Supplementary Local Rules for Genetic Modification Work involving Oncogenes or Recombinants Containing Potentially Oncogenic Nucleic Acid Sequences

1. Introduction

These local rules are produced to conform with ACGM/ HSE/NOTE 1 Advisory Committee on Genetic Modification "Guidance on Construction of Recombinants Containing Potentially Oncogenic Nucleic Acid Sequences" (2nd revision 1990) para 13, and should be applied alongside the "Local Rules for Microbiological Work" to which they are supplementary.

2. Areas Covered

These rules should be applied to known and potentially oncogenic DNA sequences, such as:

- viral oncogenes and their cellular homologues
- DNA sequences which induce tumours in experimental animals
- DNA sequences which cause transformation of cells in vitro. e.g :-
    - sequences which either cause or are associated with the "immortalisation" of cells
    - sequences whose gene products modulate the expression of growth factors, their receptors or components of the signal transduction mechanism, and which lead to escape from normal growth control
    - sequences which can involve anchorage independent growth, or which can render cells turnourigenic when inoculated into animals.

Each proposal involving sequences which might be covered by the above categories MUST be considered in detail by the above categories MUST be considered in detail by The Local Genetic Modification Safety Committee who should feel free to request further guidance from ACGM if necessary.

3. Cloning in Prokaryote or Lower Host-Vector Systems

CGM/HSE/Note 7 "Guidelines for the Risk Assessment of operations involving the contained use of Genetically Modified Micro-organisms (GMMs)" (September 1993) which assesses access, expression, damage and risk is appropriate in determining whether any hazard arises through the expression of an oncogene or related sequence and therefore the cloning of such sequences in prokaryote or lower host-vector systems.

4. Naked DNA Hazards

Possible hazards include:

- Handling naked oncogenic DNA. Recent research has shown that naked DNA can lead to tumours in mice.
- Inoculation or entry through broken skin. These are the most likely routes of exposure to DNA which might lead to tumourogenesis.
- Inhalation. This is considered to be a less significant route of exposure leading to tumourogenesis, owing to the high levels of nucleases in the lung epithelial lining, although in the absence of firm experimental evidence, it cannot be completely discounted.
- Ingestion. Oral entry is thought to be the least likely route of exposure with naked DNA which could pose a significant hazard to the operator.

5. Minimum Requirements for Working with Oncogenes and related DNA Sequences

5.1 Work may only be carried out in laboratories designated for such purposes and with access limited to authorised personnel and designated workers who should be trained beforehand in the use of good microbiological techniques and should be fully aware of the potential hazards of work with oncogenic DNA sequences.

5.2 Apparatus and equipment used in conjunction with oncogene work must be dedicated to that work and not become multi -functional. Similarly, bench space must be dedicated to oncogene work, and must not be used for other non-oncogenic work.

5.3 All designated workers and authorised personnel likely to be exposed must have a genetic modification medical prior to commencing work, subsequently at annual intervals, and at any time in between if there is cause to suspect a work-related illness (in accordance with ACGM/IISE/Note 4). Medical records should include details of which oncogcne or related sequences were used.

5.4 Cleaners and auxiliary staff are not permitted in designated laboratories, and the cleaning of fixtures, fittings. walls, floors, etc is the sole responsibility of the designated workers.

5.5 Details of good microbiological practice are defined in the "University of Sheffield Local Rules for Microbiological Work".

5.6 Gloves MUST be worn for all work with oncogenic DNA.

5.7 Sharps must not be used for oncogenic work, except where absolutely essential.

5.8 Arrangements should be formalised in writing for immediate surface decontamination after spillages. Laboratory ware should be totally immersed in an effective decontaminant which will denature DNA before normal handling. Prior to disposal, broken glassware should be treated in a similar manner. Disposables should be placed directly into a suitable container before incineration.

5.9 All experimental procedures involving naked oncogenic DNA should be performed in such a manner as to minimise aerosol production. Where aerosol production is likely, these procedures must be conducted in equipment designed for its effective containment or inside a Class 1 microbiological safety cabinet, exhausting to the outside air or laboratory extract system.

5.10 Containment levels must be commensurate with any risk assessment figure calculated according to ACGM/HSE/Note 7, and with reference to ACGM/HSE/Note 8 "Laboratory Containment Facilities for Genetic Manipulation".

6. Cloning Oncogenic Sequences in Eurkaryotic Viruses

The Local Genetic Modification Safety Committee MUST consider all such proposals, with specific reference to ACGM/HSF/Note 5 "Guidance on tile Contained Use of Eukaryotic Viral Vectors in Genetic Modification" before notification to the ACGM/HSE in each case, who can give advice if required. Work MUST NOT commence until ACGM has considered and approved the proposal.

7. Authorisation

No genetic modification work on oncogenes or recombinants containing potentially oncogenic nucleic acid sequences will be authorised until:

i. the Local Genetic Modification Safety Committee has agreed the details contained in the project proposal are accurate; AND
ii. the designated workers have read the Local Rules, are fully trained and familiar with the potential hazards of the work with oncogenic DNA sequences; AND
iii. the requirements for medicals for all designated workers are met; AND
iv. the ACGM/HSE have been notified.

When all the above conditions have been met to the satisfaction of the Local Genetic Modification Safety Committee, authorisation to proceed with the work will be issued from Safety Services.