Decision taken in the 105th meeting of the Genetic Engineering Appraisal Committee (GEAC) held on 08.12.2010.

The 105th meeting of the GEAC was held on 8.12.2010 in the Ministry of Environment & Forests under the chairmanship of Shri M. F. Farooqui, Additional Secretary, MoEF and Chairman, GEAC.

The deliberations and decision taken in the GEAC meeting in respect of Agenda items 4 to 7 are as follows:

Agenda item No. 4 Policy issue

4.1 Discussion on draft position paper on use of antibiotic resistance markers in GM plants.

4.1.1 The Committee in its meeting held on 30.7.2010 had requested Dr Ramesh Sonti, CCMB to prepare a note on the type of selectable markers used in GM crops currently in the pipeline. The following documents received from Dr Sonti were placed for consideration of the Committee:

i. Background note on use of antibiotic resistance genes (ARM) in transgenic crops
ii. EFSA Statement of the Scientific Panel on Genetically Modified Organisms on the safe use of the *npt*II antibiotic resistance marker gene in genetically modified plants adopted on 22-23 March 2007.
iii. Committee for Medicinal Products for Veterinary Use and Committee for Medicinal Products for Human Use --Presence of the antibiotic resistance marker gene nptII in GM plants for food and feed uses (EMEA/CVMP/56937/2007- Final 22 February 2007).
iv. Homology-dependent DNA transfer from plants to a soil bacterium under laboratory conditions: implications in evolution and horizontal gene transfer *(Transgenic Research* 12: 425–437, 2003).

4.1.2 At the outset, the Chairman invited Dr Sonti to brief the Committee on the substantive issues as outlined in the above documents. Subsequently members were invited to give their views on:

a. Whether scientific evidence show there is a sufficient level of risk/safety to decide:

- All transgenic plants that are to be considered for commercial release must be marker free.
- Transgenic plants that carry an antibiotic resistance marker gene for an antibiotic that is no longer in clinical use would be eligible for release can be allowed
- Plants containing genes for herbicide resistance can be considered to be eligible as long as they do not also confer resistance to antibiotics that are in clinical use.
- There would be no bar on transgenic plants containing any kind of antibiotic resistance determinant as the chances of transfer of the resistance determinant to a pathogenic microbe are deemed to be remote.
- Transgenic plants that contain a marker gene such as GUS are eligible for release as they do not contain any gene for antibiotic resistance.

- Transgenic plants with two marker genes are ineligible for release as one of the marker genes can be considered to be 'extra baggage' as it is not essential for generation of the transgenic plants.
- Transgenic plants that carry a gene for resistance to an antibiotic that is currently in clinical use are ineligible for release even if the gene is expressible only in bacteria.

b. What would be the implication of such decision?

4.1.3 During the deliberations, the following views emerged:

i. Antibiotic Resistance Market Genes have been in wide use by plant molecular biologists to develop transgenic plants since 1983. The selectable market genes such as *nptII, hpt* and *aaD* are sourced from ubiquitous bacteria such as *E. coli* (transposon 5), and gram-negative bacteria (Transposons 7 and 21) and are extensively used in the development of transgenic plants/crops/ many which are commercially cultivated globally. The biosafety of these genes/enzymes has been well established (Nap et al., 1992; EFSA, 2001 and 2007, USEPA, 2004). The likelihood of horizontal transfer of these genes from transgenic plants and foods derived thereof to bacteria and other organisms is extremely negligible. Such rare instances can occur only if there is a similar gene in the recipient bacterium by homologous recombination, which does not create an extraordinary situation. Therefore, ARM genes totally biosafe and can be continuously used without any adverse consequences.

ii. The EMEA report concludes that neomycin, and kanamycin, are of importance for veterinary and human use and that their current and potential future use cannot be classified as of no or only minor therapeutic relevance. Therefore, GM crops containing *nptII* should not be allowed.

iii. The manuscript published by Tepfer et al in Transgenic Research indicates that bacteria growing in the vicinity of plant roots/leaves can take up ARM DNA quite readily. The paper also indicates that, although the ARM DNA is taken up readily into bacterial cells, the actual integration of ARM DNA into the bacterial genome is detectable only when there is a region of homology between the ARM DNA and the bacterial genome i.e sequences similar to ARM are already present in the bacterium. Although this significantly reduces the possibility of incorporation of ARM genes into the bacterial genome, the possibility that non-homologous recombination might be used to incorporate the ARM genes into bacterial genomes cannot be ruled out.

iv. As part of the evolutionary process, lateral transfer of DNA is happening in the environment all the time. Therefore, commercial release of GM crops would in no way add to the remote risk.

v. Transgenic plants with 'extra baggage' i.e with two marker genes should not be allowed for release as it is not essential for generation of the transgenic plants. This applies irrespective of whether the two marker genes encode for antibiotic resistance or one of them encodes for an antibiotic resistance determinant and the other for a gene such as GUS.

