Decision taken in the 57th Meeting of the Genetic Engineering Approval Committee (GEAC) held on 10th August 2005.

The 57th Meeting of the Genetic Engineering Approval Committee was held on 10th August 2005 at 11.00 AM in the Ministry of Environment and Forests under the Chairmanship of Shri Suresh Chandra, Special Secretary & Chairman GEAC.

Decisions

1. Permission for import of finished formulation of anti cancer monoclonal antibody, Cetuximab (Erbitux) from Germany by MERCK.

i. The Company has completed phase III clinical studies in the European Union and in the USA. It was further noted that the product is registered internationally and marketed in 37 countries including USA, UK, European Union, Australia and Switzerland.

ii. After detailed deliberations and taking into consideration the recommendation of the Experts, the Committee approved the import of Cetuximab (Erbitux) from Germany for conduct of Phase –III clinical trials in India subject to approval of the DCGI.

2. Permission for manufacture and marketing of r-insulin by M/s Cadilla Pharmaceuticals Ahmedabad.

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3. Permission for manufacture & marketing of formulation of r-human insulin of 3 types -soluble insulin, insulin Isophane, 30:70 combination of soluble insulin + insulin Isophane, in India by M/s Lupin Ltd. Mumbai.

i. The Committee noted that the company intends to procure the bulk r-insulin from M/s Biocon and convert r-insulin crystals into smaller pack formulations as per market demand. The r-insulin developed by M/s Biocon Ltd has been approved for manufacture and marketing of the product in India by the GEAC in its meeting held on 14th July 2004. The product has also been approved by the DCGI.

ii. During the deliberations, it was noted that M/s Biocon is supplying bulk r-insulin to a number of companies. After detailed deliberations, the Committee decided to obtain the following clarifications from M/s Biocon:

a. Details of the installed capacity for production of r-insulin.
b. Names of the Companies to whom bulk r-insulin is being supplied/ proposed to be supplied and the corresponding quantities committed for supply by the company.

4. Permission for manufacture and marketing of r- human Interferon alpha 2b (r-DNA origin) by Wockhardt Ltd. Mumbai.

i. The Committee noted that the company has conducted phase-III clinical trials without the approval of GEAC. Based on the facts of the case, the Committee concluded that explanation may be called from the Company for non-compliance in respect of the following before taking a final view:

a) Reasons for not obtaining the approval of the GEAC before conduct of clinical trials.
b) Reasons for not obtaining ex-post facto approval from GEAC for conduct of Phase-III clinical trials.

5. Permission for manufacture of indigenous r-hepatitis C viral antigens core NS-3, NS-4 and NS-5 by M/s. Sudershan Biotech Ltd. Hyderabad.

i. The Committee noted that the Company has constituted the IBSC and have also obtained the approval of the RCGM prior to product development. Views were expressed that the tests carried out at the Centre for Liver Research and Diagnostics; Hyderabad to determine the efficacy of the antigen needs further clarification. Views were also expressed that the Committee may call for a validation report from the National Institute of Biologicals (NIB), which is the referral laboratory notified by the Ministry of Health.

ii. After detailed deliberation, the Committee decided to call for additional information on the tests conducted at the Centre for Liver Research and Diagnostics; Hyderabad and also direct the applicant to obtain the validation report from NIB.

6. Permission for import of r-human Erythropoietin to conduct clinical trials by M/s. ClinIvent Research Pvt. Ltd. Mumbai from Korea.

i. The Committee noted that present application is for import of r-human Erythropoietin from Seoul Korea to conduct clinical trials at KEM Hospital, Mumbai, Nizam's Institute of Medical Science, Hyderabad, P. V. S. Memorial Hospital Ltd, Cochin, Madras Institute of Nephrology, Chennai, Manipal Acunova Pvt. Ltd., Bangalore, S.M.S. Medical College and Hospital, Jaipur, Amrita Institute of Medical Science and Research Centre, Cochin.

ii. After detailed deliberation and taking into consideration the recommendations of the Expert Member and views of the ICMR, DCGI and DBT, the GEAC approved the import of the drug for conduct of human clinical trials subject to DCGI approval.

7. Revalidation Permission for import & marketing LG Euvax (r-hepatitis B vaccine) by M/s LG Life Sciences India Pvt. Ltd. New Delhi.

i. The GEAC in its 28th meeting held on 7.9.2001 had approved the import & marketing of LG Euvax (r-hepatitis B vaccine). As per the requirement under Rule 13 (2) of the 1989 Rules, the firm has requested for revalidation of the GEAC permission for import and marketing of the product in India for a further period of 2 years.

ii. The Committee conveyed their 'No Objection' for revalidation of the GEAC approval. However, the Committee requested the Member Secretary, GEAC to obtain information on the quantity of the drug marketed by the Company in India at present and during the last 3 years.

