Decisions taken in the 40th Meeting of the Genetic Engineering Approval Committee (GEAC) held on 31st March 2004.

Opening Remarks of the Chairperson

The Chairperson outlined the following actions being taken by the Ministry in the direction of greater speed, transparency, and general streamlining.

1. As an initiative to streamline the regulatory process in the Pharma sector, a consultative meeting with the major industry Associations and other Central Departments was held on 22nd March 2004 under the Chairmanship of Secretary (E&F) in the Ministry of Environment & Forests. In the above meeting it has been decided to set up a Task Force for suggesting measures to streamline the regulatory process for the recombinant Pharma sector.

2. Decisions taken in the GEAC meeting would be put up on MoEF website with the status of projects pending consideration of the GEAC.

3. All proposals (complete in terms of requisite documents) received in the Ministry 30 days prior to the next GEAC meeting would be submitted for consideration in the subsequent GEAC meeting.

DECISIONS

1. Permission for Import and marketing of Recombinant Human Erythropoitein (EPOSINO) Manufactured by M/s Sandong Kexing Pharmaceuticals Co. Ltd. people of China by M/s. Hindustan Bio-Sciences Ltd. Hyderabad.

1.1 The Committee noted that response of the experts on the additional information submitted by the company has not been received. The Committee requested DCGI and the assigned Experts to forward their comments on priority basis. The Committee concluded that the proposal will be reconsidered on receipt of comments from the Experts and DCGI. It was also agreed that the company be invited to make a presentation and provide the necessary clarifications to the GEAC.

2. NOC for use of enzyme produced from Genetically Modified Organism in preparing bread by M/s. Zytex Corp. Mumbai.

2.1 M/s Zytex Corp. Mumbai, have submitted an application vide their letter dated 9.4.2002 for manufacture of bread improvers using four enzymes produced by Novozymes namely Novamyl 1000 BG, Pentopan Mono BG, Lipopan 50 BG and Lipopan F imported from M/s Novozymes, Denmark.

2.2 Considering that the enzymes are being used for edible products, the Committee deliberated at length issues related to food safety assessment, purity profile of the enzymes and labeling of food product containing GM ingredient. The Committee also invited the representative of the company to make a presentation on the proposal.

2.3 After detailed deliberations, the Committee concluded that the company may be advised to submit the following details along with supporting documents:

- Clearance from the Codex Committee of Denmark.
- Enzyme production is listed as GRAS by the US Food & Drug Administration.
- Permission for marketing in the host country.
- Response to issues raised by ICMR.
- Purity profile of the product.

2.4 It was agreed that the proposal would be reconsidered by the GEAC on receipt of requisite information sought by the GEAC. The Committee also requested MoFP&I to expedite their comments.

3. Import of PTBIB Protein (Human recombinant) for R&D Purpose by M/s Torrent Pharmaceuticals Ltd. Ahmedabad.

3.1 Noting that the request is only for limited import for R&D purpose, and considering the comments received from the DBT and one of the experts on the proposal, the GEAC accorded approval from environmental angle subject to compliance of statutory requirements under EPA and Drugs and Cosmetic Act.

4. Permission for import and marketing of r-human growth hormone (somatropin) Formulations by M/s. Novo-Nordisk India Ltd., Bangalore from M/s Novo-Nordisk A/S. Novalle, 2880, Bagsvaerd, Denmark.

4.1 It has come to the notice of this Ministry that the product is being imported into the country without the approval of GEAC. On seeking clarification from the company, they have confirmed vide their letter dated 8.3.2004 that they have been importing the product under OGL since 1991.

4.2 The Committee agreed that Company be asked to explain the circumstances for not complying with the regulatory requirements under 1989 Rules before the request is considered.

5. Permission for import and marketing of Luveris 75 I.U. (3.4 mcg) Lutropin alpha from M/s Industria Farmaceutica Serono S.p.A. Zono Industriale dimodugno, 70123, Bari, Italy, by M/s Serum Institute India Ltd. Pune.

