

*This is a new Topic.*

**IMPORTANT NOTE** *This guidance has been prepared to provide advice on the Genetically Modified Organisms (Contained Use) Regulations 2000<sup>1</sup>. At the time of publication, the new Regulations have just been considered by ministers so this Topic may be subject to amendment when the Regulations are published and implemented. If amendments to the Regulations are made in the future, details will be provided on the National Centre for Biotechnology Education (NCBE) website: [www.ncbe.reading.ac.uk](http://www.ncbe.reading.ac.uk), and also on the ASE website.*

## 1 Introduction

Work with DNA is central to much current research in the biological sciences and to developments in modern biotechnology. There is growing public awareness of DNA technologies, their current and potential applications and the wider issues that they engender.

The science upon which these technologies are founded, and the wider concerns associated with them, feature in nearly every UK course specification in biology or science. Surveys have repeatedly shown support from both parents and pupils alike for the inclusion of modern DNA technology in the science curriculum [1, 2] (see page 105).

Despite the incorporation of the basic concepts of genetic modification into both the National Curriculum of England and Wales [3] and post-16 biology specifications for well over a decade, pupils' understanding of modern genetics generally remains poor [4, 5]. The controversy surrounding DNA technology often centres on disagreement about its potential consequences, which demands an understanding of the relevant sciences [6]. Thus Lewis *et al.* [7] found that while students of school age were able to discuss issues arising from the use of DNA technology, their misunderstandings of the underlying science made it difficult for them to come to well-reasoned and informed opinions. More recent research by Hill *et al.* [8] has hinted that students may respond negatively to teaching about genetic modification if its implications are not considered alongside the science.

Clearly, given its potential impact, there is a need for better all-round education about DNA technology. The role of practical work in developing students' understanding is complex and poorly understood. It is nevertheless accepted as an essential feature of school-based science education in most developed countries and has been strongly advocated by educationalists in the UK.

In the UK, both *Science and Plants for Schools* (SAPS) and the *National Centre for Biotechnology Education* (NCBE) have been active in promoting practical biotechnology in schools [9, 10, 11, 12]. However, practical work involving DNA has been slow to catch on in UK schools compared with several other northern European countries and the USA [13, 14, 15]. There are numerous reasons for this, a key one being uncertainty over health and safety. This has not been helped by ambiguous and inconsistent advice from school health and safety publications [16, 17].

This Topic is part of an attempt to put the record straight. Readers should be aware that policy in this area is developing. In cases of doubt, teachers should follow guidance from their employers and, if necessary, also consult one of the recognised school science health and safety organisations.

## 2 Naked DNA

DNA only gains a biological function by being inserted into a living cell. Hence work with DNA itself ('naked' DNA) is not generally thought to constitute a health hazard even if new nucleic acid molecules are formed. Risks associated with most activities that might foreseeably be undertaken with naked DNA in school laboratories, such as gel electrophoresis, cutting with restriction enzymes, ligation and the polymerase chain reaction (PCR) can therefore be controlled by normal good laboratory practice.

The one exception to this is full-length copies of viral DNA that are infectious in their own right. These are legally regarded as microorganisms even when they are not encapsulated or enveloped [18]. This means that if full-length viral DNA (such as DNA from phage lambda) were to be combined with DNA from other

<sup>1</sup> HSE (2000) *The Genetically-Modified Organisms (Contained Use) Regulations 2000*. HSE Books. ISBN 0 1101 8676 1.

sources, a genetically-modified organism would have been created. For such work to be undertaken legally, the premises would have to be registered with the Health and Safety Executive (HSE). A brief summary of the regulations governing such work is given in section 3.4.

## 2.1 DNA extraction

Simple practical tasks such as the extraction of DNA from microorganisms, plant or animal tissue, e.g., fish roe, may all be carried out, adopting relevant laboratory health and safety precautions. For instance, where microorganisms are involved, it is important to observe good microbiological practice. If DNA is to be extracted from human tissue, e.g., cheek cells, for amplification by the PCR, the sampling procedure must be designed to minimise the risk of the transmission of infective agents between participants (for example, students should only work with their own DNA samples). It should also be borne in mind that crude extracts of DNA may still contain allergens or toxins present in the source material and must therefore be handled appropriately, e.g., if the seeds of a plant that contains a toxic alkaloid have been used.

