

Open Government Status: Open	Agenda Number: SACGM/07/10/P1
Meeting Date: 21 July 2010	Type of Paper: Discussion

Draft minutes of the 18th meeting of the Scientific Advisory Committee on Genetic Modification (Contained Use)

Held on Wednesday 24th March 2010 in the BIS Conference Centre, London

Chair

Prof Janet Bainbridge

Apologies

Prof Martin Gore
Dr Penny Hirsch

Secretariat

Dr David Brown
Mr Lee Wilson

Speaker

Prof Len Seymour, University of Oxford

Members

Dr Gary Burns
Dr John Carr
Dr Peter Coyle
Prof Ernest Gould
Dr Keith Howard
Prof David Lewis
Dr Philip Minor
Mr Robert Osborne
Dr Brian Robertson
Dr Peter Searle
Dr Michael Skinner

Assessors

Dr Katherine Bainbridge, Defra

Welcome

1. The Chair welcomed everyone to the 18th meeting of the Committee and extended a warm welcome to Dr Katherine Bainbridge (new Defra assessor). Apologies were received from Professor Martin Gore and Dr Penny Hirsch.

Minutes of the previous meeting – SACGM/03/10/P1

2. The minutes were accepted as a true and accurate recording of the proceedings of the 17th meeting.

Matters arising and Secretariat report – SACGM/11/09/P2

Class 4 highly pathogenic avian influenza notification

3. Members were informed that the recommendations made at the last meeting, which included storage of higher risk samples and procedures for tracking samples had been incorporated into the additional information request made by the Competent Authority. All the recommendations had been addressed, which included robust systems for sample storage, separation and bar code identification and the

Competent Authority subsequently granted consent. A formal inspection of the facilities was deemed superfluous since a HSE inspection of the containment suite was carried out prior to the issuing of a SAPO 4 licence for the same work in September 2009.

Class 4 highly pathogenic avian influenza significant change notification

4. Members were informed that a HSE inspection had now been carried out to clarify issues and recommendations made at the last meeting, together with those of the Competent Authority. As above, these related to storage and tracking of samples and again these issues have been subsequently addressed. However, the Competent Authority was withholding consent pending a response to a query raised by them relating to justification for the use of a class 1 cabinet with respiratory protective equipment for work with highly pathogenic avian influenza strains with a history of human infection as opposed to the use of a closed fronted cabinet.
5. Members asked whether HSE had considered how other European countries dealt with laboratory containment, using A/turkey/Turkey/1/2005 as an example. The secretariat responded that it was not known how other countries handled containment and that this was not a factor when formulating our guidance. Members also asked how this applied to handling poultry. The secretariat informed Members that *in vivo* work was routinely carried out in air-fed suits.

Action: The Secretariat to keep Members informed of the progress with this significant change notification

Single regulatory framework (SRF) for contained use of human, animal and genetically modified pathogens.

6. Members were updated on the latest situation regarding the SRF, specifically the parliamentary process and the legislative reform order. The Secretariat will keep Members informed of any new developments.

Action: The Secretariat to keep Members informed of any new developments with the SRF

Reports from other relevant Scientific Advisory Committees

Advisory Committee for Releases into the Environment (ACRE)

7. The Secretariat invited Dr Katherine Bainbridge to update Members on recent developments at ACRE which included:
 - i. Recent field trial applications involving several different GM potato lines intended for release and all presenting no associated risk to human health.
 - ii. A recent application to market a gene-therapy based medicinal product in the EU.

Gene Therapy Advisory Committee (GTAC)

8. The Secretariat provided feedback from GTAC which included:
 - i. The temporary suspension in dosing within the EU for a deliberate release clinical trial due to a number of deficiencies identified by an MHRA inspection of the vaccine manufacturing facility in USA against EU GMP requirements. No new subjects will be enrolled in Europe until a new GMP certificate is issued (Dr Gary Burns registered an interest).
 - ii. Details surrounding a landmark first-in-man clinical trial involving stem cell therapy for ischaemic stroke patients.

Advisory Committee for Dangerous Pathogens (ACDP)

9. There were no significant issues relating to SACGM(CU) other than the review of ACDP guidance on 'experimental working with influenza of pandemic potential' which was a main agenda item.

Other matters of interest to Members

Synthetic Biology Workshops and research

10. A number of workshops and seminars on the topic of synthetic biology have taken place since the last meeting including:
 - i. The Nuffield Council on Bioethics held a workshop in November 2009 to explore issues raised by emerging technologies, using synthetic biology and nanotechnology as case studies. This dealt with in depth ethical and social science issues and therefore represented only a passing interest to the committee.
 - ii. The latest meeting of the Royal Society Synthetic Biology Policy Coordination Group, again this particular meeting focussed more on public dialogue and social science, as opposed to science.
 - iii. The European New Techniques Working Group met in January 2010 with the aim of finalising a document for presentation to the next Joint Contained Use/ Deliberate Release European Competent Authority meeting.
 - iv. The Secretary attended a European Commission synthetic biology workshop: from science to governance in March 2010. The impression from the meeting was that Europe is cautious about introducing new regulations for synthetic biology and may choose to address the issue with a Code of Practice.

