

**Scientific Advisory Committee on Genetic
Modification (Contained Use)**

Annual Report

January to December 2009

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Foreword

It gives me great pleasure once again, after another very busy year, to introduce the 2009 Annual Report of the Scientific Advisory Committee on Genetic Modification (Contained Use) (SACGM(CU)).

Since the Committee was established in July 2004, the underpinning science base has continued to develop and constantly becomes more complex and it is no mean feat to keep up with the changes. I am indebted to the experts on the Committee for their knowledge, integrity and independence and for giving their time and expertise, not only during our discussions but also between meetings, as the need arises. We meet as a committee three times a year, with ad-hoc meetings and specialist sub-groups being set up as required. Our work is varied but the role of the Committee can be summarised as:

- Providing advice to the Competent Authority on technical issues arising from activities notified under the Genetically Modified Organisms (Contained Use) regulations 2000.
- Providing advice on risk assessments for contained use activities involving GMO's (this covers >99% GM activities in the UK).
- Continually developing and updating the guidance on all aspects of contained use of GMO's.

To help us deliver robust risk assessments and recommendations to HSE we need to cover a diverse knowledge base, thus we work closely with other Advisory committees and Government departments who attend our meetings. In addition, we often invite scientists working on a particular notification or in a field of interest to attend, deliver presentations and answer committee queries. Thus we can reassure ourselves that our advice is supported by the best possible evidence base.

We are all committed to openness, all minutes and agendas are placed upon the website and I encourage you to look at them to see the breadth and depth of our activities.

Finally, I must express gratitude to our expert and professional secretariat. They work hard not only to service meetings, but form a necessary bridge across to our own stakeholder community and to other Government departments and are always abreast of the many changes within Government. We could not function without them. Their esteem is demonstrated by their success in gaining internal promotion and once again, I congratulate those who have moved on to new roles during the year.



Professor Janet Bainbridge, OBE
July 2010

Introduction

1. Established in 2004 in accordance with the Office of Science and Technology's Code of Practice for Scientific Advisory Committees (CoPSAC), the SACGM(CU) (hereafter referred to as the Committee) is a non-statutory scientific advisory committee. The Committee provides scientific advice to the UK Competent Authority (CA) on the contained use of genetically modified organisms, particularly in respect of hazard identification and risk assessment.
2. The Health and Safety Executive (HSE) provides the Secretariat for the Committee. The Secretariat liaises closely with the Chair, other members of the CA and prepares papers and organises the Committee's meetings. The Secretariat also prepares reports from the Committee and draft guidance arising from advice of the Committee. In addition, the Secretariat maintains the [SACGM\(CU\) website](#), where information about the Committee, its members, as well as meeting agendas and minutes may be downloaded.
3. In 2009, the Committee held two main meetings:
 - 18 March 2009 – [16th meeting](#) (& 3rd public meeting)
 - 20 November 2009 – [17th meeting](#)

Terms of Reference

4. SACGM(CU) provides scientific and technical advice to the UK CA on the risks posed to human health and to the environment from the contained use of genetically modified organisms. In particular the Committee:
 - provides advice on the technical issues of individual activities notified under the Genetically Modified Organisms (Contained Use) Regulations 2000 (as amended) (GMO(CU));
 - provides advice on risk assessments for contained use activities involving GMOs; and
 - develops and updates guidance on all aspects of contained use of GMOs including the SACGM(CU) Compendium of Guidance.
5. [The Compendium of Guidance](#) represents what the Committee considers to be safe and good practice when working with genetically modified organisms (GMOs) in a contained use setting. Whilst it is not mandatory to follow this guidance, doing so will almost certainly ensure that workers are complying with the health and safety law that governs laboratory work with GMOs. The guidance is widely used by the research community.

UK Competent Authorities for Genetic Modification (Contained Use) Activities

6. The Health and Safety Executive along with the Secretary of State for Environment, Food and Rural Affairs form the CA in England and Wales.