The extraction of DNA from calf thymus tissue is sometimes referred to in school texts, although since the advent of BSE and variant CJD, there is a risk (albeit small) of accidental exposure to the infectious agent while the extract is being prepared. Beef thymus is, however, now classified as 'specified offal' under the *Specified Bovine Offal Order* 1995, which means that butchers and abattoirs are most unlikely to supply this tissue for schools to use in practical studies.

## 2.2 DNA from laboratory suppliers

DNA from a variety of organisms is available from molecular biology and school suppliers. Sources include bacteriophage lambda, salmon sperm and even cloned human DNA. While these can generally be regarded as safe, DNA from mammalian sources may not have been screened to ensure that it is free from contaminating viruses. It is therefore recommended that such material is not used in schools. In addition, full-length viral DNA that may have been genetically modified must not be used without prior registration with the HSE (see section 3.4).

## 2.3 Manipulation of DNA *in vitro*

With the exception of full-length viral DNA mentioned above, restriction and ligation of plasmid or other DNA with enzymes, DNA gel electrophoresis and the polymerase chain reaction (PCR) may all be performed in a school laboratory.

## 2.4 Ethical considerations

Wider issues, including ethical concerns associated with the use of human DNA that may be construed as 'genetic tests', are beyond the scope of this Topic. Teachers should be aware that such issues may arise and ensure that any relevant practical procedure addresses these concerns by, for example, the random mixing of samples or the judicious selection of the DNA sequence to be investigated. Where appropriate, the relevant authorities should be consulted (e.g., the UK Human Genetics Commission: [www.hgc.gov.uk](http://www.hgc.gov.uk)).

# 3 Genetic modification

## 3.1 What is genetic modification ?

Genetic modification is officially defined as 'the alteration of genetic material (DNA or RNA) of an organism by means that could not occur naturally through mating and/or recombination' [18].

## 3.2 EU Directives and UK Regulations

Throughout most of the world, the use of all live genetically-modified organisms (GMOs) is controlled by law. There are currently two relevant sets of directives governing genetic modification throughout the European Union. Laws in the United Kingdom have been enacted to comply with these directives. In England, Wales and Scotland, genetic modification of organisms in containment, e.g., work in a laboratory, is governed by the *Genetically Modified Organisms (Contained Use) Regulations, 2000* [18]. Northern Ireland has its own separate but virtually identical legislation. Similarly, within Great Britain and Northern Ireland there are separate regulations covering deliberate releases of GMOs into the environment, e.g., field trials of genetically-modified crops. It is important to note that it is not the *techniques* of genetic modification that are controlled, but rather *activities with living organisms that are produced by these techniques*.

## 3.3 Microbial transformation

In the school context, work falling within the scope of these Regulations is most likely to involve the 'transformation' of microorganisms, that is, the introduction of DNA into microorganisms by 'artificial' means. For pre-university educational work, this almost always involves the use of plasmid DNA. Plasmids are small rings of DNA comprising just a few genes, that are found in bacteria and yeasts. They are not normally essential for the microbes, but they may help them to survive in rare and exotic environments. For instance, some plasmids enable the bacteria that carry them to resist the toxic effects of heavy metals or antibiotics, or

**Table 1** Analysis of some educational activities involving DNA for the hazards and risks, and the preventative or protective measures required to limit risks. Adapted from Richardson, J. (1995) [19].

