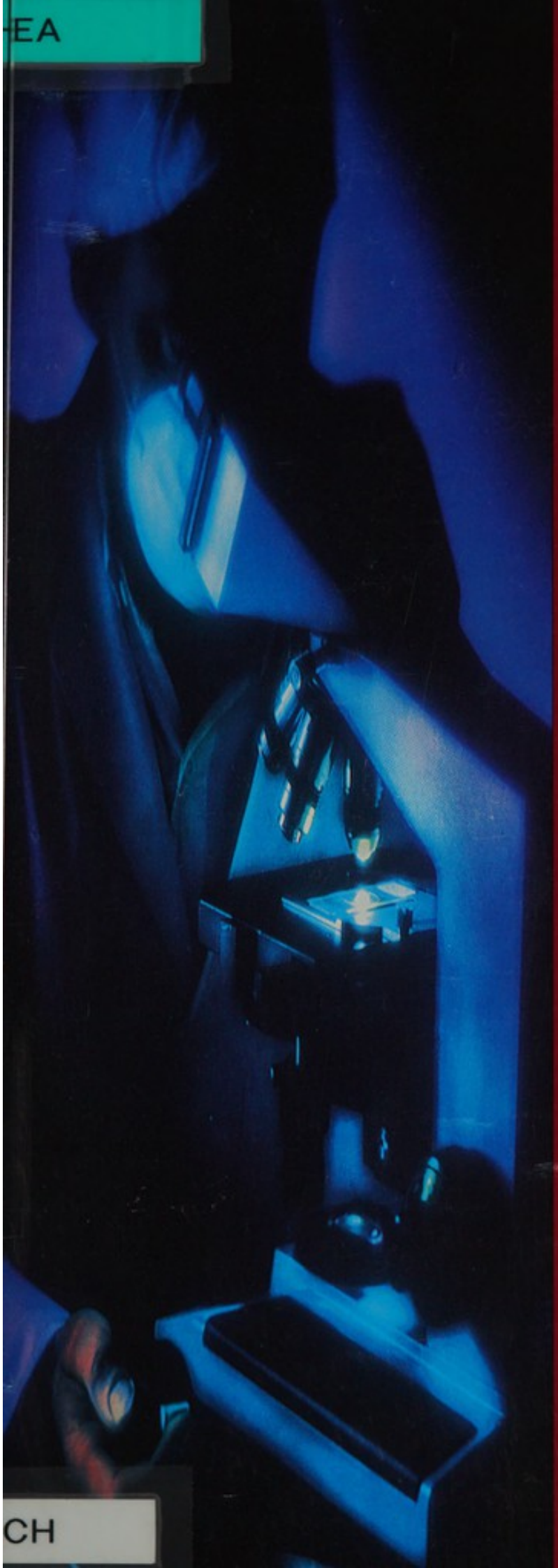
Biotechnology, health and safety in education / Education Service Advisory Committee.



Education

Service

Advisory

Committee

Biotechnology: Health and safety in education

HSC
Health & Safety
Commission

Members of the Education Service Advisory Committee

Mr D Morris	Chair, Health and Safety Executive
Mr R W Hill	Secretary, Health and Safety Executive
Mr J R Atkinson	Association of County Councils
Ms A Aziz	Association of University Teachers
Mr M W Balfour	GMB
Mr D J Bird	Independent Schools Joint Council
Mr D E Capper	Director of Education, Association of Metropolitan Authorities
Cllr T M Dair	Convention of Scottish Local Authorities
Ms H Daley	UNISON
Ms E Darbyshire	National Union of Teachers
Cllr D Eastwood	Association of Metropolitan Authorities
Mr J G Ellis	Dyfed County Council
Mr J Francey	Deputy Chief Inspector of Factories (Northern Ireland)
Mr J Greig	National Association of Governors and Managers
Ms E Harrison	UNISON
Mr R O Hellings	Committee of Vice Chancellors and Principals
Mr G A Holley	Department for Education and Employment
Mr A M Jones	Welsh Office
Mr R Kettleborough	National Association of Teachers in Further and Higher Education
Mr D Lankshear	General Synod of the Church of England
Mr G McLafferty	Convention of Scottish Local Authorities
Mr T Mellish	TUC
Mr J Owen	Association of County Councils
Mr G Richards	Transport & General Workers Union
Mr B Robinson	National Association of School Masters and Union of Women Teachers
Mr S P Rouse	Universities & Colleges Employers Association
Mrs J Short	Colleges Employers Forum
Mr C J Storr	Catholic Education Service
Mr G A Stuart	Scottish Office
Mr D Trafford	MSF Department of Pharmacology
Mr E Young	Educational Institute of Scotland

Members of the 'Biotechnology: Health and safety in education' Working Group

Mr D Morris	Chair, HSE
Mr R G Wright	Secretary, HSE
Ms K Parkinson	HSE
Ms A O'Reilly	TUC
Dr A Easton	Warwick University
Dr A Garland	Wellcome Foundation
Dr A Rankine	Committee of Vice Chancellors and Principals
Dr D Veale	Committee of Vice Chancellors and Principals
Mr N Montgomery	Department of Economic Development (N Ireland)

Observer

Dr M Iosson	HSE (Technology and Health Sciences Division)

Education

Service

Advisory

Committee

.....

Biotechnology: Health and safety in education

HSE BOOKS

First published 1996

ISBN 0 7176 0724 0

CONTENTS

CONTENTS

This guidance is prepared, in consultation with HSE, by the Education Service Advisory Committee which was appointed by the Health and Safety Commission as part of its formal advisory structures. The guidance represents what is considered to be good practice by members of the committee. It has been agreed by the Commission. Following this guidance is not compulsory and you are free to take other action. But if you do follow this guidance you will normally be doing enough to comply with the law. Health and safety inspectors seek to secure compliance with the law and may refer to this guidance as illustrating good practice.

INTRODUCTION

1 This booklet gives guidance on health and safety in the biotechnology processes used in education. It does not deal with organisms which are not micro-organisms or the development and use of transgenic animals.

2 Biotechnology is not new but recent advances have increased its use and applicability. It encompasses many technologies and has many definitions but, in general, biotechnology is the use of biological organisms or processes in research, development, manufacturing and service industries. It integrates biology, chemistry and process engineering. Potential uses include chemicals production, waste treatment, energy generation, mineral extraction and electronics. To date the health care, food, drink and agricultural industries have been most active in applying biotechnology.

3 Education establishments may be involved with biotechnology in various ways and at differing levels of expertise and competence. Work may range from undergraduates in supervised practical classes to research by postgraduate and postdoctoral researchers in semi-industrial pilot fermentation plants.

4 This publication highlights relevant risk reduction techniques. The more relevant legislation that applies to biotechnology in education is set out in the Appendix.

5 Modern biotechnology has an extremely good health and safety record attributable to careful attention to all aspects of security and the rigorous control of hazards and risks. This booklet is intended to assist those responsible for biotechnology in education in the maintenance of this record.

CONTROLLING RISKS IN BIOTECHNOLOGY PROCESSES

Risk assessment

6 Effective control of risks in biotechnology starts with an adequate assessment of those risks. Risk assessment is essentially a practical task, best done by staff in the relevant department, acting in accordance with the institution's health and safety policy and arrangements.

7 Those making risk assessments must understand the difference between hazards and risks. 'Hazard' is used to describe something with the potential to cause harm. It can include substances, processes or activities. 'Risk' is a measure of the likelihood of actual harm resulting from a hazard, combined with an indication of the frequency and likely magnitude of the consequences.

