ADVISORY COMMITTEE ON GENETIC MODIFICATION

FOURTH AND FINAL REPORT

(December 2003)

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FOURTH AND FINAL REPORT – TO DECEMBER 2003

1 Introduction

Since its Third Annual Report, namely since April 2002, the Advisory Committee on Genetic Modification (ACGM) has held one ordinary meeting to consider and advise on several matters relating to the contained use of genetically modified organisms (GMOs). In addition, in a separate meeting, ACGM members worked together with members of the Advisory Committee on Releases to the Environment (ACRE) in a special horizon-scanning exercise. This unusual session arose because the Health and Safety Commission (HSC) tasked ACGM to produce a forward look, covering the next 10-year period, in the field of the contained use of GMOs. The aim behind the task was to inform HSC's strategic plans for 2004 onwards. The horizon-scan proved a success in providing HSC with a considered view of what might be ahead in the GM field over the next few years. Bringing together two major advisory committees to pool their thoughts and predictions led to a cross-fertilization of ideas and an informative outcome.

In ACGM's Third Annual Report, an explanation was given on how the length of office of the newly reconstituted committee (appointed in December 2000) was extended to run until December 2003. This followed the Health and Safety Commission's review of its advisory committees. The Commission review required HSE to look closely at simplifying considerably the procedures for constitution, reconstitution, planning and monitoring progress of its advisory committees. The Third Annual Report also explained that towards the end of ACGM's period of office in 2003, HSE would reflect on the nature of ACGM, its membership, its Technical Sub Committee and the future and best way forward to provide advice on matters relating to the contained use of GMOs. The outcome of these reflections is described in the body of this, the fourth and final report which extends from April 2002 to December 2003. The fact that this report is entitled the 'Final' report heralds a major change in the advisory structure for the contained use of genetically modified organisms in the future.

The following paragraphs will reveal that there has been a gradual shift in advisory needs. The technological and regulatory advances, general progress and experience in the field of GMO contained use, have subtly changed the advisory requirements from the original need (going back to the 1980s) of basic policy advice in steering and shaping a developing regulatory framework, through to the present moment where a solid regulatory framework has now bedded in and the demands for advice have swung increasingly to being specific, highly technical and often related to notifications from the GM community of proposed work with GMOs in containment.

After careful consideration, it was decided that, ACGM should be replaced. HSE, acting as part of and on behalf of the sector's Competent Authorities of Great Britain has therefore been working to create a new Technical/Scientific Committee of experts to meet the specific scientific advisory needs now being encountered. The new committee came into being on 1 January 2004 and has been given the title of Scientific Advisory Committee on Genetic Modification (Contained Use)(SACGM (CU)) thus deliberately showing its parentage, but emphasising the purely scientific nature of its advice. It is expected that in addition to advising on specific notification issues and cutting edge

science, it will continue the excellent work of ACGM's Technical Subcommittee and revise and develop the Compendium of Guidance begun under the auspices of ACGM.

ACGM members have been alert to the need to question the role of the committee, its raison d'etre, and the future advisory machinery. It is with great thanks to them and their predecessors that the Health and Safety Commission and the Health and Safety Executive acknowledge their dedication, expertise and hard work. Some ACGM members have been appointed to the new Scientific Committee providing an important element of continuity and it is expected that SACGM (CU) will carry on the reputation of excellence which ACGM has set.

2 Genetic Modification (GM) and Genetically Modified Organisms

In order to clarify for the wider public who may read this Report, it is important to explain what is meant by genetic modification. Genetic modification (GM) occurs where the genetic material of an organism (either DNA or RNA) is altered by use of a method that does not occur in nature and the modification can be replicated and/or transferred to other cells or organisms. Typically, genetic modification of micro-organisms involves the removal of DNA, its manipulation outside the cell and reinsertion into the same or another organism. The aim of GM is often to introduce a new or altered characteristic to the target organism.

The organism which has been modified is referred to as a genetically modified organism (GMO). GMOs may be plants, animals or (most commonly) micro-organisms (including bacteria, viruses parasites and fungi). Where the GMO is a micro-organism it is typically referred to as a genetically modified micro-organism (GMM).

An important point to note about GMOs is that in the case of humans, even if they have undergone genetic modification as a result of, for example, gene therapy, they are not regarded as GMOs. This is because humans are specifically excluded from the definition of an organism. The result is that the contained use legislation (the Genetically Modified Organisms (Contained Use) Regulations 2000 (GMO(CU)) does not apply to humans.

