different regulatory frameworks setting out the requirements for containment of animal and human pathogens is, we think, unnecessary and potentially confusing, and as a result does not encourage compliance. We consider that this situation is not in keeping with the Hampton principles, in particular the principles that:

> *"all regulations should be written so that they are easily understood, easily implemented, and easily enforced"*
>
> and
>
> *"businesses should not have to give unnecessary information, nor give the same piece of information twice"*

7.5.2 In our view, a particularly serious example of this problem is the fact that the duty holder is different under each set of regulations. We have found that the SAPO grants a licence to an *individual* to have in his or her possession a dangerous pathogen, whereas the COSHH regulations place a duty on the employer to protect workers from dangerous pathogens. The GMO(CU) regulations on the other hand appear to grant consent to an *individual* for an *activity* (for Class 3 and 4 GMOs). This multiplicity of approaches can no doubt be explained through the *ad hoc* and piecemeal development of the particular regulations; COSHH and GMO(CU) are derived from EC Directives whereas SAPO is purely a domestic piece of legislation. However, we are concerned that there is such a variety of legal approaches to the very important issue of laboratory containment. We consider that this situation is particularly likely to lead to confusion in laboratories dealing with pathogens that affect both animals and humans, where they will be operating under two of the regulations, if not all three.

7.5.3 Even within a single facility, the current regulatory framework presents the potential for confusion over where responsibilities lie. But this is made all the more likely on sites where a number of operators share facilities, and it is particularly important in those cases that responsibilities are identified, agreed and clearly set out.

7.5.4 Given that all of the regulations we have looked at share the common goal of preventing the release of harmful pathogens, we think there is a compelling argument that the current different approaches for regulating animal and human pathogens should be replaced by a single framework.

7.5.5 **We recommend that Defra, DH, HSE and other interested parties work together to develop a single regulatory framework to govern work with human and animal pathogens.**

7.6 Cost recovery

7.6.1 In neither COSHH nor SAPO is there any provision for recovering the costs of regulation. For GMO(CU) there is partial cost recovery in that a fee is charged for notifications and applications under the Regulations, to cover the cost to HSE of processing them. There is no fee for inspections or other activity, such as providing advice.

7.6.2 We note that it is Government policy to recover costs of services wherever possible. In view of our comments about the need to increase the level of resource available to this work, we believe this is an area where cost recovery should be introduced.

7.6.3 **We recommend that Defra, DH, HSE and other interested parties work towards the introduction of cost recovery in any new regulatory framework.**

7.6.4 **We further recommend that work on this issue commence immediately.**

7.7 Risk assessment

7.7.1 The COSHH and GMO(CU) are both based on the requirement that the duty holder prepare a risk assessment relating to the use of the particular substance in question. We find this approach attractive and we think it needs to be a key feature of any regulatory framework for animal pathogens.

7.7.2 As we see it, the risk assessment is the basis of regulatory compliance by the duty holder and informs decisions about regulatory activities, such as inspections. The particular advantage we see is that it would also establish clearly the responsibility on the part of the duty holder for maintaining all of the measures reasonably practicable to prevent release of pathogens. We do not see the need to retain a system of licensing for animal pathogens, as is currently the case under SAPO. We believe that licensing can lead regulated parties to assume that the regulator accepts responsibility for the safe management of the facility. That responsibility must remain with the facility operators and managers, and we consider that both the COSHH and GMO(CU) regimes achieve a higher level of awareness in this regard then does SAPO. Compared to a licence, which is essentially static, risk assessment is a dynamic process. As such it has the effect of helping the duty holder to comply with regulatory requirements as circumstances change.

7.7.3 The concept of a risk that is "as low as reasonably practicable" (ALARP) is well-established in the area of health and safety. This concept will need to be applied in the single regulatory framework for pathogens. However, it is important to emphasise that this is, by its very nature, a fluid concept as technology changes; there will always be a societal judgement about what constitutes a tolerable level of risk.

7.7.4 **We recommend that risk assessment be a key element of the regulatory framework for handling animal pathogens, as it currently is for human pathogens and genetically modified organisms.**

7.8 ACDP advice on a common set of containment measures

7.8.1 As part of the single regulatory framework, we think there should be a common set of containment measures aimed at ensuring dangerous pathogens are not released such that they can cause harm. We have said many times that we consider the essential regulatory objective is the same regardless of the exact nature of the pathogen, namely to contain it. It seems clear to us that a common set of containment requirements should be developed which gives a clear indication of the essential measures to be taken by any laboratory dealing with human and animal pathogens.

7.8.2 The Advisory Committee on Dangerous Pathogens (ACDP) currently formulates guidance in respect of the hazards presented by human pathogens and the measures necessary to contain them in a laboratory context. There is already close collaboration between ACDP and veterinary experts in Defra. We therefore consider that ACDP is best placed to develop a single set of containment measures to apply to facilities handling animal pathogens as well as human pathogens.

7.8.3 **We recommend that ACDP be tasked with formulating a common set of containment measures to apply to both animal and human pathogens.**

7.9 Use of discretion in relation to containment measures

7.9.1 We have already noted that there is no simple relationship between a given pathogen's danger to animals and its danger to humans. We therefore accept that departures from the basic set of containment measures we have recommended above should be permitted. The approach set out in the GMO(CU) Regulations is attractive in that it gives the regulator and the operator a clear framework within which to engage in constructive dialogue about the most appropriate measures needed. We are certain that departures from the specified containment measures should be based on a thorough assessment of the risks and that the nature of the departures and the reasons for them should be agreed with the regulatory body and clearly recorded.

7.9.2 **We recommend that the regulator under the single regulatory framework be given discretion to agree with operators departures from the containment measures drawn up by ACDP, on the basis of risk assessments.**

7.10 A single regulator

7.10.1 We have concluded above that Defra should not continue as the regulator of laboratories handling animal pathogens. Defra has already considered this possibility in the recent past. The Veterinary Laboratories Agency (VLA) is already contracted to carry out inspections for all SAPO 2 and 3 laboratories and we were told that it had been agreed that the conduct of all SAPO inspections, including Category 4 laboratories, should be put out to tender. Unfortunately, it appears that this was overtaken by other priorities and progress was not made.

7.10.2 We have already noted that laboratories are currently regulated by Defra under SAPO, by HSE under COSHH, GMO(CU) and of course other more general health and safety legislation, and by a variety of other regulators under a range of regulatory instruments. In line with the principles of good regulation espoused by Philip Hampton, in particular that

> *"regulators should be of the right size and scope, and no new regulator should be created where an existing one can do the work",*

7.10.3 We believe there is a strong case for reducing the number of regulators wherever possible. Following our recommendation above that there should be a common regulatory framework for both animal and human pathogens, it seems to us that there is an obvious case for combining the regulatory roles in respect of animal and human pathogens.

7.10.4 We have found support amongst all those we have spoken to for such a move. We have talked to staff at laboratories about the approaches taken under the current arrangements by Defra and HSE inspectors. We found general agreement that the two regulators were adopting quite different approaches, although interestingly we found little agreement as to the nature of the differences and little understanding of how those differences might relate to the different regulatory regimes. This we take as an illustration of our view that greater clarity is needed within the overall legislative framework and also as regards regulatory and enforcement practices, and we conclude that this would be delivered in large part by employing a single regulator for both animal and human pathogens.

7.10.5 **We recommend that there be a single independent regulator for both animal and human pathogens, with the resources, expertise and legal powers to carry out its function effectively.**

7.11 Choice of regulator

7.11.1 We now turn to the question of who that regulator should be. We understand that when Defra previously considered handing over regulation of animal pathogens under SAPO, it identified the following bodies as potential bidders for this role:

- the Veterinary Laboratories Agency (VLA)
- Animal Health (AH) (which includes the former State Veterinary Service)
- the Health and Safety Executive (HSE)

7.11.2 We have also considered the Veterinary Medicines Directorate (VMD) as another possible candidate.

7.11.3 It is our view that VLA and AH, which are both Defra Agencies, do not have the necessary distance from Defra policy makers to count as arm's length organisations. VLA is itself a laboratory handling animal pathogens and their approach to regulatory decisions would inevitably be coloured by this. AH is an organisation that not only needs to redeploy its resources in the event of a disease outbreak, but would also have a keen interest in maintaining laboratory capacity in readiness for such situations, possibly in the face of regulatory problems. VMD is also a Defra agency and in our view it too would find it difficult to ensure an appropriate level of independence. But it is also the case that the regulatory work that VMD currently carries out in respect of medicinal production under GMP, involving the growth of pathogens in bulk (e.g. vaccines), is very different from the requirements of regulations aimed at ensuring containment. We consider that since VMD is primarily concerned with product quality, it would not be appropriate for it to take on the responsibility for biocontainment. For these reasons alone we would propose that HSE is the most suitable organisation to fulfil the regulatory role for animal pathogens.

7.11.4 Further, we note that HSE is currently the regulator for both COSHH and GMO(CU) and has considerable expertise in all of the technical areas relevant to the operation of high-containment laboratories. We note also that in recent weeks HSE has been involved in inspection visits, with Defra, of all UK laboratories operating at the highest containment levels (for both animal and human pathogens). This followed the issue of the safety alert by HSE and Defra on 7 September. We understand that this joint safety alert and the subsequent inspections have together already had a significant impact on raising standards in the laboratories concerned. We therefore conclude that HSE is well placed to carry out regulatory functions in respect of animal pathogens as well as human pathogens.

7.11.5 **We recommend that HSE become the single regulatory body for both animal and human pathogens.**

7.11.6 That said, we would emphasise the importance of effective liaison between all of the regulators with an interest in the work being carried out at laboratories and other facilities handling dangerous pathogens. In particular, VMD and MHRA, who both conduct regular inspections at laboratories which must comply with GMP, should liaise closely with HSE as the regulator of the containment requirements.

7.12 Making the regulatory changes

7.12.1 We recognise that these regulatory changes will take time to effect. But, given that the current SAPO framework does not, in our view, deliver the desired regulatory outcome, it is incumbent on us to propose a practical way forward that allows the key assurances to be provided to the general public urgently. We therefore **recommend** a phased approach to these changes.

7.12.2 Phase 1 – immediate changes (by 1 January 2008)

7.12.2.1 We envisage that the regulatory role will ultimately pass to HSE. In the interim we **recommend** that inspections under SAPO continue to be conducted by Defra, but with support from HSE. This will build on the success of the inspections conducted since the safety alert was issued and will demonstrate an urgent commitment to improve the standard of inspection of laboratories, and to assure the public that Defra's conflict of interest is being minimised.

7.12.2.2 We have previously concluded that insufficient resources have been allocated to inspections under SAPO and that a greater resource commitment is needed. HSE will therefore need to be funded for the support work they carry out under this arrangement and we believe that this can be achieved through a contracting for services arrangement with Defra, formalising the approach taken since the safety alert was issued. We **recommend** that Defra enter into immediate discussions with HSE to formalise HSE's support of SAPO inspections by 1 January 2008.

7.12.2.3 As we have already said, we do not believe that completely separate containment requirements are justified for animal and human pathogens. We therefore **recommend** that the ACDP is asked to begin work now on drawing up guidance on a single set of containment requirements for human and animal pathogens, to complement the single regulatory framework when it is introduced.

7.12.3 Phase 2 – short term changes to make HSE an inspection and enforcement body under SAPO (by April 2008)

7.12.3.1 In this phase, we consider that Defra would continue to administer the issuing of licences, but HSE would be designated as inspectors under the Animal Health Act, thus allowing them to carry out SAPO inspection functions. HSE would also be added as an enforcement authority under SAPO and thus would be able to take prosecutions under the Animal Health Act 1981. We also recommend that the powers of inspectors under the animal health act be extended to reflect the powers currently available to HSE inspectors under health and safety legislation. This would bring into play the ability to issue improvement notices and prohibition notices, which are not currently available under SAPO.