8. Revalidation Permission for import & market L. G. Espogen ™ (r-Human Erythropoietin) M/s LG Life Sciences India Pvt. Ltd. New Delhi.

i. The GEAC in its 27th meeting held on 8.8.2001 had approved the import & marketing of L. G. Espogen ™ (r-Human Erythropoietin). As per the requirement under Rule 13 (2) of the 1989 Rules, the firm has requested for revalidation of the GEAC permission for import and marketing of the product in India for a further period of 2 years.

ii. The Committee conveyed their 'No Objection' for revalidation of the GEAC approval. However, the Committee requested the Member Secretary, GEAC to obtain information on the quantity of the drug marketed by the Company in India as of date and during the last 3 years.

9. Revalidation Permission for import & market r-Interferon Injection (Intermax 3, 6,9, MIU) M/s LG Life Sciences India Pvt. Ltd. New Delhi.

i. The GEAC in its 27th meeting held on 8.8.2001 approved the import & marketing of r-Interferon Injection (Intermax 3, 6,9, MIU). As per the requirement under Rule 13 (2) of the 1989 Rules, the firm has requested for revalidation of the GEAC permission for import and marketing of the product in India for a further period of 2 years.

ii. The Committee conveyed their 'No Objection' for revalidation of the GEAC approval. However, the Committee directed the Member Secretary, GEAC to obtain information on the quantity of the drug marketed by the Company in India as of date and during the last 3 years.

10. Revalidation Permission for manufacture & marketing of r-hepatitis B vaccine produced by Pichia pastoris by M/s Bharat Biotech Hyderabad.

i. The GEAC in its 25th meeting held on 27.3.2001 approved the manufacture & marketing of r-hepatitis B vaccine produced by Pichia pastoris. As per the requirement under Rule 13 (2) of the 1989 Rules, the firm has requested for revalidation of the GEAC permission for import and marketing of the product in India for a further period of 2 years.

ii. The Committee conveyed their 'No Objection' for revalidation of the GEAC approval. However, the Committee directed the Member Secretary, GEAC to obtain information on the quantity of the drug marketed by the Company in India as of date and during the last 3 years.

11. Import of r-Leisg-111 F from USA by M/s Institute of Medical Sciences, BHU, Varanasi for conduct of phase III Clinical trials in India.

i. The Committee noted that comments from Experts and DBT are awaited but DCGI has conveyed their no objection for GEAC clearance from environmental angle. It was also noted that the Technical Advisory Committee of ICMR has recommended the case. However the Ethical Committee is yet to approve the drug for clinical trials.

ii. The Member Secretary, GEAC pointed out that the request by the company is for Phase-III clinical trials but the product has been approved by DCGI only for Phase-I clinical trials. The Committee was of the view that the import may be considered only for Phase-I trials.

iii. In view of the above stated facts, the Committee decided to await the recommendation of the ICMR Ethical Committee, Experts and DBT before taking a final view on the import of the drug for phase-I clinical trials in India.

12. Permission for Conducting phase III trials of r-Insulin Lispro Cr-DNA origin) by Wockhardt Ltd. Mumbai.

i. The Committee noted that the request for conducting Phase –III clinical trials of r insulin (Lispro) in India and scale up of r- insulin Lispro to 300 L fermenter for R&D work was deferred for want of comments from the Experts in the GEAC meeting held on 8.6.2005. Subsequently the proposal has been recommended by the RCGM and experts.

ii. After detailed deliberations and taking into consideration the views of the Expert, DCGI and RCGM, the Committee approved the conduct of Phase –III clinical trials of r insulin (Lispro) in India and scale up of r- insulin Lispro to 300 L fermenter for R&D work.

13. Permission for phase III clinical trials on r-h FSH, 75 IU u mcg by M/s. Bharat Serum and Vaccine Ltd. Mumbai.

i. The Committee noted that the pre-clinical data was considered by the RCGM in the meeting scheduled for 1.8.2005. Taking into consideration that the recommendation of RCGM on the safety and efficacy of the product is necessary before the proposal is approved for phase-III clinical trials, the Committee decided to consider the proposal after receipt of the RCGM recommendations and views of Experts.

14. Permission for import and marketing of r-human Granulocyte Macrophage Colony stimulating factor in (GM – CSF) by Emcure Biotech Ltd. Pune, from Shenghai Hygene Biopharma Company Ltd. China.

i. One of the Members pointed out certain discrepancies in the agenda note at para 4.14.3 in respect of information regarding the prior approvals granted by the GEAC for similar products. It was decided to reconsider the proposal in the next GEAC after the discrepanciy pointed out was reconciled.

