Decisions taken in the 60th Meeting of the Genetic Engineering Approval Committee (GEAC) held on 23rd November 2005.

The 60th Meeting of the Genetic Engineering Approval Committee was held on 23rd November 2005 at 10.30 AM in the Ministry of Environment and Forests under the Chairmanship of Shri Desh Deepak Verma, Joint Secretary & Vice Chairman GEAC.

Decisions

1.0 Permission for import of AVI-005 (interferon-α 2b)- from M/s. AviGenics, Inc (Athens, Georgia) USA for conducting Clinical trials in India By M/s. B.V. Feed Supplements Manufacturing Company Ltd. Pune.

1.1 The Committee noted that while M/s B V Feeds Supplements, Pune would import the product, M/s. AviGenics Inc (Athens, Georgia) USA, has contracted M/s. Siro Clinpharma in Mumbai as the CRO for conduct of human clinical trials. On this issue views were expressed that in cases where two agencies are involved it needs to be clarified as to which agency would be accountable in case of any mishappening or improper trials.

1.2 After detailed deliberations and taking into consideration the views of the Experts on the above proposal, it was decided to obtain the following clarifications from the Company:-

a. Of the two companies involved (M/s B V Feeds Supplements, Pune and M/s. Siro Clinpharma, Mumbai), who would be responsible for any exigencies during the human clinical trials?

b. Whether the patients recruited for the trials would be insured and if so the arrangement with the Insurance Company.

2.0: Permission for clinical trials of r-human Interferon alpha 2b (ReliFeron^{tm}) and NOC to manufacture trial batches for proposed clinical trials by M/s. Reliance life Sciences Pvt. Ltd (RLS), Mumbai.

2.1 The Expert Members informed the Committee that they have not received the project documents. After detailed deliberation and taking into account that representatives of DCGI and ICMR were not available to give their views, the Committee decided that comments of the Experts may be obtained in the first instance. The Committee also advised the Company to submit the requisite documents to the Members.

2.2 Decision on the proposal was therefore deferred.

3.0: Permission for manufacture of clinical supplies and conduct of human clinical trials with r-Streptokinase ('Streptokinase –A') by M/s. Shasun Chemicals & Drugs Ltd. Chennai

3.1 The Committee noted that the Company proposes to conduct a multi-center, prospective, randomized, parallel design, double blind, study to evaluate the efficacy and safety of Streptokinase – A in the treatment of acute ST elevation of myocardial infarction in the 5 at Centers Chennai, Madurai, Bangalore (two centers) and Pune. Total number of patients to be tested is about 120.

3.2 The Committee further noted that pre-clinical animal toxicity studies have been examined by the RCGM in its meeting held on 24.3.2005 wherein RCGM noted that the product is found to be safe. The Committee further noted that the product r-Streptokinase is a drug approved for marketing in India.

3.3 After detailed deliberations and taking into consideration the recommendation of RCGM and the Expert members, the Committee approved the conduct of clinical trials with ('Streptokinase –A') developed by the Company in India.

4.0: Permission for import and conduct of Phase II clinical trials of Chimerivax^{tm} –JE an Japanese Encephalitis Inactivated Mouse Brain Vaccine in children of descending age and assessment of possible interaction with concomitant Measles Vaccine by M/s. Quintiles.

4.1 The Company intends to conduct randomized, double- blind, controlled, safety, tolerability and immunogenicity Phase II trials on 128 subjects at 2 study centers in India.

4.2 It was further noted that Phase-I clinical trials involving 123 US adults' subjects and 405 adults' Australian subjects have been completed. However no safety studies in children have been carried out in these countries. The Committee also noted with concern that the present application is for phase II clinical trials in children of descending age without generating Phase-I trials in children of any JE endemic country of tropical and sub tropical region or country of origin.

4.3 The Committee expressed the need for caution regarding the use of this product in children since the end product being a LMO, the unintentional transmission of Chimerivax –JE by a mosquito feeding on a veraemic individual could be a possibility.

4.4 After detailed deliberations, and taking into consideration the views of the Expert Members, the Committee concluded that views of medical experts needs to be obtained before the request for phase-II with Chimerivax^{tm} –JE is considered. The Committee requested the Member Secretary to obtain comments of medical experts from All India Institute of Medical Science, National Institute of Immunology, New Delhi, National Institute of Virology, Pune and Indian Council of Medical Research.