5.1 The Committee noted that DBT has recommended exemption of conducting Phase-III clinical trials by the applicant and sought clarification for the basis of dispensing with Phase III clinical trials in this case. It was clarified by DBT representative in the meeting that the product per se is in the market for more then 15 years and there is a low population using the product (like 10,000 from the whole world) and therefore it takes a long time for conducting Phase III clinical trials.

5.2 Considering the recommendations of DBT and noting that the present product has been evaluated systematically for its safety and efficacy and the product is approved in 36 countries which include European & developed countries, the GEAC approved the import and marketing of the product subject to two years of PMS and other statutory requirements under EPA and Drugs and Cosmetic Act.

6. Permission for Import and marketing of r-human Hepatitis B Vaccine Hexavalent by M/s Aventis Pasteur India Ltd. from M/s Aventis Pasteur's France.

6.1 During the course of deliberations, the Committee noted that though the product is claimed to be marketed in 15 countries, the component of IPV in the Hexavalent vaccine is still not experienced in the country at large scale.

6.3 Since the comments of the experts and DCGI have not been received and the information on Quality Control data, Toxicity Data and Stability data are still under examination by the DCGI, the Committee decided to await the views of DCGI with specific reference to the purity and efficacy of the product and MOH/ICMR on the issue of bringing IPV component in the vaccine before taking a final view on the proposal**.**

7. Permission for Import and marketing of r-human Insulin from M/s. Bioton Co. Ltd, Warszawa, Poland by M/s Shreya life Sciences Pvt. Ltd. Bangalore.

7.1 The GEAC in its 35th Meeting on 6th March 2003 approved the limited import of the product for conducting Phase-III human clinical trials to establish the safety and efficacy of the product. The Phase-III clinical trial data in India for establishing safety of the product has been conducted by the applicant. The Applicant has now approached the GEAC for the import and marketing of r-human insulin to the tune of 100,000 Vials per year from M/s. Bioton Co. Ltd, Warszawa, Poland by M/s Shreya life Sciences Pvt. Ltd. Bangalore.

7.2 The Committee noted that DBT has recommended import and marketing of the product. However noting that the information on Quality Control data, Toxicity Data and Stability data are still under examination by the DCGI and recommendations of other experts have also not been received, the Committee decided to await the views of DCGI with specific reference to the purity and efficacy of the product before taking a final view on the proposal.

8. Permission for Manufacture and marketing of r-human pentavalent vaccine by M/s. Panacea Biotech Ltd., New Delhi.

8.1 M/s. Panacea Biotech Ltd., New Delhi has submitted the proposal for manufacture and marketing of r-human Hepatitis B pentavalent vaccine at Okhla Industrial Area, New Delhi. Pentavalent vaccine is for active immunization of children against disease caused by relevant organisms. The GEAC in its 33rd Meeting on 5th July 2002 accorded approval for the above product for Phase-III human clinical trials to establish the safety and efficacy of the product. The Phase-III clinical trial data in India for establishing safety of the product has been conducted by the applicant. The Applicant has now approached the GEAC for the import and marketing of r-human hepatitis B pentavalent vaccine in India. Applicant wants to manufacture 20 Million per year doses. The source of Hepatitis B is Cuba.

8.2 Since the information on Quality Control data, Toxicity Data and Stability data are still under examination by the DCGI and recommendations of other experts have also not been received, the Committee decided to await the views of DCGI with specific reference to the purity and efficacy of the product before taking a final view on the proposal.

9. Permission for Import and marketing of r-human Granulocyte colony stimulating factor rhG-CSF from M/S. Shanghai Sunway Biotech, China by M/s Emcure Biotech Ltd. Pune.