8 The aim is to identify the **significant** risks. These should not be obscured by an excess of information or by concentrating on trivial risks. The assessment needs to:

(a) address all relevant risks:

(i) first identify the hazards - the substances, micro-organisms, equipment, processes and procedures or other factors that have the potential to cause harm;
(ii) assess the risks from the identified hazards. Some risks may need to be considered when assessing the residual risk;
(iii) be systematic in looking at the hazards and the consequent risks. One approach might be to look at groups of hazards and risks (eg substances, electrical hazards, pressure systems, machinery); another might be to look at operations (eg fermentation, cell separation, fumigation, sterilisation, waste generation, collection and disposal);

(b) address what actually happens in the laboratory and during the biotechnology work:

- Actual practice may differ from the instructions laid down. This is often the way risks creep in unnoticed;
- Think about non-routine operations, eg maintenance; loading and unloading of vessels; sterilisation between experiments;
- Look at procedures for preventing, containing and clearing spillages;
- Consider what accidents might happen (eg from equipment failure, operator error etc);
- Interruptions to the work activity are a frequent cause of accidents. Look at the management of such incidents and the procedures to be followed;

(c) consider everyone at risk. Do not forget office staff, cleaners, maintenance staff, contractors, security staff and visitors;

(d) identify people who may be at particular risk, eg young and inexperienced people, students, people with disabilities, or people working alone;

(e) identify those who may be at increased risk because of immunodeficiency, ongoing medical treatment or pregnancy;

(f) take account of existing preventive or precautionary measures. Do they reduce the risk sufficiently? Are they working properly? Are they maintained?

9 Formal control validation techniques may be appropriate for the control of high risks. Validation gives assurance that equipment and procedures will operate as required. This may involve trial runs and regular recalibration or adjustment of instrumentation. For example, an autoclave should consistently achieve decontamination. Use of a protocol for regular testing for temperatures attained under load will give the necessary assurances. By contrast, a procedure such as fumigation can be pretested using a standard method, which

may need to be performed once to validate the procedure. The risk assessment will define the need for, and frequency of, validation testing.

10 Maintenance workers are often at higher risk than others, because they do non-routine work and may enter areas where others do not have access. For servicing of process plant, it may be necessary to expose hardware contaminated by potentially harmful micro-organisms. This work would require prior decontamination of equipment before work starts. A clearance certificate could be supplied to assure the worker that this process has taken place. In some circumstances a formal permit-to-work system may be needed. This will always be so where hazard group 3 pathogens are used and may also be appropriate for hazard group 2 pathogens, depending on the risk assessment. A formal permit system will always be required where access is needed inside items of plant that may contain harmful substances or asphyxiant gases.

11 Information about risk assessments can be found in References 2, 4, 5, 6, 7 and 34.

Hierarchy of risk control measures

12 There is a hierarchy of strategies that can be adopted for risk control. They are:

(a) removal or avoidance of the hazard;

(b) substitution with a lesser hazard;

(c) introduction of engineering controls;

(d) the wearing of personal protective equipment (PPE).

13 It is therefore always best to avoid a risk if possible, for example by not storing or using a particular dangerous substance if it is not essential. Hazards are best combated at source, rather than by palliative measures. Thus, if floors become slippery because of a spillage, preventing the spillage is better than either regular mopping or providing warning signs. Similarly, it is better to prevent the production of harmful aerosols by changing handling methods rather than controlling the aerosols via exhaust ventilation equipment.

14 Where changes to materials or work practices do not ensure sufficient control of risks, then additional engineering control measures may be appropriate. Spill trays or bunds will minimise the effects of spillages. Fume cupboards, microbiological safety cabinets or other extraction equipment can minimise exposure to aerosols or dusts. Further risks associated with new control measures may need to be considered. For example, will extracted air need filtration? How will the extraction equipment be maintained?

15 The control measures also need to take account of the needs of individuals. For example, an extraction system that prevents easy access to sampling points or machinery guards that ignore good ergonomic practice may rapidly fall into disuse.

16 Any control measures that are introduced need to be consistent with the institution's health and safety policy. The Management of Health and Safety at Work Regulations require that arrangements are made to ensure planning, organisation, control, monitoring and review of preventative and protective measures. Further guidance is given in References 2 and 3.

CONTROLLING HAZARDOUS SUBSTANCES

17 The Control of Substances Hazardous to Health Regulations 1994 (COSHH) apply to biological agents which include micro-organisms that are hazardous, as well as hazardous chemicals. The Regulations require an assessment of health risks created by work involving hazardous substances.

18 The Regulations cover the prevention and control of exposure and also the provision, use, maintenance and test of control measures. In some circumstances monitoring exposure in the workplace may be necessary, for example to demonstrate the effectiveness of the control measures. Guidance is given in Reference 4.

Health surveillance

19 Where appropriate to protect health, the COSHH Regulations require workers to be under suitable health surveillance. This should only be considered where the worker is exposed to an agent (including a micro-organism) known to cause adverse health effects. Consideration should be given to the competence of those carrying out the surveillance, together with the consent and confidentiality of those taking part. Further guidance on the subject is given in References 11, 12 and 13.

Training

20 The provision of appropriate instruction on the theoretical aspects of biological safety and of supervised practical training in the safe use of equipment, materials, processes and procedures are vital activities for the control of risk. The training course should be completed, with provision for refresher training and records of individuals' understanding and competence before they undertake any hazardous activity.

21 Training must be such as to ensure that workers know what they should do and understand the methods of control, what precautions they should take and when they should take them, for example when and how to use personal protective equipment. They should also know what cleaning, storage and disposal procedures are required, why they are required and when to use them, and, finally, what they should do in an emergency.

Personal protective equipment

22 The provision of personal protective equipment (PPE) needs to be underpinned by a system which ensures correct selection, fitting, maintenance, training and monitoring. Equipment needs to be suitable for the purposes of the work. It is not an alternative to preventing or minimising exposure by good working methods or engineering controls where these are reasonably practicable.

23 Respiratory protective equipment (RPE) may be needed where engineering controls are not reasonably practicable or to deal with emergencies. Examples could include fumigation or the spillage of chemicals. RPE is not specifically approved by HSE for work involving micro-organisms. However, RPE approved for use in other work situations may adequately control exposure to micro-organisms. Advice on this is given in Appendix B of Reference 8. Guidance on PPE can be found in References 9 and 10 and the General COSHH Approved Code of Practice (Reference 4).

BIOLOGICAL HAZARDS

24 Traditionally, biotechnology has involved the enhancement of desirable or the diminution of undesirable existing characteristics of naturally occurring organisms via selection or mutation. These approaches continue but modern biotechnology is increasingly harnessing recombinant DNA technology to confer entirely new capabilities and characteristics upon the resultant genetically modified organisms (GMOs). The systems used include bacteria, fungi and viruses as well as animal, insect and plant cells. Bacteria and fungi (especially yeasts) have been most commonly used. Viruses are most often used in vaccine production and as vectors in genetic modification techniques.

25 A typical biotechnology process involves several stages including inoculum preparation, growth of the organism in a bioreactor, separation of the organism from its growth medium and product recovery and purification. A bioreactor is a vessel used for the growth of organisms or the operation of the biological process. The process may be aerobic or anaerobic depending upon the organism used. The organisms or their metabolites may pose a number of potential risks to human health including infection and toxic or allergenic effects.

Categorisation of process organisms not involving genetic modification

26 Schedule 9 of the COSHH Regulations 1994 classifies biological agents according to hazard. See Reference 4.

27 Four hazard groups are defined using the following criteria:

(a) ability to cause infection

(b) severity of the disease

(c) risk that infection will spread to the community

(d) availability of vaccines and effective treatment.