In practice, these functions are delegated to HSE and the department for Environment, Food and Rural Affairs (Defra) officials. In Scotland, the CA comprises the Scottish Ministers and HSE and similarly these functions are delegated to officials of HSE and the Scottish Government. Although not part of the CA, the Welsh Assembly Government and Northern Ireland are included in all UK CA considerations.

7. The roles and responsibilities of the different members of the UK CA are set out in [Appendix 1](#).

Genetically Modified Organisms

8. Genetic engineering is different from traditional breeding methods in that the organism's genes are manipulated in a directed way. A multicellular organism that has been modified in this way is referred to as a GMO. Similarly, modified micro-organisms are referred to as genetically modified micro-organisms (GMMs).
9. Contained use (CU) is where control measures are used to limit contact between GMOs/ GMMs, humans and the environment. In practice, this involves work in laboratories, animal houses, indoor plant growth facilities and large-scale production facilities on industrial sites. The vast majority of genetic modification (GM) work includes strategies that severely incapacitate the organism so that it is unable to survive or proliferate outside of the laboratory without specified 'artificial' growth requirements. For the smaller number of activities involving organisms still capable of growth outside of the laboratory, a robust risk assessment must be submitted for scrutiny by the CA with identified appropriate and proportionate containment measures to prevent release, before work may commence. The safety record in this sector is therefore extremely good.
10. During 2009, a total of 186 GM notifications were received by the CA:

Class of Activity	Number Received
1 (New premises)	28
2	128
3	17
4	2
Significant change to work	9
Accident ¹	2

11. The majority of notified activities involved the use of replication defective viral vectors (either adenovirus or retrovirus based systems) for expression of transgenes in mammalian cells. A breakdown of work by organism type

¹ Includes accidents involving genetically modified microorganisms and transgenic organisms

may be found in [Appendix 2](#). Details of all GM work notified to HSE may be found on the electronic [Public Register](#).

Membership

12. The Committee has expertise/ representation in the following areas:
 - Molecular virology
 - Molecular bacteriology
 - Clinical applications (i.e. gene therapy, vaccine development, clinical virology, molecular oncology)
 - Molecular plant biology
 - Environmental microbiology
 - Biological safety
 - Trades Union Representative

13. The Committee comprises a Chair, Vice Chair and 14 members as follows:
 - Professor Janet Bainbridge, OBE (Chair)
 - Professor Martin Gore (Vice Chair), Royal Marsden Hospital, London
 - Dr Gary Burns, MBE, AstraZeneca Ltd, Macclesfield
 - Dr John Carr, University of Cambridge
 - Dr Martin Carrier, Queen Mary College, London
 - Dr Peter Coyle, Regional Virology Laboratory, Belfast
 - Professor Ernest Gould, Centre for Ecology and Hydrology
 - Dr Penny Hirsch, Rothamsted Research, Harpenden
 - Dr Keith Howard, Baxter Vaccines, AG, Austria
 - Professor David Lewis, St George's Hospital, London
 - Dr Philip Minor, National Institute for Biological Standards and Control
 - Mr Robert Osborne, University of Glasgow
 - Dr Brian Robertson, Imperial College, London
 - Dr Peter Searle, University of Birmingham
 - Dr Michael Skinner, Imperial College London

14. Members' biographies and interests can be found on the [SACGM\(CU\) website](#).

15. Although there have been no changes in membership in 2009, the Committee has been operating with a number of vacancies which will need to be filled in 2010.

Interactions with other advisory committees

16. The Secretariat maintains strong links with a number of other scientific advisory committees. Furthermore, several members also sit on these committees, namely:
 - The Advisory Committee on Dangerous Pathogens ([ACDP](#))
 - The Advisory Committee on Releases to the Environment ([ACRE](#))
 - The Gene Therapy Advisory Committee ([GTAC](#))
 - National Expert Panel on New and Emerging Infections ([NEPNEI](#))

17. The Committee frequently invites members from these committees to its meetings in order to inform their discussions on relevant and some of the more contentious agenda items. The meetings in 2009 included updates from cross-representing Committee members as part of the Secretariat Report. It should be noted that the Vice Chair of the Committee is also the Chair of GTAC.