9.1 The GEAC in its 37th meeting held on 16th June 2003 has accorded approval for Phase III human clinical trials to establish the safety and efficacy of the product. The Phase-III clinical trial data in India for establishing safety of the product has been conducted by the applicant. The Applicant has now approached the GEAC for the import and marketing of r-human Granulocyte colony stimulating factor rh-G-CSF from M/S. Shanghai Sunway Biotech, China by Emcure Biotech Ltd. Pune.

9.2 Since the information on Quality Control data, Toxicity Data and Stability data are still under examination by the DCGI and recommendations of other experts have also not been received, the Committee decided to await the views of DCGI with specific reference to the purity and efficacy of the product before taking a final view on the proposal.

10. Permission for production of transgenic cotton hybrid seeds and for release and Commercial marketing of RCH2 Bt in Central and South Zones, RCH 138 Bt. and RCH 144 Bt. in Central Zone and RCH 20 Bt. in South Zone, by M/s Rasi Seeds Pvt. Ltd., Salem, Tamil Nadu.

10.1. M/S. Rasi Seeds P. Ltd. Salem Tamil Nadu have submitted an application seeking approval of GEAC for commercial release, marketing and seed production (as per farmers demand) of the following hybrids:

a) RCH 2 Bt in Central and South Zone
b) RCH 138 Bt, and RCH 144Bt in Central Zone, and
c) RCH 20 Bt. South Zone**.**

10.2. The GEAC in its 37th meeting held on 13th June, 2003 had approved conduct of large scale trials in all three varieties in the respective zones. Besides, the GEAC had also accorded permission for seed production in an area of 100 ha, in case of RCH 2 Bt and in an area of 10 ha each for the remaining varieties. While according these decisions, GEAC had taken due cognizance of the fact that RCH 2 Bt hybrid is a direct derivative of the already released RCH 2 non Bt hybrid which has been released through All India Coordinated Cotton Improvement Project (AICCIP) in 1999 and notified by Department of Agriculture and Co-operation of Ministry of Agriculture on 3rd April, 2000.

10.3. The committee took note of the findings of the MEC on the large scale trials in farmers' field carried out by the company during Kharif 2003 as well as the findings of the ICAR under the AICCIP trials during Kharif 2003 & 2004.

10.4 After detailed deliberations the GEAC took the following decisions:

a. The committee concluded that RCH 2 Bt hybrid, a direct derivative of the RCH 2 non Bt hybrid which has been released through All India Coordinated Cotton Improvement Project in 1999 and notified by the Dept. of Agriculture and Co-operation of Ministry of Agriculture on 3rd April, 2000 has specific advantage over the other three hybrids in terms of agronomic benefits and fibre quality. Further, during the large scale trials, RCH 2 Bt has been tested for its adaptability over a wider representative region as compared to the other three hybrids. In view of the above and taking into consideration positive findings of ICAR and MEC regarding the superiority of RCH 2 Bt, the GEAC recommended commercial release of RCH 2 Bt for the Central and Southern zone from Kharif 2004.

b. The commercial release of RCH 2 Bt is subject to compliance of various safeguards and conditions stipulated by the GEAC while according approval to M/s Mahyco for the three hybrids (MEC 162, MEC 184 and MEC 12) released during Kharif 2002.

c. The committee further recommended that the post release monitoring of RCH 2 Bt would be carried out by MOA jointly with the State Dept. of Agriculture and Agriculture Universities. A detailed report on the performance of RCH 2 Bt would be submitted to the GEAC end of every Kharif season.

d. In the other three cases namely RCH 20 Bt, RCH 138 Bt and RCH 144 Bt, the committee concluded that for a reasonable certainty about the findings evinced as per the existing trials, it was desirable to have large scale trials for another crop season (Kharif 2004) It was felt all the more necessary since the adaptability of these hybrids during large scale trials has been tested only over a limited region. To evaluate the consistency in the performance of RCH 20 Bt, RCH 138 Bt and RCH 144 Bt, the GEAC therefore, recommended large scale trials of RCH 20 Bt in the southern zone and RCH 138 Bt and RCH 144 Bt in the Central zone during Kharif 2004 over an area of 150 ha (50 location each in the respective zones).

e. The MEC would evaluate the performance of RCH 20 Bt, RCH 138 Bt and RCH 144 Bt during the large scale trials in Kharif 2004 on a random and representative sampling basis. The MEC would submit its report for consideration of the GEAC.

