Checklist of Information Required for GMAC Review

Environmental Risk Assessment of GMO-Related Gene Therapy Products

Based on and referenced from:
EU Legislation S.I. NO. 500 2003 Second Schedule: Principles for the Environmental Risk Assessment
European Medicines Agency Guideline: Scientific Requirements for Environmental Risk Assessment of Gene Therapy Medicinal Products (GTMP)

Kindly include the following information as a pdf document for submission to the GMAC Secretariat. Applicants may skip or indicate NA for sections/points that are not applicable.

Please also include your name, designation, organisation name and date of submission in the ERA document.

Please do note that other information may be requested if needed after the initial review.

A. Technical and Scientific Info on the GMO

The following points should be included in the submission to give a scientific overview of the GMO used in the gene therapy product for release in the clinical trial or for market registration.

Please provide details on the characteristics of:

- the recipient or parental organism(s);
- the genetic modification(s), be it inclusion or deletion of genetic material, and relevant information on the vector and the donor;
- the GMO;
- the intended release or use including its scale;
- the potential receiving environment; and
- any interaction between the GMO and receiving environment

B. Environmental Risk Assessment

The following points should be addressed to draw conclusions on the level of environmental risk posed during administration of the gene therapy product.

1. Identification of characteristics of the GMO which may result in adverse effects on human health or the environment

   Please provide details of possible adverse effects that may arise from release of the GMO product.

   - Potential effects on the environment
   - Potential effects on human health-transmission/uptake of the GMO to an unintended human recipient (E.g. exposure of healthcare personnel to GMO, shedding of GMO to close contacts of patient)
     - Disease to humans including allergenic or toxic effects
   - Potential effects on dynamics of populations of species in the receiving environment and the genetic diversity of each of these populations (E.g. through GMO material disposal)
     - Disease to animals and plants including toxic and allergenic effects
     - Altered susceptibility to pathogens facilitating the dissemination of infectious diseases and/or creating new reservoirs or vectors

    - Compromising prophylactic or therapeutic medical, veterinary or plant protection treatments, for example by transfer of genes conferring resistance to antibiotics
- Likelihood of unintended transfer
    - Adverse effects may occur directly or indirectly through mechanisms which may include: spread of GMO in the environment, transfer of inserted genetic material to other organisms, interactions with other organisms, phenotypic and genetic instability

2. Evaluation of the potential consequences of each adverse effect, if it occurs

Please evaluate the magnitude of the consequences of each potential adverse effect identified in point 1. The evaluation should assume that such an adverse effect will occur.

- Provide the qualification (high, moderate, low, negligible) of severity of the consequences
- Magnitude of consequences is likely to be influenced by:
    - Genetic constitution of the GMO
    - Method of administration/Manner of release of GMO into environment (E.g. Through GMO handling by healthcare personnel, GMO material disposal)
    - Characteristics of exposed environment (E.g. Climatological conditions)
    - Health status of those likely to be exposed (E.g. Exposure of healthcare personnel, close contacts of patients receiving treatment)
    - Frequency of use of the GMO

3. Evaluation of the likelihood of the occurrence of each identified potential adverse effect

Please evaluate the likelihood of occurrence of each identified potential adverse effect. A major factor in evaluating the likelihood or probability of adverse effects occurring is the characteristics of the environment into which the GMO is intended to be released, and the manner of the release.

- Provide a worst case scenario if plausible
- Provide a judgment on the overall fitness of the GMO
- Provide the probability that rare events may occur (E.g. Likelihood of gene transfer)
- Provide data on the ability of the GMO to establish an infection *in vivo* (Level of immunity in the community, likelihood of GMO to spread in the community)

4. Estimation of the risk posed by each identified characteristic of the GMO

Please estimate the qualitative risk to human health or the environment posed by the GMO. The estimation should be made by combining the likelihood of the adverse effect occurring and the magnitude of the consequences if it occurs.

- Describe risk in qualitative terms ranging from high, moderate, low or negligible
- To take into consideration scientific uncertainty if applicable, by maximising the potential risk that may occur and taking adequate safety measurements accordingly

5. Application of management strategies for risks from the deliberate release

Please describe safety precautions and risk management strategies.

- Identify risks described above that require application of a risk management strategy, e.g. to monitor the release of the GMO during administration
- Provide examples of precautions implemented to decrease environmental risks, e.g. to reduce risk of exposure to unintended individuals or the environment

6. Determination of the overall risk of the GMO

Please describe the overall risk of the GMO release into the environment.

- Provide a summary of the overall environmental risks identified in release of the gene therapy product
- Evaluate overall risk by taking into account proposed risk management strategies and safety precautions
- Provide a qualitative rating of overall risk (e.g. negligible, very low, low, moderate, high)