Key business during 2009

18. During the two business meetings in 2009, the Committee were asked to comment on a number of recurrent issues including:

- The European Commission New Techniques Working Group- The group was established to identify and consider a list of new techniques that may challenge the definitions of what constitutes a GMO or GM technique in the GM Contained Use and Deliberate Release Directives.
- Updates on the implementation of the Callaghan review recommendations for animal and human pathogens- Significant progress was made with the development of a single regulatory framework for human pathogens/ specified animal pathogens and GMOs in 2009.

16th Meeting of SACGM(CU) on 18 March 2009

19. Eleven out of a total of fifteen members were in attendance. At the 16th meeting, members advised upon a number of matters including:

- classification of a genetically modified parasite, *Eimeria tenella*;
- the emerging field of GM stem cell therapies and;
- the successful recovery of a synthetic chimaeric human/ bat coronavirus.

Consideration of a notified activity involving *Eimeria tenella* as an heterologous vaccine vehicle

20. HSE sought advice on the appropriate classification for research involving the protozoan parasite *Eimeria tenella*, an organism which although endemic in the UK causes significant economic impact on the poultry industry. Based on the selection of control measures (e.g. room fumigation) from containment level 3, the CA were of the view that the work should be classified as class 3, whilst the notifier's view is that the proposed measure is largely based on the need for strain purity rather than environmental protection. Dr Damer Blake (Institute for Animal Health) gave an overview of the biological properties of the organism (including host range, specificity, prevalence, life cycle), the proposed genetic modifications and the containment measures for the work.

21. Following discussions, the Committee concluded that although the proposed modifications of *Eimeria* were not considered to increase the virulence of the protozoan parasite, the novel nature of the parasite and its

known pathogenicity in poultry was considered to pose a significant hazard to the environment. The proposed containment, including the necessity for whole room fumigation, whilst assisting with the need to ensure strain purity, was also recognised as necessary to prevent dissemination of the protozoa into the wider environment. Consequently, the Committee agreed that the proposed containment measures appear to be warranted and appropriate for the work, and therefore necessitate a classification of class 3.

Emerging genetically modified stem cell therapies

22. Given the rapidly evolving area of stem cell therapies, the advice of the Committee was sought on areas of potential or inherent risks of the technology and guidance on the classification requirements for such work. Professor Andrew Baker (University of Glasgow), an expert in the field and member of GTAC, gave a presentation on the approaches to genetic modification of embryonic and adult derived stem cells. Initial attempts to induce pluripotency in adult stem cells focused on the use of integrating viral vectors and involved the use of potential oncogenic sequences. For applications destined for the clinic, it was more likely that modification would involve the use of adult derived stem cells and non-viral delivery systems tailored to individual patients thereby avoiding risks related to allogenicity and tumourogenicity.
23. The Committee considered that although the pluripotent nature of some stem cells present some inherent risks (e.g. uncontrolled growth) that needed to be adequately considered, the approach to genetic modification of mammalian cells was well established (e.g. the use of viral vectors). Whilst it was anticipated that much of the development work will be aimed at clinical applications, a significant proportion of research is focussed on the use of modified stem cells to engineer models of disease. It is envisaged that such work will continue to use replication defective retroviruses to deliver oncogenes (e.g. c-myc) or a raft of genes that might induce pluripotency in cells that are exposed. SACGM(CU) existing guidance on the use of such vectors is pertinent and should be adequate to facilitate appropriate risk assessment. However, there are specific examples where further consideration by the Committee may be necessary e.g. where stem cells are developed that are intended to avoid an allogeneic immune response, which may be more hazardous given the greater potential for unchecked self renewal.

Synthetic biology - recovery of a synthetic bat SARS-like coronavirus

24. The Committee was asked to discuss a published scientific article in which a chimaeric bat/human coronavirus was successfully engineered, to address a specific evolutionary question relating to human severe acute respiratory syndrome coronavirus. The paper was an example of developments in the area of creating synthetic microorganisms.
25. The Committee were of the view that the techniques being used were not significantly different to those used for manipulation of other viruses utilising reverse genetics. Similarly the Committee felt that existing

procedures for risk assessment would have been appropriate to identify the change in tropism seen with the constructed virus and consequently existing guidance was deemed adequate.