Action: The Secretariat to make Members aware of any developments in the emerging topic of synthetic biology.

11. The Secretariat invited Dr Gary Burns to feedback from his recent trip the United States regarding regulation of gene synthesis. Dr Burns said that Industry was taking the initiative in the US and had formulated a Code of Practice/ Conduct for industry. Additionally the US Government were showing interest in the topic from a "Select Agents"

point of view, had published proposed guidelines for screening of sequence and customer and considered that there would be benefit in a broader international approach to this issue.

12. The Secretariat informed Members that HSE had commissioned a research project to identify the scope of synthetic biology work currently undertaken in the UK, together with the types of disciplines involved e.g. engineering, physics etc. The Secretariat informed Members that the project had not yet begun, but that contacts at the Royal Society would be consulted and the perception was that stakeholders were generally open to sharing information.

EU reasoned opinion that the UK has under implemented the GMO(CU) Directive

13. The Secretariat informed Members that the UK had received a 'reasoned opinion' letter from the European Commission who considered that the UK has under implemented some aspects of the GMO(CU) Directive. Specifically these were:

- **Article 5(5)** – The requirement for risk assessments to take account of the disposal of waste and effluents, and, where appropriate, to implement necessary safety measures.

14. Members asked why this was the case when the UK has actually gold-plated the requirements of the Directive for inactivation of waste at level 1 in the Compendium of Guidance. The secretariat responded that although this has been the case, the regulations don't formally specify the need to take account of disposal of waste in the risk assessment and the reasoned opinion is therefore that it fails to fulfil the requirements of the EU Directive.

- **Annex III, Part B.4** – The necessary characteristics of a GMM to be included in class 1 (negligible risk).
- **Annex IV, Table 1A, Column 10** – Biohazard notification requirements.

15. All these requirements are to be included in the new regulations but, if there was a delay in implementing the new regulations, the existing GMO(CU) regulations would need to be amended.

Incidents involving GMMs

16. HSE has received two notifications detailing accidents (as defined by the GMO(CU) regulations) involving GMMs. The first involved a needlestick injury to a researcher carrying out abdominal inoculations of *Drosophila melanogaster* with a GM strain of *Mycobacterium marinum* expressing red fluorescent protein. HSE carried out an investigation and subsequent recommendations have been made.

17. The second involved a researcher receiving a splash to their face with supernatant containing hepatitis C virus. HSE has not yet conducted an investigation, but an internal investigation has taken place.

Action: Secretariat to update Members on the outcome of the investigation at the July meeting

SAC Chairs' meeting with the Chief Scientific Advisor

18. The Secretariat invited the Chair to update Members on the outcome of a SAC meeting organised to discuss the recent dismissal of an SAC Chair and the links between SACs and policy makers. The minutes of the meeting were attached for information.

Government Office (GO) for Science workshops

19. The Secretariat informed Members of two recent workshops hosted by GO Science:
- i. The first workshop dealt with the issue of lay membership on SACs and was discussed as a main agenda item at the meeting.
 - ii. The second workshop was on openness and transparency. An integral part of this workshop was the importance placed on the review of membership, which contributed to the decision to discuss lay membership as a main agenda item.

Membership of SACGM(CU) & renewals

20. Due to other commitments and time constraints, the planned recruitment drive for new members has yet to take place, but it was anticipated that this would be addressed in the near future.
21. The Secretariat were pleased to announce that the following Members have accepted an invitation to continue on SACGM(CU) for a further 3 years:
- Janet Bainbridge
 - John Carr
 - Martin Gore
 - Keith Howard
 - David Lewis
 - Robert Osborne
 - Michael Skinner

22. The Secretariat informed Members that Dr Martin Carrier would not continue his role on SACGM(CU). The Chair thanked Dr Carrier for his contribution to the work of the Committee over the last 6 years and acknowledged the difficulty in balancing work commitments with those of the Committee.

Defra commissioned research – Review of the environmental risks from marketing GM veterinary and human medicines – SACGM/03/10/P4 (This paper was brought forward to accommodate the guest speaker.)

