Decision Taken in the 107th meeting of the Genetic Engineering Appraisal Committee (GEAC) held on 09.02.2011.

The 107th meeting of the GEAC was held on 09.02.2011 in the Ministry of Environment & Forests under the chairmanship of Shri M. F. Farooqui, Additional Secretary, MoEF and Chairman, GEAC.

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

Agenda item No.4 : Policy issues

It was noted that two industry associations namely Association of Biotechnology Lead Enterprises (ABLE) and National Seed Association of India (NSAI) made a brief presentation to the GEAC in the meeting held on 12.01.2011 on several issues. After a brief discussion on the issues, it was decided to consider the matter in the next GEAC meeting.

Decisions taken by the GEAC in this meeting in respect of the following issues are given under:

4.1 Duration during BRL-1 and BRL-II trials

4.1.2 The Committee noted that the issue has already been clarified in the previous meeting wherein it has been informed that the duration of BRL-I trials would be for a minimum period of two years and BRL-II trials would be for a minimum period of one year.

4.2 Data Generation during BRL-1 and BRL-II trials

4.2.1 The Committee considered the request of ABLE to expedite the finalization of the e "Draft Guidance for information/Data Generation and Documentation for Safety Assessment of Regulated/Genetically Engineered (GE) Plants" developed by DBT and MoEF.

4.2.2 It was noted that finalization of the document is pending for two reasons, namely (i) it has been linked with the Bt. Brinjal review process, and (ii) Policy decision on use of ARM in GM food crops. As the Bt. Brinjal review and decision may take some time, the Committee opined that finalization of the draft Guidance Document for data generation should be completed at the earliest which can be subsequently used in Bt. Brinjal review process. Further, it was noted that the GEAC in its meeting held on 8.12.2010, has concluded that "the GM crops containing ARM genes currently in the pipeline may be evaluated on a case-by-case basis unless scientific evidence established otherwise". The Committee opined that this aspect may also be taken into consideration while finalizing the document so that appropriate data requirement is prescribed.

4.2.3 Member Secretary, GEAC further informed that the GEAC has taken several initiatives to streamline the regulatory process but most of the policy decisions including the data generation are camouflaged in the minutes of the GEAC meeting which is put on the website or in the approval letters. In the absence of a handbook or guidance document on the regulatory requirements, there is a lot of public criticism regarding the lack of transparency on the regulatory procedure. This issue has been repeatedly cropping up in the PILs filed in the Hon'ble Supreme Court.

4.2.4 After detailed deliberations, it was agreed that the guidance document would be discussed thread bare in the next GEAC meeting with a view to finalize the same.

4.3 Implementation of Event Based Approval Mechanism (EBAM):

4.3.1 The Committee noted that the GEAC in its meeting held on 02.04.2008 had adopted the event-based approval Mechanism (EBAM) in respect of Bt. cotton hybrids expressing approved events on the grounds that the biosafety profile of an event does not change when it is transferred to other genetic backgrounds of the same crop through back-crossing to develop new hybrids/parents. Accordingly the earlier practice of approving hybrid by hybrid was dispensed with as it does not involve any biosafety issues. Subsequent to the adoption of the EBAM, the Ministry vide OM No. 13/39/2007-CSII dated 20.2.2009 /17.4.2009 had constituted a 'Standing Committee' to review applications for commercial release of Bt cotton hybrids expressing approved events under the new EBAM. As per the new procedure, the 'Standing Committee' is being serviced by the DBT. It was noted that the Standing Committee has convened five meetings during Kharif 2009 and Kharif 2010. The tenure of the Standing Committee is upto Kharif 2011.

4.3.2 The Committee considered the request of DBT to transfer the responsibility under the EBAM mechanism for Bt cotton from DBT to the State Governments or ICAR. The Committee opined that the tenure of the 'Standing Committee' is for a period of three years of which only two years have been completed. The Chairman, GEAC opined that putting in place a new mechanism for a short period may not be advisable and would send wrong signals. He requested Member Secretary, RCGM to continue with the current mechanism until the tenure of the Standing Committee is complete, subsequent to which the matter may be reviewed again. Member Secretary RCGM informed that Dr. P. Balasubramanian, former Director, Centre for Plant molecular Biology, TNAU and Chairman of the Standing Committee is now working with a private company and therefore, it may not be appropriate for him to continue as Chairman of the Standing Committee. It was decided to nominate Dr. N Gopalkrishnan, ADG (Commercial Crops) as Chairman of the Standing Committee.

