

**IN CONFIDENCE**

**BIOTECHNOLOGY AND BIOLOGICAL SCIENCES RESEARCH COUNCIL**

**REVIEW OF ARRANGEMENTS FOR THE RISK ASSESSMENT AND SAFE  
MANAGEMENT OF PATHOGEN-HANDLING PROCEDURES IN LABORATORIES AT  
THE INSTITUTE FOR ANIMAL HEALTH**

**REPORT OF THE VISIT OF THE EXTERNAL REVIEW GROUP TO THE PIRBRIGHT  
LABORATORY: 10 APRIL 2008**

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Biotechnology and Biological Sciences Research Council  
June 2008

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### SUMMARY AND LIST OF RECOMMENDATIONS

1. An external review group was of the opinion that the process and outcome of an internal review by IAH of arrangements for the risk assessment and safe management of pathogen-handling procedures at the Pirbright Laboratory were appropriate and adequate. In the group's view, the procedure followed by the Institute in the light of the Government response to Recommendation 5 of the report of the *Independent review of the safety of UK facilities handling foot-and-mouth disease virus* had been soundly based and well executed. The suites of risk assessments, SOPs and methods - and arrangements for managing and monitoring their implementation - were considered to be fit for purpose, and no significant gaps were identified. The system now in place gave the group significant confidence that, if they continued to be implemented effectively, the Laboratory's current procedures for handling pathogens should minimise the risk of accidental release. The staff with whom the group met were to be commended for their effort and commitment in carrying out a very substantial task over a period of just a few months.
2. With the aims of helping IAH to build on the considerable work that had been done, and ensuring that the biosafety management system now in place at Pirbright continued to be implemented effectively, the review group made the following recommendations:

#### **Recommendation 1**

(paragraph 17)

**The Director of IAH should ensure that the operational context of Pirbright's two-tier biosafety management system of top-level risk assessments and SOPs, and group-specific SOPs and methods, is presented appropriately in relation to the policy framework of the Institute's high-level risk register and overall risk-management strategy.**

#### **Recommendation 2**

(paragraph 19)

**The Director of IAH should review the Institute's committee structure, with the aims of reducing its current complexity, and ensuring that all reporting lines and relationships between bodies are clear, particularly with regard to those which have roles in the management of biosafety.**

### **Recommendation 3**

(paragraph 20)

To assist the induction and training of new staff - and respond to the forthcoming introduction of a common regulatory regime for work with human and animal pathogens - the Director of IAH should arrange for the Institute to produce local codes of safety practice that offer an appropriate guide to safe working practices on the Pirbright site, and which underpin and guide the biosafety management structure and operational practices detailed in SOPs and other documents.

### **Recommendation 4**

(paragraph 21)

To ensure that the necessary changes in laboratory practice are both implemented and documented in a timely manner, the Director of IAH should assign to a designated coordinator responsibility for reviewing and communicating changes in top-level risk assessments and SOPs to research groups, and for verifying that the implications of those changes are appropriately reflected in group-specific SOPs and methods in accordance with site biosafety and quality management policies.

### **Recommendation 5**

(paragraph 22)

To enhance consistency, and reduce the complexity of existing arrangements, the Director of IAH should work towards ensuring that all laboratory activities at Pirbright are carried out in compliance with the ISO 9001 quality management standard (and, where relevant, ISO 17025).

### **Recommendation 6**

(paragraph 23)

The Director of IAH should put in place policies and procedures for the establishment of regular external audits of the biosafety management system that has been developed at Pirbright, with a view to monitoring that it continues to be implemented effectively over the coming years.

## **BACKGROUND**

3. The outbreak of foot-and-mouth disease (FMD) in the UK early in August 2007, on farms in Surrey, was caused by a strain of the FMD virus (FMDV) which was believed not to be circulating in nature, but which had been recently used in research at the nearby Pirbright Laboratory of the Institute for Animal Health (IAH), and for vaccine production by Merial Animal Health Ltd, a tenant of IAH based in separate premises on the Institute's Pirbright site. Following the outbreak, the UK Government immediately commissioned an independent inquiry into arrangements for biosecurity at the facilities operated by IAH and Merial.
4. A group chaired by Professor Brian Spratt FRS was established to carry out an *Independent review of the safety of UK facilities handling foot-and-mouth disease virus*. The group's report ("the Spratt report"<sup>1</sup>) was presented to the Secretary of State for Environment, Food and Rural Affairs, and the Chief Veterinary Officer on 31 August 2007.