vi. Transgenic plants that carry a gene for resistance to an antibiotic that is currently in clinical use should not be allowed even if the gene is expressible only in bacteria. This is because of the concern that the gene becomes readily

expressible in pathogenic bacteria to which it might be passed in the human/animal body or in the soil.

vii. Since technology for generating marker free transgenic plants is available, transgenic plants that are commercialized should be marker free.

viii. The development of marker free GM crops is highly expensive and/or cumbersome cannot be a criteria for deciding the policy on whether GM crops containing ARM genes is safe or not.

ix. Decision to allow commercial release of only marker free GM crops would make almost all transgenic plants that are under consideration of GEAC/RCGM ineligible for release.

x. Any policy decision to disallow ARM genes in GM food crops should be based on scientific evidences substantiated by studies commissioned by the GEAC.

xi. As regards the policy decision not to allow GM crops containing two genes, it was pointed out that there are several GM crops under various stages of research and development containing more than two genes. It was clarified that the policy under consideration is specific to use of ARM genes only and would not be applicable to the gene of interest.

4.1.4 After detailed deliberations, the Committee agreed on the following:

(i) The GM crops containing ARM genes currently in the pipeline may continue to be evaluated on a case-by-case basis unless scientific evidence established otherwise.

(ii) The Member Secretary, GEAC would prepare a base paper for consideration of the Committee based on the deliberations in the meeting and invite comments from various experts/institutions by posting it on the GEAC website before taking a view on the matter. The paper would include information on decisions taken by other countries.

Agenda item No. 5: Consideration of applications for confined field trials of transgenic crops (Event selection, BRL-I and BRL-II) as recommended by the RCGM.

5.1 Request from M/s Monsanto for conducting BRL-2 trials of MON89034 x NK603 corn during Rabi 2010-2011

5.1.1 The Committee noted that the GEAC in its meeting held on 15.11.2010 had approved the request of M/s. Monsanto India Ltd., New Delhi to conduct BRL-II trials with two transgenic corn hybrids namely 900M Gold and Hishell, containing stacked cry2Ab2, cry1A.105 (Event MON 89034) & cp4epsps (Event NK603) genes at nine locations during Kharif 2011 on the grounds that the sowing season for corn during Rabi is over.

5.1.2 The Committee considered the present request of the Company to conduct BRL-2 trials during late Rabi season (Dec-2010-Jan-2011) at the following five locations in addition to the nine trials to be conducted during Kharif 2011 for which they have obtained consent letters from the respective SAUs:

1. Begusarai / Samastipur, Bihar;

2. Bhagalpur Bihar;
3. TNAU Coimbatore;
4. UAS Dharwad;
5. ANGRAU Karimnagar;

5.1.3 After detailed deliberations, the Committee was of the view that the trials to be conducted during Rabi 2010 are additional trials suggested by the applicant to generate additional information during the Rabi period and would not be in lieu of the BRL-II trials at nine locations approved by the GEAC in its meeting held on 15.11.2010.

5.1.4 On the request of the Company for limited seed production in an area of 25 acres during Rabi, the Committee noted that the GEAC has already approved seed production in an area of 25 hectares during the Kharif season. The Committee was of the view that the applicant may be advised to provide justification for the additional requirement. The Committee gave an opportunity for a personal hearing to the representative of the Company wherein it was clarified that the request for seed production is only for 25 acres. However, some flexibility needs to be provided so they can produce the seeds either during the Rabi or Kharif as in the southern zone, seed production is undertaken during the Rabi season.

5.1.5 After detailed deliberation, the Committee conveyed it's no objection for (i) conducting BRL-II trials at 5 locations during Rabi 2010 in addition to 9 locations during Kharif 2011; and (ii) limited seed production in an area of 25 acres either during Rabi or Kharif.

5.2 Permission to conduct Biosafety Research Trials I (BRL-1) on two Bt sorghum lines containing cry 1B gene NRCSCRY1B event 4 and NRCSCRY 1B event 19 along with non transgenic lines (M35-1) by Directorate of Sorghum (DSR), Hyderabad, formerly known as National Research Centre for Sorghum.

5.2.1 The Committee noted that the GEAC in its meeting held on 15.11.2010 had considered the request of the Directorate of Sorghum Research (DoSR), Hyderabad to conduct BRL-1 trials on two Bt transgenic Sorghum (Sorghum bicolor (L) Moench) lines containing *cry1B gene NRCSCRY1B* event 4 and NRCSCRY1B event 19 during Rabi season, 2010.