4.3.3 The Committee also considered the following issues raised by Able and NSAI:

A. Operationalising the EBAM mechanism

i. EBAM should be put in place at the earliest as once the event(s) is declared safe as opposed to the present practice of declaring the event bio-safe only after 3 years of commercialization.
ii. The policy to allow only one or two hybrids for BRL-1 and BRL- 2 trials, restricts the applicant to commercialize only these hybrids till the event(s) are declared bio-safe.
iii. The process by which new hybrids can be brought into the market within 3 years after the first approval of an event is not clear at the moment.
iv. Once an event has been declared bio-safe, release of an event in a given germplasm should be similar to a conventional germplasm release process as long as the technology provider certifies an appropriate level of event/trait purity and expression of the protein in the specific hybrid.

B. Streamlining the approvals under the Standing Committee

i. The meetings of the Standing Committee may be held well in advance of the crop seasons.

ii. The Standing Committee may approve hybrid(s) based on submission of information as prescribed by the GEAC.
iii. Standing Committee may not mention any agro climatic zone in its approval letter as agronomic data is not submitted to the Committee. The applicant based on the hybrids agronomic evaluation would approach the State Government for release in the respective States.

4.3.4 After a brief discussion on the matter, the Committee decided to constitute a Sub-committee to review the matter and submit its recommendations to the GEAC.

4.4 Use of imported germplasm for field trials in India

4.4.1 This issue pertains to the policy decision taken by the GEAC not to approve applications for field trials to generate biosafety data with imported seed materials. ABLE has requested the GEAC to reconsider its decision as the background of germplasm, whether it is imported or indigenously produced seeds does not have any relevance for conduct of field trials and also for generating biosafety data on the particular event(s).

4.4.2 The Committee reiterated its earlier decision dated 9.9.2009 not to allow the use of imported GM seeds for field trials in India.

4.5 Acceptance of laboratory biosafety data from overseas

4.5.1 The Committee considered the suggestion from ABLE regarding acceptance of laboratory biosafety data generated in GLP certified laboratory outside the country. The Committee opined that a detailed note on the biosafety data requirements as per the prevailing national and international guidelines may be prepared subsequent to which a view on the matter may be taken.

4.6 Deregulation of stacked events and subsequent regulatory status of single event parental lines in the approved stacked events for seed production

4.6.1 The Committee considered the suggestion for deregulation of stacked events (breeding stack) in a given transgenic crop wherein the environmental clearance given to a stacked product would automatically translates to the parental lines expressing single event for open environmental cultivation for the purpose of bulking up the parental lines and also to be used in commercial seed expressing stacked event.

4.6.2 The Committee opined that each event is considered as a new product and therefore biosafety clearance is mandatory.

4.7 Zone classification for different crops

4.7.1 Regarding the suggestion to dispense with the need for generating zone specific biosafety data for the purposes of deregulation, it was decided to refer the matter to the Sub-Committee constituted under Agenda No.4.3.4

4.8 State Agricultural Universities (SAU) trials

4.8.1 It was noted that most applicants are conducting field trials in the SAUs, as universities are able to provide the required isolation distances for the trials. However, SAUs are often reluctant to undertake trials for fear of protests on their campuses and experimental fields. Regarding the request to explore ways and means of bringing SAUs to be partners in progress in the spirit of public-private partnership it was opined that the matter may be referred to DG-ICAR.

4.9 Minimize the time for application processing & time limits for issuing the permit letter.

4.9.1 The Committee opined that all efforts will be made to convene meetings of the GEAC/RCGM as per the standard timetable. Further, it was also agreed that time lines for approval of BRL-I trials can be minimized by adopting the following procedure:

(i) The applicants may submit their application for two years BRL-1 instead of one year BRL-1.

(ii) In case of change in location, the applicant may inform the RCGM/GEAC / State Governments of the exact location within 15 days of the sowing. While identifying the alternate locations, the applicant may strictly follow the following decisions taken by the GEAC in its earlier meetings:

- All event selection trials will be carried out within the Company's institutional research farm.
- BRL-I/BRL-II trials will be conducted within the research farm of the SAU/ICAR/company including long leased land.
- No trials will be conducted within the farmer's field.