11. Permission for Import and marketing of Interleukin –2(r IL-II) from M/s Benging Four Rings Bio-engineering Product Factory China by M/s. Kee Pharma Ltd. New Delhi.

11.1 The company intends to import and market at least 300,000 Vials of 100, 000 or 200, 000 or 500,000 or 1000,000 IU/vials in a year. The product is approved for marketing in the host country only and did not apply for registration in any other country. The Phase-III clinical trials have been done in country of origin only.

11.2 The Committee noted that DBT has approved only limited import of the product for conducting Phase-III clinical trials. However, noting that the proposal is under evaluation concerning with quality, safety and efficacy, the Committee decided to await specific comments of DCGI on the above matter before taking a final view on the proposal.

12. Permission for Import and marketing of r-human interferon alpha –2b from M/s Tianjin Hualida Biotechnology Company Ltd. P.R. China by M/s. Kee Pharma Ltd. New Delhi.

12.1 The Committee noted that comments from DBT have not been received. Further the proposal is under evaluation concerning with quality, safety and efficacy by the GEAC. The Committee decided to await specific comments of DBT & DCGI on the above matter before taking a final view on the proposal.

13 Permission for Seed Production of Transgenic Cotton Hybrids and Release and commercial Marketing of RCH-134 Bt. 250 Hectare and RCH-138 Bt. 250 Hectare in North Zone by M/s Rasi Seeds Pvt. Ltd. & MRC 6301 and MRC 6304 Bt in North zone by M/s Mahyco.

13.1. M/s Rasi Seeds Pvt. Ltd. Salem and M/s Mahyco requested for GEAC's permission to undertake seed production and commercial release of transgenic cotton hybrids namely RCH-134 Bt and RCH 138 Bt and MRC 6301 and MRC 6304 Bt (containing Cry 1 Ac gene) respectively in the northern region.

13.2 The matter of feasibility of the request of immediate commercial release of Bt cotton hybrids made by Govt of Punjab was also considered by the Committee. The committee was of the view that the company has conducted only contained trials under RCGM for Kharif 2002 & 2003 and one year of ICAR trials during Kharif 2003. As per the current practice, a minimum of two years of large scale trials and two years of ICAR trials are mandatory prior to approval for commercial release. Further, in the northern zone the issue of the susceptibility of the Bt hybrids to CLCuV is an area of serious concern which needs to be addressed before commercial release is permitted. The ICAR has specifically indicated that at this stage no specific inference could be drawn based on one year ICAR trials. Both ICAR and Chairman MEC conveyed that the proposal based on the present findings is too pre-mature for its consideration for commercial release. They have however conveyed their no objection to GEAC recommending the proposal for large scale trials.

13.3 In view of the above stated facts and noting the findings of the contained field trials and one year ICAR trials and the recommendations made by ICAR & MEC, it was decided that in accordance with the current regulatory practice, commercial release would be considered by the GEAC only after evaluation of the large scale trial data and two years of ICAR trials. The Committee recommended large scale trials of the RCH 134 Bt, MRC 6301 and MRC 6304 in an area of 50 ha each in the northern zone.

14. Permission for manufacture and marketing of r- Hepatitis B Vaccine by M/s Biological E. Ltd., Hyderabad.

14.1 The above proposal was considered by the GEAC in the meeting held on 27th November 2003 and 3rd February 2004.

14.2 In its meeting held on 31st March 2004, the GEAC had taken the view that since the documents submitted by the company did not adequately address issues regarding containment facilities and other aspects of environmental safety, it was decided that a sub-committee would carry out a site inspection for on the spot verification. A sub-committee comprising of representative of DBT, DCGI & Expert Member visited the unit on 14th February 2004.

