Guidelines for the health surveillance of those involved in genetic manipulation at laboratory and large-scale / Advisory Committee on Genetic Manipulation.

ACGM/HSE/NOTE 4

ADVISORY COMMITTEE ON GENETIC MANIPULATION

GUIDELINES FOR THE HEALTH SURVEILLANCE OF THOSE INVOLVED IN GENETIC MANIPULATION AT LABORATORY AND LARGE-SCALE

This guidance has been prepared by a specialist ACGM Working Group

INTRODUCTION

This note sets out a system for the health surveillance of those involved in genetic manipulation, outlines medical contraindications to work and gives guidance on procedures to be followed if occupationally acquired illness is suspected. The guidance is applicable to those involved in the large scale* growth of genetically manipulated organisms as well as to those involved in genetic manipulation in the laboratory.

This note supersedes and replaces the guidance in GMAG Note 6 and GMAG Note 14, page 8.

HAZARDS

Laboratory Scale Work

There are no known health hazards that are specific to genetic manipulation. However, as in other microbiological work not involving genetic manipulation, micro-organisms capable of infecting man may be used. But, because hazards beyond those associated with non-manipulated micro-organisms may be envisaged, ACGM advises that there must continue to be special arrangements to keep under review the health of those engaged in genetic manipulation. This should apply regardless of the category of containment of any particular project, although this guidance differentiates in its recommendations between the higher and lower levels of risk.

Large-Scale Work

The hazards posed by large-scale fermentation of genetically manipulated organisms arise from the scale of operation and the opportunity for greater degree of exposure to an organism and it. biologically active products relative to laboratory work. In general terms large-scale hazards can be considered under three headings:

Infection
Allergenicity
Toxicity

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* Guidance on other aspects of such work is given in GMAG Note 12, available from the ACGM Secretariat.

In more detail these hazards relate to the pathogenicity of the organism being used, toxicity and biological activity of its products and allergenicity to the organism's molecular components or its products. These hazards are no different to those posed by large-scale fermentation of micro-organisms generally.

However it can be postulated that genetic manipulation may give rise to complications of these hazards eg.

- infection with an rDNA organism which facilitates delivery of a biologically active gene product to target tissue;

- seroconversion to a gene product possibly leading to therapeutic complications if treatment with that product should be required or, to autoimmune disease;

- enhanced immune response to proteins expressed as fusions with bacterial proteins;

- possibility that microbial protein may act as an adjuvant to product exposure.

Although there is at present no evidence establishing the existence of health hazards specific to large-scale growth of genetically manipulated organisms, ACGM believes that it is prudent to institute health surveillance for those workers involved. It is intended that a scheme based on the following recommendations will cover both the established hazards of large scale fermentation of micro-organisms as well as those envisaged as possibilities for genetically manipulated organisms.

Large-scale Process Risks

The nature of large-scale fermentation means that there is potential for greater exposure to micro-organisms or their products than in the laboratory. Furthermore, there are discrete stages such as the steps involved in downstream processing each of which require individual assessment. For

example, any consideration of risk must take account of factors such as whether the organism is killed in the fermenter before downstream processing. Methods of processing micro-organisms on a large-scale such as harvesting, centrifuging or otherwise concentrating and washing cells, in breaking them and in extracting the required products, have the potential for widespread contamination and aerosol generation unless appropriate precautions are taken.

RECOMMENDATIONS

1 The Supervisory Medical Officer

A Supervisory Medical Officer (SMO) must be appointed for each workplace. The SMO should have experience in some related field of medicine such as community medicine, infectious diseases or occupational medicine. It may be possible for an occupational medical officer or a member of a university's health service to undertake the duties. During an SMO's absence, arrangements should be made for a deputy to act in case of emergency.

2 Medical Contact Cards

The purpose of issuing medical contact cards is to alert medical personnel outside the workplace to the possibility of occupationally acquired illness. ACGM advises that such cards should continue to be issued to workers involved in genetic manipulation at Category I or above on commencement of work. However, the wording on such cards should reflect differing levels of risk as indicated below:

CARD A

Although this person is working in a laboratory where genetically manipulated organisms are handled, neither these organisms or their products are known to

be able to produce disease. However, in case of unexplained illness detailed information can be obtained from the

Supervisory Medical Officer
Dr ..... Tel .....

CARD B

This person is working in a workplace where genetically manipulated organisms are handled. Exposure to these organisms and/or their products may have adverse clinical effects. In the event of unexplained illness detailed information concerning the health hazards involved SHOULD be obtained from the

Supervisory Medical Officer
Dr ..... Tel .....

It is recommended that the local genetic manipulation safety committee in conjunction with the SMO should make recommendations for its particular site using these two forms of wording and the flexible system of application shown schematically below:

GM RISK CATEGORY	MEDICAL CONTACT CARD
0 (GMP)	No Card or Card A
I)	Card A
II)	
III)	Card B
IV)	

With respect to work carried out under conditions of Good Microbiological Practice, the local genetic manipulation safety committee may recommend that the issue of a card is not necessary.

It is recommended that Card B is used for large-scale workers.

A copy of the card should be carried by the worker and a second copy provided which the worker may give to his/her family practitioner for attachment to the worker's records.

3. Health Surveillance and Reviews

The SMO is responsible for continuous surveillance of the health of workers involved in genetic manipulation.

Included in the purposes of health surveillance and review are these:-

(a) To provide an initial baseline to assist in the identification of any subsequent illness and in investigating possible causes.

(b) To identify conditions that, because they place the worker at special risk, contraindicate the commencement or continuation of work.

(c) To identify and control occupationally acquired illness.

(d) To initiate and guide action in emergencies.

(e) To provide evidence of the efficacy or failure of safety precautions.