15. Permission for Phase III Clinical trials on r-h GCSF manufactured by M/s. Wockhardt Ltd. Mumbai.

i. The Committee noted that the above proposal was earlier considered by the GEAC in its meeting on 12.1.2005 wherein it was decided to seek clarification from RCGM on the safety and purity profile of the product. The Committee considered the clarifications received from the Member Secretary, RCGM and also noted that the Company has adequate containment facilities at R & D and production unit to meet the environmental safety regulations.

ii. In view of the above stated facts, the Committee approved the Phase III Clinical trials on r-h GCSF manufactured by the Company.

16. Permission to import Erythropoietin (EPREX- with HAS, EPREX-without HAS and Neorecormon) for Test Analysis by M/s Wockhardt Ltd. Mumbai.

i. The Committee noted that the request for import of the above products from Europe for isolating API and testing the same for detailed structural analysis was considered by the GEAC in its meetings held on 8.12.2004 and 10.2.2005. However decision on the proposal was deferred as the company had not submitted its application for revalidating the GEAC clearance for manufacture and marketing of Erythropoietin in India which had expired in July 2004. The Committee noted that the explanation provided by the Company and their request for revalidation of the GEAC clearance was considered and approved by the GEAC in its 56th meeting held on 8.6.2005.

ii. After detailed deliberation and taking into consideration that the present request for import of EPREX-with HAS, EPREX-without HAS and Neorecormon is for the purpose of test analysis only, the Committee approved the proposal.

17. Permission to export limited quantity seed of transgenic cotton containing 'vip 3A' insect-resistance gene Event COT-202 for research purposes to Burkina Faso, Africa Permit by M/s Syngenta Seeds India Pvt. Ltd.

i. The Committee noted that the above proposal was considered by the GEAC in its 56th meeting held on 8.6.2005 wherein it was decided to obtain certain clarifications from the Company

regarding the purpose of import of *vip* 3 A gene from USA, source of Indian material and geographical indication of the background into which the *vip* 3 a gene has been transferred and justification for withdrawing the product from large-scale trials in India. The Committee considered the clarifications received from the Company. The Committee also gave an opportunity to the representative of the Company to present their views on the matter. The following points were noted:

a) With the approval of RCGM, the Company has imported seeds of different events, Viz., COT-102, COT-202 and COT-203, of transgenic cotton containing vip 3A gene from USA for the purposes of testing and evaluation, crossing/back-crossing with various elite germplasm lines and development of hybrids suitable for cultivation.

b) The material intended for export is Vip Cotton Hybrid (F1 Seed) of Event COT-202 whereas the GEAC approval was for conduct of large-scale trials (LST) of Vip Cotton hybrid (F1 Seed) of Event COT-102. To a query regarding the reasons for not conducting the LST it was clarified that few experimental hybrids prepared with other events showed higher efficacy against the target pest as compared to COT-102. Also taking into consideration that the efficacy could be further increased by stacking vip 3A with cry gene it was considered prudent to pursue LST only after further testing of other events especially when so many Bt hybrids have been recently released.

c) Regarding the reason for export it was clarified that the Syngenta affiliated Company in Burkina Faso has initiated preliminary testing and evaluation of Vip Cotton in the country and the purpose of export is to compare the performance of Vip Cotton pure lines received from USA with a hybrid of Vip Cotton which is available only in India.

d) Vip Cotton of event COT-202 is a first generation experimental hybrid suitable only for testing the efficacy of the gene against target pests and has not been bred for agronomic parameters required for commercialization.

ii. The Committee deliberated at length on the comments received from Chairman NBA and explanation given by the Company. Views were expressed that LRA-5166 is one of our best available cotton germplasm and some members concern as it involves outflow of germplasm from the country without any economic benefit. Some Members cautioned that India may be used as a testing ground for various bio-materials, in future, if export of genetic material at the trial stage is permitted. Views were also expressed that outflow and inflow of genetic material is necessary in the scientific interests.

iii. After detailed deliberations, the Committee decided to await the recommendation of the Agro Biodiversity Task Force constituted by NBA and also refer the proposal to NBPGR for their comments. Decision on the proposal was, therefore, deferred.