These may be used to determine the required containment . Table 1 illustrates the four hazard groups, with examples.

28 Hazard group 1 organisms do not normally cause infections in humans, although the hazard groups above do not take into account the allergenic properties of micro-organisms, the toxic hazards of their products and metabolites and people who may be at increased risk because of immunodeficiency, ongoing medical treatment, or pregnancy. Thus a hazard group 1 biological agent (unlikely to cause human disease by infection) will still present a risk of ill health in other ways. Hazard group 4 agents pose the greatest hazard to operators and may only be used in facilities designed for the purpose, and even then only after notification with HSE.

Table 1

Hazard Group	*Description of organism*	*Example organisms*
1	Unlikely to cause human disease	*Aspergillus niger* *Cyanobacter spp*
2	Can cause human disease; May be a hazard to workers; Is unlikely to spread to the community; There is usually effective prophylaxis or treatment available.	*Vibrio cholerae* *Escherichia coli* (pathogenic strains) Polio viruses
3	Can cause severe human disease; May be a serious hazard to workers; May spread to the community; There is usually effective prophylaxis or treatment available.	*Yersinia pestis* *Histoplasma spp* Hepatitis B virus Human retrovirus
4	Causes severe human disease; Serious hazard to workers; Is likely to spread to the community; There is usually no effective prophylaxis or treatment available.	Lassa virus Marburg virus Ebola virus

29 Some organisms used in biotechnology may pose a greater threat to the environment than to human health or safety. Certain pathogens of agricultural animals, birds, bees, fish and plants are subject to controls on importation and/or use by statutory orders made by the Ministry of Agriculture for Fisheries and Food (MAFF), who should be consulted for advice.

Notification to HSE

30 Schedule 9 of the COSHH Regulations 1994 (Reference 4) requires notification of storage and use for the first time of any biological agent in hazard groups 2, 3 or 4. There are additional requirements for notification of storage or

use for the first time of each subsequent biological agent specified in part V of Schedule 9, and each subsequent group 3 organism which does not appear in the approved classification of biological agents.

31 Where notification is required, the employer must notify HSE in writing 30 days in advance of the intended work. Notification of activities involving genetic modification is also required under separate legislation. See paragraph 44.

Risk assessment and risk control

32 Before commencing any process using micro-organisms the risks need to be assessed.

33 The risk associated with a process will relate to the intrinsic hazard of the organism(s) and the potential for exposure during the process. Some organisms (for example *S. cerevisiae*) may not present a hazard. Others may introduce significant hazards. Exposure to organisms can be by inhalation, ingestion, inoculation or transmission through mucous membranes or broken skin. The effects on health depend on the route of entry, the organism itself, its viability, the dose received and the status of the exposed person's immune system. Accidental inoculation of biological agents due to contaminated 'sharps' (syringe needles, scalpel blades, scissors, broken glassware etc) is a particular hazard. A sharps policy should specify those procedures where the use of sharps should be minimised or prohibited, for example during the handling of oncogenes, naked DNA or viable organisms which could pose a risk. It should also set out the action to be taken in the event of a sharps injury.

34 Health hazards may also arise from adventitious contamination of cultures. This could be a particular concern where viruses may be present in cell cultures of animal and, especially, human origin. Wherever possible, animal cellular material should be taken from 'specific pathogen free' strains.

35 Micro-organisms used in biotechnology need to be chosen carefully, especially if scaling-up is intended. A volume of ten litres has been suggested as an arbitrary division between small and large scale culture work but this is not to be taken literally when considering the risks of scale-up. It is the hazard of the organism and the potential for exposure to the hazardous organism that determines the risk to operators. This potential for exposure, which is also related to the procedures employed, is therefore a major factor when defining the necessary control measures. See paragraph 61 for scale-up of operations with genetically modified micro-organisms.

36 The COSHH Regulations require that for any work with a hazardous substance (which includes micro-organisms), exposure must be prevented, or if it cannot be prevented, be adequately controlled. If at all possible, non-hazardous micro-organisms or hazard group 1 should be selected. If organisms allocated to a higher hazard group need to be used, for operational or process reasons, the measures adopted to control exposure need to be commensurate with the risks. This may include the use of microbiological safety cabinets or other forms of secondary containment where appropriate.

Further guidance on containment measures is given in References 4 and 8.

37 Risks can also be reduced by proper consideration of health and safety issues when designing and constructing experimental rigs. Formal risk management techniques such as 'Hazop' or 'Hazan' studies can usefully be applied at this stage. Attention to issues such as decommissioning and refurbishing when designing a rig can substantially reduce the risks to staff. Specialist guidance on these topics should be consulted.

Use of genetically modified micro-organisms

38 A **micro-organism** is a microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material. An **organism** is a biological entity capable of replication or of transferring genetic material. Thus the definition of 'organism' is much more wide ranging than that of 'micro-organism'. 'Organisms' include animals and plants as well as micro-organisms. Animal or plant cell culture artificially sustained in the laboratory are 'micro-organisms' as defined under the Genetically Modified Organisms (Contained Use) Regulations 1992 (Reference 15). **This document only deals with micro-organisms**.

39 Much of the current interest in biotechnology comes from the use of techniques to develop micro-organisms expressing gene products from a variety of sources. Potential donor and/or recipient organisms for this process include bacteria (prokaryotes), fungi and higher animals and plants (eukaryotes). The collection of techniques used is called 'genetic modification', (formerly 'genetic manipulation') but may also be known as 'genetic engineering' or 'recombinant DNA (rDNA) technology'.

40 Laboratory-based activities involving genetically modified organisms are controlled by the Genetically Modified Organisms (Contained Use) Regulations 1992 (Reference15). For the purposes of the regulations, genetically modified micro-organisms (GMMs) are divided into groups. Group I GMMs are those which satisfy the criteria in Schedule 2 of the GMM Regulations (Reference 15), and are, as a general guide, non-pathogenic and free from harmful sequences, and not capable of causing human disease or harm to the environment. Organisms which cannot satisfy these criteria are classified as Group II GMMs.

41 The Regulations also require that all operations involving GMMs should be classified as either **Type A** or **Type B**. Type A operations are those used for teaching, research or development or for non-industrial or non-commercial purposes, which are on a scale (number of organisms/culture volume) such that the containment system reflects both good microbiological practice and good occupational safety and hygiene and for which standard laboratory decontamination techniques can be employed.

42 Group I classification depends on the host, insert, vector, etc. Examples of organisms likely to be suitable as Group I hosts include:

(a) *Saccharomyces cerevisiae*

(b) some *Bacillus spp*

(c) *Streptomyces spp*

(d) some disabled laboratory strains of *Escherichia coli*

The final classification will depend on the inserted DNA.

It should be noted that Group II GMMs could be derived from organisms allocated to any one of the HSC-approved categories of biological agents. For example, GMMs derived from wild-type *E.coli* would probably be classified as Group II GMMs, unless all sequences coding for functions related to pathogenicity had been removed. This would be unlikely, as some of the pathogenic or harmful sequences may not be known.

43 HSE and the Department of the Environment, in conjunction with the Advisory Committee on Genetic Modification (ACGM), have published a series of guidance notes on operational matters relating to the use of GMOs (References 7 and 13).

44 The Genetically Modified Organisms (Contained Use) Regulations 1992 require that HSE is notified of activities involving genetic modification. Prior consent may also be required. The notification requirements differ depending on whether the activity is a Type A or Type B operation and whether the micro-organism is of Group I or Group II. Guidance on these Regulations is given in Reference 15.

