Record of the 58th Meeting of the Genetic Engineering Approval Committee (GEAC) held on 14th September 2005.

The 58th Meeting of Genetic Engineering Approval Committee was held on 14th September 2005 at 10.30 AM in the Ministry of Environment and Forests under the Chairmanship of Shri Suresh Chandra, Special Secretary & Chairman GEAC. List of participants is annexed.

At the outset of the Chairman welcomed all the members and requested the Member Secretary to take up the agenda items for discussion.

1.0 Leave of Absence

1.1 The Committee noted that Dr. A. K. Bhatnagar, Member GEAC has informed that he will not be able to participate in the meeting due to other prior commitments. Leave of absence was granted.

2.0 Confirmation of Minutes of 57th Meeting of the GEAC held on 10th August 2005.

2.1 The Member Secretary informed the committee that the minutes were circulated on 30.8.2005 and no written comments on the minutes have been received. However, one Member desired to redraft the minutes agenda item 6.1, para 6.1.2 and 6.1.3 as follows:

6.1.2 One of the expert Members pointed out that there was nothing ***unusual or startling*** in the findings of the CICR report and the variability in the quantitative levels of ***expression of the same gene in different genetic background, different tissues of the organisms and in different environment are a common occurrence***. This does not necessarily mean that the Bt technology is inadequate to confer protection from bollworms in cotton plants.

6.1.3 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 ***misinterpreted*** by the NGOS and is ***quoted*** 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".

2.2 The Minutes were confirmed subject to above amendment.

3.0 Follow up on the decisions taken in the 57th GEAC Meeting.

3.1 The Member Secretary informed the Committee that GEAC decisions have been communicated to the project proponents, concerned government departments and

other agencies. Details of action taken were placed before and noted by the Committee.

A. Pharmaceuticals

Agenda Item No. 4:- Consideration of Proposals.

4.1: Permission for import of bulk r-Erythropoietin from BioGenerics, Germany for formulations and subsequent export to Germany, by M/s Gland Pharma Ltd., Hyderabad

The Committee noted that M/s Gland Pharma intends to import bulk material of Erythropoietin concentrate from M/s BioGenerix Germany. The Company is not going to manufacture bulk material in their facility. They will formulate the bulk received from M/s BioGenerix into prefilled syringes (PFS) for the purpose of 100% export. The facilities for PFS set up by M/s Gland Pharma Ltd. have been approved by USFDA.

The Committee also gave an opportunity to the representative of the Company to present their case wherein it was clarified by them that the facility for PFS has the approval of USFDA and the product r-Erythropoietin is being imported from M/s Biogenerix which is a European Directorate of Quality Medicines (EDQM) certified company. Subsequently they confirmed this in writing. Since the proposal is for 100% export, information on the prescribed import-export norms was also sought. It was clarified that the Advance License Committee under DGFT will consider the proposal only after approval of the GEAC.

In view of the declaration submitted by the Company and taking into consideration that the proposal is for 100% export, the Committee approved the request for import of bulk material of Erythropoietin concentrate from M/s BioGenerix Germany and subsequent export of PFS.

4.2: Permission for import of Actilyse (recombinant human tissue type plasminogen activator) 50 mg for use in clinical study from Germany by M/s Sanofi Aventis, Mumbai.

4.2.1 The Committee noted that the present proposal is for import of Actilyse (recombinant human issue type plasminogen activator) 50 mg for ExTRACT study from Germany by M/s Sanofi Aventis .from Mumbai. The Company requires Actilyse as a fibrinolytic agent for use in clinical study of Enoxaparin which has been initiated in India since 2003. The Member Secretary informed that as per the information furnished by the Company, the product r-Actilyse is already in use in India, since the Company was purchasing the product locally from German Remedies Ltd. who was marketing this product for Boehringer Ingelheim. As German Remedies Ltd. has stopped marketing the product, it is not available in India and therefore the Company now proposes to import the same directly from Germany.

4.2.3 During the deliberations, it was also noted that DCGI vide their later dated 2nd August 2005 has accorded approval for import (test license) of Actilyse for the purpose of examination, test or analysis to be conducted in India. However, even though the product has been in use for quite some time, approval of GEAC has not been obtained for import of r-Actilyse by M/s German Remedies. Therefore, the Committee was of the view that the present request may be considered afresh as a new case.

4.2.4 After detailed deliberations, it was decided to obtain the following:

a. How long the product has been in use by the Company and the quantity imported so far?
b. Whether the product has been earlier imported with the approval of DCGI?
c. Reasons for not obtaining the approval of GEAC earlier.