Type and source of hazard	Nature of the risk	Type of activity in which risks may arise	Means of limiting risks
<b>CHEMICAL HAZARDS</b>			
Antibiotics	Toxicity	Preparation and use of media for maintaining microbial cultures that harbour plasmids; selective media for transformation experiments.	Selection of appropriate antibiotics. Scale of use and dilution. Care in handling powdered antibiotics when preparing solutions to avoid contact and raising dusts, e.g., use a fume cupboard and wear eye protection and suitable gloves. Destruction before disposal by autoclaving.
Buffer solutions	Toxicity; irritancy	Making up solutions for extracting or dissolving DNA or for gel electrophoresis.	Choice of buffer type; use of prepared solutions needing only dilution; limited scale of use. Precautions such as the use of a fume cupboard and gloves where appropriate.
Detergents	Allergenic reactions	Making up solutions from concentrates or powders. Use to break down membranes when extracting DNA, etc.	Detergent type SDS (sodium dodecyl sulfate (also known as sodium lauryl sulfate) as used in domestic detergents, shampoos, etc.); dilution; limited scale of use.
DNAs	Infection from certain types of viral DNA or from contaminants	Making up and handling DNA solutions and digests.	With the types of DNA used in the kits designed for schools, e.g., plant and phage lambda, the risks are insignificant. Avoid potentially hazardous sources.
DMF (N,N-dimethyl formamide)	Toxicity	DMF is a solvent for X-Gal which is often employed as an indicator in microbiological media used for transformation experiments.	Prepare solutions in a fume cupboard. Wear eye protection and gloves. Limit the scale of use. Store DMF in appropriate conditions.
Dyes and stains	Toxicity; allergenic reactions	Staining DNA fragments on electrophoresis gels.	School kits typically use thiazin dyes such as methylene blue or Azure A and B, or Nile blue sulfate for staining DNA. Avoid breathing in the powders when making up solutions, e.g., use a fume cupboard and control spills. Keep dyes off the skin — gloves of an appropriate type may be needed. Avoid the use of other stains such as ethidium bromide (which is a mutagen).
Enzymes	Allergenic reactions	Restriction enzymes used to cut DNA. Proteases used when extracting DNA.	Scale and containment: only very small quantities of restriction enzymes are used. Spills of protease should be rinsed with water and wiped up promptly.
Ethanol	Toxicity and fire Explosion	Stains such as methylene blue used in ethanolic solution.  Precipitating DNA extracts.	Limited scale — small volume technique. Keep off skin — use gloves of a suitable type.  When preparing cold ethanol, ensure that it is placed in a sealed, vapour-tight container to avoid explosions in non-spark-proof freezers.

(continued)

Type and source of hazard	Nature of the risk	Type of activity in which risks may arise	Means of limiting risks
Electrophoresis gels	Toxicity (if polyacrylamide gels are cast) Burns or scalds from molten gels	Making up and using gels.	Make agarose gels only and follow good practice in preparation. Exercise caution if using a microwave oven to liquefy gel — do not use sealed containers and beware of superheated liquids which may froth up unexpectedly. If polyacrylamide gels are used, do not make up or cast your own — buy them ready-made.
<b>MICROBIAL HAZARDS</b>			
Bacteria, fungi	Infection; genetic transfer; accidental release of a GMO into the environment	Transformation.	The use of appropriate non-pathogenic strains, and non-mobile genetic elements, coupled with good microbiological practice. All cultures must be destroyed by autoclaving after use. <b>IMPORTANT!</b> Non-self cloning work requires registration with the HSE and the establishment of a GMSC; see section 3.4.
Pathogenic microorganisms including viruses	Infection	Collection and handling of human DNA samples, e.g., from cheek cells for amplification by the PCR.  Preparation of DNA extracts from bovine thymus glands.	Ensure that the sampling method is non-invasive and the procedure is explicitly designed to prevent cross-infection.  Since the occurrence of BSE and variant CJD, bovine thymus tissue should no longer be available and should not be used in schools.
DNAs other than those provided in school kits, especially if unknown or incompletely characterised	Infection (more likely — transfection) via skin with viral DNA contaminants	Extraction of DNA	Use only UK school kits. Good microbiological practice should reduce risks from other material to an acceptable minimum.
<b>ELECTRICAL HAZARDS</b>			
Gel electrophoresis tanks and power supplies	Electrical shock, burns and fire	Connecting and disconnecting power supplies and using gel tanks. The buffer solution is highly conductive and gels are directly handled within it. Gels may have to be run unattended overnight.	Use low voltage (< 50 V) supplies from dry cells or a well-designed mains-to-low voltage and low-current device. If higher voltages are used to shorten run times, professionally-designed apparatus must be employed (e.g., <i>interlocked</i> tank terminals; current limited; <i>shrouded</i> leads). Teachers use only, unless pupils are aged over 16 years and trained.
<b>OTHER PHYSICAL HAZARDS</b>			
Centrifuges	Physical injuries	Centrifuging extracts and DNA, e.g., in the extraction of plasmid, nuclear and chloroplast DNA.	Proper use of a centrifuge of an appropriate design, with the correct type of tubes, observing the usual precautions.
Microwave ovens	Explosion of sealed containers; burns and scalds from hot containers and liquids	Preparation of microbiological media and agarose gels.	Ensure that containers are not sealed and that hot containers and liquids are handled with great care, e.g., wear heat-proof gloves.
Ultraviolet radiation (UVR)	Carcinogenic effects on skin. Damage to eyes	Examining stained gels using short-wave UVR.	If the use of ethidium bromide (mutagenic) is avoided, short-wave UVR will not be needed.

to live on particular nutrients. Sequences of DNA can be 'spliced' into plasmids, allowing them to be used as vectors for transferring genes between organisms.