GMM risk assessment and control

45 It is theoretically possible that genetic modification could exacerbate or complicate the hazards associated with micro-organisms. Examples of the mechanisms for this could include:

(a) infection with a GMO which facilitates delivery of a biologically active product to its target tissue;

(b) induction of an immune response to a gene product possibly leading to therapeutic complication if treatment with that product was required;

(c) enhanced immune response to products expressed as fusions with bacterial proteins.

46 An additional concern is that exposure to cloned oncogenes or genetically modified retroviruses might initiate or aid the progression of carcinogenesis. In a few reported cases of laboratory infection the causative agents were pathogenic organisms such as (genetically modified) vaccinia virus. Some organisms, while not representing a threat to human health, may be hazardous to the environment. They may be pathogenic to plants or animals or otherwise damage the environment and have the potential to cause heavy economic

losses. Such organisms may be subject to statutory controls and licensing by the Ministry of Agriculture for Fisheries and Food (MAFF).

47 There are no generic hazard categories for GMOs, as even when derived from the same organism, the hazards may depend on the function of the inserted nucleic acid sequences. Any hazard categorisation will depend on factors which may include:

(a) properties of the donor and recipient organisms;

(b) genetic modification itself, including the techniques used and any associated vector sequences;

(c) properties of the organism derived by genetic modification.

These factors also need to be taken into account in order to classify organisms as Group I or Group II.

48 The properties of the donor and recipient organisms to consider include the nature of the DNA sequence from the donor as well as the genetic, physiological and ecological characteristics of the recipient (host) organism. Examples of such properties are included in Schedule 3 of the GMO (Contained Use) Regulations 1992 (Reference 15). In general, the techniques used to modify an organism may provide information on its likely properties. If a eukaryotic viral vector is used then this may pose a hazard to workers, particularly if the virus has a human host range. An important factor when categorising genetically modified organisms is the extent to which the host organism's characteristics may have been altered by the inserted nucleic acid. This will include the degree of expression of the introduced genetic material and hence the level of production of any biologically active product with increasing potential for causing damaging effects. GMMs, as with pathogenic organisms, are assigned to one of four groups dependent on their potential hazard to human health. **This categorisation of hazard potential should not be confused with the 'Group I / Group II' status of GMMs, which is solely for the purposes of the Regulations.**

49 Advice on risk assessment and risk reduction for GMMs may be found in Reference 7.

Microbiological safety cabinets

Safety cabinets

50 A microbiological safety cabinet can reduce the risk of exposure to micro-organisms. A cabinet is necessary for handling organisms in hazard group 3 or for high-risk procedures with organisms in lower groups, for example where aerosols are generated. There are three classes of cabinets:

(a) **Class I.** Cabinets are open-fronted and air is drawn into the front over the work area. Air passes through a High Efficiency Particulate Absorption

(HEPA) filter before being exhausted to the outside air or laboratory extract system. The extract should be discharged from the building and not be recirculated from room to room.

(b) **Class II.** Cabinets are also open-fronted but differ from Class I cabinets in having a lower air inflow velocity. A fraction of the air is recirculated within the cabinet through a HEPA filter to provide a protective screen of sterile air over the work area. The remainder of the air is discharged through one or more HEPA filters to the outside air.

(c) **Class III.** Cabinets are sealed during operation and work within the cabinet involves the use of impermeable gloves sealed into the front of the cabinet. Air from the laboratory is passed through a HEPA filter before flowing over the work area. Exhaust air then passes through two or more HEPA filters before discharge to the outside air. Use of Class III cabinets is uncommon in education establishments and requires special training.

51 In some circumstances Class II open fronted cabinets may provide operators with protection equivalent to Class I cabinets. If this can be consistently demonstrated in use such cabinets may be used with hazard group 3 pathogens. It is common for Class II cabinets to discharge the exhaust air into the laboratory. This should always pass through double HEPA filters unless the risk assessment indicates otherwise.

52 Events such as doors opening or closing, operator movements or people passing close to the cabinet can cause turbulence. Correct siting of cabinets in relation to doors and traffic routes will minimise disturbance. Consider also the procedures used in cabinets: centrifuges can cause severe disruption of air flows in open-fronted cabinets, as can bunsen burners. If the use of wire inoculating loops is essential, an electric loop heater would minimise air flow disturbance.

53 An additional factor to be considered when assessing the suitability of particular types of cabinets is the need to ensure that fumigation can safely be done. Special arrangements may be needed for 'recirculating' type cabinets to ensure that fumigants can be discharged safely.

54 Microbiological safety cabinets and other extraction systems need to be thoroughly examined and tested at least once every 14 months. An increase in frequency of testing may be necessary, depending on the hazard of the organism(s) and the cabinet usage. Proper fumigation of the cabinet is necessary before any work which requires access to the filters: this will ensure that the filters are safe to handle. Both sides of each filter need to be exposed to the action of the fumigant. BS 5726:1992 *Microbiological safety cabinets*, Parts 1 to 4, gives detailed specification for design, siting, testing, use, disinfection and maintenance (Reference 16).

Flexible film isolators

55 Like Class III cabinets, flexible film isolators also separate the operators from the work but they differ in structure. They are commonly used to house small laboratory animals or to ensure product sterility because they minimise transfer of micro-organisms or allergens in and out of the work area.

56 The work surface is totally enclosed by a plastic tent-like structure over a rigid frame. Access to the work is via specially designed sleeves with gloves. The isolator has both the air inlet and outlet fitted with HEPA filters. There are also sample ports and transfer ports for movement of equipment used inside. Correct maintenance is vital to their safe use. Although the plastic film is relatively tough, it could be torn by sharp objects such as metal animal cages. It may be stretched or strained during careless handling. Internal lighting may cause heat damage, therefore lighting is best mounted outside the isolator. Similarly bunsen burners should not be used inside. Seals and welds need to be tested to locate any leaks especially as some isolators may be used under positive pressure.

57 HEPA filters fitted to the isolator also need to be tested for integrity as with conventional safety cabinets. It is preferred that the isolator exhausts outside the building. Where this is not possible it may be necessary to recirculate the air into the laboratory via double HEPA filters. Before such action is taken, a thorough risk assessment of the work to be undertaken in the isolator should be made. Advice relating to the use of flexible film isolators is detailed in an ACDP document (Reference 17).

58 Appropriate training is essential prior to the use of safety cabinets or flexible film isolators.

Processes involving foodstuffs

59 Biotechnology is often used to develop or produce foodstuffs for human or animal consumption. Examples include brewing, cheese making and other dairy processes and producing animal feed from waste brewer's yeast. This presents an anomaly: on the one hand, the laboratory needs to control microbiological or chemical risks, on the other the products will be tasted or eaten. Food tasting and similar work is 'clean work' and special precautions in excess of normal housekeeping standards may be needed. In such cases, the product should be consumed outside the main process area. Access to the tasting room by people from incompatible areas will need to be prevented.

60 Food under test must be stored in a separate refrigerator for food use only. Any apparatus in the area should also be dedicated to food use. Items such as glassware ought not be used in other laboratories and need to be labelled accordingly. Clean laboratory coats exclusive to the area will be needed and hands should be washed before entry. Traffic between the process area and the tasting laboratory needs to be minimised. Ideally, clean work is best done before process work, necessitating advance planning of the work schedule. Food, or food components, that have been produced with the aid of genetically modified organisms should not be entered into tasting trials or otherwise consumed without first obtaining advice from the Advisory Committee on Novel

Foods and Processes (ACNFP). The ACNFP can be contacted c/o the Department of Health, Hannibal House, Elephant and Castle, London SE1 6TE.