5.0: Permission for conducting Phase III clinical trials of r-DTwPHb-Hib Pentavalent Combination Vaccine by M/s. Shantha Biotechnics Ltd. Hyderabad.

5.1 The Committee noted the vaccine is for a pediatric use in immunization program. Pentavalent vaccine contains Diphtheria (D) and Tetanus toxoids (T) and the purified major surface antigen of the hepatitis B virus (HBV), Hib poly-saccharide adsorbed on aluminum salts and mixed with inactivated whole cell pertussis (P).

5.2 The Company proposes to conduct a multi-centric, randomized, single blind, three arm study to compare the immunogenicity and safety of indigenously developed DTPwHB-HIB (Liq) Pentavalent combination vaccine with Easyfive^{tm} (Liq) and Tritrantrix^{TM} + Hberix^{TM} in about 400 children. The route of administration is intra-muscular injection and duration of the study period per subject will be 12-15 weeks.

5.3 The Committee further noted that the pre-clinical animal toxicity studies has been examined by the RCGM in its meeting held on 27.10.2005 wherein RCGM noted that the product is found to be safe.

5.4 After detailed deliberations and taking into consideration the recommendation of RCGM and the Expert members, the Committee approved the conduct of clinical trials with of r-DTwPHb-Hib Pentavalent Combination Vaccine developed by the Company.

6.0: Permission to import r-human granulocyte colony stimulating factor (rhg-GSF) from China for conduct of clinical trials in India by M/s. Sun Pharmaceuticals Industries Ltd. Mumbai.

6.1 The Committee noted that the Company proposes to conduct an open label, non-comparative, multi-centric trials in a total of 10 patients as an adjunctive therapy in the nonmyeloid

malignancies. The trials will be conducted at the two centers, Jaslok Hospital and Research Centre, Mumbai and Haemato- Oncology Clinic, Nursing Home and Laboratory, Ahmedabad.

6.2 It was noted that information furnished by M/s Sun Pharmaceuticals Industries Ltd indicates that bulk formulation will be imported from China. The normal practice has been to import the drug in finished formulation at the clinical trial stage and only after market authorization has been granted; the Company imports the drug as bulk for further formulation in the country. The Committee was of the view that the Company may be advised to clarify whether they propose to import finished formulation or in bulk at this stage. In case bulk import is proposed clarification on whether the Company has complied with the requirements of IBSC/ RCGM approvals along with the details of in-house facility for formulation also needs to be obtained.

6.3 Decision on the proposal was deferred till the above information is received.

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

7.1 The Committee noted that the RCGM has examined the pre-clinical toxicological studies data in its meeting held on 21.9.2005 and concluded that the product is safe for human clinical trials. The Committee also noted that the Expert Member and DCGI have conveyed their 'no objection' to the proposal.

7.2 After detailed deliberations and taking into consideration the recommendation of RCGM, DCGI and the Expert members, the Committee approved the conduct of clinical trials with r-h FSH, 75 IU u mcg by M/s Bharat Serum in India.

8.0: 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.

8.1 The Committee noted that the request of the Company for import of additional 1000 vials was considered by the GEAC in its meeting held on 14.9.2005 wherein the Committee was of the view that the Company may be advised to submit results of the clinical trials conducted so far and clarification on the need for additional import.

8.2 The Committee considered the clarifications submitted by the Company and noted that as of date only 20 subjects of the proposed 80 subjects have completed the treatment cycle and it is also proposed to recruit additional 45 more subjects for the clinical trials. Further, it is anticipated that the requirement of h-R3 would increase in treating the enrolled subjects since 1160 vials out of 1500 vials imported have already been used in the clinical trials.

8.3 After detailed deliberations and taking into consideration the clarification submitted by the Company and recommendation of the Expert Members, the Committee approved the import of additional 1000 vials of EGF-R Neutralizing monoclonal antibodies hR3 Thera CIM,

9.0: Request for manufacture and marketing of r-insulin from M/s. Biocon by the following companies:-

- **M/s. Ranbaxy, Gurgaon.**
- **M/s. Lupin Ltd. Mumbai**
- **M/s. Cadilla Pharmaceuticals Ahmedabad**

9.1 The Committee noted that the request of the above Companies to procure bulk insulin from M/s Biocon for further formulation and marketing in India was considered by the GEAC in the meeting held on 10.10.2005 wherein it was decided to obtain the following information from M/s. Biocon:-

- Detailed information regarding the installed capacity for production of r-insulin.
- Names of the Companies to whom bulk r-insulin is being supplied/proposed to be supplied and the corresponding quantities committed for supply by M/s. Biocon.