(f) To provide data for epidemiological studies aimed at assessing long-term health hazards.

The health review need not always entail a medical examination but it would be valuable for the SMO to interview each worker on starting genetic manipulation work to record previous medical history and advise accordingly. It is recommended that for laboratory work at Categories II, III and IV and for large-scale work, the SMO should review the health of all workers before potential exposure and subsequently at intervals of one year whilst the worker is still involved in genetic manipulation. The annual review should detail any absences on account of illness, should record the

reason for and results of any medical examinations undertaken by the SMO and should note any accidents in which the worker was involved. There should be a final review when ceasing genetic manipulation with the same employer or when the worker's appointment terminates.

For work at GMP or Category I, it is sufficient to maintain health records for each worker as detailed in paragraph 8.

4. Medical Examinations

A medical examination may be necessary at the discretion of the Supervisory Medical Officer.

5. Serum Samples

The storage of serum samples is a sensible precaution at all levels of work, providing baseline information in the event of an unexplained illness and for use in any epidemiological study, subject to ethical committee control.

A sample of approximately 5 ml of serum should be requested by the SMO from each worker on starting work involving genetic manipulation and, ideally, when involvement with the work ceases or when the worker moves to another employment. There may also be a need to request a further sample as part of a follow up to any ill health. At the time of the initial request the individual should be informed that the sample may be used for two types of purpose:-

5.1 to protect the individual in the event of some medical enquiry concerning his/her own health.

5.2 for possible use in a epidemiological study as a coded sample with the permission of an ethical committee constituted according to a recognised standard.

The individual has the right of access to the results of any analysis of the sample.

The serum need not be tested routinely but should be stored indefinitely at minus 40°C or below, for testing if needed. It would be simplest if the samples were stored in the laboratory where they have been taken and retained there even if the worker moves elsewhere.

6. Epidemiological Monitoring

On the standard proposal form for the notification of experiments involving genetic manipulation, HSE asks for the NHS number of all workers, which would facilitate subsequent epidemiological monitoring to be undertaken. Should any possible untoward pattern of illness be suspected it may be desirable to request information from the health records of individual workers. The SMO should therefore ask workers to authorise the disclosure of information on their health, in confidence, for epidemiological study if the need should arise. It is expected that the SMO will bring any disease known or suspected to have been acquired occupationally by working with genetically manipulated organisms to HSE's attention.

7. Records

Records for every worker must be kept, by the employer, under the control of the SMO. They will be of value to enable identification of defects in procedures causing laboratory contracted illness and hence enable appropriate preventive action to be taken.

They should be kept separate from any clinical record and should contain:

Surname
Forenames
Surname at Birth
Sex
Date of Birth
Place of Birth
Permanent Address
Present Address
National Insurance Number
NHS Number (if known)
Date of commencement of present employment
Previous periods of employment with the organisation or company
Nature of work

These records may be of particular value in providing information on the health history of certain workers in the event of serious illness or for epidemiological monitoring. With this in mind, the records should be kept for at least 30 years and preferably indefinitely after termination of employment.

A specimen Health Record Form is available from the Secretariat of ACGM in HSE.

8. Records of Work

Any hazards involving genetic manipulation are likely to be specific to the particular organisms used and to the products expressed. Therefore in assessing whether the work has contributed to an illness it is necessary to know details of the experiments with which workers have been involved. This would need to include detail of the organisms used and the products expressed. The employer, usually through the Biological Safety Officer, must ensure that the appropriate occupational records are kept.

9. Considerations which may contraindicate a worker engaging in or continuing work with genetically manipulated organisms

It is for clinical judgement and decision, in each instance, whether a particular medical condition should limit a worker's involvement in genetic manipulation.

In common with other areas of microbiological risk, some general considerations that might be borne in mind are:-

(a) relevant medical history (eg history of asthma, recurrent infections);

(b) evidence of defective barriers to infection (disorders of skin, respiratory tract and alimentary canal);

(c) immune competence;

(d) treatment with antibiotics, especially those used in the experimental programme, or the therapeutic use of steroids;

(e) some forms of self-medication may influence the chances of infection.

The routine health review may provide warning of contraindications, and individual workers should be advised to consult the SMO if there is any reason to believe that risk has been, even temporarily, increased due to changes in their medical condition, for example (d) and (e) above.

10. Pregnancy

Workers may be exposed during genetic manipulation at laboratory or large-scale to microbiological and chemical risks. Beyond this, there is no known risk to the fetus. However, if a worker expects to conceive or believes herself to be pregnant, she may wish to discuss her work with the SMO.

11. Unexplained Illness

Incidents of unexplained illness should be drawn to the attention of the SMO by the worker. The SMO should take appropriate action and consider:

(a) are the symptoms in any way relatable to the material being handled?

(b) have any other workers had the same symptoms?

(c) has an accident occurred? Was the worker involved?

(d) is there evidence of infection by an organism in use?

(e) communication with the worker's general practitioner?

(f) risk to others in the work environment.

12. Accidents

It is the responsibility of the BSO to draw up a contingency plan (which includes notification to the SMO) for emergency action and to ensure its implementation should an accident occur. All accidents and subsequent action

should be carefully logged. Incidents considered to be of clinical significance should be notified to HSE.

13. Liaison

To ensure the effectiveness of the local arrangements for health surveillance consideration must be given to the working relationships between the BSO, the SMO, management, appropriate safety committees and the local medical community - in particular General Practitioners and Medical Officers for Environmental Health. Such consideration may best be made initially by the SMO.

14. Enquiries

Any queries arising from the guidance should be directed to the Secretariat of ACGM, HSE, Baynards House, 1 Chepstow Place, London W2 4TF. (Tel: 01-229-3456 ext 6612).