Numerous practical kits have been developed for demonstrating microbial transformation. These are particularly common in the USA where they have become a routine part of high school biology courses. A search of the World Wide Web will unearth many sites describing practical exercises for schools.

### IMPORTANT NOTE

Although many of these procedures may be freely used in the USA, within the European Union such work is more strictly regulated, and teachers could easily be in breach of the law were they or their students to carry out the majority of the genetic modification exercises that are currently described on the Web.

### 3.4 Working with DNA in the UK

Under the UK Regulations referred to in section 3.2, before genetic modification (other than 'self cloning', as defined in section 3.5) is undertaken, the premises involved must be registered with, and approved by, the HSE. There is a fee for this and, in addition, a local 'Genetic Modification Safety Committee' (GMSC) will need to be established, consisting of individuals who are suitably qualified to advise on any risks to human health and the environment of all activities before they begin. Records of such risk assessments must be retained for at least 10 years after the relevant activity has ceased.

**Schools wishing to undertake such work are advised to contact the HSE for further details.**

These stringent requirements would seem to preclude most schools from carrying out practical genetic modification. There is, however, one important exception to this rule, namely, 'self cloning'.

### 3.5 Self cloning

Microbial transformation in which DNA (or RNA) is returned to a species in which it could naturally occur is known technically (and rather confusingly) as 'self cloning'. In this context, 'cloning' means making copies of plasmid DNA within an organism. Because the plasmids used are made entirely from DNA that could occur naturally within the species involved, the work is called 'self cloning'.

The official definition of self cloning runs as follows:

*... the removal of nucleic acid sequences from a cell ... followed by the re-insertion of all or part of that nucleic acid ... into cells of the same species or into cells of phylogenetically closely-related species with which it can exchange genetic material by homologous recombination.'* [18]

In other words, if the transfer of genetic information is largely confined to that which could naturally occur within a single species, the work is regarded as 'self cloning'. The nucleic acid may have been subject to modification by enzymic, chemical or mechanical steps so as to produce a novel order of genes or bases, to remove sequences, to produce multiple gene copies, etc.

Self cloning, *where the resulting organism is unlikely to cause disease in humans, animals or plants*, is exempt from the 'Contained Use' Regulations. Schools and others may therefore undertake such work without licensing their premises or setting up a GMSC. However, somewhat unusually (since these microbes could in theory be found in nature), the organisms produced *are* covered by the 'Deliberate Release' Regulations.

### 3.6 Containment

Under current legislation it is an offence to release any GMO into the environment or to allow it to escape without prior consent of the Secretary of State. It is therefore essential that even 'self-cloned' organisms are adequately contained and that a 'release' does not occur. A key point is that an accidental release of a GMO might be considered to be deliberate if the steps taken to ensure containment are deemed to have been inadequate. Note that if a GMO cannot survive in, or transmit genes to, other organisms in the environment, it is regarded as being 'biologically contained', and an accidental escape is *not* regarded as a 'release'.

Fortunately, containment can be ensured simply by following good microbiological practice (e.g., effective aseptic technique and autoclaving materials before disposal) and good occupational safety and hygiene, coupled with the careful selection of suitable host organisms and plasmids. The latter would usually involve, for example, using host strains that are weakened and 'non-mobilisable' plasmids that cannot transfer their genes into the host's chromosome, or be transferred into other organisms by natural means such as bacterial conjugation.

Kits from reputable suppliers (e.g., from the NCBE), that have been designed for use in UK schools, should comply with these requirements.

### 3.7 Host strains

The species of bacterium that is most commonly used for cloning work is *Escherichia coli*, strain K 12. Unlike the wild type, K 12 strains of *E. coli* are usually unable to inhabit the mammalian gut. This strain's origins can be traced back to work in the USA in 1922. Biochemical and genetic studies by Edward Tatum in the 1940s made the strain popular with researchers and, after many millions of generations of laboratory cultivation, it is

now known to have undergone significant changes. These have altered the lipopolysaccharides that comprise the outer membrane of the bacterial cell, so that it can no longer infect mammals.