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<sup>1</sup> [www.defra.gov.uk/FootandMouth/investigations/pdf/spratt\\_final.pdf](http://www.defra.gov.uk/FootandMouth/investigations/pdf/spratt_final.pdf)

5. Concurrently with the inquiry by Professor Spratt's group, a separate investigation was undertaken by the Health and Safety Executive (HSE), which submitted an initial report to Government on 7 August 2007, and its *Final report on potential breaches of biosecurity at the Pirbright site 2007* ("the HSE report"<sup>2</sup>) four weeks after the first outbreak of FMD had been confirmed on 3 August.

6. The Spratt report made a number of recommendations, including the following:

Recommendation 5

IAH should have a thorough review of the safety of all laboratory activities to ensure that procedures which could release infectious FMDV into the containment laboratories are eliminated. This is particularly important for aerosol-producing procedures.

7. In the light of the Spratt and HSE reports, a *Government Statement in response to investigations into the probable release of FMD virus from Pirbright*<sup>3</sup> was published on 7 September 2007, together with the two reports. The Government's response to Recommendation 5 of the Spratt report was as follows:

IAH should have a thorough review of the safety of all laboratory activities to ensure that procedures which could release infectious FMDV into the containment laboratories are eliminated. *We agree, and believe that IAH should carry out a more far-reaching review of the safety of management procedures for all pathogens. IAH will appoint an independent person to lead the review. The Biotechnology and Biological Sciences Research Council will work with IAH to assist in undertaking the review and applying any findings from it.*

## FRAMEWORK AND SCOPE OF THE REVIEW

8. Taking account of:

- (i) Recommendation 5 of the Spratt report;
- (ii) the broader nature of the Government's response to the recommendation;
- (iii) the uncertainties arising from the drafting of the response with regard to (a) the scope of the review, and (b) the respective roles within it of IAH and the Institute's parent body, the Biotechnology and Biological Sciences Research Council (BBSRC);

a framework for the conduct of the proposed review was agreed between BBSRC and IAH, in which a clear distinction would be maintained between the roles of the Council and the Institute.

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<sup>2</sup> [www.hse.gov.uk/news/archive/07aug/finalreport.pdf](http://www.hse.gov.uk/news/archive/07aug/finalreport.pdf)

<sup>3</sup> [www.defra.gov.uk/footandmouth/investigations/pdf/govstatement\\_fmd2007.pdf](http://www.defra.gov.uk/footandmouth/investigations/pdf/govstatement_fmd2007.pdf)

9. In order to implement the actions required in response to Recommendation 5 of the Spratt report, it was agreed that:
- (i) IAH would carry out an internal review of the management of its pathogen-handling procedures.
  - (ii) BBSRC would establish and service an external group to carry out a review of the internal activity undertaken by the Institute. The external group would independently assess - but not formally validate - the process and outcome of the work carried out by IAH. The group would report to the Institute's Governing Body and to BBSRC.
  - (iii) The terms of reference and membership of the external group would be defined by BBSRC after consultation with the Institute.
  - (iv) Reflecting the broad scope of the Government's response to Recommendation 5 ("all pathogens"), as distinct from the narrower focus of the recommendation itself ("FMDV"), the review would cover laboratory activities involving all pathogens at both IAH's Pirbright and Compton sites. However, coverage of the two sites would require a phased approach. The Pirbright phase should be completed as soon as possible, with Compton to follow later in 2008. This report is concerned only with activities at Pirbright.
  - (v) For the purpose of the review, "laboratory activities" would include all activities that directly involve the handling of pathogens for experimental or testing purposes. More general biosecurity or maintenance procedures that are associated with, but do not directly involve, the handling of pathogens for scientific purposes would be outside the scope of the exercise.