17th Meeting of SACGM(CU) on 20 November 2009

26. Eight out of a total fifteen members were in attendance. At the 17th meeting, members advised upon a number of matters including:

- host range restriction of avian influenza in both avian and mammalian cells
- adaptation of avian influenza to mammalian cells

The determinants of replication of avian influenza viruses in avian and mammalian cells

27. The Secretariat introduced a paper on the proposed submission of a new GM class 4 notification with the aim of elucidating the determinants of influenza host-range restriction in mammals and birds. The proposal was to use reverse genetics to identify mutations or combinations of mutations that increase viral replication in mammalian cells compared to avian cells.

28. The principal investigator associated with the proposal gave an overview presentation on the work outlining the scientific goals, proposed genetic modifications and the risk assessment and associated containment measures. The Committee asked the researcher a number of questions associated with the scope and management of the project. These included whether they intended to cover all of the work described in the risk matrix and a number of questions related to the management of samples such as storage, item tracking, identity of stock material, transport of samples and numbers of viruses manipulated at any one time. Further discussions focussed on the risk matrix and the rationale behind the final assignment of risk levels.

29. The Committee was of the opinion that consent for the work could be granted by the CA following the provision of satisfactory answers to the questions raised.

Pathogenesis of avian influenza virus infections in avians and investigation of adaptation to mammalian swine cells

30. HSE sought scientific advice on the risks posed to humans and the environment following a class 4 notification received by the CA to undertake *in vivo* studies in pigs with genetically modified highly pathogenic avian influenza viruses. The proposed work was a significant change to an existing class 4 project for work with influenza. As the project had been submitted prior to the 17th SACGM(CU) meeting, the CA had already requested additional information from the notifiers. The response to the additional information request was not received prior to the meeting.

31. The Committee agreed that the additional information, already requested by the CA would be critical to adequately assess the risks posed by the work. In addition to the questions already asked by the CA, the Committee felt it was necessary to raise a number of new questions with the notifiers regarding management procedures for the work e.g. sample tracking, storage, transport etc.
32. The Committee was of the opinion that consent for this project could be granted by the CA following the provision of satisfactory answers to the questions raised.

Working Groups

ACDP working group on common containment measures

33. Following the outbreak of foot and mouth disease from Pirbright in August 2007, several Government sponsored reviews took place. One of those led by Sir Bill Callaghan, proposed several recommendations to improve the way animal pathogens are regulated; all of these recommendations were accepted by Government. The recommendations included the development of a single regulatory framework for human, animal and genetically modified pathogens, broadly utilising the risk-based framework of the Genetically Modified Organisms (Contained Use) regulations.
34. As part of this process, the Advisory Committee for dangerous Pathogens (ACDP) were tasked with formulating a set of common containment measures for these pathogens. Two Members of SACGM(CU), namely Dr Gary Burns and Dr Mike Skinner, were co-opted to the ACDP Common Containment Measures Working Group. The working group met in January, March and May 2009. Considerable progress was made and the working group delivered a finalised containment table with supporting guidance to ACDP in October 2009.

Future Work

35. In addition to the normal 'reactive' business of the Committee, the plan of work for 2010 will include the following topics:
 - Further input into the development of a single regulatory framework for human, animal and genetically modified pathogens;
 - The emerging topic of 'Synthetic Biology' will be advised upon from a risk assessment perspective;
 - Revision of the Compendium of Guidance, as required, following the introduction of the single regulatory framework;
 - Contribution to the European Commission working group on new techniques;
 - Recruitment of new Committee members to restore the membership to full cadre.