4.10 Need for Pollen flow studies

4.10.1 Regarding the suggestion to accept established pollen flow data available from a variety of internationally accepted publications, the Committee opined that only India specific data if available will be accepted. In all other cases, the applicant will have to conduct pollen flow studies as part of the biosafety assessment.

4.11 Joint application and registration process

4.11.1 The Committee noted that this issue pertains to the policy decision taken by the GEAC to allow confined field trials to only those companies/organizations that are involved in the development of the technology and are responsible for conducting biosafety studies. The Committee decided to refer the matter to the Sub-Committee constituted under Agenda No.4.3.4

4.12 Protecting the field trials from vandalis

4.12.1 The Committee noted that attack on GM crop field trials is a law and order issue. Such kind of sabotage is highly risky as it may lead to release of untested GM material and therefore strict action against the violators should be initiated by the State Govt. It was agreed that a letter in this regard would be sent to all Chief Secretaries of states where field trials are being conducted.

4.13 Web based mechanism for submission of applications

4.13.1 The Committee opined that the suggestion for online submission and tracking of applications merits consideration. Member Secretary GEAC clarified that revamping of the GEAC website is underway wherein the above suggestion has already been incorporated.

4.14 Opportunity to meet and discuss applications with the Member Secretary of RCGM/GEAC.

4.14.1 The Committee opined that in view of the multi-disciplinary nature of the subject matter, it would be more useful if applicants are provided an opportunity to make a presentation on the proposal or provide clarifications to issues raised by the Experts in the GEAC meeting. This practice is already being followed by the GEAC. The Committee further advised that applicants may depute only technical representatives who are familiar with the subject matter for the GEAC meetings.

4.15 Refuge/IRM strategy for insect resistance crops

4.15.1 The Committee opined, to ensure long term sustenance of benefits from Bt cotton technology, a science based refuge strategy which is also practically implementable by seed companies and farmers must be developed which will increase on-ground compliance of the required refuge planting by farmers. The Committee considered the following suggestions received from NSAI:

1. **Permit planting of non-Bt refuge as a single patch adjoining Bt cotton field** since the farmers find the current requirement of planting refuge all around Bt cotton as practically challenging. The planting of the non-Bt refuge as a single patch makes it easier for planting, managing and fits well for any land holding size.

2. **Permit use of non-Bt cotton variety, having similar maturity and fiber characteristics as that of the Bt cotton hybrid, as refuge** since any non-Bt cotton plant, regardless of whether it is a hybrid or a variety, would provide the required refuge to bollworms. The GEAC, in its 71st meeting (item 1.4.5) had concluded "non Bt counterpart of the same species, similar duration and fiber quality may be used as refugia in place of same non Bt counter part". However, GEAC approval letters issued to applicants require the refuge to be "non-Bt cotton seeds of popular hybrids". This inconsistency may please be corrected.

3. **Reduce the size of refuge (non Bt cotton or pigeon pea) required for Bt cotton stacked with two or more Bt genes.** The added efficacy of stacked *Bt* genes can be translated to a requirement of a smaller refuge size (Zhao *et al*. 2003, *Nature Biotechnology* 21: 1493-14). Published scientific data clearly demonstrates that stacking of *Bt* genes with diverse modes of action in the same plant increases product durability and could reduce the refuge requirement due to greater efficacy of the product and reduced survivorship of target pests (Roush, 1977, Pesticide Sci. 51, 328; Roush, 1998, Phil. Trans. Proc.R. Soc. Lond. Ser B 353: 1777; Zhao et al., 2003, Nature Biotech. 21(12), 1493). Consequently, in most countries such as US, South Africa, Brazil, Australia etc, either there is no requirement of structured refuge in the case of stacked Bt genes or the requirement is much less (5%).

4.15.2 On this issue the Committee agreed with the suggestion given by DDG-ICAR that a lengthy discussions with some experts on the subject to develop a short/medium and long term strategy for a sustainable Bt technology is necessary. The Committee decided to refer the matter to the Sub-Committee constituted under Agenda No.4.3.4. The Sub-Committee in consultation with other Experts may submit its recommendation to the GEAC.

4.16 Approval for transgenic parent lines of GEAC approved Bt Cotton hybrids

4.16.1 The Committee noted that all applications for registration of transgenic parental lines have been kept in abeyance by the PVP&FR Authority on the ground that 'GEAC

has approved only hybrids; and parents of these GEAC approved hybrids cannot be considered as approved by GEAC'.