7.12.3.2 These changes should, in our view, be straightforward to implement, given that they would make no changes to the essential regulatory requirements under SAPO. The changes would have the effect of strengthening the effectiveness of the enforcement mechanisms under SAPO.

7.12.3.3 **We recommend that changes be made to SAPO, by April 2008, to designate HSE as an inspection and enforcement body.**

7.12.4 Phase 3 – putting in place a single regulatory framework (during 2008)

7.12.4.1 The measures described in phases 1 and 2 will deliver many advantages over the current regulatory framework. They will, in our view, serve to assure the public that laboratories handling dangerous pathogens are being regulated responsibly while work progresses on the introduction of a new single regulatory framework. Meanwhile, Defra, DH, HSE and other interested parties should work together to introduce the more far reaching changes we have recommended, with the aim of arriving at a single risk based regulatory framework for animal and human pathogens as soon as possible during 2008.

7.12.4.2 **We recommend that Defra, DH, HSE and other interested parties begin work urgently with a view to bringing in the single regulatory framework before the end of 2008.**

7.13 Conclusion

7.13.1 We have outlined above a process of changes to the existing regulatory framework which will bring about a range of benefits, most importantly simplification of what is currently a complex system, and greater transparency in regard to the relationship between the regulator and the regulated.

ANNEX 1

The Review Team members

Sir Bill Callaghan	Chair Health and Safety Commission October 1999 to September 2007 and Chief Economist TUC until 1999. Member of the Low Pay Commission 1997 -2000. Chair British Occupational Health Research Foundation and Chair Policy Advisory Committee Centre for Risk and Regulation at LSE. Visiting Fellow Nuffield College Oxford.
Tim Brooks	Head, Novel & Dangerous Pathogens Department, Health Protection Agency (HPA)
Kären Clayton	Head of Biological Agents Unit, Specialised Industries Division, Health and Safety Executive (HSE)
Prof. George Griffin	Professor of Infectious Disease at St George's Hospital, London; Chairman of the Advisory Committee on Dangerous Pathogens (ACDP)
Richard Percy	Farmer, Environment Agency Board Member, NFU Mutual Board Member, and NFU Council member
Mike Piggott	Head of Enforcement Policy Section, Defra

The Secretariat

Nafees Meah

Peter Grimley

Jo Withers

Matt Guenigault

ANNEX 2

We spoke to the following individuals during the Review:

Fred Landeg (Defra, Acting CVO)
Nick Coulson (Defra, Assistant CVO)
Dr Bob Watson (Chief Scientific Adviser, Defra)
David Dawson (Director of Animal Health & Welfare, Defra)
Paul Manser (Deputy Veterinary Head of Food & Farming Group, Defra)
Ruth Lysons (Deputy Director in Food & Farming Group, Defra)
David Mouat (Head of Veterinary Exotic Notifiable Diseases Unit, Defra)
Geoffrey Podger (Chief Executive, HSE)
Justin McCracken (Deputy Chief Executive[Operations], HSE)
Alex Brett-Holt (Legal Advisor to HSC and HSE)
Charles Milne (CVO Scotland)
Christianne Glossop (CVO Wales)
Robert Houston (CVO Northern Ireland)
Andrew Voas (Veterinary Adviser, Scottish Executive)
Prof. Sir David King (Government Chief Scientist)
Dr Paul Logan (Health & Safety Executive)
Dr Heather Sheeley (Safety Manager, HPA)
Ben Walsh (Biological Investigations Group Manager, HPA)
Nigel Silman (Operations Manager, HPA)
Allan Bennett (Head of Biosafety Research & Services Group, HPA)
Howard Tolley (Lab Manager, HPA)
Simon Caidan (Safety and Security Manager, National Institute for Medical Research, Mill Hill)
Malcolm Broster (Facility Manager, DSTL)
Dr Mark Fulop (Department Manager, DSTL)
Dr Paul Williams (Director of Research Council Directorate, DIUS)
Dr David Harper (Department of Health)
Maggie Tomlinson (Department of Health)
Prof. Steve Edwards (CEO, VLA)
Chris Thorns (VLA)
Steve Dean (CEO, VMD)
Prof. Martin Shirley (Director of IAH Pirbright)
Dr John Anderson (Head of Laboratory at IAH Pirbright)
Dr Uwe Mueller-Doblies (Head of Biosecurity, IAH Pirbright)
Dr Timothy Doel (Site Manager, Merial Animal Health Ltd.)
Dr Duncan Fawthrop (Disease Safety Officer, Merial Animal Health Ltd.)
Dr Paul Burr (Veterinary Director, Biobest Laboratories Ltd.)

Peter Baxter (Independent Biological Safety Officer, Biobest Laboratories Ltd.)
Prof. Julie Fitzpatrick (Moredun Research Institute)
Dr Colin McInnes (Moredun Research Institute)
David Windsor (Mycoplasma Experience Ltd.)
Helena Windsor (Mycoplasma Experience Ltd.)
Dr Chris Bowles (Safety Adviser, University of Liverpool)
Jillian Deans (Assistant Safety Adviser, University of Liverpool)
Prof. Brian Spratt (Head of Department of Infectious Disease Epidemiology, Imperial College London)
Dr Filippa Lentzos (Senior Research Fellow, BIOS Centre, London School of Economics)
Prof. Sir Andy Haines (Director, LSHTM)
Prof. Hazel Dockrell (Chair of Safety Committee, LSHTM)
Mr Michael Smith (Safety Manager, LSHTM)
Dr Iain Anderson CBE (Chairman, Foot and Mouth Review: 2007)

We also received written submissions from:

The BBSRC

The Institute for Animal Health

The Veterinary Laboratories Agency

Professor Keith Gull

ANNEX 3

We visited the following laboratories during the Review

Health Protection Agency (HPA), Porton Down

Defence Science and Technology Laboratory (DSTL), Porton Down

Institute for Animal Health (IAH), Pirbright

Moredun Research Institute, Edinburgh

Merial Animal Health Ltd, Pirbright

Biobest Laboratories Ltd., Edinburgh

Mycoplasma Experience, Reigate

University of Edinburgh, Easter Bush Veterinary Centre

University of Liverpool

London School of Hygiene & Tropical Medicine (LSHTM)

ANNEX 4

Advisory Committee on Dangerous Pathogens (ACDP)

The Advisory Committee on Dangerous Pathogens (ACDP) is a non-statutory advisory non-Departmental Public Body. The Committee comprises a Chairman and 16 members. The membership is tripartite, with scientific experts, employer and employee representatives. The current Chairman is Professor George Griffin, St George's Hospital Medical School.

The work of the ACDP cuts across a number of Government Departments. The Committee is thus 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 Advisory Committee on Dangerous Pathogens' terms of reference are:

> *"To advise the Health and Safety Commission, the Health and Safety Executive, Health and Agriculture Ministers and their counterparts under devolution in Scotland, Wales and Northern Ireland, as required, on all aspects of hazards and risks to workers and others from exposure to pathogens."*

The remit of ACDP is to provide advice to workers and others on risks from exposure to dangerous pathogens (also known as biological agents and infectious agents). Workers and others can be exposed to a range of dangerous pathogens in the workplace and through workplace activities.

Dangerous pathogens include infectious agents that cause diseases transmissible between animals and man (zoonoses). Such agents are controlled under human health (DH/HPA remit). (The primary purpose of the latter legislation is to prevent the introduction and spread of animal diseases that affect farmed livestock and poultry).

One of ACDP's roles is to advise on worker health and safety, and much of its advice supports health and safety legislation on the control of exposure to hazardous substances such as dangerous pathogens. Health and safety legislation (principally the Control of Substances Hazardous to Health (COSHH) Regulations 2002 (as amended) requires employers to assess the risks from dangerous pathogens in their workplace and to prevent or control exposure. Further information can be obtained from the HSE website

(http://www.hse.gov.uk/biosafety/index.htm).

The work of ACDP can be broadly divided into three areas:

- Production of guidance relating to safety at work and protection of public health;
- Provision of advice to Government on the formulation and implementation of legislation;
- Provision of advice to Government on specific pathogen risk issues and their impact.

ACDP makes a significant contribution to the assessment of risks to employees and the general public from infectious agents, and to ensuring that appropriate controls are in place. It has produced several guidance documents that give practical advice on the application of health and safety measures for a range of occupational groups and on a range of public health issues. For example, *Infection at Work: Controlling the Risk and TSE agents: Safe working and the prevention of infection*. Information on the range of publications available from the ACDP can be found at
http://www.advisorybodies.doh.gov.uk/acdp/publications.htm

ANNEX 5

Scientific Advisory Committee on Genetic Modification (Contained Use) Introduction

The Scientific Advisory Committee on Genetic Modification (Contained Use) (SACGM (CU)) was established in January 2004 to provide technical and scientific advice to the UK Competent Authorities (UK CA) on all aspects of the human and environmental risks of the contained use of genetically modified organisms (GMOs).

SACGM (CU) replaces the Health and Safety Commission's long-running Advisory Committee on Genetic Modification (ACGM) together with its Technical Subcommittee (TSC). ACGM, and latterly the TSC, played a key role in the development of the comprehensive and highly successful legislation now in place for the contained use of GMOs, namely the Genetically Modified Organisms (Contained Use) Regulations 2000 (GMO(CU)).

The SACGM (CU) was set up as a Government scientific advisory committee in accordance with the Office of Science and Technology's Code of Practice for scientific advisory committees and operates in accordance with the Nolan principles. Compliance with Government good practice relating to scientific advisory committees is intended to ensure that independent expert scientific advice is provided when considering key scientific issues relating to the contained use of GMOs.

UK Competent Authorities for Genetic Modification (Contained Use) Activities

The Health and Safety Executive (HSE) and the Secretary of State for the Department for Environment, Food and Rural Affairs (Defra) form the Competent Authority in England and Wales for GMO(CU). In practice, these functions are delegated to HSE and Defra officials. In Scotland, the Competent Authority comprises the Scottish Ministers and HSE and similarly these functions are delegated to officials of HSE and the Scottish Executive. Although not part of the Competent authority, the National Assembly for Wales and Northern Ireland are included in all UK CA considerations and are invited to all SACGM(CU) meetings.

HSE provides the Secretariat for SACGM(CU). The Secretariat liaises closely with the Chair and prepares papers, organises and hosts SACGM(CU) meetings.

Terms of Reference

The SACGM(CU) terms of reference are:

To provide technical and scientific advice to the UK Competent Authorities on all aspects of the human and environmental risk of the contained use of GMOs. In particular:

- At the request of the UK CAs, to advise on technical issues on individual activities notified under GMO(CU);
- To provide advice on risk assessments for contained use activities involving GMOs other than Genetically Modified Microorganisms (GMMs);

- To develop and update guidance on all aspects of contained use of GMOs including the Compendium of Guidance;

- To provide advice and guidance to others on the technical aspects of genetic modification contained use activities.

ANNEX 6

WHO Classification of Hazard Groups

Classification of infective microorganisms by risk group

Risk Group 1 *(no or low individual and community risk)*

A microorganism that is unlikely to cause human or animal disease.

Risk Group 2 *(moderate individual risk, low community risk)*

A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to laboratory workers, the community, livestock or the environment. Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread of infection is limited.

Risk Group 3 *(high individual risk, low community risk)*

A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another. Effective treatment and preventive measures are available.

Risk Group 4 *(high individual and community risk)*

A pathogen that usually causes serious human or animal disease and that can be readily transmitted from one individual to another, directly or indirectly. Effective treatment and preventive measures are not usually available.