#### **TERMS OF REFERENCE**

10. The terms of reference of the external review group, agreed between BBSRC and IAH, were as follows:

In the light of Recommendation 5 of the report of the *Independent review of the safety of UK facilities handling foot-and-mouth disease virus*, and of the *Government Statement in response to investigations into the probable release of FMD virus from Pirbright*:

- (i) to make an independent assessment of the process and outcome of an internal review by the Institute for Animal Health of arrangements for the risk assessment and safe management of pathogen-handling procedures in its laboratories at Pirbright and Compton;
- (ii) to report to the Institute's Governing Body and to BBSRC.

#### **MEMBERSHIP**

11. The membership of the review group is listed in **Annex 1**.

## METHOD OF WORKING

12. The safe management of procedures for work with pathogens at IAH's Pirbright Laboratory is based on a two-tier system of:
  - (i) "top-level", generic risk assessments and standard operating procedures (SOPs) for handling viruses;
  - (ii) more specific, secondary-level SOPs and methods followed by individual research groups.
13. The rationale for, and nature and scope of IAH's internal review of the risk assessment and implementation of those procedures was set out in a paper for the external review group *Internal review of virus handling procedures at the Institute for Animal Health Pirbright Laboratory - January 2008*. In particular, the paper described the process that has been carried out by the Institute, together with plans for its future management. In addition, the external group was provided with a CD-ROM containing copies of all (as at 8 February 2008) of the top-level (25 documents) and group-specific (270) SOPs, methods and risk assessments.
14. The external group was asked to make an independent assessment of the process and outcome of the internal review undertaken by IAH, but that assessment should not be regarded as a formal validation of the work carried out by the Institute. The quantity of written material arising from the internal activity - nearly 300 documents in total - was such that the group was able to consider only a proportion of it. Of necessity, the group had to adopt a relatively "light touch" approach, focusing mainly on the overall process and top-level risk assessments and SOPs, and using a "dipstick" approach to examine samples of some of the many group-specific SOPs and methods. During its visit to Pirbright on 10 April 2008, the group engaged in discussions about the process and outcome of the internal review with the Pirbright Virus Handling Procedures Review Team, and with senior IAH staff, including the Institute Director and the Acting Head of the Pirbright Laboratory.

## CONCLUSIONS AND RECOMMENDATIONS

15. Drawing on its members' relevant experience, the external group made an independent assessment of IAH's internal review of arrangements for the risk assessment and safe management of pathogen-handling procedures at the Pirbright Laboratory. The group was of the opinion that the process and outcome of the internal review were appropriate and adequate. In the group's view, the procedure followed by the Institute in the light of the Government response to Recommendation 5 of the Spratt report had been soundly based and well executed. The suites of risk assessments, SOPs and methods - and arrangements for managing and monitoring their implementation - were considered to be fit for purpose, and no significant gaps were identified. The system now in place gave the group significant confidence that, if they continued to be implemented effectively, the Laboratory's current procedures for handling pathogens should minimise the risk of accidental release.
16. The IAH staff with whom the group met were to be commended for their effort and commitment in carrying out a very substantial task over a period of just a few months. Consideration of biosafety procedures at Pirbright had been an ongoing process, which was greatly accelerated - and broadened to involve a much wider range of staff - following the outbreak of FMD in August 2007. It was a process that would continue to evolve, and the documentation considered by the group represented a "snapshot" of the situation at the time it had been submitted by the Institute to BBSRC in February 2008.

17. In the group's view, the system of top-level, generic risk assessments and SOPs that had been devised by the Pirbright Virus Handling Procedures Review Team provided a conceptually appropriate and workable framework for the development of consistency of approach and practice in the large number of more specific, secondary-level methods and SOPs of individual research groups. Presentationally, however, the group was of the view that the operational context of this two-tier system for the safe management of work with pathogens should be linked more explicitly to IAH's high-level risk register and wider risk-management strategy. The review group recommended:

#### **Recommendation 1**

**The Director of IAH should ensure that the operational context of Pirbright's two-tier biosafety management system of top-level risk assessments and SOPs, and group-specific SOPs and methods, is presented appropriately in relation to the policy framework of the Institute's high-level risk register and overall risk-management strategy.**