Many strains of *E. coli* K 12 have been specially selected for transformation work. Usually these do not harbour any extra-chromosomal DNA of their own, but can be transformed efficiently by plasmids. Compared to the wild type *E. coli*, these 'cloning strains' are severely weakened and would find it difficult to thrive outside the laboratory. They may have unusual nutritional requirements, and are often susceptible to damage, e.g., from the ultraviolet component of sunlight.

### 3.8 Plasmids

Plasmids can pass from one bacterial cell to another of the same or a related species by a natural 'mating' process called conjugation. During conjugation, a tube (pilus) is formed between adjacent cells, through which the plasmid passes. The genes required for the formation of the pilus are also carried on a plasmid (an F or fertility plasmid). Host strains used for transformation experiments in schools usually have no F plasmid, so that they cannot pass on genetic material by conjugation. They often also lack phages, so that DNA cannot be picked up and passed on by viral infection (transduction).

The use of non-conjugative strains of bacteria that lack phages, coupled with the use of non-mobilisable plasmids (see section 3.9), significantly reduces the risk of DNA being transferred between microorganisms, and hence the unwanted transfer of characteristics such as antibiotic resistance [20].

The transformation of bacterial cells with plasmid DNA is very inefficient and only a small proportion of the cells treated will take up the DNA. Therefore a means of selecting those cells that have been transformed is needed. The incorporation of one or more antibiotic-resistance genes into the plasmid DNA used to transform cells is the commonest method of achieving this. In the presence of appropriate antibiotics, such plasmid-bearing cells thrive while their less well-endowed (untransformed) neighbours perish. In this way, selection pressure is applied to maintain the plasmid in the population of cells. Without that pressure, the few transformed cells would be swamped by their untransformed neighbours.

### 3.9 Missing genes

For a plasmid to travel through a pilus, two additional requirements must be met. The plasmid must possess a gene encoding a mobility protein (*mob*) and have a *nic* site. The mobility protein nicks the plasmid at the *nic* site, attaches to it there and conducts the plasmid through the pilus. Plasmids for school demonstration

experiments usually have neither a *nic* site nor the *mob* gene. This means that once a plasmid has been introduced into a bacterial cell by artificial means (transformation), it cannot naturally transfer (by conjugation) into other cells that do not possess it.

### 3.10 Incubation at 37 °C

Although model risk assessments for microbiological work normally warn against incubating cultures at 37 °C to avoid the growth of contaminating pathogens, the delicate strains of *E. coli* used for cloning work often will not grow quickly or reliably unless maintained at this temperature. Good microbiological practice, coupled with the use of selective growth media, will ensure that contaminating human pathogens are not inadvertently cultivated at this temperature.

### 3.11 Physical and chemical containment

In addition to the biological containment measures described above, good microbiological practice must be followed to ensure that the microorganisms are physically and chemically contained during the investigation and destroyed afterwards. UK law requires that genetically-modified microorganisms must be inactivated after use by a *validated* means. In practice in a school, this means that any cultures must be destroyed by autoclaving them.

The containment and the destruction of cells when such work is undertaken will prevent the spread of antibiotic-resistant populations. In addition, most of the antibiotics used for such work are heat-labile and readily break down when media are autoclaved after use.

Together, these methods of physical, chemical and biological containment will ensure that educational exercises which demonstrate the principles of genetic modification are as safe as possible.

## 4 Useful addresses

For addresses of CLEAPSS and SSERC, see 'Introduction' page 2.

### National Centre for Biotechnology Education (NCBE)

The University of Reading, Whiteknights, PO Box 228, Reading RG6 6AJ.

Tel: 0118 987 3743

Fax: 0118 975 0140

E-mail: NCBE@reading.ac.uk

Website: www.ncbe.reading.ac.uk

### Microbiology in Schools Advisory Committee (MISAC).

c/o Society for General Microbiology (SGM)  
Marlborough House, Basingstoke Road, Spencer's  
Wood, Reading RG7 1AG.

Tel: 0118 988 1835

Fax: 0118 988 5656

E-mail: education@sgm.ac.uk

Website: www.biosci.org.uk/MISAC

### Science and Plants for Schools (SAPS)

Homerton College, Hills Road, Cambridge CB2 2PH

Tel: 01223 507168

Fax: 01223 215004

E-mail: hom-saps@lists.cam.ac.uk

Website: www-saps.plantsci.cam.ac.uk

## 5 Suppliers of plasmids, cultures, etc.

Plasmids and cells for transformation experiments should only be obtained from recognised suppliers.