ANNEX 7

OIE Terrestrial Animal Code (2007)

CHAPTER 1.4.5.

INTERNATIONAL TRANSFER AND LABORATORY CONTAINMENT OF ANIMAL PATHOGENS

Article 1.4.5.1.

Object

To prevent the introduction and spread of animal *diseases* caused by pathogens.

Article 1.4.5.2.

Introduction

1. The consequences of the introduction into a country of an infectious disease or an animal pathogen or new strain of animal pathogen from which it is currently free, are potentially very serious. This is because animal health, human health, the agricultural economy and trade may all be adversely affected to a greater or a lesser degree. Countries will already have in place a range of measures, such as requirements for pre-import testing and quarantine, to prevent such introductions through the importation of live *animals* or their products.

2. However, there is also the risk that disease may occur as a result of the accidental release of animal pathogens from laboratories that are using them for various purposes such as research, diagnosis or the manufacture of vaccines. Such pathogens may already occur in the country or they may have been imported deliberately or inadvertently. It is therefore necessary to have in place measures to prevent their accidental release. These measures may be applied either at national borders by prohibiting or controlling the importation of specified pathogens or their carriers (see Article 1.4.5.7.) or within national boundaries by specifying the conditions under which laboratories must handle them. In practice, a combination of external and internal controls is likely to be applied depending on the risk to animal health posed by the pathogen in question.

Article 1.4.5.3.

Purpose

1. To provide guidance on the laboratory containment of animal pathogens according to the risk they pose to animal health and the agricultural economy of a country, particularly when the disease they cause is not enzootic.

2. To provide guidance on the import conditions applicable to animal pathogens.

3. Where animal pathogens also pose a risk to human health, guidance on their laboratory containment should be sought from the *Terrestrial Manual* and other relevant published documents.

Article 1.4.5.4.

Classification of animal pathogens

1. Animal pathogens should be categorised on the risk they pose to animal health, should they be introduced into a country or accidentally released from a laboratory. In categorising pathogens into four groups according to containment requirements, the following factors should be taken into account: the organism's pathogenicity, the biohazard it presents, its ability to spread, the economic aspects and the availability of prophylactic and therapeutic treatments.

2. Some pathogens need to be transmitted by specific vectors or require intermediate hosts to complete their life cycles before they can infect animals and cause disease. In countries where such vectors or intermediate hosts do not occur, or where climatic or environmental factors mitigate against their survival, the pathogen poses a lower risk to animal health than in countries where such vectors or intermediate hosts occur naturally or could survive.

3. When categorising animal pathogens into specific groups, the following criteria should be taken into account:

   a. Group 1 animal pathogens

      Disease producing organisms which are enzootic but not subject to official control.

   b. Group 2 animal pathogens

      Disease producing organisms which are either exotic or enzootic but subject to official control and which have a low risk of spread from the laboratory.

      i. They do not depend on vectors or intermediate hosts for transmission.

      ii. There is a very limited or no transmission between different animal species.

      iii. Geographical spread if released from the laboratory is limited.

      iv. Direct animal to animal transmission is relatively limited.

      v. The need to confine diseased or infected non-diseased animals is minimal.

      vi. The disease is of limited economic and/or clinical significance.

   c. Group 3 animal pathogens

      Disease producing organisms which are either exotic or enzootic but subject to official control and which have a moderate risk of spread from the laboratory.

      i. They may depend on vectors or intermediate hosts for transmission.

      ii. Transmission between different animal species may readily occur.

iii. Geographical spread if released from the laboratory is moderate.

iv. Direct animal to animal transmission occurs relatively easily.

v. The statutory confinement of diseased, infected and in-contact animals is necessary.

vi. The disease is of severe economic and/or clinical significance.

vii. Prophylactic and/or therapeutic treatments are not readily available or of limited benefit.

d. Group 4 animal pathogens

Disease producing organisms which are either exotic or enzootic but subject to official control and which have a high risk of spread from the laboratory.

i. They may depend on vectors or intermediate hosts for transmission.

ii. Transmission between different animal species may occur very readily.

iii. Geographical spread if released from the laboratory is widespread.

iv. Direct animal to animal transmission occurs very easily.

v. The statutory confinement of diseased, infected and in-contact animals is necessary.

vi. The statutory control of animal movements over a wide area is necessary.

vii. The disease is of extremely severe economic and/or clinical significance.

viii. No satisfactory prophylactic and/or therapeutic treatments are available.

Article 1.4.5.5.

Containment levels

1. The principal purpose of containment is to prevent the escape of the pathogen from the laboratory into the national animal population. Some animal pathogens can infect man. In these instances the risk to human health may demand additional containment than would otherwise be considered necessary from purely animal health considerations.

2. The level of physical containment and biosecurity procedures and practices should be related to the group into which the pathogen has been placed, and the detailed requirements should be appropriate to the type of organism (i.e. bacterium, virus, fungus or parasite). The lowest containment level will be required for pathogens in group 1 and the highest level for those in group 4. Guidance on the containment requirements for groups 2, 3 and 4 is provided in Table 1.

3. Arthropods may be pathogens or vectors for pathogens. If they are a vector for a pathogen being used in the laboratory, the appropriate containment level for the pathogen will be necessary in addition to the containment facilities for the arthropod.

Article 1.4.5.6.

Possession and handling of animal pathogens

1. A laboratory should be allowed to possess and handle animal pathogens in group 3 or 4 only if it can satisfy the relevant authority that it can provide containment facilities appropriate to the group. However, depending on the particular circumstances of an individual country, the authority might decide that the possession and handling of certain pathogens in group 2 should also be controlled. The authority should first inspect the facilities to ensure they are adequate and then issue a licence specifying all relevant conditions. There should also be a requirement for appropriate records to be kept and for the authority to be notified if it is suspected that a material being handled contains a pathogen not covered by the licence. The authority should visit the laboratory periodically to ensure licence conditions are being complied with. It is important that authority staff carrying out the visit should not have any contact with species susceptible to the pathogens being handled at the laboratory for a specified period after visiting the laboratory. The length of this period will depend on the pathogen.

2. Licences should specify:

    a. how the pathogen is to be transported and the disposal of the packaging;

    b. the name of the person responsible for the work;

    c. whether the pathogen may be used *in vivo* (and if so whether in laboratory animals or other animals) and/or only *in vitro*;

    d. how the pathogen and any experimental animals should be disposed of when the work is completed;

    e. limitations on contact by laboratory staff with species susceptible to the pathogens being used;

    f. conditions for the transfer of pathogens to other laboratories;

    g. specific conditions relating to the appropriate containment level and biosecurity procedures and practices.

Article 1.4.5.7.

Importation of animal pathogens

1. The importation of any animal pathogen, *pathological material* or organisms carrying the pathogen should be permitted only under an import licence issued by the relevant authority. The import licence should contain conditions appropriate to the risk posed by the pathogen and, in relation to air transport, the appropriate standards of the International Air Transport Association concerning the packaging and transport of hazardous substances. The import licence for group 2, 3 or 4 should only be granted to a laboratory that is licensed to handle the particular pathogen as in Article 1.4.5.6.

2. When considering applications to import *pathological material* from other countries, the authorities should have regard to the nature of the material, the animal from which it is derived, the susceptibility of that animal to various diseases and the animal health situation of the country of origin. It may be advisable to require that material is pre-treated before import to minimise the risk of inadvertent introduction of a pathogen.

Table 1. Guidance on the laboratory requirements for the different containment groups

	Containment Group		
REQUIREMENTS OF THE LABORATORY	**2**	**3**	**4**
A) Laboratory siting and structure			
1. Not next to known fire hazard	Yes	Yes	Yes
2. Workplace separated from other activities	Yes	Yes	Yes
3. Personnel access limited	Yes	Yes	Yes
4. Protected against entry/exit of rodents and insects	Yes	Yes	Yes
5. Liquid effluent must be sterilised		Yes and monitored	Yes and monitored
6. Isolated by airlock. Continuous internal airflow		Yes	Yes
7. Input and extract air to be filtered using HEPA or equivalent		Single on extract	Single for input, double for extract
8. Mechanical air supply system with fail-safe system		Yes	Yes
9. Laboratory sealable to permit fumigation		Yes	Yes
10. Incinerator for disposal of carcasses and waste	Available	Yes	Yes on site
B) Laboratory facilities			
11. Class 1/2/3 exhaust protective cabinet available	Yes	Yes	Yes
12. Direct access to autoclave	Yes	Yes with double doors	Yes with double doors
13. Specified pathogens stored in laboratory	Yes	Yes	Yes
14. Double ended dunk tank required		Preferable	Yes
15. Protective clothing not worn outside laboratory	Yes	Yes	Yes

	Containment Group		
REQUIREMENTS OF THE LABORATORY	**2**	**3**	**4**
16. Showering required before exiting laboratory			Yes
17. Safety Officer responsible for containment	Yes	Yes	Yes
18. Staff receive special training in the requirements needed	Yes	Yes	Yes
C) Laboratory discipline			
19. Warning notices for containment area	Yes	Yes	Yes
20. Laboratory must be lockable	Yes	Yes	Yes
21. Authorised entry of personnel	Yes	Yes	Yes
22. On entering all clothing removed and clean clothes put on		Yes	Yes
23. On exiting all laboratory clothes removed, individual must wash and transfer to clean side		Yes	
24. Individual must shower prior to transfer to clean side			Yes
25. All accidents reported	Yes	Yes	Yes
D) Handling of specimens			
26. Packaging requirements to be advised prior to submission	Yes	Yes	Yes
27. Incoming packages opened by trained staff	Yes	Yes	Yes
28. Movement of pathogens from an approved laboratory to another requires a licence	Yes	Yes	Yes
29. Standard Operating Procedures covering all areas must be available	Yes	Yes	Yes

ANNEX 8

Containment measures for Health and Veterinary care facilities, laboratories and animal rooms under the Control of Substances Hazardous to Health (COSHH) Regulations 2002 (as amended)

Containment measures	Containment levels		
	2	3	4
1 The workplace is to be separated from any other activities in the same building.	No	Yes	Yes
2 Input air and extract air to the workplace are to be filtered using HEPA or equivalent.	No	Yes, on extract air	Yes, on input and double extract air
3 Access is to be restricted to authorised persons only.	Yes	Yes	Yes, via airlock key procedure
4 The workplace is to be sealable to permit disinfection.	No	Yes	Yes
5 Specified disinfection procedure.	Yes	Yes	Yes
6 The workplace is to be maintained at an air pressure negative to atmosphere.	No	Yes	Yes
7 Efficient vector control e.g. rodents and insects.	Yes, for animal containment	Yes, for animal containment	Yes
8 Surfaces impervious to water and easy to clean.	Yes, for bench	Yes, for bench and floor (and walls for animal containment)	Yes, for bench, floor, walls and ceiling
9 Surfaces resistant to acids, alkalis, solvents, disinfectants.	Yes, for bench	Yes, for bench and floor (and walls for animal containment)	Yes, for bench, floor, walls and ceiling
10 Safe storage of biological agents.	Yes	Yes	Yes, secure storage

Containment measures	Containment levels		
	2	3	4
11 An observation window, or alternative, is to be present, so that occupants can be seen.	No	Yes	Yes
12 A laboratory is to contain its own equipment.	No	Yes, so far as is reasonably practicable	Yes
13 Infected material, including any animal, is to be handled in a safety cabinet or isolator or other suitable containment.	Yes, where aerosol produced	Yes, where aerosol produced	Yes
14 Incinerator for disposal of animal carcases.	Accessible	Accessible	Yes, on site

ANNEX 9

Containment Requirements for Laboratories to be Licensed to Handle Defra Category 2 Pathogens under the Specified Animal Pathogens Order 1998

The laboratory – siting and structure

1. Whereas the laboratory need not be physically separated from other laboratories it should not be sited next to a known fire hazard (e.g. the solvent store) or be in danger of flooding.