Scaling-up processes and pilot plant

61 Larger scale operations may increase the risk of exposure to harmful quantities of hazardous substances, whether they are organisms, medium components or products. Scaling-up and pilot plant operations therefore need careful planning and effective risk management. These larger scale operations may be 'Type B' operations for the purposes of the Genetically Modified Organisms (Contained Use) Regulations 1992 (Reference 15).

62 The preparation of inocula usually involves the handling of microbiological material of high titre. Extra care needs to be taken during these procedures. During the growth phase in the bioreactor and in subsequent purification, any exposure is most likely to be to the growth medium, the organism being cultured or its products, including metabolites and toxins. Exposure may be to viable or non-viable cells or to survival forms such as spores. Organisms may be released from seals, gas outlets, inoculation/sample ports and bursting discs/pressure relief valves. In addition, release may occur if the bioreactor is ruptured or if culture fluid leaks into the vessel jacket or cooling baffles, leading to contamination of the cooling water system. The role of spillage containment (bunds) needs to be considered. Pipework systems, in particular connections/couplings, valves or flanges, may also release organisms, either as fugitive emissions or as a consequence of component failure. Properly evaluated operating procedures and trained process operators will help avoid inadvertent releases of process organisms. Contingency plans and practice drills will ensure that accidental releases are dealt with promptly and properly.

63 Downstream processing may also cause exposure to organisms, cell components or products. In particular, cell separation and disruption processes may generate substantial aerosols. Centrifuges and rotary vacuum filters may also produce contaminated aerosols. Homogenisation, bead milling and sonication can generate aerosols both of the whole organism and of components such as endotoxins. Effluent from the process may contain viable organisms, cell components or product. It may therefore be an additional source of exposure not only to workers but also to the environment.

64 The aim is effective control of risks from exposure by primary containment through good engineering design of the equipment. Primary containment protects personnel (and the facility) from exposure to the organism being handled by immediate physical barriers to release. For bioreactors this includes seals, gas filters for exhaust gases and sampling devices to contain the fermentation process.

65 Depending on the risk assessment, additional secondary containment may also be required. This is intended to protect the environment outside the laboratory or process plant and may include provision of waste treatment, room air filtration, and balanced air pressures to prevent contaminated air leaking out into other areas.

66 Guidance on containment measures for dealing with Group II micro-organisms in 'Type B' operations is given in Table 2 (see page 15). An individual risk assessment may indicate that a higher degree of containment is required for specific operations or items of plant.

67 Good design of plant will allow for easy dismantling when needed for cleaning and disinfecting. Inoculation and sample ports may have to be removed for autoclaving and so should be constructed of impervious, low-corrosion materials. In some types of fixed plant, sterilisation will require a supply of steam 'in situ'. Perishable components such as seals need to be checked regularly for integrity and replaced where necessary. Secondary screens on glassware would mitigate the effects of breakage. Where possible, access to process laboratories or plant rooms should be restricted. Traffic in the area should be minimised.

68 In very large volume systems people may need to enter vessels for cleaning and maintenance. Such vessels are 'confined spaces' and appropriate precautions will be needed before entry to prevent exposure to a low-oxygen environment or to toxic vapours. Permit-to-work procedures will be required. The additional risks from any microbiological hazards will also have to be considered.

CHEMICAL HAZARDS

69 Biotechnology uses many chemicals and ensuring control of the associated risks may be overlooked in the emphasis on biological hazards. The risk assessment for the work will highlight any hazardous chemicals, either as supplied commercially or as produced during the work. The assessment, or an action summary of it, should be easily accessible to students and staff alike - ideally immediately next to the working area.

70 Hazardous chemicals used in biotechnology may include flammable, explosive or toxic solvents, acids or alkalis, mutagens, carcinogens, teratogens and toxic products of metabolism. Dusty materials such as dry culture media may be allergenic or irritant upon inhalation or skin contact. Certain disinfectants are toxic or may cause allergic sensitisation; others may cause defatting of the skin leading to dermatitis if handled incorrectly. Toxic gases such as sulphur dioxide are also used. Other hazardous substances likely to be used include fumigants, asphyxiant gases and metabolic inhibitors.

Risk control techniques

Storage

71 Storage of all chemicals, either in bulk or smaller volumes, needs careful managing. Incompatible materials need to be kept apart. Material safety information sheets from manufacturers or suppliers should provide useful data and indicate the necessary precautions. Contact the suppliers if their data are inadequate or difficult to understand. Flammable substances (for example 70%

TABLE 2 Containment provisions to be used for work with Group II micro-organisms in Type B operations are set out in Schedule 6 to the GMO(CU) Regs. 1992, at three levels: B2, B3, B4. These were previously used under the GM Regs 1989 for large scale categories LS1, LS2, LS3.

		CONTAINMENT LEVELS		
Specifications		*B2*	*B3*	*B4*
1	Viable micro-organisms should be contained in system which physically separates the process from the environment (closed system).	Yes	Yes	Yes
2	Exhaust gases from the closed system should be releatreated so as to:	Minimise release	Prevent release	Prevent release
3	Sample collection, addition of material to a closed system and transfer of viable micro-organisms to another closed system, should be performed so as to:	Minimise release	Prevent release	Prevent release
4	Bulk culture fluids should not be removed from the closed system unless the viable micro-organisms have been:	Inactivated by validated means	Inactivated by validated chemical or physical means	Inactivated by validated chemical or physical means
5	Seals should be designed so as to:	Minimise release	Prevent release	Prevent release
6	Closed system should be located within a controlled area.	Optional	Yes	Yes, and purpose built
	(a) Biohazard signs should be displayed.	Optional	Yes	Yes
	(b) Access should be restricted to nominated personnel only.	Optional	Yes	Yes, via airlock
	(c) Personnel should wear protective clothing.	Yes, work clothing	Yes	Yes, a complete change
	(d) Decontamination and washing facilities should be provided for personnel.	Yes	Yes	Yes
	(e) Personnel should shower before leaving the controlled area.	No	Optional	Yes
	(f) Effluent from sinks and showers should be collected and inactivated before release.	No	Optional	Yes
	(g) The controlled area should be adequately ventilated to minimise air contamination.	Optional	Optional	Yes
	(h) The controlled area should be maintained at an air pressure negative to atmosphere.	No	Optional	Yes
	(i) Input air and extract air to the controlled area should be HEPA filtered.	No	Optional	Yes
	(j) The controlled area should be designed to contain spillage of the entire contents of the closed system	Optional	Yes	Yes
	(k) The controlled area should be sealable to permit fumigation	No	Optional	Yes
7	Effluent treatment before final discharge.	Inactivated by validated means	Inactivated by validated chemical or physical means	Inactivated by validated physical means

alcohol) need to be stored in accordance with recognised guidelines (see Reference 18).

72 Chemical containers need proper labelling to inform users of hazards. The practice of transferring chemicals from suppliers' containers should be discouraged unless the new container is suitable for the purpose and is labelled with the supplier's information. 'Temporary' use of unsuitable containers (for example soft drink bottles) should be proscribed.

Handling

73 In general, only the smallest possible quantity of hazardous chemicals should be handled manually. Properly designed and installed bulk distribution systems are better where large quantities are needed. Where manual handling is required, controlling the potential risk of physical injury (for example back or muscle damage) is as important as dealing with the 'chemical' risks such as skin or eye contact. Using appropriate personal protective equipment (PPE) such as overalls, gloves and eye protectors will minimise the risks of skin and eye contact. Make sure that the PPE is suitable. Unsuitable gloves, for example, may allow solvents to penetrate to the wearer's skin very quickly.

