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ANNEX II

PART A

Techniques or methods of genetic modification yielding micro-organisms to be excluded from this Directive on condition that they do not involve the use of recombinant-nucleic acid molecules or GMMs other than those produced by one or more of the techniques/methods listed below:

1. Mutagenesis.

2. Cell fusion (including protoplast fusion) of prokaryotic species that exchange genetic material by known physiological processes.

3. Cell fusion (including protoplast fusion) of cells of any eukaryotic species, including production of hybridomas and plant cell fusions.

4. Self-cloning consisting in the removal of nucleic acid sequences from a cell of an organism which may or may not be followed by reinsertion of all or part of that nucleic acid (or a synthetic equivalent), with or without prior enzymic or mechanical steps, into cells of the same species or into cells of phylogenetically closely related species which can exchange genetic material by natural physiological processes where the resulting micro-organism is unlikely to cause disease to humans, animals or plants.

   Self-cloning may include the use of recombinant vectors with an extended history of safe use in the particular micro-organisms.

PART B

Criteria establishing the safety of GMMs for human health and the environment

This Annex describes in general terms the criteria to be met when establishing the safety of types of GMMs for human health and the environment and their suitability for inclusion in Part C. Technical guidance notes may be developed in accordance with the regulatory procedure referred to in Article 20(3) in order to facilitate the implementation and explanation of this Annex.

1. **Introduction**

Types of GMMs listed in Part C in accordance with the regulatory procedure with scrutiny referred to in Article 20(2) are excluded from the scope of this Directive. GMMs will be added to the list on a case-by-case basis and exclusion will relate only to each clearly identified GMM. This exclusion applies only when the GMM is used under conditions of contained use as defined in point (c) of Article 2. It does not apply to the deliberate release of GMMs. For a GMM to be listed in Part C, it must be proved that it meets the criteria given below.

2. **General criteria**

2.1. Strain verification/authentication

Identity of the strain must be precisely established. Modification must be known and verified.

2.2. Documented and established evidence of safety

Documented evidence of the safety of the organism must be provided.

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2.3. Genetic stability

Where any instability could adversely affect safety, evidence of stability is required.

3. **Specific criteria**

3.1. Non-pathogenic

The GMM should not be capable of causing disease or harm to a healthy human, plant or animal. Since pathogenicity includes both toxigenicity and allergenicity, the GMM should therefore be:

3.1.1. Non-toxigenic

The GMM should not produce increased toxigenicity as a result of the genetic modification nor be noted for its toxigenic properties.

3.1.2. Non-allergenic

The GMM should not produce increased allergenicity as a result of the genetic modification nor be a noted allergen, having, for example, allergenicity comparable in particular with that of the micro-organisms identified in Directive 2000/54/EC.

3.2. No harmful adventitious agents

The GMM should not harbour known harmful adventitious agents such as other micro-organisms, active or latent, existing alongside or inside the GMM, that could cause harm to human health and the environment.

3.3. Transfer of genetic material

The modified genetic material must not give rise to harm if transferred; nor should it be self-transmissible or transferable at a frequency greater than other genes of the recipient or parental micro-organism.

3.4. Safety for the environment in the event of a significant and unintended release

GMMs must not produce adverse effects on the environment, immediate or delayed, should any incident involving a significant and unintended release occur.

GMMs that do not meet the above criteria may not be included in Part C.

PART C

Types of GMMs which meet the criteria listed in Part B:

… (to be completed in accordance with the regulatory procedure with scrutiny referred to in Article 20(2))