2. Access to the laboratory should be limited to laboratory personnel and other specified persons.

3. The entrance to the laboratory should have a clearly defined clean and dirty side over which staff don or remove protective clothing and wash their hands.

4. The laboratory must be proofed against entry or exit of animals or insects. This is particularly important in the case of diseases which can be spread by insect vectors.

5. Liquid effluent containing specified pathogens should be treated by a procedure known to kill the relevant pathogens. Since this procedure may take some time, it may be necessary to have more than one standing tank if work is to be carried out continuously. The standing tank(s) and recording equipment form parts of the facilities of the laboratory, so the Safety Officer is responsible for ensuring their proper functioning.

Laboratory facilities

1. The laboratory must be equipped with a Class I, II or III exhaust protective cabinet where procedures likely to generate aerosols will be used e.g. homogenisation.

2. All waste biological material containing specified pathogens must be sterilised prior to removal from the laboratory site. Therefore, each laboratory should have access to an autoclave. There should be no possibility of removing the load without the autoclave cycle having been completed. As soon as practicable after the completion of the autoclave cycle, the load should be taken to an incinerator and immediately incinerated. Autoclaves should be monitored to ensure that time/temperature cycles are completed and records should be kept.

3. Each member of staff working in the laboratory must have adequate working space.

4. Specified pathogens should be stored in the laboratory and in suitable containers (depending on the mode of storage, frozen or freeze-dried) in a cabinet reserved for specified pathogens and kept under lock and key. A key should be available on demand only to nominated individual(s). Where storage in the laboratory is not reasonably practicable, material must be transported and stored without spillage in

properly labelled robust containers which must only be opened in the Category 2 laboratory. Physical security measures similar to those in place at the laboratory must be in place at the site of storage.

Protective clothing

1. Laboratory gowns must wrap over the chest and fit tightly at the wrists. Ordinary white laboratory coats are UNSUITABLE. Staff should have a clean gown for each uninterrupted period spent in the laboratory. Other types of clothing giving the same degree of protection may be acceptable.

2. Gowns must be not be used outside the laboratory suite. They should be autoclaved before they are removed from the laboratory.

3. Gloves must be worn for all work with infective materials and workers must wash hands before leaving the laboratory.

Safety Officer

NOTE: Throughout this document the term Safety Officer refers to a person having responsibility for work with specified pathogens.

1. A Safety Officer able to advise on infectious hazards, and a deputy, must be appointed or designated. The establishment may have a Safety Officer with general responsibility for such hazards. If not, an additional individual must be designated.

2. A Safety Officer should have appropriate qualifications and laboratory experience in working with specified pathogens.

3. The Safety Officer will act as adviser to the Head of the Department in all matters which may affect the containment of the pathogens and should be authorised to stop practices considered unsafe, pending guidance when necessary, from the laboratory Head.

4. He or she will take control, implement first aid in, and investigate all accidents in laboratories and take what other action he considers necessary.

5. Where their responsibilities are not sufficient to warrant their full-time employment as Safety Officer, provided that they are readily accessible to the laboratory during normal hours, they may hold another appointment.

6. He or she will be responsible for the safe storage of specified pathogens and the maintenance of the inventory.

7. He or she will be responsible for organising the admission to the laboratory of cleaners and maintenance personnel and for the disinfection of any apparatus, etc. which is to be removed.

8. He or she will be responsible for advising staff on all aspects of the application of these Safety Precautions.

Training in handling specified pathogens

1. The Safety Officer will organise the initial training of staff in the safe handling of specified pathogens.

2. Training will cover, e.g. the correct use of safety hoods, exhaust protective cabinets, pipettes, syringes/needles, hot/cold rooms, centrifuges, blenders, freeze-driers, shaking machines, ultrasonic disintegrators, glassware and the disposal of contaminated protective clothing and laboratory materials.

3. Staff should only work with specified pathogens if they have some previous experience in microbiology and have had a course of training supervised by the Safety Officer.

Supervision

1. Work in the laboratory must, at all times, be carried out by, or be supervised by, a senior, trained and experienced member of the staff.

2. The supervisor will be personally responsible to the Safety Officer for the safety of the work actually in progress at any time, although he or she may not be responsible for the overall project.

Laboratory discipline

1. The containment area of each laboratory must be identified clearly with appropriate warning notices.

2. When unoccupied, the laboratory must be locked. The key(s) must be kept under the supervision of the Safety Officer, and released only to authorised persons. A key, however, should be kept at a secure control point, available at all times, in case of emergency.

3. In normal hours the supervisor will be responsible to the Safety Officer for ensuring that no unauthorised person enters the laboratory.

4. Only the Safety Officer or his deputy may authorise staff to enter the laboratory, and he or she will hold a list of names of personnel so authorised.

5. Unlisted persons (e.g. visitors, observers, cleaners or maintenance/repair personnel must not enter the laboratory unless they have received a signed statement from the Safety Officer that it is safe for them to do so.

6. The Safety Officer will be responsible for confirming when a laboratory and its apparatus have been disinfected.

7. The laboratory door must be closed whilst work is in progress. No food, drink, tobacco, make-up, etc. may be taken inside. Clean protective clothing should be put on. The ‘clean’ and ‘dirty’ areas should be clearly distinguished physically.

8. On the way out, over garments should be removed and before leaving the laboratory the individual must wash hands.

9. This procedure should be adhered to whenever, and for whatever purposes, the room is vacated.

10. All accidents or spillage of potentially dangerous material in the laboratory must be reported IMMEDIATELY to the Safety Office. EVERY SUCH INCIDENT MUST BE REGARDED AS A FULL MEDICAL OR ANIMAL DISEASE HAZARD.

11. The day-to-day cleanliness of the laboratory is the responsibility of those working in it. Only when the Safety Officer has confirmed that it has been disinfected can other cleaning/maintenance work be carried out.

12. At the end of a working day benches and working surfaces should be disinfected.

13. Work with specified animal pathogens must be kept separate at all times from other work in the laboratory.

Handling of specimens

1. All in-coming packages which may contain specified pathogens must be opened by trained staff in the laboratory.

2. Senders should be advised that a liquid sample should be externally identified and sealed in a can filled with sufficient absorbent material wholly to mop up a spill. The can may, if necessary, be cooled in solid carbon dioxide or liquid nitrogen. Similarly solid samples should be double wrapped so that, in the event of the outer container rupturing, there can be no leakage of contents.

3. Chapter 6 of "Laboratory-Acquired Infections" by C H Collins (4th edition, Butterworth and Co. 1999) gives general advice on packing and unpacking specimens, but in the present context all such unpacking must be carried out in the containment facility.

4. Particular care must be taken when biological material which cannot be autoclaved, is to be removed from the laboratory. The Safety Officer must be consulted before unsterilised material is removed. Precautions must be taken to sterilise the outer surface of containers and to sterilise the material itself, as far as possible.

5. The movement of specified pathogens from an approved laboratory to any other premises is prohibited except under the provisions of a licence issued by Defra.

Security

1. It is imperative that the laboratory and animal rooms must be secure against intruders or vandals. An intruder alarm system must be fitted.

2. Security patrols, etc. must not enter laboratories, or animal rooms. If it appears that an adjacent fire or water hazard threatens the room then the Safety Officer should be informed immediately.

3. A key to the laboratory should be held centrally for emergency access but must only be released on the instruction of the Safety Officer or their deputy.

4. The Safety Officer must maintain a list of the specified pathogens used at the laboratory. This list must indicate the number of vials of pathogen under storage.

Standard operating procedures

1. SOPs must be written and issued to staff covering:

   (i) receipt and unwrapping of incoming specimens;

   (ii) handling of specified pathogens in vitro;

   (iii) handling of specified pathogens in vivo (where appropriate);

   (iv) disposal of all waste and surplus pathogens;

   (v) storage of specified pathogens; and

   (vi) emergency procedures.

2. All staff must be familiar with these SOPs and have access to them on a day to day basis. Adherence to the SOPs will be a condition of a licence issued under the Specified Animal Pathogens Order 1998 and they must not be altered without prior approval from the Defra licensing office. Any plans to amend SOPs must be forwarded, via the Defra inspector, to the appropriate HQ licensing office.

Animal room

NOTE: All relevant regulations in these Safety Precautions apply to any room in which animals are in contact with specified pathogens. There are, in addition, hazards arising from the natural diseases of animals which may be transmissible to man. Diseases can be contacted following bites, scratches, droplet infection or the bites of insect vectors. There are particular hazards associated with the generation of aerosols in animal rooms.

In addition to the staff utilising the animals, others may be engaged to clean and feed them and the Safety Precautions also apply to them.

1. DRAINS: See THE LABORATORY – SITING AND STRUCTURE, paragraph 5.

2. DEAD ANIMALS, BEDDING, DUNG etc.: see LABORATORY FACILITIES, paragraph 2. Where autoclaving followed by incineration would create a radiological hazard, carcases must be first sealed in a suitable bag.

3. CAGES AND ASSOCIATED EQUIPMENT: must be autoclaved or disinfected before being cleaned and returned to store.

4. ESCAPES: in no circumstances should there be a direct exit to the outside. The Safety Officer and the licensing authority of Defra must be informed if an animal cannot be accounted for.

5. VERMIN: suspected or obvious infestation with insects or wild rodents must be reported at once to the Safety Officer and the licensing authority of Defra.

6. MONKEYS: the principal hazard in monkey handling not common to the handling of other animals is the risk of infection with monkey viruses which can produce serious disease in man. The established basic rules for handling must be observed.

7. RESPONSIBILITY: servicing of specified pathogen rooms in the animal house must not be carried out by general animal house staff. Suitably trained staff approved by the Safety Officer should carry out these duties under the day-to-day supervision of the person in charge of the animal house.

Containment Requirements for Laboratories to be Licensed to Handle Defra Category 3 Pathogens under the Specified Animal Pathogens Order 1998

The laboratory – siting and structure

1. Whereas the laboratory need not be physically separated from other laboratories it should not be sited next to a known fire hazard (e.g. the solvent store) or be in danger of flooding.

2. The laboratory should be isolated by an air lock. A continuous internal air flow must be maintained by one of the following means:

   (a) extracting the laboratory air through independent ducting to the outside air through a HEPA filter;

   (b) ducting the exhaust air from a microbiological safety cabinet to the outside air through a HEPA filter.

3. In laboratories which have a mechanical air supply system, the supply and extract airflow must be interlocked to prevent positive pressurisation of the room in the event of failure of the extract fan. The ventilation system must also incorporate a means of preventing reverse air flows.

4. The laboratory must be sealable so as to permit fumigation.

5. The laboratory must be proofed against entry or exit of animals or insects. This is particularly important in the case of diseases which can be spread by insect vectors.

6. Liquid effluent should be treated by a procedure known to kill the relevant pathogens. This procedure must be confirmed as having operated satisfactorily before the effluent is discharged to the public sewer, e.g. if heat treatment is to be used, temperature recording facilities should be provided to monitor the process. Since treatment and tests may take some time, it may be necessary to have more than one standing tank if work is to be carried out continuously. The standing tank(s) and recording equipment form parts of the facilities of the laboratory, so the Safety Officer is responsible for ensuring their proper functioning.

Laboratory facilities

1. The laboratory must be equipped with a Class I, II or III exhaust protective cabinet. All laboratory manipulations with live pathogens may be carried out with the cabinet in any mode with the exception of homogenisation which should be carried out with the cabinet in the Class I or III mode.