18. In the course of the internal review, the group SOPs and methods had been updated in the light of the new top-level SOPs and risk assessments. Inevitably, some of these many documents - almost 300 in total - were more "mature" than others, and some were perhaps over-complicated. Although they were presented in common formats, there were also conceptual differences in the nature of the documents: some were concerned specifically with biosafety, some with research practice, and some with statutory testing activities. In the group's view, however, the outcome of this process had been appropriately consistent, and could be considered satisfactory at this stage, but implementation of the new system would need to be kept under review (see also paragraph 23). The group had a minor concern about the inclusion in some of the SOPs of references to named individuals. This was not good practice, and would necessitate the updating of documents if those people left the Institute or changed jobs within it. If it was essential for those documents to refer explicitly to people with specific roles, they should be identified by the titles of their posts, not by name.
19. The group particularly welcomed the extension of the remit - and corresponding broadening of its membership - of the Laboratory's Biological Agents and Genetic Modification Safety Committee (BAGMSC) to include responsibility for approving new (or significantly amended) risk assessments, SOPs and methods not covered by existing assessments or protocols. Amongst many other duties, this had previously been the responsibility of IAH's Head of Biosecurity, with the potential for a "single point of failure". However, the group was concerned about the apparent complexity of the Institute's overall committee structure - covering both the Pirbright and Compton sites - as presented diagrammatically in the paper mentioned in paragraph 13 above, from which reporting lines were not clear, and the role of the Pirbright BAGMSC in relation to other bodies was not obvious. This complexity would be potentially compounded in future, following the proposed relocation to IAH of the virology work of the Veterinary Laboratories Agency (VLA) currently carried out at Weybridge (see paragraph 24 below). The review group recommended:

#### **Recommendation 2**

**The Director of IAH should review the Institute's committee structure, with the aims of reducing its current complexity, and ensuring that all reporting lines and relationships between bodies are clear, particularly with regard to those which have roles in the management of biosafety.**

20. On the basis of the evidence available to it, the group was of the view that appropriate arrangements were being put in place for the induction and training of staff - and associated record-keeping - in the new system of biosafety management. However, in view of the large numbers of documents involved in the system, the group thought that the induction of new staff would be eased by the production of local codes of safety practice (e.g. for laboratory areas, animal facilities etc) that formed part of the introductory process of providing information about safe working, offering an appropriate guide to safe working practices on the Pirbright site. Specific information about the arrangements for working safely on a day-to-day basis could be best set out in local codes of practice. Guidance on their contents was available in a booklet published by the HSE<sup>4</sup>. Laboratory codes of practice of this kind were an existing requirement for the management, design and operation of microbiological containment laboratories. Although the organisms currently studied at Pirbright did not cause human disease<sup>5</sup>, similar codes might be required in future for work involving animal pathogens, with the forthcoming introduction of a common regulatory regime under the auspices of the HSE. The review group recommended:

### **Recommendation 3**

**To assist the induction and training of new staff - and respond to the forthcoming introduction of a common regulatory regime for work with human and animal pathogens - the Director of IAH should arrange for the Institute to produce local codes of safety practice that offer an appropriate guide to safe working practices on the Pirbright site, and which underpin and guide the biosafety management structure and operational practices detailed in SOPs and other documents.**

21. The group was concerned, however, that existing arrangements for promulgating changes in the top-level risk assessments or SOPs did not appear to be optimal to ensure that they would be incorporated rapidly and consistently in corresponding amendments to group-specific SOPs and methods. In discussion with staff, it appeared that although the alterations to laboratory practice required by such changes were effected quickly, the necessary updating of the associated documents might currently be subject to inappropriate delay. In the group's view, it would be desirable for a designated coordinator to have responsibility for communicating changes to top-level risk assessments and SOPs to research groups, and for verifying that the implications of such changes are appropriately reflected in the relevant group-level documents in a timely manner. The review group recommended:

### **Recommendation 4**

**To ensure that the necessary changes in laboratory practice are both implemented and documented in a timely manner, the Director of IAH should assign to a designated coordinator responsibility for reviewing and communicating changes in top-level risk assessments and SOPs to research groups, and for verifying that the implications of those changes are appropriately reflected in group-specific SOPs and methods in accordance with site biosafety and quality management policies.**

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<sup>4</sup> *The Management, Design and Operation of Microbiological Containment Laboratories*: ISBN 0 7176 2034 4.

