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Ministry of Environment and Forests
(HSM Division)

Subject: Minutes of the 22nd Meeting of Genetic Engineering Approval Committee held on 10th April, 2000.

The twenty second meeting of the Genetic Engineering Approval Committee (GEAC) was held on 10th April, 2000 under the Chairmanship of Shri Vinod Vaish, Special Secretary, Ministry of Environment & Forests. The following is the list of participants:

1) Shri Vinod Vaish, Special Secretary, Ministry of Environment & Forests, New Delhi – **Chairman**
2) Dr. Sushil Kumar, Director, Central Institute of Medicinal and Aromatic Plants, Lucknow (U.P.) – **Co-chairman**
3) Shri V. Rajagopalan, Joint Secretary, Ministry of Environment & Forests, New Delhi.
4) Dr. Vasantha Muthuswamy, Deputy Director General, Indian Council of Medical Research, New Delhi.
5) Prof. A.K. Bhatnagar, Department of Botany, University of Delhi, Delhi
6) Shri A.B. Ramteke, Deputy Drugs Controller, Ministry of Health, New Delhi
7) Dr. T.V. Ramanaiah, PSO, Department of Biotechnology, New Delhi
8) Shri K.D. Bhardwaj, National Productivity Council, New Delhi
9) Dr. R.R. Khan, Director, Ministry of Environment & Forests, New Delhi
10) Smt. Madhu Gupta, Research Assistant, Ministry of Environment & Forests, New Delhi

2. Welcoming the members, Chairman referred to the minutes of the 21st Meeting of GEAC held on 8th November, 1999 which was circulated to all the members. There were no comments from the members. The minutes were confirmed.

3. Chairman referred to para 6 of the minutes of the last meeting of GEAC and enquired from DBT representative about the status of preparation of a paper on the monitoring mechanism to be evolved for manufacture and use of recombinant products in the country. DBT had earlier agreed to prepare such a paper. Representative of DBT mentioned that a proforma to facilitate monitoring in respect of recombinant products has been prepared and was discussed by RCGM in its last meeting held on 4.4.2000. Chairman mentioned that while such a check-list would be useful, a more comprehensive paper on the procedure for monitoring the production, import, export and use of products based on hazardous micro-organisms and other recombinant products like drugs, vaccines, diagnostic aids, transgenic seeds and pollution control organisms is required to be prepared. While suggesting the procedure, it may be kept in mind that instead of creating a new institutional mechanism, the existing mechanisms operating under DCGI, IVRI, State Agriculture Directorates and CPCB may be involved with such monitoring. An indicative approach in this regard could be as follows:

DCGI, State Drug Inspectors and IVRI	:	Recombinant drugs, vaccines & diagnostic aids
ICAR, Plant Protection Directorate & State Directorate of Agriculture	:	Transgenic seeds, crops, fruits, biofertilizers and biopesticides
CPCB, SPCBs & Regional Offices of MoEF	:	Microbes for pollution control and remediation of contaminated sites

4. In respect of drugs and pharmaceuticals, it was noted that the system is fairly well-established. Besides routine monitoring and post-marketing surveillance undertaken by DCGI with the help of experts, the local drug administration responsible for licensing the drug manufacturing units renews their license every two years. Before renewal of license, local inspector examines various facilities existing at the manufacturing unit. Dr. Vasantha Muthuswamy, DDG, ICMR mentioned that the data generated during post-marketing surveillance are a good source of monitoring for drug-related activities. This, however, needs to be done on a regular basis and feedback given to MoEF through DCGI. Chairman enquired as to whether the Institutional Bio-safety Committee (IBSC) set up under HMO/GMO Rules, 1989 could also be involved in monitoring work. The representative of DBT mentioned that involvement of IBSC is only to ensure good laboratory and manufacturing practices. Involvement of IBSC in post-marketing surveillance of recombinant drugs will be difficult. Local drug inspectors who are in touch with marketing of such products and medical experts are in a better position to collect necessary details. Chairman requested DBT that these aspects should be taken into consideration while making the paper on the subject. DBT representative agreed to work on this paper and present it to GEAC at the earliest.

Import and marketing of r-Cattle Tick Vaccine (GAVAC) by M/s Kee Pharma Ltd., New Delhi (Agenda Item No. 3) and Import of Tickgard by Hoechst Roussel Vet. Pune, (Agenda Item No. 4)

5. The proposals submitted by M/s Kee Pharma Ltd., New Delhi and Hoechst Roussel Vet. Pvt. Ltd., Pune are about import and marketing of recombinant vaccines administered to cattles to protect them against the infestation of ticks. M/s Kee Pharma intends to import the product from Cuba under the brand “Gavac” while M/s Hoechst Roussel intends to import the same from Australia under the brand named “tickgard”. It was pointed out that the Department of Animal Husbandry and Dairy Development has some reservations to allow import of the vaccine. Other experts from the Central Drug Research Institute (CDRI), Lucknow and DBT have supported the proposal on the basis of its safety from environmental angle. However, as a general policy, a new product to be imported in the country is required to undergo certain tests. It was noted that DBT has already given a protocol for generating data on the above vaccines in the country. It was agreed that the product may be cleared from the environmental angle for the import of 200 ml each by M/s Kee Pharma and Hoechst Roussel Vet. Pune for generating the necessary data as per the protocol suggested by DBT. The Committee was however clearly of the view that this approval is only from the environmental angle and that it was for the Department of Animal Husbandry & Dairy Development to consider the matter for determining its essentiality and decide on its import and marketing accordingly, which should be done in fulfilment of the conditions and adherence to the protocol as mentioned above.