74 Incorrect handling techniques for large bottles continue to cause incidents which result in spillage of chemicals. Always use suitable carrying baskets for such bottles. Staff and students will need training and instruction in their use.

Minimising exposure

75 Exposure to airborne vapours, dusts and mists can be reduced by minimising work at open vessels, or operations involving pouring from one vessel to another. Where such transfers are essential, risks can be reduced by applying control techniques which might include complete or partial enclosures and properly designed and maintained extraction systems. If engineering controls cannot be applied appropriate personal protective equipment may be needed.

76 Good laboratory practice is essential. People may ingest chemicals if they pipette by mouth or do not wash their hands. Eating, chewing, drinking or smoking in laboratories is very bad practice, as is applying contact lenses or cosmetics. Such activities should be prohibited. Accidental injection of chemicals is uncommon but may occur through cuts from contaminated glass or metal or where hypodermic syringes are used. Any cuts or abrasions to the skin should be appropriately covered to minimise exposure. See also the Approved Code of Practice to COSHH (Reference 4).

Spillages

77 Good experiment or pilot plant design will minimise the risk of spillage and, where possible, containment trays or bunds are a useful secondary defence.

Spillage control procedures are needed. Students, and technical and academic staff should know about the procedures and, if necessary, be trained to use them. Appropriate equipment ranging from emergency showers and eyewash stations to quenching agents, mops and vacuum cleaners fitted with HEPA filters will be needed. In some circumstances appropriate respiratory protective equipment for emergency use may need to be kept readily available for use by trained personnel.

Liquid nitrogen

78 Liquid nitrogen is often used to store biological material. Its low temperature (-196°C) means that it needs careful handling. There are risks of burns or necrosis if the liquid (or objects cooled by it) contact the skin. Eye splashes can cause irreparable damage. The liquid quickly evaporates at room temperature to form large volumes of cold gaseous nitrogen, which is initially heavier than air. This may lead to risks of asphyxiation in unventilated rooms. Beware also of the propensity of liquid nitrogen to concentrate oxygen on the surface when stored in open containers.

79 Large liquid nitrogen tanks are best sited outside and away from sumps and sewers. Where this is not possible, a dedicated storage room, with at least one external wall, may be used. A mechanical extraction ventilation system that discharges to a safe place will usually be needed and low-level oxygen alarms may also be considered. Access should be for authorised people only.

80 Everyone using liquid nitrogen needs to understand the risks and the necessary precautions and be trained as appropriate. Training will usually include first-aid procedures in the event of skin or eye contact and the use of personal protective equipment (PPE). PPE should be kept close to hand and needs to be regularly checked for damage. When vessels are being filled impervious aprons, cryogenic gauntlets, visors and sturdy shoes should be worn.

81 Ampoules stored in liquid nitrogen have been known to explode upon removal due to the sudden increase in temperature. Risks can be reduced by using plastic rather than glass ampoules. Similarly there is usually less risk if biological materials are stored in the vapour phase above the liquid rather than in the liquid itself. However the higher temperature (-80°C) may reduce storage life. Where liquid phase storage is necessary then adequate control of risks associated with the higher volumes of liquid nitrogen needed will be a priority.

82 It should be assumed that liquid nitrogen used for storing cultures is potentially contaminated and should be handled accordingly.

Disinfectants

83 Where micro-organisms are in use in a laboratory, an effective disinfection policy is needed to deal both with routine situations such as decontamination of work surfaces and to control spills of culture fluid or other contaminated substances. The disinfection policy will usually be fully described in the local rules for the laboratory and include recommendations for use, working dilutions and renewal frequency for each type of disinfectant. Everyone concerned will

need training in the use and limitations of disinfectants.

84 The disinfectant used will depend on the organism(s) and the circumstances of use. It is advisable to have a selection of agents which are designed and validated for particular purposes. For example, 70% v/v ethanol or 60% v/v propanol are useful as surface decontaminants on cleaned equipment, but are totally unsuitable for decontamination of large volumes of spilled culture fluid. By contrast, a gelling chlorine based disinfectant would contain and decontaminate a liquid spill, but would be unsuitable for decontaminating equipment or metal surfaces such as a safety cabinet. The fire risks associated with alcohols are best controlled by minimising the quantity used. The alcohol should be transported and dispensed in suitable safety containers and no sources of ignition should be permitted in the vicinity.

85 Advice on the application and properties of various disinfectants is given in References14 and 19. Suppliers will also be able to help.

86 Disinfectants may present risks to the user and such risks need to be assessed and controlled. Some disinfectants are incompatible with other cleaning agents. For example, mixing bleach with certain household cleaning products may produce chlorine gas. Glutaraldehyde is a powerful biocide, useful for items that cannot be heat sterilised. Formaldehyde is another aldehyde widely used as disinfectant and preservative. Aldehydes are also potent respiratory sensitisers, particularly as aerosols, causing asthma or rhinitis in those sensitised. They are best avoided unless alternative, lower-risk techniques cannot be used or are ineffective (Reference 20). Where such chemicals need to be used then good occupational hygiene practice should be applied to reduce exposure so far as is reasonably practicable.

87 The manufacturer's instructions need to be carefully followed and the correct concentrations made up as needed. Some solutions may usually need to be made up freshly each day. Certain disinfectants are corrosive to metals causing pitting of the surface. This both facilitates protection of micro-organisms in microscopic cracks and fissures and could lead to structural failure of highly stressed components in plant such as centrifuges. See paragraph 72 on labelling of chemical containers.

Fumigation

88 Fumigation releases a gaseous substance into the atmosphere in order to inactivate contaminating organisms in an area. It may be required, for example, in clean areas such as tissue culture preparation where avoidance of contamination is paramount or as a prelude to servicing or maintenance of laboratories and equipment. It may also be needed where accidental spillage has contaminated the laboratory area, presenting a risk to workers. Use for emergency control is unlikely to be common in education except in containment level 3 laboratories. 'Local rules' should advise on correct methods. Where fumigation is to take place there needs to be adequate provision for venting of the gas to a safe place. In addition, smoke tests will usually be needed to show that the fumigant will be safely contained.

89 Fumigation operations should be assessed under the COSHH Regulations. The Approved Code of Practice *Control of substances hazardous to health in fumigation operations* (Reference 33), explains the procedures to be followed, such as informing and notifying relevant personnel, using respiratory protective equipment for re-entry and monitoring requirements for fumigant levels. Only competent, trained people ought to carry out fumigations.

90 The COSHH Regulations 1994 require that laboratories be sealable for fumigation in certain circumstances, ie it should be possible to prevent escape of the gas during the process. A false ceiling may allow gas to escape and enter other areas of the building. The vapour should not be able to penetrate either the walls or the ceiling; for example, they may be painted with solvent-based paint to prevent absorption. If it is necessary to decontaminate a laboratory for reasons other than control of known pathogens, for example on completion of a project, the same criteria apply.

91 Modern microbiological safety cabinets are usually provided with fumigation apparatus which allows fumigation of the whole interior. It is important to follow manufacturers' instructions.

92 Older cabinets may not be so equipped. In such cases a timer controlled, thermostatically regulated hot plate should be used to evaporate formalin. Mixing formalin and potassium permanganate can give rise to a rapid and uncontrolled release of formaldehyde and should be discouraged.

93 Particular difficulties may arise when a class II cabinet is fumigated. If the exhaust gases are recirculated into the laboratory, special arrangements must be made to ensure that the fumigant is dispersed to a safe place or otherwise rendered safe.