2. All waste biological material must be sterilised prior to removal from the laboratory. Therefore, each laboratory should have direct access to an autoclave. There should be no possibility of removing the load without the autoclave cycle having been completed. As soon as practicable after the completion of the autoclave cycle the load should be taken to an incinerator and immediately incinerated. Autoclaves should be monitored to ensure that time/temperature cycles are completed and records should be kept.

3. All waste materials must be made safe before disposal or removal to the incinerator. Where materials cannot be autoclaved, a means must be provided for their immersion in an effective disinfectant.

4. Each member of staff working in the laboratory must have adequate working space.

5. Specified pathogens should be stored in the laboratory and in suitable containers (depending on the mode of storage, frozen or freeze-dried) in a cabinet reserved for specified pathogens and kept under lock and key. A key should be available on demand only to nominated individual(s). Where storage in the laboratory is not reasonably practicable, material must be transported and stored without spillage in properly labelled robust containers which must only be opened in the Category 3 laboratory. Physical security measures similar to those in place at the laboratory must be in place at the site of storage.

Protective clothing

1. Laboratory gowns must wrap over the chest and fit tightly at the wrists. Ordinary white laboratory coats are UNSUITABLE. Staff should have a clean gown for each uninterrupted period spent in the laboratory. Other types of clothing giving the same degree of protection may be acceptable.

2. Gowns must be not be used outside the laboratory suite. They should be autoclaved before they are removed from the laboratory.

3. Gloves must be worn for all work with infective materials and workers must wash hands before leaving the laboratory.

Safety Officer

NOTE: Throughout this document the term Safety Officer refers to a person having responsibility for work with specified pathogens.

1. A Safety Officer able to advise on infectious hazards, and a deputy, must be appointed or designated. The establishment may have a Safety Officer with general responsibility for such hazards. If not, an additional individual must be designated.

2. A Safety Officer should have appropriate qualifications and laboratory experience in working with specified pathogens.

3. The Safety Officer will act as adviser to the Head of the Department in all matters which may affect the containment of the pathogens and should be authorised to stop practices considered unsafe, pending guidance when necessary, from the laboratory Head.

4. He or she will take control, implement first aid in, and investigate, all accidents in laboratories and take what other action he considers necessary.

5. Where their responsibilities are not sufficient to warrant their full-time employment as Safety Officer, provided that they are readily accessible to the laboratory during normal hours, they may hold another appointment.

6. He or she will be responsible for the safe storage of specified pathogens and the maintenance of the inventory.

7. He or she will be responsible for organising the admission to the laboratory of cleaners and maintenance personnel and for the disinfection of any apparatus, etc. which is to be removed.

8. He or she will be responsible for advising staff on all aspects of the application of these Safety Precautions.

Training in handling specified pathogens

1. The Safety Officer will organise the initial training of staff in the safe handling of specified pathogens.

2. Training will cover, e.g. the correct use of safety hoods, exhaust protective cabinets, pipettes, syringes/needles, hot/cold rooms, centrifuges, blenders, freeze-driers, shaking machines, ultrasonic disintegrators, glassware and the disposal of contaminated protective clothing and laboratory materials.

3. Staff should only work with specified pathogens if they have some previous experience in microbiology and have had a course of training supervised by the Safety Officer.

Supervision

1. Work in the laboratory must, at all times, be carried out by, or be supervised by, a senior, trained and experienced member of the staff.

2. The supervisor will be personally responsible to the Safety Officer for the safety of the work actually in progress at any time, although he or she may not be responsible for the overall project.

Laboratory discipline

1. The containment area of each laboratory must be identified clearly with appropriate warning notices.

2. When unoccupied, the laboratory must be locked. The key(s) must be kept under the supervision of the Safety Officer, and released only to authorised persons. A key, however, should be kept at a secure control point, available at all times, in case of emergency.

3. In normal hours the supervisor will be responsible to the Safety Officer for ensuring that no unauthorised person enters the laboratory.

4. Only the Safety Officer or his deputy may authorise staff to enter the laboratory, and he or she will hold a list of names of personnel so authorised.

5. Unlisted persons (e.g. visitors, observers, cleaners or maintenance/repair personnel must not enter the laboratory unless they have received a signed statement from the Safety Officer that it is safe for them to do so.

6. The Safety Officer will be responsible for confirming when a laboratory and its apparatus have been disinfected.

7. The laboratory must be entered through a 'clean-side' changing area (locker room) separated from the 'dirty-side' by an airlock. All clothing, rings, watches, etc. must be removed into a locker. No food, drink, tobacco, make-up, etc. may be taken through the airlock. Clean protective clothing should be put on. The 'clean' and 'dirty' areas should be clearly distinguished physically.

8. On the way out, over garments should be removed on the 'dirty-side' of the airlock. The individual must then wash hands, transfer to the 'clean-side' and dress.

9. This procedure should be adhered to whenever, and for whatever purposes, the room is vacated.

10. All accidents or spillage of potentially dangerous material in the laboratory must be reported IMMEDIATELY to the Safety Office. EVERY SUCH INCIDENT MUST BE REGARDED AS A FULL MEDICAL OR ANIMAL DISEASE HAZARD.

11. The day-to-day cleanliness of the laboratory is the responsibility of those working in it. Only when the Safety Officer has confirmed that it has been disinfected can other cleaning/maintenance work be carried out.

12. At the end of a working day benches and working surfaces should be disinfected.

13. Work on specified animal pathogens must be kept separate at all times from other work in the laboratory.

14. Periodically, the rooms and everything in them must be fumigated with gaseous formaldehyde.

Handling of specimens

1. All in-coming packages which may contain specified pathogens must be opened by trained staff in the laboratory.

2. Senders should be advised that a liquid sample should be externally identified and sealed in a can filled with sufficient absorbent material wholly to mop up a spill. The can may, if necessary, be cooled in solid carbon dioxide or liquid nitrogen. Similarly solid samples should be double wrapped so that, in the event of the outer container rupturing, there can be no leakage of contents.

3. Chapter 6 of "Laboratory-Acquired Infections" by C H Collins (4th edition, Butterworth and Co. 1999) gives general advice on packing and unpacking specimens, but in the present context all such unpacking must be carried out in the containment facility.

4. Particular care must be taken when biological material which cannot be autoclaved, is to be removed from the laboratory. The Safety Officer must be consulted before unsterilised material is removed. Precautions must be taken to sterilise the outer surface of containers and to sterilise the material itself, as far as possible.

5. The movement of specified pathogens from an approved laboratory to any other premises is prohibited except under the provisions of a licence issued by Defra.

Security

1. It is imperative that the laboratory and animal rooms must be secure against intruders or vandals. An intruder alarm system must be fitted.

2. Security patrols, etc. must not enter laboratories, or animal rooms. If it appears that an adjacent fire or water hazard threatens the room then the Safety Officer should be informed immediately.

3. A key to the laboratory should be held centrally for emergency access but must only be released on the instruction of the Safety Officer or their deputy.

4. The Safety Officer must maintain a list of the specified pathogens used at the laboratory. This list must indicate the number of vials of pathogen under storage.

Standard Operating Procedures

1. SOPs must be written and issued to staff covering–

   (i) receipt and unwrapping of incoming specimens;

   (ii) handling of specified pathogens in vitro;

   (iii) handling of specified pathogens in vivo (where appropriate);

   (iv) disposal of all waste and surplus pathogens;

   (v) storage of specified pathogens; and

   (vi) emergency procedures.

2. All staff must be familiar with these SOPs and have access to them on a day to day basis. Adherence to the SOPs will be a condition of a licence issued under the Specified Animal Pathogens Order 1998 and they must not be altered without prior approval from the Defra licensing office. Any plans to amend SOPs must be forwarded, via the Defra inspector, to the appropriate HQ licensing office.

Animal room

NOTE: All relevant regulations in these Safety Precautions apply to any room in which animals are in contact with specified pathogens. There are, in addition, hazards arising from the natural diseases of animals which may be transmissible to man. Diseases can be contacted following bites, scratches, droplet infection or the bites of insect vectors. There are particular hazards associated with the generation of aerosols in animal rooms.

In addition to the staff utilising the animals, others may be engaged to clean and feed them and the Safety Precautions also apply to them.

1. DUST: Pre-filters are required to protect the HEPA filters and should be changed as necessary with the air-steam working. Used filters should be immediately placed into bags, autoclaved and then incinerated.

2. DRAINS: See THE LABORATORY – SITING AND STRUCTURE paragraph 6.

3. DEAD ANIMALS, BEDDING, DUNG etc.: see LABORATORY FACILITIES paragraph 2. Where autoclaving followed by incineration would create a radiological hazard, carcases must be first sealed in a suitable bag.

4. CAGES AND ASSOCIATED EQUIPMENT: must be autoclaved or disinfected before being cleaned and returned to store.

5. ESCAPES: in no circumstances should there be a direct exit to the outside. The Safety Officer and the licensing authority of Defra must be informed if an animal cannot be accounted for.

6. VERMIN: suspected or obvious infestation with insects or wild rodents must be reported at once to the Safety Officer and the licensing authority of Defra.

7. MONKEYS: the principal hazard in monkey handling not common to the handling of other animals is the risk of infection with monkey viruses which can produce serious disease in man. The established basic rules for handling must be observed.

8. RESPONSIBILITY: servicing of specified pathogen rooms in the animal house must not be carried out by general animal house staff. Suitably trained staff approved by the Safety Officer should carry out these duties under the day-to-day supervision of the person in charge of the animal house.

Containment Requirements for Laboratories to be Licensed to Handle Defra Category 4 Pathogens under the Specified Animal Pathogens Order 1998

The laboratory – siting and structure

1. Whereas the laboratory need not be physically separated from other laboratories it should not be sited next to a known fire hazard (e.g. the solvent store) or be in danger of flooding.

2. The laboratory should be isolated by an air lock and provided with a suitably placed shower. Air locks and rooms must be ventilated by an exhaust air system. The air pressure in the laboratory should be monitored and displayed both within and immediately outside the laboratory. The laboratory should be maintained at a differential negative pressure of 75 Pascal's (Pa) (0.3 inches or 7.6 mm water pressure) to ambient. An alarm should sound if the air pressure falls below this.

3. The exhaust air must be filtered before discharge through two HEPA filters. The system must include a device to prevent back flow through the filters. The air intake should be protected by a single HEPA filter in case of power failure.

4. The laboratory must be sealable so as to permit fumigation.

5. The laboratory must be proofed against entry or exit of animals or insects. This is particularly important in the case of diseases which can be spread by insect vectors.

6. Effluent should be sterilised by a procedure known to kill the relevant pathogens. This procedure must be confirmed as having operated satisfactorily before the effluent is discharged to the public sewer, e.g. if heat sterilisation is to be used, temperature recording facilities should be provided to monitor the process. Since sterilisation and tests may take some time, it may be necessary to have more than one standing tank if work is to be carried out continuously. The standing tank(s) and recording equipment form parts of the facilities of the laboratory, so the Safety Officer is responsible for ensuring their proper functioning.

Laboratory facilities

1. The laboratory must be equipped with a Class I/II/III exhaust protective cabinet. All laboratory manipulations with live pathogens should be carried out in the cabinet in any mode with the exception of homogenisation which should be carried out with the cabinet in the Class I or Class III mode.

2. All waste biological material must be sterilised prior to removal from the laboratory. Therefore, each laboratory should have direct access to an autoclave which should have double doors. There should be no possibility of removing the load without the autoclave cycle having been completed. As soon as practicable after the completion of the autoclave cycle the load should be taken to an incinerator and immediately incinerated. Autoclaves should be monitored to ensure that time/temperature cycles are completed and records should be kept.