4.2.5 Decision on the proposal was meanwhile deferred.

4.3: Revalidation Permission for manufacture and marketing r-human Granulocyte Colony stimulating factor (G-CSF) by M/s Dr. Reddy's Lab. Ltd., Hyderabad.

4.3.1 The Member Secretary informed that the GEAC in its 25th meeting held on 27.3.2006 had approved the manufacture and marketing r-human Granulocyte Colony stimulating factor (G-CSF).

4.3.2 As per Rule 13(2) of the 1989 Rules, the approval of GEAC is valid for four years at the first instance and in the subsequent years renewal is required every two years. The firm has requested for revalidation of the GEAC permission for a period of two years.

4.3.3 The Committee conveyed their 'No Objection' for revalidation of the GEAC clearance dated 11.04.2005.

4.4: Permission for import of EGF-R Neutralizing monoclonal antibodies hR3 TheraCIM from Centre of Molecular Immunology, Cuba to conduct phase II Clinical Trials by M/s Biocon Biopharmaceuticals.

4.4.1 The Committee noted that the GEAC in the 46th Meeting held on 8.9.2004 had approved the import of 1500 vials of the EGF-R Neutralizing monoclonal antibodies hR3 TheraCIM, for conduct of phase-II clinical trials in India.

4.4.2 In respect of the company's present request for import of additional 1000 vials of EGF-R Neutralizing monoclonal antibodies hr3 Thera CIM for conduct of phase II clinical trials in India, the Committee was of the view that results of the clinical trials conducted so far and clarification on the need for additional import may be obtained.

4.4.3 Decision on the proposal was therefore deferred.

B. Reconsideration Cases

4.5: Permission for import and marketing of r-human Insulin APIDRA by M/s Sanofi Aventis Pharma Ltd. Mumbai.

4.5.1 The Committee noted that the above proposal was considered by the GEAC in its 53rd meeting held on 13.4.2005 wherein it was decided to seek additional information in respect of the observations made by the Expert Member.

4.5.2 The Committee considered and deliberated on the following information submitted by the Company:-

> "The study under reference at a above is a repeated dose toxicity study wherein normoglycemic animals have been dosed once or twice daily, in the Toxicological studies in dogs, human insulin was not used as a comparator to glulisine as this was done in rats. However, in pharmacological studies in dogs, human regular insulin was used as a comparator to insulin glulisine. In these studies the pharamacodynamic property i.e. the blood glucose lowering activity in vivo, was similar for insulin glulisine and human regular insulin. Therefore we conclude that the same effects induced by hypoglycaemia can be expected for human regular insulin as this was seen for insulin glulisine.
>
> Apidra (insulin glulisine) is the global Aventis product and has already undergone extensive clinical trials abroad including PhaseI, II and III. In fact this product has already been approved for marketing in Germany and USA. We would be directly importing the finished formulation of Apidra and hence are not required to repeat Phase I and II trials in India as per Drug Rules. As mentioned before the need to conduct Phase III clinical trials is decided by the DCGI in the Ministry of Health and Family Welfare. We will consult the same for further discussion separately."

4.5.3 The need for using such intensive Protocols whereby the animals have to be euthanized after the study was also discussed. It was clarified that "significant hypoglycemia associated with deteriorating clinical conditions" observed in the two dogs tested was a drug induced symptom and not because of the intensity of the protocol or dosage.

4.5.4 After detailed deliberations and taking into consideration the views of DBT, ICMR and Expert Member, the Committee approved the request for import and marketing of r-human Insulin APIDRA subject to DCGI clearance.

4.6: Permission for import and marketing of r-human Granulocyte Macrophage Colony stimulating factor in (GM - CSF) from M/s Shanghai Hygiene –Biopharma Company Ltd., China by M/s Emcure Biotech Ltd., Pune.

4.6.1 The Member Secretary informed that the GEAC in its meeting held on 27.11.2003 had approved the import of r-human Granulocyte Macrophage Colony stimulating factor in (GM CSF) imported from Shanghai Hygiene Biopharma Company Ltd., China for conducting phase III cinical trials in India. The Phase -III clinical trials have been completed and the present request is for import and marketing the product in India. The Company has conducted an open - label clinical study at Jehangir Hospital and Ruby Hall Clinic, Pune as per the protocol approved by the DCGI and with the approval of Medical Ethical Committee.

