SCHEDULE 2

CRITERIA FOR THE CLASSIFICATION OF ORGANISMS

PART II

Guidelines as applicable for classification of micro-organisms in Group I

For classification into Group I the following guidelines should be used to further interpret Part I of this Schedule.

Characteristics of the recipient or parental organism(s)

5.—(1) Non-pathogenic

The recipient or parental organisms can be classified as non-pathogenic if they satisfy the conditions of one of the following sub-paragraphs—

(a) the recipient or parental strain should have an established record of safety in the laboratory and/or industry, with no adverse effects on human health and the environment;

(b) the recipient or parental strain does not meet the conditions of sub-paragraph (a) above but it belongs to a species for which there is a long record of biological work including safety in the laboratory and/or industry, showing no adverse effects on human health and the environment;

(c) if the recipient or parental organism is a strain which does not satisfy the conditions of sub-paragraph (a) above and belongs to a species for which there is no record of biological work including safe use in the laboratory and/or industry, appropriate testing (including, if necessary, animals) must be carried out, in order to establish non-pathogenicity and safety in the environment;

(d) if a non-virulent strain of an acknowledged pathogenic species is used, the strain should be as deficient as possible in genetic material that determines virulence so as to ensure no reversion to pathogenicity. In the case of bacteria, special attention should be given to plasmid or phage-borne virulence determinants.

(2) No adventitious agents

The recipient or parental strain/cell line should be free of known biological contaminating agents (symbionts, mycoplasms, viruses, viroids, etc.), which are potentially harmful.

(3) The recipient or parental strain/cell line should have proven and extended history of safe use or built-in biological barriers, which, without interfering with optimal growth in the reactor or fermenter, confer limited survivability and replicability, without adverse consequences in the environment (applicable only for Type B operations).

Characteristics of the vector

6.—(1) The vector should be well characterised

For this purpose the following characteristics should be taken into account.

(a) Information on composition and construction

(i) the type of the vector should be defined (virus, plasmid, cosmid, phasmid, transposable element, minichromosome, etc.);

(ii) the following information on the constituent fragments of the vector should be available—

(aa) the origin of each fragment (progenitor genetic element, strain of organism in which the progenitor genetic element naturally occurred),

(bb) if some fragments are synthetic, their functions should be known;

(iii) the methods used for construction should be known.

(b) Information on vector structure

(i) the size of the vector should be known and expressed in basepairs or D;

(ii) the function and relative positions of the following should be known—

(aa) structural genes,

(bb) marker genes for selection (antibiotic resistance, heavy metal resistance, phage immunity, genes coding for degradation of xenobiotics, etc.),

(cc) regulatory elements,

(dd) target sites (nic-sites, restriction endonuclease sites, linkers, etc.),

(ee) transposable elements (including provirus sequences),

(ff) enes related to transfer and mobilisation function (eg with respect to conjugation, transduction or chromosomal integration),

(gg) replicon(s).

(2) The vector should be free from harmful sequences

The vector should not contain genes coding for potentially harmful or pathogenic traits (eg virulence determinants, toxins, etc.) unless for Type A operations, such genes constitute an essential feature of the vector without, under any conditions or circumstances, resulting in a harmful or pathogenic phenotype of the genetically modified micro-organism.

(3) The vector should be limited in size as much as possible to the genetic sequences required to perform the intended function.

(4) The vector should not increase the stability of the genetically modified micro-organism in the environment (unless that is a requirement of the intended function).

(5) The vector should be poorly mobilisable

(a) If the vector is a plasmid—

(i) it should have a restricted host-range;

(ii) it should be defective in transfer-mobilisation factors eg Tra, MobS.036, for Type A operations or Tra, Mob, for Type B operations.

(b) If the vector is a virus, cosmid or phasmid—

(i) it should have a restricted host-range;

(ii) it should be rendered non-lysogenic when used as a cloning vector (eg defective in the cI-lambda repressor).

(6) It should not transfer any resistance markers to micro-organisms not known to acquire them naturally (if such acquisition could compromise use of drugs to control disease agents).

Required characteristics of the insert

7.—(1) The insert should be well characterised

For this purpose, the following characteristics should be taken into account.

(a) The origin of the insert should be known (genus, species, strain).

(b) The following information on the library from which the insert originated, should be known—

(i) the source and method for obtaining the nucleic acid of interest (cDNA, chromosomal, mitochondrial, etc.);

(ii) the vector in which the library was constructed (eg lambda gt 11, pBR322, etc.) and the site in which the DNA was inserted;

(iii) the method used for identification (colony, hybridization, immuno-blot, etc.);

(iv) the strain used for library construction.

(c) If the insert is synthetic, its intended function should be identified.

(d) The following information on the structure of the insert is required—

(i) information on structural genes, regulatory elements;

(ii) size of the insert;

(iii) restriction endonuclease sites flanking the insert;

(iv) information on transposable elements and provirus sequences.

(2) the insert should be free from harmful sequences—

(a) the function of each genetic unit in the insert should be defined (not applicable for Type A operations);

(b) the insert should not contain genes coding for potentially harmful or pathogenic traits (eg virulence determinants, toxins, etc.), (unless for Type A operations, such genes constitute an essential part of the insert without, under any circumstances, resulting in a harmful or pathogenic phenotype of the genetically modified microorganism).

(3) The insert should be limited in size as much as possible to the genetic sequences required to perform the intended function.

(4) The insert should not increase the stability of the construct in the environment (unless that is a requirement of intended function).

(5) The insert should be poorly mobilisable.

For instance, it should not contain transposing or transferable provirus sequences and other functional transposing sequences.

Required characteristics of the genetically modified micro-organism

8.—(1) The genetically modified micro-organism should be non-pathogenic.

This requirement is reasonably assured by compliance with all the requirements above.

(a) (2) (a) The genetically modified micro-organism should be as safe (to man and the environment) as the recipient or parental strains (applicable only for Type A operations);

(b) the genetically modified micro-organisms should be as safe in the reactor or fermentor as the recipient or parental strains, but with limited survivability and/or replicability outside the reactor or fermenter without adverse consequences in the environment (applicable only for Type B operations).

Other genetically modified micro-organisms that could be included in Group I if they meet the conditions in paragraph 8 above

9.—(1) Those constructed entirely from a single prokaryotic recipient (including its indigenous plasmids and viruses) or from a single eukaryotic recipient (including its chloroplasts, mitochondria, plasmids, but excluding viruses).

(2) Those that consist entirely of genetic sequences from different species that exchange these sequences by known physiological processes.