5.2.2 Decision on the proposal was deferred as the applicant did not provide information on gene construct and vector map (pCAMBIA 3300). The Committee noted that the requisite information submitted by the applicant subsequently is in order. Accordingly, the GEAC approved the conduct of BRL-I trials with two Bt transgenic Sorghum (Sorghum bicolor (L) Moench) lines containing *cry1B gene NRCSCRY1B* event 4 and NRCSCRY1B event 19 during Kharif 2011 as the sowing season for Rabi is over.

Agenda item No. 6: Consideration of applications related to Pharmaceuticals

6.1 Permission for Phase III clinical trials to conduct controlled study of the safety and immunologencity of Japanese Encephalitis Chimeric Virus Vaccine (JE-CV) by M/s Sanofi Pasteur India Pvt Ltd. New Delhi (former *Acambis Inc)*

6.1.1 The Committee noted that the GEAC in its meeting held on 30.7.2010 had advised the applicant to submit the following information:

i. Seroconversion rate of JE-CV vaccine in comparison with the available brain mouse vaccine.
ii. Complete Phase-II clinical trial and safety data which includes information on adverse reactions, if any.
iii. Whether the Phase-II trials have been conducted without involving measles vaccine as directed by the GEAC in its letter dated 28.1.2008?
iv. Number of patients and age group to be tested in Phase-III clinical trials.

6.1.2 The Committee noted that the requisite information submitted by the applicant is in order. Accordingly, the Committee approved the conduct of Phase III clinical trials to conduct controlled study of the safety and immunologencity of Japanese Encephalitis Chimeric Virus Vaccine (JE-CV) by M/s Sanofi Pasteur India Pvt Ltd. New Delhi.

Agenda item No. 7: Other items:

7.1 Permission for Export of 2500 Bt Cauliflower seeds to National Collection of Industrial, Food and Marine Bacterial NCIMB, United Kingdom by Mahyco.

&

7.2 Permission for Export of 2500 Bt Brinjal seeds to National Collection of Industrial, Food and Marine Bacteria (NCIMB), Ltd. United Kingdom by Mahyco.

7.2.1 The Committee considered the request of M/s Mahyco to export 2500 Bt cauliflower transgenic seeds of event CFE-4 containing cry 1Ac gene and 2500 Bt brinjal transgenic seeds of event EE-6726 containing cry 2Ab gene to National Collections of Industrial, Food and Marine Bacteria (NCIMB) Ltd, Ferguson Building, Craibstone Estate, Bucksburn, Aberdeen AB21 9YA, United Kingdom for event identification pattern.

7.2.2 The Committee noted the following points:

- The applicant is in the process of filing patent application for Bt Cauliflower transgenic event CFE-4 and Bt Brinjal transgenic EE-6726 event for which they have been asked by the International Search Authority under the PCT, to deposit the biological material to satisfy the requirement of Article 5 of the PCT for sufficiency of disclosure. As per the said article, the invention cannot be said to be disclosed adequately unless the biological material is deposited.

- As per law, both in India and under the PCT, the biological material may only be deposited in an International Depository Authority (IDA) under Budapest Treaty on International Recognition of the Deposit of Micro-organisms for the purposes of Patent Procedure, to which India is a signatory.

- World Intellectual Property Organization (WIPO) which administers the Budapest treaty has recognized 37 IDAs (Intellectual Depository Authorities). Out of 37 Depository Authorities only 5 accepts seeds.

- There is one recognized depository in Chandigarh, India but they do not accept seeds.

- The GEAC in its 93rd meeting held on 13.5.2010 had allowed the export of 2500 seeds of Bt okra of event OE-17A expressing cry 1Ac gene Bt and 2500 seeds of Bt. rice of 3 events PE-2, PE-4 and PE-7 expressing cry 1Ac gene to National

Collections of Industrial, Food and Marine Bacterial (NCIMB) Ltd., U.K for the purpose of patent.

7.2.3 During the deliberations, several issues such as approvals from the competent authority under the relevant domestic law for export of seed material, mechanism to ensure that the exported material is used for the intended purpose and approval of the country of import were discussed.

7.2.4 After detailed deliberations, the Committee conveyed its 'no-objection' for export of 2500 Bt Cauliflower seeds and 2500 Bt. Brinjal seeds to National Collection of Industrial, Food and Marine Bacterial NCIMB, United Kingdom by Mahyco subject to:

i. The applicant would obtain the necessary approvals under the prevailing domestic laws, as applicable, prior to export of the seed material.
ii. The applicant shall submit a copy of the acknowledgement from NCIMB confirming that the seed material has been deposited in the depository of the institute.
iii. The applicant shall also submit a copy of the approvals obtained under the domestic law and copy of the acknowledgement from NCIMB with respect to export of Bt okra transgenic seeds of event OE-17A expressing cry 1Ac gene and Bt rice transgenic seeds of 3 events PE-2, PE-4 and PE-7 expressing cry 1Ac gene which were earlier exported to NCIMB.

Date of next GEAC Meeting: 12th January 2011.

****