Appendix 1: United Kingdom Competent Authority Role

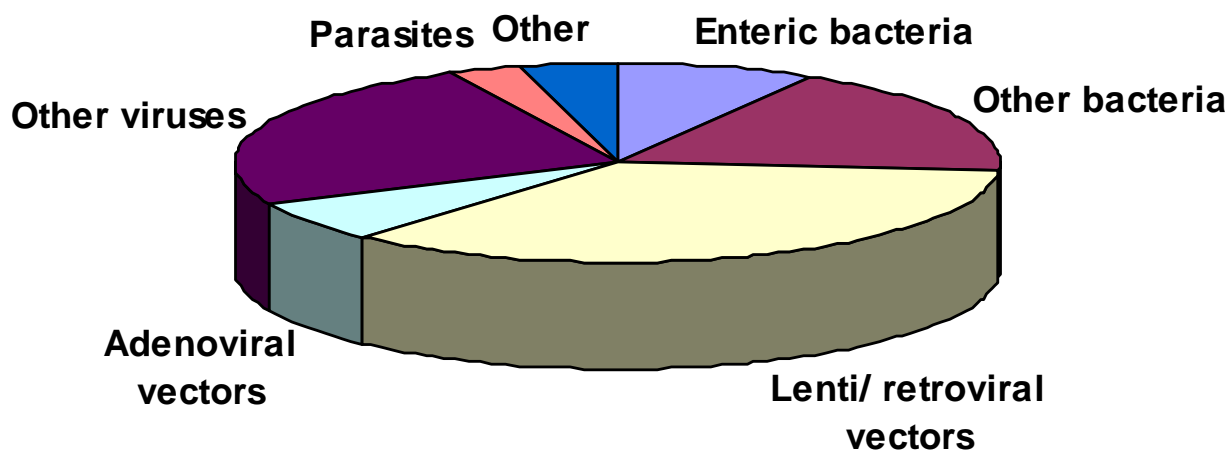
Health and Safety Executive (HSE): HSE has lead responsibility for human health and safety throughout Great Britain. HSE administers the permissioning process for the whole of the competent authority, and its Biological Agents Unit (BAU) maintains the [Public Register](#) and provides technical comment on the notifications. HSE's BAU undertakes inspections of notified premises and activities to check compliance and support the GMO(CU) regulatory framework. Permissioning provides intelligence for inspection and inspection provides intelligence for permissioning.

The Department for Environment, Food and Rural Affairs (Defra): Acts on behalf of the Secretary of State. It has lead responsibility in England and Wales for all effects from the contained use of GMMs on the environment or living organisms supported by the environment, including indirect effects on human health that may result from environmental pathways. It is also responsible for the environmental effects of GM animals and plants in England and Wales in relation to contained uses that affect the former Ministry of Agriculture, Fisheries and Food's interests, e.g. farmed animals (including fish and shellfish), plant varieties and seeds, veterinary medicines, fertilizers, animal feedstuffs, food and forestry, as well as the marine environment.

The Scottish Government: Has the same responsibility in Scotland for the effects of contained use of GMMs on the environment as Defra has in England and Wales, and for the environmental effects of GM animals and plants as Defra has in England. It is also responsible for those aspects of public health that do not come within the scope of the Health and Safety at Work etc. Act 1974.

The Welsh Assembly Government: Has no legal responsibilities for contained use activities involving GMMs, but are consulted upon the environmental aspects of such activities when they occur in Wales. The assembly has the same responsibility for the environmental effects of GM animals and plants in Wales, as Defra in England or the Scottish Government in Scotland. This means that they have a legal responsibility to comment on environmental aspects of contained use activities involving GM animals and plants.

Appendix 2: Breakdown of GM activities by organism type



Abbreviations

ACDP	Advisory Committee on Dangerous Pathogens
ACRE	Advisory Committee on Releases to the Environment
BAU	Biological Agents Unit
CA	Competent Authority
CoPSAC	Code of Practice for Scientific Advisory Committees
Defra	Department for Environment, Food and Rural Affairs
GM	Genetic Modification
GMM	Genetically Modified Microorganism
GMO	Genetically Modified Organism
GMO(CU)	Genetically Modified Organisms (Contained Use) Regulations
GTAC	Gene Therapy Advisory Committee
HSE	Health and Safety Executive
NEPNEI	National Expert Panel on New and Emerging Infections
SACGM(CU)	Scientific Advisory Committee on Genetic Modification (Contained Use)