3 Contained Use

It is similarly important to clarify what is meant by 'contained use'. ACGM's remit is limited to consideration of 'contained use'. Contained use is where control measures are used to limit contact between GMOs and humans and the environment so as to provide a high level of safety. In practice, this involves work in laboratories, animal houses, plant growth facilities (including growth rooms in buildings and suitable glasshouses) and large-scale production facilities on industrial sites. All of these activities are regulated under GMO (CU). There are also controls on the environmental aspects of GM animals and plants under the Environmental Protection Act 1990.

Matters that do <u>not</u> fall under contained use and are hence outside of the remit of ACGM include:

- Deliberate release of GMOs into the environment (e.g. crop plants in fields):
- Food safety aspects;

- Product approval/marketing approval.

ACGM also does not get involved in some areas closely related to contained use, but for which there are other specific advisory bodies. These include matters of animal welfare and patient safety (e.g. in relation to gene therapy). Whilst ACGM does not advise on patient safety with regard to gene therapy, where the therapy administers GMMs, this has usually, and until recently, constituted a contained use activity and may have involved asking ACGM or TSC to advise on safety in relation to the medical safety of staff, patients' relatives and other close contacts of the patient.

4 ACGM's Terms of Reference (from April 2000)

To advise the Health and Safety Commission and Executive, the Secretary of State, the First Minister of the National Assembly for Wales and Scottish Ministers on all aspects of human and environmental safety of the contained use of genetically modified organisms. In developing its advice, ACGM shall take account of the work of the Food Standards Agency (FSA), the Human Genetics Commission (HGC) and, in particular, the Agriculture and Environmental Biotechnology commission (AEBC).

These Terms of Reference have not changed since the committee was newly constituted in 2000 other than to exclude reference to the MAFF Minister since MAFF no longer exists as a Ministry (its function having been absorbed by the Department for the Environment, Food and Rural Affairs (DEFRA)).

5 Membership of ACGM from April 2002 to December 2003

Member	Nominated by / Independent	Employer
Mrs Sandra Caldwell (Chair)	HSE, Director of Health	HSE
Dr Gary Burns	CBI[1] (employer organisation)	AstraZeneca
Dr Jonathan Butler	Independent	MRC
Mrs Dot Carey	TUC[2] (employee organisation)	Retired, formally of NERC Centre for Ecology and Hydrology, Oxford
Dr Robert Dalziel	Independent	University of Edinburgh
Mr Spyros Elia	Independent	Thomas Tallis School
Dr Lynn Frewer	Independent	Institute of Food Research
Dr Penny Hirsch	Independent	Rothamsted Research
Dr John Keddie	CBI (employer organisation)	GlaxoSmithKline
Prof. Julian Kinderlerer	TUC (employee organisation)	University of Sheffield
Dr Tom Loeffler (appointed from April 2001)	TUC (employee organisation)	BBSRC
Mr Robert Osborne	CVCP[3] (employer organisation)	University of Glasgow
Professor Bert Rima	Independent	Queens University Belfast
Dr Brian Robertson	Independent	Imperial College
Mr Roger Spiller	TUC (employee organisation)	MSF Union
Prof. Anthony Trewavas FRS	Independent	Institute of Cell and Molecular Biology, Edinburgh
Dr Bruce Whitelaw	Research Councils (employer organisation)	Roslin Institute
Professor David Wynford-Thomas	Independent	University of Wales College of Medicine

[1]CBI - Confederation of British Industry.
[2]TUC - Trades Union Congress.
[3]CVCP - Committee of Vice Chancellors and Principals.

(The Register of Members interests is given at Annex 1)

6 Technical Sub Committee

ACGM's Technical Sub Committee was set up to provide detailed technical advice to ACGM and to HSE on scientific developments involving GM. It has continued in this role, providing advice on a number of emerging topic areas, as well as giving detailed comments on a number of notifications made under the Genetically Modified Organisms (Contained Use) Regulations. (The membership of the TSC was primarily drawn from independent experts selected to reflect current developments in the field. There was also a nominee from the TUC, and a nominee from the CBI, and up to 10 independent experts.) Membership for the period from April 2002 to December 2003 is shown below:

Member	Nominated by / independent	Employer
Mr Steve Vranch (chair)	Independent	Jacobs Engineering
Dr Gary Burns	Independent	Astra Zeneca
Dr Iain Cooper	Independent	Institute for Virology and Environmental Microbiology
Mr Steve Eley	Independent	DERA, Porton Down
Dr Penny Hirsch	Independent	Rothamstead Research
Dr Julian Kinderlerer	TUC (employee organisation)	University of Sheffield
Dr Joanna Marshall	Independent	Oxford University
Dr Sue Mayer	Independent	GeneWatch
Dr Phil Minor	Independent	National Institute for Biological Standards and Control
Professor Tony Minson	Independent	Cambridge University
Professor Rick Randall	Independent	University of St. Andrews
Mr John Thorley	CBI (employer organisation)	Consultant
Professor Douglas Young	Independent	St. Mary's Hospital, London

In April 2003, John Thorley retired from TSC on health grounds after a long and valued service. Thanks and best wishes of all his friends and colleagues go with him in his retirement.
Two new members joined TSC - Dr Peter Coyle and Dr Peter Searle, both of whom are experienced in the field of gene therapy, an area of GMM activity which is expanding and raising new issues requiring advice on health and safety matters.

TSC met three times between April 2002 and December 2003. A range of topics were covered resulting from notifications and technical enquiries to HSE, as well as broader developments in the field of GM. Issues covered included:

- the use of plant viruses as gene vectors from risk assessments submitted to HSE for work with Potato Virus X (PVX) and Tobacco Mosaic Virus (TMV) vectors which were being used to express foreign proteins in plants and for use in gene silencing;
- construction of chimaeric viruses of bovine viral diarrhoea virus and hepatitis C virus which had arisen from a couple of similar notifications to HSE which had raised a number of issues;
- the use of an adenovirus-FGF construction in coronary gene therapy;
- difficulties arising from the application of the Contained Use Regulations in a clinical setting;
- draft guidance on the interpretation of the term 'sequences associated with pathogenicity' used in Schedule 5 of the Anti-Terrorism, Crime and Security Act.

Advice on individual notifications was fed into the notification procedure, whilst more general advice was sent to individual centres, or is being used to update the ACGM Compendium of Guidance.

7 Extract from the Second Annual Report (April 2002 – March 2003) to the Competent Authority on notifications processed under the Genetically Modified Organism (Contained Use) Regulations 2000 as amended

To give a general idea of types and numbers of notifiable GM activities which have been the backdrop to ACGM's work, the year's figures for 2002/3 are given below.

NUMBERS AND TYPES OF NOTIFICATIONS

A breakdown is provided below of the number of GMO(CU) notifications processed over the last year with a comparison to the figures for the previous year. The year runs from 1 April to 31 March. This therefore includes notifications received prior to 31 March 2002 but processed during 2002/2003.

Notification Type	Reg	England		Scotland		Wales	
		02/03	01/02	02/03	01/02	02/03	01/02
Class 2 (1st)	10	21	54	5	11	1	6
Class 2 (Subsequent)	10	127	131	17	23	5	3
Class 3 (1st)	11	4	12	2	2	0	0
Class 3 (Subsequent)	11	12	17	3	1	0	0
Class 4 (1st)	11	1	1	0	0	0	0
Class 4 (Subsequent)	11	0	0	0	0	0	0
Premises (for Class 1 only)	9	29	29	2	7	0	1
Premises (for other classes)	9	7	15	1	2	0	0
Significant change	15	19	16	2	0	0	0
Compliance with conditions of consent	-	0	0	0	1	0	0
Compliance with imposed conditions	-	2	6	0	0	0	0
Derogation after notification	18	4	12	3	1	0	0
Confidentiality claim after notification	-	0	0	0	1	0	0
Total		**226**	**293**	**35**	**49**	**6**	**10**

8 ACGM's 48th Meeting on 14 November 2002

At ACGM's 48th meeting, on 14 November 2002, members considered and gave their advice on several issue:

- Exclusions from the Public Register of GM premises and activities maintained under the Genetically Modified Organisms (Contained Use) Regulations 2000 (GMO (CU)) for national security reasons and in line with wider government policy.
- Developments arising from the Cartagena Protocol on Biosafety to the Convention on Biological Diversity (concerning transboundary movements of GMOs) and the Aarhus convention (concerning access to information, public participation in decision making and access to justice) in relation to GMOs.
- Proposed minor amendments to GMO(CU).
- An industry perceived legislative overlap between GMO(CU) and the Plant Health (Great Britain) Order 1993

In addition to secretariat papers being put before members for advice, several members requested more information about notifications, enforcement action and significant developments in the CU arena. The secretariat agreed to produce an annual synopsis of information. Such a synopsis was in fact included in the Third Annual Report last year and has similarly been provided at '7' above.