3. All material must be made safe before being removed from the laboratory unit. A double ended dunk tank filled with an effective disinfectant is required for the removal of materials that cannot be autoclaved. The dunk tank should be sealed during fumigation if the disinfectant is incompatible with the fumigant.

4. Each member of staff working in the laboratory must have adequate working space.

5. Specified pathogens should be stored in the laboratory and in suitable containers (depending on the mode of storage, frozen or freeze-dried) in a cabinet reserved for specified pathogens and kept under lock and key. A key should be available on demand only to nominated individual(s).

Protective clothing

1. Laboratory gowns must wrap over the chest and fit tightly at the wrists. Ordinary white laboratory coats are UNSUITABLE. Staff should have a clean gown for each uninterrupted period spent in the laboratory. Other types of clothing giving the same degree of protection may be acceptable.

2. Gowns must be autoclaved before they are removed from the laboratory.

3. Gloves must be worn for all work with infective materials and workers must shower before leaving the laboratory.

Safety Officer

NOTE: Throughout this document the term Safety Officer refers to a person having responsibility for work with specified pathogens.

1. A Safety Officer able to advise on infectious hazards, and a deputy, must be appointed or designated. The establishment may have a Safety Officer with general responsibility for such hazards. If not, an additional individual must be designated.

2. A Safety Officer should have appropriate qualifications and laboratory experience in working with specified pathogens.

3. The Safety Officer will act as adviser to the Head of the Department in all matters which may affect the containment of the pathogens, and should be authorised to stop practices considered unsafe, pending guidance when necessary, from the laboratory Head.

4. He or she will take control, implement first aid in, and investigate, all accidents in laboratories and take what other action he considers necessary.

5. Where their responsibilities are not sufficient to warrant full-time employment as Safety Officer, provided that they are readily accessible to the laboratory during normal hours, they may hold another appointment.

6. He or she will be responsible for the safe storage of specified pathogens and the maintenance of the inventory.

7. He or she will be responsible for organising the admission to the laboratory of cleaners and maintenance personnel and for the disinfection of any apparatus, etc. which is to be removed.

8. He or she will be responsible for advising staff on all aspects of the application of these Safety Precautions.

Training in handling specified pathogens

1. The Safety Officer will organise the initial training of staff in the safe handling of specified pathogens.

2. Training will cover, e.g. the correct use of safety hoods, exhaust protective cabinets, pipettes, syringes/needles, hot/cold rooms, centrifuges, blenders, freeze-driers, shaking machines, ultrasonic disintegrators, glassware and the disposal of contaminated protective clothing and laboratory materials.

3. Staff should only work with specified pathogens if they have some previous experience in microbiology and have had a course of training supervised by the Safety Officer.

Supervision

1. Work in the laboratory must, at all times, be carried out by or be supervised by a senior, trained and experienced member of the staff.

2. The supervisor will be personally responsible to the Safety Officer for the safety of the work actually in progress at any time, although he or she may not be responsible for the overall project.

Laboratory discipline

1. The containment area of each laboratory must be identified clearly with appropriate warning notices.

2. When unoccupied, the laboratory must be locked. The key(s) must be kept under the supervision of the Safety Officer, and released only to authorised persons. A key, however, should be kept at a secure control point, available at all times, in case of emergency.

3. In normal hours the supervisor will be responsible to the Safety Officer for ensuring that no unauthorised person enters the laboratory.

4. Only the Safety Officer or their deputy may authorise staff to enter the laboratory, and he or she will hold a list of names of personnel so authorised.

5. Unlisted persons (e.g. visitors, observers, cleaners or maintenance/repair personnel must not enter the laboratory unless they have received a signed statement from the Safety Officer that it is safe for them to do so.

6. The Safety Officer will be responsible for confirming when a laboratory and its apparatus have been disinfected.

7. The laboratory must be entered through a 'clean-side' changing area (locker room) separated from the 'dirty-side' by a shower and an airlock. All clothing, rings, watches, etc. must be removed into a locker. No food, drink, tobacco, make-up, etc. may be taken through the airlock. Clean protective clothing should be put on. The 'clean' and 'dirty' areas should be clearly distinguished physically.

8. On the way out, over garments should be placed in a bin on the 'dirty-side' of the showers and all remaining clothing also removed to a bin. The individual must then shower, transfer to the 'clean-side' and dress.

9. This procedure should be adhered to whenever, and for whatever purposes, the room is vacated.

10. All accidents or spillage of potentially dangerous material in the laboratory must be reported IMMEDIATELY to the Safety Office. EVERY SUCH INCIDENT MUST BE REGARDED AS A FULL MEDICAL OR ANIMAL DISEASE HAZARD.

11. The day-to-day cleanliness of the laboratory is the responsibility of those working in it. Only when the Safety Officer has confirmed that it has been disinfected can other cleaning/maintenance work be carried out.

12. At the end of a working day benches and working surfaces should be disinfected.

13. Work on specified animal pathogens must be kept separate at all times from other work in the laboratory.

14. Periodically, the rooms and everything in them must be fumigated with gaseous formaldehyde.

Handling of specimens

1. All in-coming packages which may contain specified pathogens must be opened by trained staff in the laboratory.

2. Senders should be advised that a liquid sample should be externally identified and sealed in a can filled with sufficient absorbent material wholly to mop up a spill. The can may, if necessary, be cooled in solid carbon dioxide or liquid nitrogen. Similarly solid samples should be double wrapped so that, in the event of the outer container rupturing, there can be no leakage of contents.

3. Chapter 6 of "Laboratory-Acquired Infections" by C H Collins (4th edition, Butterworth and Co. 1999) gives general advice on packing and unpacking specimens, but in the present context all such unpacking must be carried out in the containment facility.

4. Particular care must be taken when biological material which cannot be autoclaved, is to be removed from the laboratory. The Safety Officer must be consulted before unsterilised material is removed. Precautions must be taken to sterilise the outer surface of containers and to sterilise the material itself, as far as possible.

5. The movement of specified pathogens from an approved laboratory to any other premises is prohibited except under the provisions of a licence issued by Defra.

Security

1. It is imperative that the laboratory and animal rooms must be secure against intruders or vandals. An intruder alarm system must be fitted.

2. Security patrols, etc. must not enter laboratories, or animal rooms. If it appears that an adjacent fire or water hazard threatens the room then the Safety Officer should be informed immediately.

3. A key to the laboratory should be held centrally for emergency access but must only be released on the instruction of the Safety Officer or their deputy.

4. The Safety Officer must maintain a list of the specified pathogens used at the laboratory. This list must indicate the number of vials of pathogen under storage.

Standard Operating Procedures

1. SOPs must be written and issued to staff covering:

   (i) receipt and unwrapping of incoming specimens;

   (ii) handling of specified pathogens in vitro;

   (iii) handling of specified pathogens in vivo (where appropriate);

   (iv) disposal of all waste and surplus pathogens;

   (v) storage of specified pathogens; and

   (vi) emergency procedures.

2. All staff must be familiar with these SOPs and have access to them on a day to day basis. Adherence to the SOPs will be a condition of a licence issued under the Specified Animal Pathogens Order 1998 and they must not be altered without prior approval from the Defra licensing office. Any plans to amend SOPs must be forwarded, via the Defra inspector, to the appropriate HQ licensing office.

Animal room

NOTE: All relevant regulations in these Safety Precautions apply to any room in which animals are in contact with specified pathogens. There are, in addition, hazards arising from the natural diseases of animals which may be transmissible to man. Diseases can be contacted following bites, scratches, droplet infection or the bites of insect vectors. There are particular hazards associated with the generation of aerosols in animal rooms.

In addition to the staff utilising the animals, others may be engaged to clean and feed them and the Safety Precautions also apply to them.

1. DUST: Pre-filters are required to protect the HEPA filters and should be changed as necessary with the air-steam working. Used filters should be immediately placed into bags, autoclaved and then incinerated.

2. DRAINS: See THE LABORATORY – SITING AND STRUCTURE paragraph 6.

3. DEAD ANIMALS, BEDDING, DUNG etc.: see LABORATORY FACILITIES paragraph 2. Where autoclaving followed by incineration would create a radiological hazard, carcases must be first sealed in a suitable bag.

4. CAGES AND ASSOCIATED EQUIPMENT: must be autoclaved or disinfected before being cleaned and returned to store.

5. ESCAPES: in no circumstances should there be a direct exit to the outside. The Safety Officer and the licensing authority of Defra must be informed if an animal cannot be accounted for.

6. VERMIN: suspected or obvious infestation with insects or wild rodents must be reported at once to the Safety Officer and the licensing authority of Defra.

7. MONKEYS: the principal hazard in monkey handling not common to the handling of other animals is the risk of infection with monkey viruses which can produce serious disease in man. The established basic rules for handling must be observed.

8. RESPONSIBILITY: servicing of specified pathogen rooms in the animal house must not be carried out by general animal house staff. Suitably trained staff approved by the Safety Officer should carry out these duties under the day-to-day supervision of the person in charge of the animal house.

ANNEX 10

Containment Measures for activities involving Genetic Modification of Micro-organisms in laboratories under the Genetically Modified Organisms (Contained Use) Regulations 2000 (as amended)

Containment Measures	Containment Levels			
	1	**2**	**3**	**4**
1 Laboratory suite: isolation **(Note 1)**	not required	not required	required	required
2 Laboratory: sealable for fumigation	not required	not required	required	required
EQUIPMENT				
3 Surfaces impervious to water, resistant to acids, alkalis, solvents, disinfectants and decontamination agents and easy to clean	required for bench	required for bench	required for bench and floor	required for bench, floor ceiling and walls
4 Entry to lab via airlock **(Note 2)**	not required	not required	required where and to extent the risk assessment shows it is required	required
5 Negative pressure relative to the pressure of the immediate surroundings	not required	required where and to extent the risk assessment shows it is required	required	required
6 Extract and input air from the laboratory shall be HEPA filtered	not required	not required	HEPA filters required for extract air	HEPA filters required for input and extract air **(Note 3)**

Containment Measures	Containment Levels			
	1	2	3	4
7 Microbiological safety cabinet/enclosure	not required	required where and to extent the risk assessment shows it is required	required, and all procedures with infective materials required to be contained within a cabinet/ enclosure	Class III cabinet required
8 Autoclave	required on site	required in the building	required in the laboratory suite **(Note 4)**	double ended autoclave required in laboratory
SYSTEM OF WORK				
9 Access restricted to authorised personnel only	not required	required	required	required (via airlock key procedure)
10 Specific measures to control aerosol dissemination	not required	required so as to minimise	required so as to prevent	required so as to prevent
11 Shower	not required	not required	required where and to extent the risk assessment shows it is required	required
12 Protective clothing	suitable protective clothing required	suitable protective clothing required	suitable protective clothing required; footwear required where and to extent the risk assessment shows it is required	complete change of clothing and footwear required before entry and exit

Containment Measures	Containment Levels			
	1	2	3	4
13 Gloves	not required	required where and to extent the risk assessment shows they are required	required	required
14 Efficient control of disease vectors (eg rodents and insects) which could disseminate GMMs	required where and to extent the risk assessment shows it is required	required	required	required
15 Specified disinfection procedures in place	required where and to extent the risk assessment shows they are required	required	required	required
WASTE				
16 Inactivation of GMMs in effluent from handwashing sinks and showers and similar effluents	not required	not required	required where and to extent the risk assessment shows it is required	required
17 Inactivation of GMMs in contaminated material and waste	required by validated means	required by validated means	required by validated means	required by validated means
OTHER MEASURES				
18 Laboratory to contain its own equipment	not required	not required	required, so far as is reasonably practicable	required

Containment Measures	Containment Levels			
	1	2	3	4
19 An observation window or alternative is to be present so that occupants can be seen	required where and to extent the risk assessment shows it is required	required where and to extent the risk assessment shows it is required	required	required
20 Safe storage of GMMs	required where and to extent the risk assessment shows it is required	required	required	secure storage required
21 Written records of staff training	not required	required where and to extent the risk assessment shows they are required	required	required

NOTES

1. In the Table above, "isolation" means, in relation to a laboratory, separation of the laboratory from other areas in the same building, or being in a separate building.
2. Entry must be through an airlock which is a chamber isolated from the laboratory. The clean side of the airlock must be separated from the restricted side by changing or showering facilities and preferably by interlocking doors.
3. Where viruses are not retained by the HEPA filters, extra requirements will be necessary for extract air.
4. Where the autoclave is outside the laboratory in which the activity involving genetic modification of micro-organisms is being undertaken, but within the laboratory suite, there shall be validated procedures for the safe transfer of material into that autoclave, which provide a level of protection equivalent to that which would be achieved by having an autoclave in that laboratory.