23. At the 17th SACGM(CU) meeting in November 2009, Members were informed that the GM team at the Department for Environment, Food and Rural Affairs (Defra) had commissioned a desk study to increase the understanding of the risks posed to the environment and wider human health that may be associated with the deliberate release of GM medicines.
24. Although the report was intended to cover potential future applications for medical and veterinary use, it concentrated on current applications that are at/ approaching a clinical trial phase. In order to appraise Members on current developments, Professor Len Seymour from the University of Oxford's Department of Clinical Pharmacology was invited to present on potential future applications in the field of gene & cell therapy.
25. Professor Seymour's presentation covered a number of applications which were showing promising preclinical results and described several strategies that were emerging to overcome problems of insertional mutagenesis associated with the treatment of single gene disorders. The approaches discussed included the development of safer lentiviral vectors (self-inactivating mutations, tissue-specific promoters etc.), the use of adeno-associated virus vectors, herpes simplex virus amplicons and other lytic viruses as candidates for virotherapy. In addition to the approaches using GM microorganisms, transposons were also covered as a potential future application.
26. Particularly with regard to cancer gene therapy, the main conclusions from the presentation were that targeted delivery of the therapeutic agent to the correct cells is essential, and the safety of replication-competent/oncolytic viruses can be improved by appropriate tumour/tissue-specific control of viral replication. While replication-competent viruses with increased potency appear likely to offer greater therapeutic potential in patients, their safety is an important consideration, not only for the patient, but also importantly for the clinical and nursing staff, and other patient contacts. Shedding must be assessed for all new vectors, and co-ordination of regulatory procedures between Defra (deliberate release) and HSE (contained use) is essential.
27. Professor Seymour's presentation was well received by Members and provoked some interesting discussions. These discussions covered recombination and reversion to wild-type pathogens as well as potential concerns over the future use of viruses which, in the wild-type form, show a degree of neurotropism.
28. Members were also asked to comment on the Defra commissioned report, specifically its content and relevance for contained use activities involving GMM constructs with potential therapeutic application. Members felt that as a generic document on gene therapy it was quite

useful, although in parts it lacked detail, e.g. whether recombination had been sufficiently addressed. Other comments related to the general currency and accuracy of the report. Members enquired whether the report could be linked to the minutes or referenced in the SACGM(CU) Compendium of Guidance.

Action: The Secretariat to seek approval from Defra to link the report to the minutes or the Compendium of Guidance

http://randd.defra.gov.uk/Document.aspx?Document=CB02047_7832_FRP.pdf

ACDP Guidance – Advice on Experimental working with Influenza Viruses of Pandemic Potential – SACGM/03/10/P3

29. As part of the review of the ACDP guidance on working with strains of influenza viruses that were novel or had pandemic potential, the views of SACGM(CU) were sought on the GM aspects and the general purpose and scope.

30. Members, including those directly involved in the initial drafting stage, were generally unhappy with the current draft. In summary, they felt it lacked clarity in terminology e.g. SAPO 4 vs HG3, it failed to take account of activities such as clinical trials e.g. challenge studies using influenza and, in its current form, presented an obstacle to laboratories wishing to develop an influenza vaccine in the early stages of a pandemic. Concerns were also raised as to whether the guidance was suitable and sufficient to minimise the risks posed to workers in diagnostic facilities during an outbreak.

Action: The Secretariat to feed back the comments made by Members to the ACDP Secretariat. Members will be updated on progress made with this guidance at future meetings.

SACGM(CU) Compendium of Guidance – update options following implementation of the single regulatory framework – SACGM/03/10/P5

31. The Secretariat introduced this paper aimed at beginning the process of considering how the Compendium of Guidance should be altered when the new single regulatory framework is introduced.

32. Members were generally happy with the minimal changes suggested by the Secretariat, although it was agreed that any future developments should look to keep all the relevant information in one place for ease of use and continuity.

Lay membership on Scientific Advisory Committees – SACGM/03/10/P6

33. The Secretariat introduced this paper, which aimed to review SACGM(CU)'s current set-up and seek Members' views regarding lay membership on the committee.

34. The issue of lay membership provoked a very useful discussion and suggested options including:

- Co-opting a different lay member for each meeting – However, it was agreed that this would place an unnecessary burden on the Secretariat.
- Co-opting a lay member at specific meetings where public perception issues were to be discussed - Members discussed whether this could be achieved through our open meetings, but agreed that this was unlikely, as members of the public did not tend to show much interest based on past audiences.
- Appointing a permanent lay member to the Committee - Members generally felt that because the Committee's remit excluded looking at ethics, a lay member would need a certain degree of understanding of the subject matter and it was difficult to envisage what difference this could make.
- Maintaining the current situation in which Members represented the lay point of view by continuing to offer opinion on information that was outside their area of expertise.

35. Members generally felt that the current situation worked best for the Committee, but that should the need arise we could co-opt someone to represent the lay point of view as and when required. The Secretariat was content that Members were aware of their dual roles as lay members and scientific experts.

Any Other Business

36. None

Close

37. The Chair thanked everyone for their attendance and contribution and drew the meeting to a close.

Date of next meeting(s)

38. 21st July 2010 & 25th November 2010.