4.16.2 On the request from NSAI to issue appropriate orders to PVP&FR Authority clarifying that Bt parents of approved Bt cotton hybrids may also be considered as approved under EPA, it was opined that the GEAC is involved only in the biosafety assessment of the hybrids prior to commercialization. Therefore, the matter does not fall under the mandate of the GEAC.

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

5.1 Permission to conduct event selection on 20 transgenic rice (*Oryza sativa L.*) events containing *cry1Ac* gene for the evaluation of the Bt events for resistance against lepidopteron insects and to identify events which are true-to-type agronomically by M/s. JK Agri Genetics Ltd., Hyderabad.

5.1.1 The Committee noted that the GEAC in its 106th meeting held on 12.1.2011 had considered the request of the company to conduct event selection on 20 transgenic rice (*Oryza sativa L.*) events containing *cry1Ac* gene for the evaluation of the Bt events for resistance against lepidopteron insects and to identify events which are true-to-type agronomically.

5.1.2 Decision on the proposal was deferred as the applicant did not provide information pertaining to: (i) location of the event selection trials; and (ii) the marker used for selection of events.

5.1.3 The Committee considered the clarification submitted by the applicant and noted that information pertaining to (i) vector map, (ii) complete construct and (iii) Insert map have not been submitted. It was agreed that the same may be obtained from the applicant under the confidentiality clause. Accordingly, it was decided to defer the matter to the next GEAC.

5.2 Permission to conduct event selection trials on 20 transgenic rice (*Oryza sativa L.*) events namely Cry2AxE 001-to Cry 2AxE 020 containing *cry2Ax1* gene containing for the evaluation of the Bt events for resistance against lepidopteran insects and to identify events which are true-to-type agronomically by JK Agri Genetics Ltd., Hyderabad

5.2.1 The Committee noted that the GEAC in its 106th meeting held on 12.1.2011 had considered the request of the company to conduct event selection on 20 transgenic rice (*Oryza sativa L.*) events namely Cry2AxE 001-to Cry 2AxE 020 containing *cry2Ax1* gene containing for the evaluation of the Bt events for resistance against lepidopteron insects and to identify events which are true-to-type agronomically.

5.2.2 Decision on the proposal was deferred as the applicant did not provide information pertaining to: (i) location of the event selection trials; and (ii) the marker used for selection of events.

5.1.3 The Committee considered the clarification submitted by the applicant and noted that information pertaining to (i) vector map, (ii) complete construct and (iii) Insert map have not been submitted. It was agreed that the same may be obtained from the applicant under the confidentiality clause. Accordingly, it was decided to defer the matter to the next GEAC.

Agenda Item No 6: Consideration of applications related to pharma.

6.1 Permission to conduct phase I clinical trials of recombinant- Salmonella *Typhi strain Ty21* a expressing Human Papilloma virus vaccine (HPV) major protein L1 as a oral vaccine in India by M/s Indian Immunological Limited. Hyderabad.

6.1.1 The Committee considered the request of M/s Indian Immunologicals Limited for conduct of Phase I clinical trials of recombinant *Salmonella Typhi strain Ty21a* expressing Human Papilloma Virus vaccine (HPV) major capsid protein L1 as an oral vaccine.

6.1.2 The Committee observed that the company in collaboration with Dr Denise Nardelli-Haefliger of University of Lausanne, Switzerland has developed a prophylactic vaccine that is ideally suited for low resource setting. One of the major strengths of the vaccine is that that it uses attenuated *Salmonella typhi Ty21a* as delivery vehicle for the major capsid protein L1 of HPV type 16 and 18. The vaccine is developed for oral delivery, which is expected to improve the vaccine coverage and compliance in the rural population.

6.1.3 The Committee also noted that the Oral HPV Vaccine will be used for prevention of the following diseases caused by Human Papilloma Virus (HPV) types 16, and 18:

- Cervical Cancer
- Cervical intraepithelial neoplasia (CIN) grade 2 or worse
- Cervical adenocarcinoma in situ, and
- Cervical intraepithelial neoplasia (CIN) grade I

6.1.4 The Committee also noted that DCGI vide their letters dated 6.12.2006 and 21.5.2010 had permitted to import of *Salmonella typhi* strain Ty21a LIS from Singapore for manufacture of *prophylactic Salmonella* based vaccine against HPV for experimental batches against HPV for the purpose of examination, test or analysis respectively.