OTHER HAZARDS

Waste disposal

94 The risks associated with waste collection, storage and disposal need to be assessed and controlled as necessary. The risks will depend on the type and volume of waste and this depends in turn on the work being done. Waste may include toxic, flammable, explosive and carcinogenic materials, and effluent containing viable micro-organisms. The risks should be assessed **before** the processes producing the wastes start. It may be possible to reduce the quantity of waste from a proposed project and thus minimise the risks associated with its disposal.

95 All waste from laboratories is 'controlled waste' (see the Environmental Protection Act 1990, Reference 21). Therefore management procedures will be needed to ensure that the waste is described correctly, is kept safely and where necessary is transferred to an authorised carrier for correct disposal. Audit trails need to be established for 'special wastes', as defined in the Control of Pollution (Special Wastes) Regulations 1988 (Reference 22).

96 Risks to personnel can be reduced by correct collection techniques, segregation, proper labelling, safe storage and effective pre-treatment before disposal. Waste containers need to be clearly labelled. Colour coding can help. Sharps and glass and aerosol cans should be kept separate from other wastes. Sharps bins help prevent needle stick injuries but they should not be overfilled. If contaminated sharps containing liquid are discarded into a bin it should be leak proof as well as sealable. Waste storage in working areas needs to be minimised. Regular clearance of unwanted chemicals and biological materials can help.

97 In general, all biologically active waste will need pre-treatment (typically autoclaving) before disposal. Waste treatment is dealt with in the COSHH Regulations 1994 (Reference 4). The GMO (Contained Use) Regulations (Reference 15) have specific requirements for waste. Advice on disposal of clinical waste may be found in References 23 and 24.

98 Non-hazardous chemicals may (if miscible with, or soluble in, water) be suitably diluted before flushing down the foul drainage system. In all cases the local waste disposal authority and the water company should be consulted for advice since it may be defined as Trade Effluent.

99 Waste incinerators need to be registered with the local authority, and emissions to atmosphere are also subject to the controls of the Environmental Protection Act 1990 (Reference 21).

Use of radioactive substances

100 Radioactive materials may be used for tracer work and other purposes. Radioactive iodine, carbon, phosphorus, sulphur and tritium have all been used in biotechnology. The advice of the radiation protection adviser appointed under the Ionising Radiations Regulations 1985 (Reference 25) will be needed before starting work with ionising radiations. Notification under the Radioactive Substances Act 1960 will also be required.

Noise

101 Some biotechnology processes may cause noise levels in excess of the action levels in the Noise at Work Regulations 1989 (Reference 26). Centrifuges, homogenisers and compressors are typical noise sources. If appropriate, noise surveys will be needed and steps taken to reduce noise levels, for example by enclosing noisy plant. Guidance on this is given in References 27 and 28. Hearing protection can only be regarded as a temporary expedient and not a permanent solution.

Pressure systems

102 The Pressure Systems and Transportable Gas Containers Regulations 1989 (Reference 29) may apply to some processes, particularly if the bioreactor or culture vessel and any associated pipework need to withstand increased pressures due to the build-up of fermentation gases or the use of compressed air or steam sterilisation. All compressed gas/air and steam pressure systems, including autoclaves and gas cylinders, are covered by the Regulations and will be subject to a scheme of regular inspection by a competent person. Gas cylinders present a particular hazard. Consideration should be given to safe

transport, use and secure storage (References 30 and 31).

Peripatetic workers

103 The university or college workforce may include many peripatetic workers, ranging from cleaning contractors to specialist service engineers. They may be exposed to risks from biotechnology processes just as may academic staff, technicians or students. They need the information and guidance necessary for them to be protected against the risks. Visiting academics or research staff from other institutions should also be properly briefed. They may have experience in other specialities and may be quite senior in their own discipline but may not always be experienced in the field of biotechnology (for example MD students).

104 For contracted staff both their employer and the university/college have a duty to consider possible risks and take appropriate measures to prevent or control them. The HSE booklet *COSHH and peripatetic workers* (Reference 32) gives advice on this important issue.

APPENDIX: MANAGEMENT SYSTEMS AND HEALTH AND SAFETY LAW

1 Everyone at work has obligations and duties under health and safety law. The main duties are placed on employers. But managers and other employees also have duties, as do people who control premises. In addition, self-employed people have duties.

2 The law aims to protect both employees and non-employees from risks to their health and safety arising from work activities.

Who is the employer?

3 In most universities and colleges the employer is the body corporate established by the act of parliament that founded the institution.

What do employers need to do?

4 Employers need to ensure, so far as is reasonably practicable, the health, safety and welfare at work of their employees. They also need to ensure, so far as is reasonably practicable, the health and safety of non-employees who may be affected by the work activity.

5 Thus, education employers have to protect academic, ancillary and support staff, including maintenance staff and cleaners (employees), and students and visitors (non-employees). They also need to ensure that employees of contractors working in the premises and self-employed contractors are properly informed about any risks to their health or safety in the premises, and about any precautions they need to take.

6 These general duties are supplemented by more detailed requirements. Examples include requirements to assess risks to the health and safety of both employees and non-employees and to have effective arrangements for planning, organising, controlling, monitoring and reviewing any measures necessary to control risks. Employers have to prepare a statement of their health and safety policy and arrangements and tell their employees about it.

7 Employers need to appoint competent people to assist them undertake the measures needed to comply with health and safety law. Employees need to be given understandable, relevant information on the risks of their work and the measures to control those risks. They also need to be adequately trained and properly supervised (References 1 and 2).

What do employees need to do?

8 Employees need to take reasonable care for their own health and safety and for that of anyone else who may be affected by their acts or omissions at work. They have to co-operate with their employer (and anyone else who has legal duties under health and safety law) so far as is necessary to enable those legal duties to be complied with.

9 This means that staff should always follow the health and safety advice and instructions from their employers. They need to tell their employers about any unsafe conditions or practices they know about.

10 The exact responsibilities of employees will depend in part on the extent of their management control. Thus Principals and Heads of Department are expected to carry greater responsibilities than lecturers or technicians.

What about non-employees?

11 Non-employees (students and visitors, for example), like everyone else, must not intentionally or recklessly interfere with or misuse anything required by law to be provided in the interests of health, safety or welfare. In addition, any non-employee carrying out activities involving genetically modified organisms is deemed to be self-employed for the purpose of the legal controls on such work.

Cost and risk

12 When considering what health and safety measures are necessary it is legitimate to take cost into account. Whenever possible, relevant good practice should be followed, or a similar level of precaution applied.

13 What is relevant good practice in a particular case may be apparent from authoritative guidance. Where this is not so, or where there is doubt:

(a) the magnitude of the risks (both their extent and likelihood) need to be **assessed** (trivial risks can be ignored altogether);

(b) the risks should then be roughly balanced against the cost of reducing them;

(c) measures must be taken to reduce or eliminate the risks unless the cost of doing so is obviously unreasonable compared to the risk.

14 Common sense is often all that is necessary. But remember the human consequences: **The balance must firmly be on the side of health and safety.**

Management systems

15 Guidance has been published by HSE on the importance of effective management systems in assessing and controlling risks. See for example *Successful health and safety management* (HSE Books ISBN 0 7176 0425 X), *Five steps to successful health and safety management* (HSE Books IND(G)132L) and *Health and safety management in further and higher education: Guidance on inspection, monitoring and auditing* (Reference 3).

16 The Management of Health and Safety at Work Regulations 1992 now make explicit the obligation on employers to make and give effect to arrangements for the effective planning, organisation, control, monitoring and review of the protective and preventive measures needed to minimise risks at work.