14.3 In course of the inspection, it has been reported that as per the company records Phase-III trials had been completed. The Member Secretary informed necessary approval of the GEAC had not been obtained by the company for this purpose.

14.4 The committee decided to request the members of the sub-committee to submit the final inspection report expeditiously. On the issue of the procedural lapse, it was decided to seek explanation from the company as to why the Phase-III clinical trials were conducted without the approval of the GEAC.

15. Permission for manufacture and marketing of r-Streptokinase by M/s Shantha Biotechnics Pvt. Ltd., Hyderabad.

15.1 In its last meeting held on 3rd February 2004 GEAC had decided to condone the procedural lapse by the company with a strict warning & recommended ex-post facto approval for Phase-III clinical trials. As regards the request of the company to permit manufacture & marketing of r-Streptokinase, it was decided to obtain the copy of the IBSC report & corresponding reports of the RCGM from DBT relating to environmental safety aspects. It was further decided to obtain relevant information from the DCGI in the matter of the alleged tests during the clinical trials.

15.2 The matter was discussed and it was noted by the committee that the desired report from the DBT containing the copy of the IBSC report & the minutes of the RCGM meeting has not still been received. This was necessary before taking a final view by the Committee regarding the adequacy or other wise about the contained facilities and other environmental safety aspects. Further, the committee noted that there were few gaps in various reports received from the DCGI and the company in the matter of the reported deaths which needed to be suitably explained.

15.3 After deliberation the Committee took the following decisions:

a) DBT may be requested to forward a copy of IBSC report & the minutes of the RCGM relevant to the issue at hand. In case this had not been duly considered by the RCGM, this may be done accordingly & the minutes furnished.

b) The DCGI may be requested to furnish supplementary information in the light of the discussions held in the GEAC meeting.

16. Permission for revalidation to import and marketing of Injection Human Insulin Lispro (r-DNA) by M/s Eli Lilly & Company (India) Pvt. Ltd., Gurgaon

16.1 M/s Eli Lilly &Company (India) Pvt. Ltd., Gurgaon had submitted the proposal for revalidation to import and marketing of Injection Human Insulin Lispro (r-DNA).

16.2 The committee noted that the GEAC in its 13th Meeting held on 14.11.1996 had approved manufacture and marketing of the Injection Human Insulin Lispro (r-DNA) for a period of four years.

Subsequently the approval was revalidated for a period of two years by the GEAC in the 27th Meeting of GEAC held on 8th August 2001. The present request is for the extension of the approval for two years, This is in accordance with the sectrion 13(2) of the 1989 Rules which stipulates that the approvals of GEAC are valid a period of four years at the first juncture and renewable for two years at a time.

16.3 The committee conveyed their No Objection for revalidation of the GEAC approval.

17. Transfer of approval given by GEAC for import and marketing of Ovidrel – 250 mcg (Recombinant Human Chorionic Gonadotropin/ Chorionogonadtopin Alfa) from M/s Serum International Ltd., Pune to M/s Serum Institute of India Ltd. (Sister Company), Pune.

17.1 The Committee noted that the GEAC in its 39th Meeting held on 3rd February 2004 accorded approval for import and marketing of Ovidrel – 250 mcg (Recombinant Human Chorionic Gonadotropin/ Chorionogonadtopin Alfa) from M/s Serum International Ltd., Pune. The present request made by the company is for transfer of the clearance given by GEAC to M/s Serum International Ltd. Pune, to M/s Serum Institute of India Ltd. (Sister Company), Pune.

17.2 The Committee noted the request made by the applicant and conveyed "No Objection" for transfer of the clearance to M/s. Serum Institute of India Ltd. (Sister Company), Pune.

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