9 Horizon-scan – a joint ACGM/ACRE venture on November 14 2002

Whilst the morning session of the November meeting was given to the ordinary business of ACGM, the afternoon session was specially arranged to engage members in a joint horizon-scanning exercise with members of the Advisory Committee on Releases into the Environment (ACRE).

The impetus for this exercise arose from the Health and Safety Commission's (HSC) need for strategic advice from its expert committees (of which ACGM is one) on the scientific and technological trends and developments HSC should take into account in developing its strategic plans for 2004 and beyond. The forward look was to cover the next 10-year period looking at key scientific and technological developments, likely innovations and new technologies and so would assist HSC/E in assessing the possible impact of this on its future work in the field of health and safety in the workplace.

ACRE is not an HSC committee. It is based within the Department for the Environment, Food and Rural Affairs (Defra). However, like HSC, Defra was also interested in scanning the horizon pro-actively. ACGM and ACRE reflect and advise on the two major regulatory aspects of GM activity (contained use and deliberate release respectively) in Great Britain and it was considered that a joint horizon-scan would be of mutual benefit allowing a cross-fertilization of ideas and greater breadth of knowledge. It would:

- provide advance notice of the likely applications that may come forward from contained use and deliberate release activities in the future;

- allow time to prepare policy and regulatory positions as appropriate; and
- allow time to research biosafety questions – to ensure safety to human health and the environment.

Accordingly ACGM invited ACRE to its special horizon-scan meeting and Mrs Sandra Caldwell and Professor Alan Gray (respective Chairs) jointly presided over the ensuing brainstorming sessions. Members put forward many ideas on what the future might hold in the GM field and ACGM secretariat compiled these for presentation to HSC.

A resulting paper was put to HSC and while making clear that it was neither appropriate nor necessarily an accurate reflection of the many ideas resulting from the horizon-scanning session it, nevertheless, flagged up several general points which arose out of the session:

- The GM medical field is burgeoning.
- The future of GM food/agriculture/animal husbandry is uncertain.
- The UK is likely to continue as a home to GM research.
- There is a need to 'think globally' where GM in concerned.

All of these could have implications for the GM regulatory system administered by HSE and also Defra in the future.

At the Health and Safety Commission meeting in May 2003, HSC invited representatives of each Advisory Committee to make a brief presentation in connection with the horizon-scan exercise. ACGM's Chair, Secretariat, and members as well as HSC were very grateful to Dr Penny Hirsch for kindly giving up her time to do this on behalf of ACGM.

10 Farewell and thank you to ACGM members

The Health and Safety Commission and the Health and Safety Executive would like to take this opportunity to thank all the members of both ACGM and TSC for their time and commitment to ACGM matters during the final period of office ending on December 31 2003.

GLOSSARY

ACGM	Advisory Committee on Genetic Modification
ACRE	Advisory Committee on Releases into the Environment
AEBC	Agricultural & Environmental Biotechnology Commission
CBI	Confederation of British Industries
CVCP	Committee of Vice Chancellors and Principals
DNA	Deoxyribonucleic acid – present in almost all living cells and contains information coding for cellular structure, organisation and function
Defra	Department for the Environment, Food and Rural Affairs
FSA	Food Standards Agency
GM	Genetic Modification
GMM	Genetically Modified Micro-organism
GMO	Genetically Modified Organism
GMO(CU)	Genetically Modified Organisms (Contained Use) Regulations 2000
HGC	Human Genetics Commission
HSC	Health and Safety Commission
HSE	Health and Safety Executive
MAFF	Ministry of Agriculture, Fisheries and Food
MOD	Ministry of Defence
RNA	Ribonucleic acid – the alternative reservoir of genetic information to DNA
TSC	Technical Sub Committee (of ACGM)
TUC	Trades Union Congress

ANNEX 1 REGISTER OF ACGM MEMBERS' INTERESTS

ACGM members have declared the following commercial and non-commercial interests deemed relevant to their appointment to the ACGM.