6.1.5 The Committee further noted that the prophylactic vaccine made from recombinant virus like particle of HPV has proven highly efficacious in preventing the onset of cervical cancer in vaccinated women. Since the vaccine contains virus like particle (VLP), which requires rigorous purification processes, it remains out of the reach of people who require this prophylactic vaccine the most. A low cost prophylactic HPV vaccine has the potential to augment the public health service even in low resource setting.

6.1.6 The host strain used for the delivery of vaccine antigen into human is highly attenuated strain of *Salmonella typhi Ty21a*. They have been used as live oral vaccine against typhoid infection and have an safety record.

6.1.7 It was observed by the Committee that the pre-clinical trials done at NIN, Hyderabad to evaluate the acute toxicity, sub-toxicity and allergenicity potential of the vaccine formulation in mice, rats and rabbits has been considered by the RCGM in its 92nd meeting held on 25.8.2010. RCGM approved the proposal.

6.1.8 It was also noted that the GEAC in its 63rd meeting held on 8.2.2006 had approved the import of Cervarix ^{tm} Human Papilloma Virus vaccine for conduct of Phase III clinical trials in India by M/s Glaxo Smith Kline (GKS) Pharmaceuticals Ltd. Mumbai.

6.1.9 In view of the above stated facts and taking into consideration the recommendations of the Experts and the RCGM, the Committee approved the request for conduct of phase I clinical trials of recombinant Salmonella *Typhi strain Ty21*a expressing Human Papilloma Virus Vaccine (HPV) major protein L1 as an oral vaccine in India subject to DCGI approval.

Agenda Item No 7: other items:

7.1 Permission to import transgenic Liberty Link Soybean Oil from USA by M/s. Bayer BioSciences Pvt. Ltd, Gurgaon.

7.1.1 The Committee noted that the request of the Company to import transgenic Liberty Link Soybean Oil from USA, was considered by the GEAC in its meeting held on 8.7.2009, wherein the applicant was advised to clarify whether the safety approval obtained from other countries is for glyphosate tolerant trait or for glufosinate tolerant trait. The applicant was also advised to provide information on queries raised by FSSAI.

7.1.2 The Committee considered the following information submitted by the applicant:

1. All the safety approvals have been taken for Glufosinate Tolerant trait.
2. A study was conducted to validate an ELISA method (QualiPlateKit for PAT, cat#AP014NWV10, EnviroLogix) for the determination of phosphinothricin acetyltransferase (PAT) in soybean oil under Good Laboratory Practice Standards (GLPs). In all of the tested LL Soybean (gene event A2704-12 and A 5547-127) oil samples, PAT protein can't be detected (was below detectable level) (Carringer and Langevin 2010 M-395304-01-1 and Carringer and Langevin 2010 M-395296-01-1. In the case of detection of the PAT protein the lowest limit of quantification is 0.063 ng/mL oil (Carringer and Langevin 2010 M-395304-01-1).
3. 23 countries are importing GM Soybean oil. The Liberty Link Soybean has been approved for cultivation in 1996 and for food/feed in 1998.
4. Worldwide, approximately 35 countries have developed some form of labeling requirement (both mandatory and voluntary) for GM foods, including European Union (EU), China, Australia, New Zealand, Japan, South Korea and Taiwan.

7.1.3 During the discussions, one of the members pointed out that, as per the information submitted by the applicant, countries have imposed mandatory labeling of soybean oil and in the absence of such a policy in India, the product should not be approved for consumption. It was clarified that there is no specific labelling requirement for GM Soybean oil in a Country of Import, but many Countries have general Food labelling requirements. Many countries do not require labelling for processed food like oils (which may not contain GM). Further, there is no international agreement about labelling of food or food components or about the wording of the label. It was also pointed out that mandate of the GEAC is to accord approval based on biosafety assessment in accordance with scientific facts whereas issues related to labelling are trade related matters.

7.1.4 After detailed deliberations, the Committee requested Member Secretary GEAC to prepare a detailed agenda note highlighting: (i) requirement of labelling soybean oil in other countries; (ii) position on the matter under various laws existing in the country; (iii) role and mandate of GEAC. Accordingly decision on the proposal was deferred.

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