17 The Regulations also make clear that the starting point for effective health and safety management is a suitable and sufficient assessment of the risks to both employees and non-employees. The Approved Code of Practice *Management of health and safety at work* (Reference 2) gives more information.

Specific legislation relevant to biotechnology

18 The techniques and processes used in biotechnology mean that the following Regulations may be particularly relevant:

- The Ionising Radiations Regulations 1985 SI 1985/1333 HMSO ISBN 0 11 057333 1
- The Control of Substances Hazardous to Health Regulations 1994 SI 1994/3246 HMSO ISBN 0 11 043721 7
- The Pressure Systems and Transportable Gas Containers Regulations 1989 SI 1989/2169 ISBN 0 11 0981169 3
- The Electricity at Work Regulations 1989 SI 1989/635 HMSO ISBN 0 11 096635 X
- The Genetically Modified Organisms (Contained Use) Regulations 1992 SI 1992/3217 HMSO ISBN 0 11 025332 9
- The Genetically Modified Organisms (Deliberate Release) Regulations 1992 SI1992/3280 HMSO ISBN 0 11 025216 0
- The Noise at Work Regulations 1989 SI 1989/1790 HMSO ISBN 0 11 097790 4

Other Regulations to be considered include:

- The Management of Health and Safety at Work Regulations 1992 SI 1992/2051 HMSO ISBN 0 11 025051 6
- The Manual Handling Operations Regulations 1992 SI 1992/2793 HMSO ISBN 0 11 025920 3
- The Health and Safety (Display Screen Equipment) Regulations 1992 SI 1992/2792 HMSO ISBN 0 11 025919 X
- The Provision and Use of Work Equipment Regulations 1992 SI 1992/2932 HMSO ISBN 0 11 025849 5
- The Personal Protective Equipment at Work Regulations 1992 SI 1992/2966 HMSO ISBN 0 11 025832 0
- The Workplace (Health, Safety and Welfare) Regulations 1992 SI 1992/3004 HMSO ISBN 0 11 025804 5

REFERENCES

1 *A guide to the Health and Safety at Work etc Act 1974* L1 HSE Books ISBN 0 7176 0441 1

2 *Management of health and safety at work* Management of Health and Safety at Work Regulations 1992 Approved Code of Practice L21 HSE Books 1992 ISBN 0 7176 0412 8

3 *Health and safety management in higher and further education: Guidance on inspection, monitoring and auditing* HSE Books 1992 ISBN 0 11 886315 0

4 Control of Substances Hazardous to Health Regulations 1994 and Approved Codes of Practice L5 HSE Books ISBN 0 7176 0819 0

5 *A step by step guide to COSHH assessment* HS(G)97 HSE Books 1993 ISBN 0 11 886379 7

6 *COSHH: Guidance for universities, polytechnics and colleges of further and higher education* HSE Books 1990 ISBN 0 11 885433 X

7 *Guidelines for the risk assessment of operations involving the contained use of genetically modified micro-organisms* (GMMs) Advisory Committee on Genetic Modification (ACGM), ACGM/HSE/DOE Note 7 (Available free from ACGM Secretariat, c/o Health and Safety Executive, Health Policy Division B2, Rose Court, 2 Southwark Bridge, London SE1 9HS)

8 *Categorisation of biological agents* HSE Books 1995 ISBN 0 7176 1038 1

9 *Respiratory protective equipment: a practical guide for users* HS(G)53 HSE Books 1990 ISBN 0 11 885522 0

10 *Personal protective equipment* Personal Protective Equipment at Work Regulations 1992. Guidance on Regulations L25 HSE Books 1992 ISBN 0 7176 0415 2

11 *Surveillance of people exposed to health risks at work* HS(G)61 HSE Books 1990 ISBN 0 11 885574 3

12 *Occupational health services in higher education* HSE Books 1991 ISBN 0 11 885560 3

13 *Guidelines for the health surveillance of those involved in genetic modification at laboratory and large scale* ACGM/HSE/DOE Note 4 (free, see Reference 7 for availability)

14 *Safety in health service laboratories: Safe working and the prevention of infection in clinical laboratories* HSE Books 1991 ISBN 0 11 885446 1

15 *A guide to the Genetically Modified Organisms (Contained Use) Regulations 1992* L29 HSE Books ISBN 0 11 882049 4

16 BS 5726:1992 *Microbiological safety cabinets* Parts 1 to 4

17 *Guidance on the use, testing and maintenance of laboratory and animal flexible film isolators* Advisory Committee on Dangerous Pathogens (ACDP) (Available free from HDB2, Rose Court, 2 Southwark Bridge, London SE1 9HS)

18 *The storage of flammable liquids in containers* HS(G)51 HSE Books 1990 ISBN 0 7176 0481 0

19 BS 7152:1991 *Guide to choice of chemical disinfectants*

20 *Glutaraldehyde and you* IAC(L)64 HSE Books (free leaflet)

21 Environmental Protection Act 1990, Chapter 43, HMSO ISBN 0 10 544390 5

22 Control of Pollution (Special Waste) Regulations 1980 SI 1980/1709 HMSO ISBN 0 11 007709 1

23 *Safe disposal of clinical waste* HSE Books 1992 ISBN 0 7176 0447 0

24 Department of Environment Paper No 25 *Clinical waste: A technical memorandum on arisings, treatment and disposal including a code of practice* HMSO 1983 ISBN 0 11 751719 4

25 Ionising Radiations Regulations 1985 SI 1985/1333 HMSO ISBN 0 11 057333 1

26 Noise at Work Regulations 1989 SI 1989/1790 HMSO ISBN 0 11 097790 4

27 *Noise at work. Noise guide No 1: Legal duties of employers to prevent damage to hearing. Noise guide No 2: Legal duties of designers, manufacturers, importers and suppliers to prevent damage to hearing.* The Noise at Work Regulations 1989 HSE Books 1989 ISBN 0 17176 0454 3

28 *Noise at work. Noise guides 3 to 8: Noise assessment, information and control* HS(G) 56 HSE Books 1990 ISBN 0 11 885430 5

29 *A guide to the Pressure Systems and Transportable Gas Containers Regulations 1989* HS(R)30 HSE Books 1990 ISBN 0 11 885516 6

30 *Safety of Pressure Systems* COP 37 Pressure Systems and Transportable Gas Containers Regulations 1989. Approved Code of Practice HSE Books 1990 ISBN 0 11 885514 X

31 *Safety of transportable gas containers* COP 38 Pressure Systems and Transportable Gas Containers Regulations 1989. Approved Code of Practice HSE Books ISBN 0 11 885515 8

32 *COSHH and peripatetic workers* HS(G)77 HSE Books 1992 ISBN 0 11 885733 9

33 *Control of substances hazardous to health in fumigation operations: Control of Substances Hazardous to Health Regulations* 1988 Approved Code of Practice COP 30 HSE Books 1988 ISBN 0 11 885469 0

34 HS(G)122 *New and expectant mothers at work - A guide for employers* HSE Books HS(G)122 1995 ISBN 0 7176 0826 3

Printed and published by the Health and Safety Executive C50 3/96

HSE BOOKS

MAIL ORDER
HSE priced and free publications are available from:
HSE Books
PO Box 1999
Sudbury
Suffolk CO10 6FS
Tel: 01787 881165
Fax: 01787 313995

RETAIL
HSE priced publications are available from good booksellers.

HEALTH AND SAFETY ENQUIRIES
HSE InfoLine
Tel: 0541 545500
or write to:
HSE Information Centre
Broad Lane
Sheffield S3 7HQ

£6.95 net