Note: Share holdings only declared if over £25,000

Member's Name	Interest
Chair	
Mrs Sandra Caldwell	**Employer:** ☒ Health and Safety Executive **Commercial Interests:** ☒ None **Non-commercial Interests:** ☒ None
Employer Nominees	
Dr Gary Burns	**Employer:** ☒ AstraZeneca **Commercial Interests:** ☒ None **Non-commercial Interests:** ☒ None
Mr Robert Osborne	**Employer:** ☒ University of Glasgow **Commercial Interests:** ☒ None **Non- commercial Interests:** ☒ None
Dr C Bruce A Whitelaw	**Employer:** Roslin Institute (Edinburgh) **Commercial Interests**: ☒ None **Non-commercial Interests:** ☒ Most research is funded by the BBSRC. Currently some research is funded through a consortium of Pharmaceutical Companies (AstraZeneca; Aventis; Cyclacel; GlaxoSmithKline; Novartis; Novo Nordisk; Pharmacia; Pfizer; Schering Plough and Wyeth) - approx funding 200K per annum. ☒ Editor of internationally peer reviewed scientific journal, Transgenic Research, published by Kluwer (Netherlands).
Dr John R Keddie	**Employer:** ☒ GlaxoSmithKline **Commercial Interests:** ☒ GlaxoSmithKline Shares held by Dr Keddie and his spouse. **Non-commercial Interests:** ☒ None
Employee Nominees	
Mrs Dot Carey	**Employer:** Retired (Formerly of IVEM of Oxford) **Commercial Interests:** ☒ None **Non-commercial Interests:**

Member's Name	Interest
	☒ None
Mr Roger Spiller	**Employer:** ☒ MSF(Management, Science, Finance) **Commercial Interests:** ☒ None **Non-commercial Interests:** ☒ None
Dr Julian Kinderlerer	**Employer:** ☒ University of Sheffield **Commercial Interests:** ☒ Occasional consultancy to UNEP and UNIDO re GMOs. **Non-commercial Interests**: ☒ Adviser to UNEP, UNIDO and various governments including Namibia and South Korea on safe use of GMOs.
Dr Tom Loeffler	**Employer:** ☒ Biotechnology and Biological Sciences Research Council (BBSRC) **Commercial Interests:** ☒ None **Non-commercial Interests:** ☒ None
Independent Members	
Dr Lynn Frewer	**Employer:** ☒ Consumer Science Section, Institute of Food Research **Commercial Interests:** ☒ None **Non-commercial Interests:** ☒ BBSRC - CASE award with Unilever - in the area of food risk communication.
Professor Anthony Trewavas FRS	**Employer:** ☒ Institute of Cell and Molecular Biology **Commercial Interests:** ☒ None **Non-commercial Interests:** ☒ Helps administer a grant from AKFADIX (California) to five plant science academic staff in the University of Edinburgh. No payment or research support is received from this grant. The grant is for a gene discovery programme. ☒ On the Governing Council of the John Innes Centre
Dr P. Jonathan G. Butler	**Employer:** ☒ The Medical Research Council, Laboratory of Molecular Biology **Commercial Interests:** ☒ None **Non-commercial Interests:** ☒ Acts as Biological Safety Officer in MRC Laboratory of Molecular Biology and as Biological Safety Adviser to several MRC units

Member's Name	Interest
	in Cambridge (and occasionally MRC Safety Section). ☒ Acts as paid consultant in biological safety to the Sanger Centre, Hinxton, Cambridge. (This is a non - commercial laboratory established and supported by the Wellcome Trust and MRC).
Dr Robert G Dalziel	**Employer:** ☒ University of Edinburgh. **Commercial Interests:** ☒ None **Non-commercial Interests:** ☒ Project Grant."Characterisation of a model of Post Herpetic Neuralgia", GlaxoSmithKline - £200,000 until 30/07/03.
Dr Brian D. Robertson	.**Employer:** ☒ Imperial College of Science, Technology and Medicine. **Commercial Interests:** ☒ None **Non-commercial Interests:** ☒ None
Dr Penny Hirsch	**Employer:** ☒ Rothamsted Research **Commercial Interests:** ☒ None **Non-commercial Interests:** ☒ BBSRC - CASE studentship. ☒ Industrial sponsor Syngenta, to start 2001 (Syngenta give some support to the student, none to Rothamsted or Dr Hirsch).
Professor Bert Rima	**Employer:** ☒ Queen's University Belfast **Commercial Interests:** ☒ Consultant to Lovells (65 Holborn Viaduct, London **Non-commercial Interests:** ☒ Director of Ulidia Housing Association Limited in Northern Ireland.
Mr Spyros Elia	**Employer:** Thomas Tallis School **Commercial Interests:** ☒ None **Non-commercial Interests:** ☒ None
Professor David Wynford -Thomas	**Employer:** ☒ University of Wales College of Medicine **Commercial Interests:** ☒ None **Non- commercial Interests:** None