ANNEX 11

Animal pathogens by SAPO and ACDP categories

	ACDP				
		4 *Causes severe human disease and is a serious hazard to employees; it is likely to spread to the community and there is usually no effective prophylaxis or treatment available.*	**3** *Can cause severe human disease and may be a serious hazard to employees; it may spread to the community, but there is usually effective prophylaxis or treatment available.*	**2** *Can cause human disease and may be a hazard to employees; it is unlikely to spread to the community and there is usually effective prophylaxis or treatment available*	**1** *Unlikely to cause human disease*
SAPO	**4** *Disease producing organisms which are either exotic or produce notifiable disease and have a high risk of spread from the laboratory.*	Hendra virus; Nipah virus;	rabies virus; highly pathogenic avian influenza viruses		African swine fever virus; FMD virus; Newcastle disease virus; Peste des petits ruminants virus; Rinderpest virus; swine vesicular disease virus; Teschen virus
SAPO	**3** *Disease producing organisms which are either exotic or produce notifiable disease and have a moderate risk of spread from the laboratory.*		Bacillus anthracis; Brucella abortus; Brucella melitenis; Brucella suis; Burkholderia mallei; Eastern and Western encephalomyelitis; Histoplasma farciminosum; Japanese encephalitis virus; Rift Valley fever; Venezuelan equine encephalomyelitis; West Nile Fever;	Vesicular Stomatitis	African Horse Sickness; Bluetongue; Brucella ovis; Classical Swine Fever; Cochliomya hominivorax; equine infectious anaemia; Lumpy skin disease; sheep & goat pox;

	ACDP				
		4 *Causes severe human disease and is a serious hazard to employees; it is likely to spread to the community and there is usually no effective prophylaxis or treatment available.*	**3** *Can cause severe human disease and may be a serious hazard to employees; it may spread to the community, but there is usually effective prophylaxis or treatment available.*	**2** *Can cause human disease and may be a hazard to employees; it is unlikely to spread to the community and there is usually effective prophylaxis or treatment available*	**1** *Unlikely to cause human disease*
SAPO	**2** *Disease producing organisms which are either exotic or produce notifiable disease, but have a low risk of spread from the laboratory.*		Echinococcus granulosus; Echinococcus multilocularis	Trichinella spiralis; Trypanosoma brucei	Aujeszky's disease; Babesia bigemina; Babesia bovis; Babesia cabilli; Bovine leucosis; Ehrlichia ruminantium; Mycoplasma agalactiae; Mycoplasma capricolum subspecies capripneumoniae; Mycoplasma mycoides var capri; Mycoplasma mycoides sub species mycoides, SC and mycoides LC variants; Theileria annulata; Theileria equi; Theileria parva; Trypanosoma congolense; Trypanosoma equiperdum; Trypanosoma evansi; Trypanosoma simiae; Trypanosoma vivax, Viral haemorrhagic disease of rabbits virus

	ACDP				
		4 *Causes severe human disease and is a serious hazard to employees; it is likely to spread to the community and there is usually no effective prophylaxis or treatment available.*	**3** *Can cause severe human disease and may be a serious hazard to employees; it may spread to the community, but there is usually effective prophylaxis or treatment available.*	**2** *Can cause human disease and may be a hazard to employees; it is unlikely to spread to the community and there is usually effective prophylaxis or treatment available*	**1** *Unlikely to cause human disease*
SAPO	**1** *Disease-producing organisms which are enzootic and do not produce notifiable disease.*				

ANNEX 12

International Standards for Microbiological Containment Laboratories

The World Health Organisation (WHO)

The World Health Organization (WHO) published the first edition of its "*Laboratory Biosafety manual*" in 1983. The third edition was published in 2004. The manual encourages countries to accept and implement basic concepts in biological safety and to develop national codes of practice for the safe handling of pathogenic micro- organisms in laboratories within their geographical borders. Since 1983, many countries have used the guidance in the manual to develop such codes of practice.

The manual specifies 4 containment levels, designated according to a risk assessment, and the risk group of micro-organisms for both laboratories, and for animal facilities.

The 2004 edition stresses throughout the importance of personal responsibility. It also contains chapters on **risk assessment**, transportation of infectious diseases, 'new' risks such as recombinant DNA technology, and new threats to public health and biosecurity.

WHO – Managing Biorisks in Laboratory Environments

WHO's "*Laboratory Biosecurity – WHO Guidance*" outlines an approach to managing biorisks in the laboratory environment. It covers the identification of roles and responsibilities of different stakeholders, as well as the tools and mechanisms needed to support the implementation of a biosecurity strategy.

Laboratory biosecurity concepts describe a culture of responsibility and accountability for valuable biological materials that:

- affirms the importance of keeping dangerous pathogens and toxins safe in laboratories worldwide;
- recognizes biosafety and laboratory biosecurity as complementary and essential activities for managing biological risks in the laboratory environment;
- teaches about the laboratory risk issues that are important to different regions;
- highlights efforts by various international organizations to manage laboratory biological risks, including WHO, Office International des Epizooties (OIE), the Food and Agriculture Organization of the United Nations (FAO), and the International Centre for Genetic Engineering and Biotechnology (ICCEB);
- discusses available guidance for managing laboratory biological risks.

OIE Guidance on International Transfer and Laboratory Containment of Animal Pathogens

The Office International des Epizooties (OIE) – the World Organisation for Animal Health – publishes its "*Terrestrial Animal Health Code 2007*" , Chapter 1.5.4 on the International Transfer and Laboratory Containment of Animal Pathogens provides a framework and guidance on the transfer of animal pathogens and laboratory containment levels similar to COSHH. It is based on risk assessment and categorizes animal pathogens into risk groups.

It describes containment levels – in terms of lab requirements; entry and exit requirements; specimen manipulation procedures, and provides guidance on 1. the laboratory requirements for the different containment groups; 2. possession and handling, and 3. importation.

The OIE Code is an influential document that provides a framework for a wide range of animal health regulations in OIE member countries. Its primary purpose is to establish international animal health standards in order to facilitate international trade in animals and animal products. In that regard, the health standards published by the OIE are recognised under the Sanitary and Phytosanitory (SPS) agreements within the World Trade Organisation. However, the laboratory safety standards referred to in the code have no status in international law and apply as guidance only.

European Union law

All EU Member States have had to implement the following European Directives:

- Council Directive 90/219/EEC, on the contained use of genetically modified micro-organisms (as amended by Council Directive 98/81/EC)

- Directive 2000/54/EC, on the protection of workers from risks related to exposure to biological agents at work

These are transposed into UK law by the GMO(CU) Regulations and the COSHH Regulations respectively.

We note that there is no EU legislation that bears directly on the containment of animal pathogens.

Some countries maintain human and veterinary pathogens on the same Register and under the same regime, other countries do not.

In respect of FMDV, all FMD labs in the EU are obliged to follow the security standard for FMD laboratories. This was developed in 1985 and further refined in 1992. It is currently being revised. This is the basis of EU inspections of FMD laboratories. If this was strengthened, a certification system for these laboratories would be conceivable provided conflicting interests between the specialists from different EU labs could be managed effectively.

Examples from Other Countries

Canada

In Canada, human pathogens are regulated under the Dept. of Health Act, and the Human Pathogens Importation Regulations. *The Office of Laboratory Safety* (within the Public Health Agency of Canada (PHAC)) are responsible for developing and applying national biosafety policies and guidelines for human pathogens. They permit applications for the importation of human pathogens , certify level 3 and 4 containment facilities (there are 4 containment categories), and provide training.

PHAC develop polices, procedures and guidelines for biosecurity (biosafety emergencies and threat reduction initiatives), control and track the use of dangerous pathogens in Canada and monitor the accidental release of biological materials from certified and non-certified facilities and the instances of laboratory-acquired infections. They also have general responsibility for developing and managing safety programs for all Public Health labs and produce Laboratory Safety Guidelines.

Animal Pathogens are mandated under the Health of Animals Act which covers the importation and use of animal pathogens. This is regulated by the Canadian Food Inspection Agency (CFIA) which establishes the 4 biocontainment levels, procedures and protocols that are needed to work safely with animal and zoonotic pathogens, chemical hazards, and plant pests of quarantine significance, and to protect laboratory staff, the Canadian public, and the environment.

Developed and enforced by the CFIA, the Containment Standards for Veterinary Facilities (1st ed 1996) sets out the design and operational requirements for facilities working with animal pathogens. The CFIA also issue import permits and certification for animal pathogens.

Canada's Containment Standards and Guidelines are based on the World Health Organisation's Laboratory Safety Manual (ref above).

The United States

The historical development of the US regulatory framework in place for managing risks related to human pathogens.

The risks of working with biological agents were initially perceived as limited to the exposure of lab researchers, of the general public and of the environment. Responding to surveys published in the 40s, 50s, 60s, and 70s documenting numerous laboratory-associated cases of infection, the Public Health Service of the Department of Health, Education and Welfare (the predecessor to the current Department of Health and Human Services) outlined, in 1969, a classification system for biological agents. The *Classification of Etiologic Agents on the Basis of Hazard* categorised bacteria, fungi and viruses known to infect humans into four classes, or risk groups as they are now known.

Soon after this publication came out, concern grew about another safety hazard. In the early 70s university researchers developed the recombinant DNA technique where genes are transferred from one organism to another unrelated organism, i.e. one with which it would not normally reproduce. The National Institutes of Health (NIH) – also of the previous

Department of Health, Education and Welfare – responded by establishing a Recombinant DNA Molecule Program Advisory Committee, later shortened to the Recombinant DNA Advisory Committee, or the RAC. The RAC produced a set of guidelines, first published in 1976, which suggested that the hazards associated with genetic modification could be categorised using the risk group classification developed for biological agents, and that each of the four risk groups could be matched with a particular set of containment precautions. Accordingly, four biosafety levels consisting of various combinations of laboratory practices and techniques, safety equipment, and laboratory installations were developed.

The *NIH Guidelines for Research Involving Recombinant DNA Molecules* (NIH Guidelines) were closely followed by another biosafety publication, this time a joint endeavour by the Centers for Disease Control and Prevention and the National Institutes of Health. This publication – Biosafety in Microbiological and Biomedical Laboratories – drew heavily on the risk classification systems outlined in the previous two biosafety guides. It assigned biological agents to four risk groups and described four biosafety levels to contain the hazards associated with the particular risk groups. The criteria used in assigning agents to Risk Groups 1 – 4 were consistent with the general criteria used in the *Classification of Etiologic Agents on the Basis of Hazard*, and the descriptions of Biosafety Levels 1 – 4 paralleled those in the *NIH Guidelines*.