<sup>5</sup> Although the animal pathogens currently studied at Pirbright did not cause human disease, staff demonstrated a good awareness of the potential hazards of contamination of clinical material with zoonotic organisms, particularly in samples from tropical areas.

22. The group also had some concern about the existing situation in which activities at Pirbright were executed under different quality assurance arrangements. Some experimental work was carried out under systems accredited to ensure compliance with the BBSRC/DEFRA/FSA/NERC Joint Code of Practice for Research<sup>6</sup>, and some to the international quality management system standard ISO 9001. In addition, the Laboratory was working towards accreditation to the more stringent ISO 17025 standard - specifying general requirements for the competence of testing and calibration laboratories - for some of its statutory testing activities. In the interests of consistency, and to reduce the complexity of the current arrangements, the group was of the view that it would be desirable for IAH to work towards ensuring that all of its activities were carried out in compliance with ISO 9001 (and, where relevant, ISO 17025). The review group recommended:

#### **Recommendation 5**

**To enhance consistency, and reduce the complexity of existing arrangements, the Director of IAH should work towards ensuring that all laboratory activities at Pirbright are carried out in compliance with the ISO 9001 quality management standard (and, where relevant, ISO 17025).**

23. In addition, the group was of the view that there would be both operational and reputational benefits for IAH if implementation of the biosafety management system that had been developed at Pirbright were to be subject to regular external monitoring - perhaps involving "scenario testing", for example, to rehearse the emergency procedures that would be followed in the event of a virus spillage. The review group recommended:

#### **Recommendation 6**

**The Director of IAH should put in place policies and procedures for the establishment of regular external audits of the biosafety management system that has been developed at Pirbright, with a view to monitoring that it continues to be implemented effectively over the coming years.**

24. Looking ahead, implementation of the system would need to have regard to the proposed redevelopment of the Pirbright site and, in particular, to the relocation to IAH of the virology work of the VLA currently carried out at Weybridge. Following the transfer, it would be essential that Institute and VLA staff operated under a common biosafety and quality management culture, with clear and unambiguous reporting lines and management structures, and uniform risk management policies and procedures. Preparations for this would need to begin well in advance of the relocation of VLA staff to Pirbright, in order to ensure that jointly agreed systems for biosecurity, safety and quality management were in place from the outset.

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<sup>6</sup> [www.defra.gov.uk/science/documents/QACoP\\_V8.pdf](http://www.defra.gov.uk/science/documents/QACoP_V8.pdf)

25. More generally, the review group emphasised the crucial roles that biosafety, disease security and quality assurance played in enabling IAH to undertake internationally leading research at Pirbright. However, the provision of a suitable containment regime for work with pathogens incurred substantial costs. Although not strictly within its remit, the group highlighted the need for adequate and stable future funding to enable the Institute's staff to continue to carry out science not only at the leading-edge of its field, but in a safe and secure manner under an appropriate system of quality management, the financial implications of which had to be taken into account by funding bodies. Those implications related not only to the requirement for suitable physical infrastructure, but also to the costs of developing, implementing, monitoring, auditing and enhancing the associated biosafety and quality management systems necessary for it to be used safely and effectively.

## **ACKNOWLEDGEMENTS**

26. The external review group was very grateful for the cooperation extended to it by IAH's Director and staff. The arrangements for its visit to Pirbright, and the Institute's hospitality were much appreciated. The group acknowledged the considerable amount of work, undertaken by many people over a short time, which had been involved in carrying out the Institute's internal review, and in compiling the documentation to inform the group's independent assessment of the process and outcome of that exercise.

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10 APRIL 2008**

**MEMBERSHIP OF THE REVIEW GROUP**

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