9.2 The Committee considered the information submitted by M/s Biocon and noted that the information lacks clarity in respect of the actual installed capacity utilized for captive use by M/s Biocon (commercial sale of insulin as drug and in house R & D), quantity presently being sold to other Companies in bulk and quantity proposed to be sold. It was therefore decided to obtain the above information from the Company and reconsider the proposal in the next meeting.

10.0: Permission for manufacture and marketing of r-human interferon alpha (r-DNA Origin) by M/s. Wockhardt, Mumbai.

10.1 The Committee noted that the RCGM in its meeting held on 27.10.2005 has considered the recommendation of IBSC on the adequacy of the containment facility and concluded that the containment facilities available are adequate to meet the environmental norms.

10.2 After detailed deliberations and taking into consideration the recommendation of RCGM, DCGI and the Expert members, the Committee approved the manufacture and marketing of r-human interferon alpha (r-DNA Origin) by M/s. Wockhardt, Mumbai.

11.0: Permission to import parental lines of herbicides tolerant corn by M/s. Monsanto India Ltd., from Monsanto Republic of South Africa.

11.1 The Committee noted that the above request was considered by the GEAC in the 49th meeting held 11.8.2005 wherein MOA, the nodal Ministry for agriculture and food security issues was advised to submit their considered opinion in consultation with ICAR and any other organization they deem fit on whether the country would benefit from the commercial cultivation of herbicide tolerant corn.

11.2 The Committee considered the views of MOA communicated vide their letter dated 3rd October 2005 and noted that the ICAR has advised that the herbicide tolerant maize and its testing, needs to be considered cautiously since the production of maize has been increasing continuously in the country for last five years and the crop has high potential for export in future. However MOA is also of the view that the permission to import 250 gm of seeds from Monsanto, Republic of South Africa by GEAC would not in any case give a blanket authority to Monsanto India Ltd to release whatever products they might develop for commercial release in India as the import is exclusively for research purposes. MOA has also advised that whenever any Company applies for similar permission, they may be advised that India's preference is for drought and insect pests/diseases resistant seeds. Subject to the above condition, MOA has conveyed their no objection.

11.3 After detailed deliberation, the Committee approved the import of transgenic corn seed (250 gm), 50 gm each of four inbred lines and one single cross by M/s. Monsanto India Ltd subject to the following conditions:-

a. The import of transgenic corn seeds shall be exclusively for the purpose of research and shall be carried out in accordance with conditions and safe guards stipulated by the Review Committee on Genetic Manipulation (RCGM) and National Bureau on Plant Genetics and Research (NBPGR), the authorized agencies for granting permission to import transgenic materials for the purpose of research.
b. The research proposal shall have the prior approval of RCGM before initiating the research activity.
c. The clearance will not be treated as blanket approval for product development. The product development if any shall be done in accordance with the procedure prescribed by RCGM and GEAC.

d. In terms of product development, India's preference is for drought and insect pests/diseases resistant crops and not herbicide tolerant crops.

12.0: Permission for bulk seed production and commercialization of transgenic cotton hybrids for South Zone by M/s. Ankur Seeds Pvt. Ltd. Nagpur.

12.1 The Committee noted that the Company has not complied with the mandatory testing procedure and Ankur 651 Bt has not been evaluated in respect of its performance for the south zone. The Committee therefore concluded that the above request does not merit consideration.

13.0: Report of the Sub-Committee on Bt cotton and related issues.

13.1 The Member Secretary presented the recommendation of the Sub Committee constituted by MoEF under the Chairmanship of Dr S Nagarajan, Director IARI and presently Chairman, Protection of Plant Varieties and Farmers Rights (PPVFR) Authority for consideration of the GEAC.

13.2 After a brief discussion on the various issues, the Committee opined that a final view may be taken on the recommendations of the Sub-Committee after obtaining the response/ views of various stakeholders. After detailed deliberations it was decided that "specific recommendation" of the sub-Committee along with a foot note in the form of a qualifying statements on the prevailing practice would be placed on MoEF website for inviting stakeholder response for a period of two weeks. Decision on the above matter was therefore deferred.

13.3 The Committee also appreciated the efforts made by Dr Nagarajan and members of the sub-Committee in rationalizing the complex issues related to Bt Cotton trials.

Date of the Next GEAC Meeting

It was decided that the next GEAC meeting would be held on 14.12.2005.

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