The National Research Council also published its own guide for working with biological agents. Having published two reports in the early 1980s on chemical safety in the laboratory, a Committee on Hazardous Biological Substances in the Laboratory was formed in 1985. Four years later, the Committee produced its report entitled Biosafety in the Laboratory: *Prudent Practices for the Handling and Disposal of Infectious Materials*. The guide reinforced the principles established in *Biosafety in Microbiological and Biomedical Laboratories* for handling biological agents.

Specific guidelines for working with human immunodeficiency virus, hepatitis B virus, and other bloodborne pathogens were developed in the early 1990s by the Occupational Safety and Health Administration, and were enshrined in law through the Bloodborne Pathogen Standard of the Occupational Safety and Health Act.

The 1990s saw an expansion in the perceived risks associated with biological agents. In addition to accidental infections and releases of biological agents from research laboratories, the risks associated with work on biological agents were now seen to also include their deliberate theft, diversion, and malicious use. The earliest regulation in the US recognising this second type of risk was the Biological Weapons Anti-Terrorism Act of 1989. Its primary purpose was to incorporate the long overdue[28] Biological Weapons Convention into national legislation and it accordingly prohibits anyone from knowingly developing, producing, stockpiling, transfering, acquiring, retaining, or posessing any biological agent, toxin or delivery system for use as a weapon, or knowingly assisting a foreign state or any organisation in doing so.

[28] John Isaac argues that the long delay in enacting US legislation to implement the Biological Weapons Convention is unlikely due to any organized opposition, but rather the result of normal bureaucratic procrastination as well as to different and more pressing arms control priorities. (Isaac, J. (1990) 'Legislative Needs' in Wright, S. *Preventing a Biological Arms Race*, MIT Press)

The Aum Shinrikyo nerve gas attacks on the Tokyo underground, the Oklahoma City bombing, and the Aryan Nations member Larry Wayne Harris arrest for possession of Yersinia pestis, all within a three month period in the early spring of 1995, formed the key impetus behind the Antiterrorism and Effective Death Penalty Act of 1996. The core objective of this Act, in terms of biosecurity, was to draw up a select agents list[29] recording 'each biological agent that has the potential to pose a severe threat to public health and safety' (42 USC §262a(a)(1)(A)). The Act also mandated the development of safety and security measures for the transfer of these agents.

Biosecurity risks were managed in greater detail still in the USA PATRIOT Act of 2001 and in the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, which followed September 11 and the ensuing anthrax attacks. The USA PATRIOT Act amended the Biological Weapons Anti-Terrorism Act of 1989 by instructing that 'restricted persons'[30] were not to ship, transport, possess, or receive any of the biological agents listed as select agents in the Antiterrorism and Effective Death Penalty Act of 1996. Focused solely on biosecurity, the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 was designed 'to provide protection against the effects of misuse of select agents and toxins whether inadvertent or the result of terrorist acts against the United States homeland or other criminal acts' (42 CFR §73.2). Reemphasising the necessity of a select agents list, it called for the creation of standards and procedures governing listed agents over and above those provided for in the 1996 Act. The resulting regulations required, among other things, that persons working with listed agents obtain a certificate of registration from the Department of Health and Human Services and that facilities develop their own safety, security and emergency response plans.

Animal Pathogens

In the United States the Department of Agriculture (USDA) has five biosafety levels, of which four are universally recognized across the US. (In the US there is no single Federal Agency with a mission to track containment laboratories, and a recent GAO report found that no one anency even knows the exact number of high containment level – level 3 and 4 – laboratories in the United States).

These levels consist of combinations of laboratory practices and techniques, safety equipment, and facility design features appropriate for the dangers posed by the biohazardous materials, and by the procedures to be performed with these agents.

These five biosafety level designations are applicable to all types of containment spaces, including laboratories, animal rooms, corridors, greenhouses, necropsy rooms, insect rearing facilities, carcass disposal facilities, etc. The five biosafety levels, and the general types of biohazardous materials they are meant to contain, are:

---

[29] Examples of agents included on this list are the Ebola, Herpes B, Lassa, Marburg, Monkeypox, and Smallpox viruses; the *Yersinia pestis, Clostridium Botulinum*, and *Bacillus anthracis* bacteria; and the abrin and ricin toxins (42 CFR §73.4 and §73.5).

[30] The term 'restricted person' referred to an individual who a) is under indictment for or has been convicted of a crime punishable by imprisonment for a term exceeding 1 year; b) is a fugitive from justice; c) is an unlawful user of any controlled substance; d) is an alien illegally or unlawfully in the US; e) has been adjudicated as a mental defective or has been committed to any mental institution; e) is an alien who is a national of a country as to which the Secretary of State has made a determination that such country has repeatedly provided support for acts of international terrorism; or f) has been discharged from the Armed Services of the US under dishonorable conditions (18 USC §175b(d)(2)).

A. Biosafety Level 1 (BSL-1). Used with agents of no known or minimal potential hazard to facility personnel, animals or the environment. They present no potential economic loss to the agricultural industries.

B. Biosafety Level 2 (BSL-2). Used with agents of moderate potential hazard to personnel, animals, and the environment, with minimal economic loss to the animal industries. Most research and diagnostics laboratories are at this level. It is the policy of ARS that any laboratory where research is being conducted on infectious agents will be designed, built and operated at a BSL-2 standard at a minimum.

C. Biosafety Level 3 (BSL-3). Used with agents which may be indigenous or exotic to the United States that can be contracted by the respiratory route, and may cause serious or lethal diseases to man, animals, or cause moderate economic loss to the animal industries.

D. Biosafety Level 3 Agriculture (BSL-3Ag). Used with pathogens that present a risk of causing infections of animals and plants and causing a great economic harm. (Foot and Mouth Disease is the premier example.)

E. Biosafety Level 4 (BSL-4). Used with highly lethal exotic agents which pose a high individual risk of life-threatening disease to man. Certain of these viruses also infect food animals and have the potential to cause severe economic loss to animal industries.

   In certain instances, enhancements may be required to the standard design features of a given BSL classification under certain conditions.

Detailed descriptions of acceptable work practices, procedures, and facilities, described as biosafety levels 1 through 4, are presented in the CDC/NIH publication *Biosafety in Microbiological and Biomedical Laboratories*.

Norway

As in the UK, research on human pathogens is regulated under the Working Environment Act (the Norwegian equivalent of the Health and Safety at Work Act) and implemented by the Norwegian Labour Inspection Authority.

The genetic modification of organisms is regulated through a separate act: the Gene Technology Act. The competent authority for deliberate releases is the Ministry of the Environment and the competent authority for approval for contained use is the Ministry of Health and Care Services.

The Gene Technology Act (in English) is available here:
http://www.regjeringen.no/en/doc/Laws/Acts/Gene-Technology-Act.html?id=173031

The Norwegian Food Safety Authority (established on 1 Jan 2004 and merged the Norwegian Animal Health Authority, the Norwegian Agricultural Inspection Service, the Norwegian Food Control Authority, the Directorate of Fisheries' seafood inspectorate, and local government food control authorities) has overall responsibility for animal health and welfare in Norway.

Animal research laboratories are regulated generally through ISO accreditation 17025: 2005, which corresponds to EU directive 882/2004 on animal health. There are also more specific regulations relating to certain pathogens, e.g. FMDv, burd flu, etc. There is a rather limited webpage available: http://www.mattilsynet.no/english/animal_disease_control

Animal research is also regulated through the Animal Welfare Act:
http://www.animallaw.info/nonus/statutes/stnoapa1995.htm

Switzerland

There is there is no difference for containment regulations for human or animal pathogens. They are covered under the same regime – one Einschlussverordnung ("containment order")which covers all pathogens (human, veterinary, plant).

The containment requirements are not very detailed, and do not accommodate specific requirements for FMDV. (This has resulted in problems around the CL4 requirement for supply HEPA filters for laboratory spaces, which is in Switzerland a requirement for human CL4 laboratories, while the security standard only calls for this in animal accommodation).

Licences and inspection

The government issues the licence (either the Office of Public Health for human pathogens or the Environment Office for animal or plant pathogens).

The inspection and the control of the safety measures is done by the local (cantonal) authority. This is a weak point in Switzerland, since they have 23 inspectorates.

The differences between these local inspections are very large and here are thoughts that a centralized system might be better especially for high containment laboratories.

*Differences between regulations for **import** for human or animal pathogens*

The only difference are the import permits: for animal pathogens: Swiss Veterinary Office and for human pathogens it is the Office of Public Health.

It may be that some issues can easily be covered under the same regime and others not (eg. animal is not always a containment and the animal room is then the primary containment etc.).

Standardisation

The European BioSafety Association (EBSA), founded in June 1996, is a not for profit organisation which aims to provide a forum for its members to discuss and debate issues of concern and to represent those working in the field of biosafety and associated activities. The Association has individual members, representing over 15 countries in Europe, as well as other regions.

EBSA's mission is to enhance the knowledge and understanding of biological safety issues throughout Europe. It strives to establish and communicate best practices amongst its members and to encourage dialogue and discussions on developing biosafety and

biosecurity issues. EBSA seeks to influence and support emerging legislation and standards in the areas of biological safety, biosecurity, biotechnology, transport and associated activities and acts as a focal point for the consolidation of views on these issues.

Projects EBSA are participating in to help harmonise legislation and standards include:

- An *International Biorisk Laboratory Management Standard* to safeguard life, property and the environment from biological risks through the development and adoption of recognized standards in the area of management of biological organisms and their products within laboratory environments.

- A *Biosafety Pofessional Competence* for biosafety professionals agreed by the International Biosafety Working Group (IBWG), and by several national organizations, including the WHO.

- *Biosafety Europe* – Coordination, harmonization and exchange of biosafety and biosecurity practices within a pan-European network. A project mandated by the European Commission within the 6 th Framework Programmme on Research and Technological Development.

This EU funded project will look at cross country comparisons. Full data is not yet available from this study.

Conclusions

There is general agreement on principles for laboratory biosafety, however it appears there are many systems out there, and work has only just begun on international standardisation.

ANNEX 13

List of Abbreviations

ACDP – Advisory Committee on Dangerous Pathogens
ACOP – Approved code of practice
ALARP – as low as reasonably practicable
BAU – Biological Agents Unit, HSE
BBSRC – Biotechnology and Biological Sciences Research Council
CFIA – Canadian Food Inspection Agency
COSHH – Control of Substances Hazardous to Health Regulations 2002
DIUS – Department for Innovation, Universities and Skills
EBSA – European Biosafety Association
EC – European Commission
FAO – Food and Agriculture Organisation, of the United Nations
FMD – Foot and mouth virus
GMOs – genetically modified organisms
GMO(CU) – Genetically Modified Organisms (Contained Use) Regulations 2000
GMP – Good manufacturing practice
HEPA – High efficiency particle abstraction (filter)
HPA – Health Protection Agency
HSE – Health and Safety Executive
HSWA – Health and Safety at Work Act
ICCEB – International Centre for Genetic Engineering and Biotechnology
MHSWR – The Management of Health and Safety at Work Regulations 1999
PHAC – Public Health Agency of Canada
SACGM – Scientific Advisory Committee on Genetic Modification
SAPO – Specified Animal Pathogens Order 1998
SPS – sanitary and phytosanitory
USDA – United Stated Department of Agriculture
USPHS – United States Public Health Service
VLA – Veterinary Laboratories Agency
VMD – Veterinary Medicine Directorate
WHO – World Health Organisation

Published by the Department for the Environment, Food and Rural Affairs,

Printed on material that contains a minimum of 100% recycled fibre
for uncoated paper and 75% recycled fibre for coated paper.

www.defra.gov.uk