18. Permission for export of Bt Eggplant transgenic seeds containing Cry 1 Ac gene to institute of Plant Breeding, College of Agriculture, University of Philippines, East West Seeds (Bangladesh) Ltd, and Bangladesh Agriculture Research Institute by M/s. Mahyco.

i. The Committee noted that the above application is for export of Bt Eggplant transgenic seeds containing Cry 1 Ac gene to Bangladesh and Philippines.

ii. The Committee considered the comments of Chairman NBA and noted the above proposal is similar to the proposal of M/s Syngenta at agenda 4.17 and therefore the decision taken therein would be applicable in this case. One of the members pointed out that this case is different from that of M/s Syngenta as in the present proposal M/s Mahyco has obtained the non-transgenic bringal

seeds from Bangladesh and Philippines and transgressed the Bt gene into the Bangladesh and Philippines germplasm by backcrossing with the Indian parental lines.

iv. After detailed deliberations, the following decisions were taken: -

a. Await the recommendation of the Agro Biodiversity Task Force constituted by NBA
b. Refer the proposal to NBPGR for their comments.
c. Obtain the following clarifications from the Company:

- The purposes of import of cry 1 Ac gene from USA as per the original application from RCGM.
- Details of the source of Indian material into which the Cry 1 Ac gene has been transferred.
- Geographical indication of the background into which the Cry 1 Ac gene has been transferred.

v. Decision on the proposal was therefore deferred.

19. Permission to scale up of r- Insulin produced by Pichia pastoris R & D work to 300 L fermenter by Wockhardt Ltd. Mumbai

i. The Committee noted that above request was considered by the GEAC in the meeting held on 8.6.2005, but deferred for want of comments from DBT and other experts. The Member Secretary informed that the Expert has subsequently recommended the case.

ii. After detailed deliberations and taking into consideration that the proposed scale-up operation is only for the purpose of R&D, the Committee approved the proposal.

20. Representation from J K Seeds regarding permission for large-scale trials and seed production of Bt Cotton varieties containing cry 1 Ac gene (Event 1) developed by the company.

i. The request of the Company to reconsider the earlier GEAC decision regarding seed production and number of years for LST was deliberated at length.

ii. The Committee noted that the decision of 8.6.2005 has given rise to some anomalies and inconsistency in the GEAC decision with the previous decisions of 4.3.2005 wherein the GEAC, while considering proposals for the North Zone, had permitted Bt cotton seed production in an area of 100 ha during first year LST for all hybrids/ varieties irrespective of the whether it was a hybrid containing a new gene /event or an approved event. Similarly, no specific condition on the two-year requirement of LST was stipulated for the North Zone.

iii. The recommendations made by Dr. S. Nagarajan, Chairman of the sub-Committee was also placed before the GEAC. The Committee noted that the report of the sub-Committee is expected by end of August by which time the sowing season even in the South Zone would be over.

iv. After detailed deliberations and taking into consideration the need for removing the anomaly in the decision and for maintaining consistency, it was decided that seed production may be permitted in an area up to 100 ha during the first year LST. The Committee also decided that the decision pertaining to increased seed production would be applicable to all similar proposals containing new gene/event approved by the GEAC for LST during Kharif 2005.

v. On the request for relaxation of the condition pertaining to two years of LST, views were expressed that there is no seasonality involved with this request as the second year LST can be initiated only in Kharif 2006 and therefore it was decided that this matter may be taken up after receipt of the report of the Sub-Committee on Bt cotton and related issues.

21. Proposal for alternate Monitoring Mechanism to evaluate large scale trials and post release monitoring of transgenic crops.

i. The Committee briefly discussed the proposal for alternate Monitoring Mechanism to evaluate large-scale trials and post release monitoring of transgenic crops prepared by DBT.

ii. The Committee requested the Member Secretary GEAC to forward the proposal to the respective State Govts and Vice Chancellors of the SAUs for their comments and submit the consolidated views for consideration of the Committee in its next meeting.

22. Representations from NGOs with reference to the findings of CICR, Nagpur reported in "Current Science" , July 2005.

i. The Committee discussed the CICR article 'Temporal and intra-plant variability of Cry1Ac expression in Bt-cotton and its influence on the survival of the cotton bollworm, *Helicoverpa armigera* (Hubner) (Noctuidae: Lepidoptera)' by K.R. Kranthi et al., from the Central Institute for Cotton Research (CICR) which was recently published in the Current Science, 89 (2):291-298, 2005 (July 25, 2005) and the allegations made by the NGOs in respect of the findings of the CICR study.

ii. One of the expert Members pointed out that there was nothing new or unnatural in the findings of the CICR report and the variability in the quantitative levels of Cry1Ac among different hybrids and the variability in the Cry1Ac expression between different plant parts are established facts and it does not necessarily mean that the Bt technology is inadequate to confer protection from bollworms in cotton plants.

iii. Dr Kranthi, Scientist from CICR and one of the authors of article published in the Current Science stated that the findings of the study have been misquoted by the NGOS and is out of context. In the meeting he provided the Committee with a written response on the various allegations/representations received in the Ministry. Views were also expressed that CICR, as a scientific organization, should take necessary action to counter the allegations and put the issues in proper perspective as the findings of CICR are being quoted by NGOs all over the World.

iv. After a brief discussion on the matter and taking into consideration the request by Members for more time to go through the written submissions provided by Dr Kranthi, it was decided to consider the matter in the next GEAC meeting.

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