4.6.2 After detailed deliberations, the Committee decided to refer the proposal and clinical trials study report to the following Experts:

a. Dr. Vinod Kochupulla, AIIMS
b. Dr. K. T. Dimsha, Tata Memorial Cancer Hospital, Mumbai
c. Director, Rajiv Gandhi Cancer Memorial Hospital, New Delhi

4.6.3 Decision on the proposal was therefore deferred

Agenda Item No. 5. Other Items

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

5.1.1 The Committee noted that the response of the concerned State agencies on the above proposal is awaited. As adoption and implementation of the alternate monitoring mechanism will take some more time, the Committee requested RCGM to extend the tenure of the MEC which has expired on 4.9.2005 so that the monitoring and evaluation of the large scale trials authorized by GEAC during Kharif 2005 are carried out in a timely manner. In view of the fact that the cotton crop season is likely to be over by end of October in the North Zone, the Committee advised that this matter may be given utmost priority by RCGM.

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

5.2.1 The Committee discussed the findings of CICR, Nagpur as reported in "Current Science" and representation received from some NGOs on the above matter.

5.2.2 The Committee was of the view that the facts presented in Dr. Kranthi's papers do not speak against the efficacy and safety of the Bt gene in cotton. The decision to approve Bt technology was based on extensive laboratory and field data and none of the results presented by CICR negate that. The GEAC was aware that there is a possibility of variation in the Cry 1Ac protein expression in specific tissue of the plant depending on the genetic background of the host and the environment in which it is deployed. Taking into consideration the above fact the GEAC has taken a decision to approve the Bt hybrids on a case-by-case basis. All hybrids approved by the GEAC for release have been

tested at several sites in the various zones. It is also a fact that Bt technology does not confer 100% elimination of bollworms and therefore there is a need to follow the prescribed IPM approach. It may be noted that the conditions stipulated by GEAC require that information on Bt based Integrated Pest Management is included in the seed packet. The Committee was of the view that the ongoing initiatives to increase awareness of farmers on the use of Bt technology should continue and should include this aspect specifically. In view of the biotechnological advancements, the Committee concluded that the present practice of reviewing the performance of released Bt cotton hybrids after every three years should also continue.

Agenda Item No. 6. Any Other item with the permission of the Chair.

6.1 The Member Secretary informed the Committee that the report of the sub-Committee on Bt Cotton and related issues under the Chairmanship of Dr S Nagarajan, Director, IARI and the report of the Task Force on r-Pharma under the Chairmanship of Dr RA Mashelkar, DGCSIR have been received. A copy of the reports was given to the Members for their comments and consideration of the GEAC in one of its subsequent meetings.

6.2 Shri D D Verma, JS & Vice Chair also briefed the Committee on the recent proposal mooted by MOA to set up a National Biotechnology Regulatory Authority under the aegis of MOA. The Ministry is preparing the comments on the proposal and the same would be send to MOA soon.

Date of Next GEAC Meeting

It was decided that in view of Dusshera, the next GEAC meeting will be held on **10th October, 2005 at 1.30 PM** instead of 12.10.2005.

The meeting ended with a vote of thanks to the Chair.

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List of the participants who attended the 58th meeting of the GEAC held on 14th September, 2005 in the Ministry of Environmental & Forests, New Delhi

S. No.	Name of the participants
1.	Shri Suresh Chandra, Chairman, GEAC
2.	Dr. Amit Ghosh, Co-Chairman GEAC
3.	Shri D. D. Verma, JS, MoEF and Vice-Chair
4.	Dr. Sushil Kumar, Expert Member GEAC
5.	Dr. V. Vasantha Muthuswamy, Chief BMS, ICMR
6.	Dr. T. V. Ramaniah, Director DBT, Member GEAC
7.	Dr. S. K. Mahajan, Member GEAC
8.	Dr. R. P. Sharma, Member GEAC
9.	Prof. Subhash Chand, Member GEAC
10.	Shri Harish Prasad, Director (Seeds) MOA
11.	Shri K. C. Jain, ICAR
12.	J. P. Charasuia, Scientist, RPBD, Council for Scientific & Industrial Research
13.	Dr. Chetan Brat, Sr. Dy. Advisor, RPBD, CSIR
14.	Dr. (Mrs.) S. Kulshreshtha, Directorate of Plant Protection Quarantine and Storage
15.	Dr. B. K. Chaudhary, Senior Environmental Engineer, CPCB
16.	Dr. R. Warrier, Additional Director & Member Secretary GEAC
17.	Ms. Madhu Gupta, Research Officer, MoEF

Special Invitees

1.	Dr. K. K. Tripathi, Advisor, DBT

Company Representatives

1.	Shri P. Ramesh Kumar, Gland Pharma Ltd., Hyderabad