Some bacterial strains that are commonly used for transformation experiments lack an enzyme required for DNA repair, and this means that they can be subject to mutations if they are maintained on slope cultures. Fresh cultures should therefore be obtained as required from suppliers, rather than being maintained in school. This will ensure that the host cells are the correct species and strain and thereby avoid disappointment or the inadvertent transformation of contaminating microorganisms.

As noted above, many of the kits and protocols supplied by US firms may not be appropriate for use in UK schools. Even if a school was to register with the HSE so that it could undertake non-self cloning work, most of the US school kits currently provide insufficient information about the host strains and/or plasmid construction for an adequate risk assessment to be made.

## 6 References

1. IGD (1997) *Consumer attitudes to genetically-modified foods*. Institute of Grocery Distribution, Watford.
2. Osborne, J. and Collins, S. (2000) *Pupils and parents views of the school science curriculum*. A study funded by The Wellcome Trust. King's College London.
3. Department for Education and Employment and the Qualifications and Curriculum Authority (1999) *The National Curriculum. Key Stages 3 and 4*. Stationery Office. Website: www.nc.uk.net
4. House of Commons Science and Technology Committee (1995) *Third Report — Human Genetics: The Science and its Consequences, Volume 1*. HMSO.

5. Lock, R., Miles, C. and Hughes, S. (1995) The influence of teaching on knowledge and attitudes in biotechnology and genetic engineering contexts: implications for teaching controversial issues and the public understanding of science. *School Science Review*, **76**(276), 47–59.
6. Straughan, R. and Reiss, M. (1996) *Improving Nature? The science and ethics of genetic engineering*. Cambridge: Cambridge University Press.
7. Lewis, J. M., Driver, R. H., Leach, I. T. and Wood-Robinson, C. (1997) *Opinions on and attitudes towards genetic engineering. Acceptable limits: a discussion task. Working Paper 7 of the Young People's Understanding of, and Attitudes to, The New Genetics Project*. Centre for Studies in Science and Mathematics Education, The University of Leeds.
8. Hill, R., Stanistreet, M. and Boyes, E. (2000) What ideas do students associate with biotechnology and genetic engineering? *School Science Review*. **81**(297), 77–83.
9. Madden, D. (ed) (1995) *Investigating plant DNA* (2nd edn). National Centre for Biotechnology Education, The University of Reading. Web site: www.ncbe.reading.ac.uk.
10. Madden, D. (1996) *The Lambda Protocol* (2nd edn). National Centre for Biotechnology Education, University of Reading. Website: www.ncbe.reading.ac.uk.
11. Madden, D. (2000) *Illuminating DNA*. National Centre for Biotechnology Education, University of Reading. Website: www.ncbe.reading.ac.uk.
12. Madden, D. (2000) *The Transformer Protocol*. National Centre for Biotechnology Education, University of Reading. Website: www.ncbe.reading.ac.uk.
13. Micklos, D. and Freyer, G. (1990) *DNA Science. A first course in recombinant DNA technology*. Carolina Biological Supply Company/Cold Spring Harbor Laboratory Press.
14. Bloom, M., Freyer, G. and Micklos, D. (1996) *Laboratory DNA Science. An introduction to recombinant DNA techniques and methods of genome analysis*. The Benjamin/Cummings Publishing Company.
15. Agensen, H. et al. (1992) *Experimental gene technology in education* [English edition]. Nucleus Forlag ApS, Studsgade 28, 8000 Arhus C, Denmark.
16. DES (1985; 1990) *Microbiology. An HMI guide for schools and further education*. HMSO.
17. DfEE (1996) *Safety in science education*. Stationery Office.
18. Health and Safety Executive (2000) *A guide to the genetically-modified organisms (contained use) Regulations 2000*. HSE Books.
19. Richardson, J. (1995) Practical work with DNA. *Education in Science*, **162**, 16–18.
20. Timms-Wilson, T. M., Lilley, A. K. and Bailey, M. J. (1999) *A review of gene transfer from genetically-modified microorganisms*. Stationery Office. [Health and Safety Executive Contract Research Report 221/1999]
21. ACGM Compendium of Guidance. *Guidance from the Health and Safety Commission's Advisory Committee on Genetic Modification* (2000). Stationery Office. Website: www.hse.gov.uk.