Import and marketing of rhG-CSF (Jilifen) Recombinant human granulocyte colony stimulating factor by M/s United Biotech Pvt. Ltd., Delhi (Agenda Item No. 5), Import and Marketing of r-interleukin-2 (r-IL-2) by M/s Ambalal Sarabhai Enterprises Ltd., Baroda (Agenda Item No. 6) & Import of Intron-A multidose pen by M/s Fulford (India) Ltd,. Mumbai (Agenda Item No. 8).

6. The above three proposals relate to recombinant medicines used in anti-cancer therapy. It was pointed out that since the recombinant vaccines used for anti-cancer therapy are quite expensive, the firms find it difficult to import them only for conducting clinical trials. The vaccines have long been in use in the country of origin and have been approved by the respective regulatory authorities. It was agreed that the import and marketing of above medicines be allowed and the firms may be asked to conduct Post-Marketing Surveillance (PMS) data on about 100 patients for a period of two years. The results of PMS data may be examined by DCGI and the reports of adverse drug reaction, if any, may be communicated to MoEF. The quantity of the respective product to be allowed for import and marketing will be 5000 ampoules per year.

7. Another proposal concerning recombinant human interleukin by M/s Wyeth Lederle Ltd., Mumbai (Agenda Item No. 10) approved during the last meeting of GEAC held on 8th November, 1999 for phase-III clinical trials was also discussed. The firm has made a representation requesting for exemption from phase-III clinical trials in view of the high cost of the medicine like in case of anti-cancer vaccines. It was agreed that M/s Wyeth Lederle should also be allowed to conduct PMS data on 100 patients for two years. The quantity of the product to be allowed would be 5000 vials per year.

Import and marketing of Twinrix brand of Hepatits A/B Combination vaccine (Agenda Item No. 7) & Import and marketing of Tritanrix HB (Combined Diptheria, Tetanus and Pertusis & r-Hepatitis B) (Agenda Item No. 12) by M/s Smithkline Beecham Pharmaceuticals (India) Ltd.

8. The Hepatits A/B combination product is proposed to be imported by M/s Smithkline Beecham Pharmaceuticals (India) Ltd. the clinical trials of this product have been done at G.B. Pant Hospital, New Delhi which were found to be without any adverse effects. The product is widely used in over 50 countries. Dr. Vasantha Muthuswamy, DDG, ICMR felt that a combination vaccine like Hepatitis A and B may not be required since Hepatitis A is not a serious problem the country. Moreover, by administering the combination vaccine, the population will be needlessly exposed to the other virus. She informed the Committee that the Toxicological Review Panel of ICMR had gone into this question and averred that such a combination may not be allowed in the country at the moment. In view of the comments received from PGIMER, Chandigarh and IVRI, Bareilly that the product may not lead to environmental problems, it was decided that the product can be cleared from the environmental angle. The broader issue of import of combination vaccine may be decided by DCGI in consultation with ICMR.

9. As regards another proposal submitted by M/s Smithkline Beecham regarding combined vaccine (Diptheria, Tetanus, Pertusis and r-Hepatitis-B). Dr. Vasantha Muthuswamy mentioned that ICMR has not yet examined this proposal. Representative of DCGI mentioned that there is a global initiative to combine vaccines in areas where the population is exposed to a number of diseases. It was decided that as far as environment is

concerned, the combined vaccine will not pose any problem. The clearance from environmental angle is subject to clearance under the Drugs & Cosmetics Act.

Refilling of r-Hepatits B Vaccine manufactured by M/s Bharat Biotech, Hyderabad (Agenda Item No. 9)

10. This Ministry had earlier approved manufacture of r-hepatitis-B surface protein by M/s Bharat Biotech Ltd., Hyderabad vide letter dated 2nd September, 1998. The firm has now applied to DCGI for permission to sell final bulk vaccine in 50 litre packs in steel containers to M/s Biological Evans, Hyderabad who would refill the said vaccine in smaller packs for retail marketing under the brand name BEVAC. A reference to this effect has been received from DCGI.

11. Since the issue of packaging/sale is handled by DCGI after GEAC has accorded its approval, DBT was consulted in the matter. DBT has recommended such bulk packaging with the condition that a separate filing and sealing facility must be installed and inspected by a representative nominated by the GEAC. It was decided that such bulk refilling should be done under close observation of Institutional Bio-safety Committee who should give periodical reports to GEAC.

Manufacturing and marketing of Tetanus Toxoid (Absorbed) I.P. (Agenda Item No. 11)

12. Non-recombinant tetanus toxoid vaccine has long been manufactured in the country. It is produced from Clostridium tetani which is a hazardous micro-organism under HMO/GMO Rules, 1989. DCGI suggested that the firm may obtain permission from State Licensing Authority. However, the State drug authority is asking the firm to get the clearance from MOEF since the source organism is covered by HMO/GMO Rules, 1989. It was decided that since the product is available in the market, GEAC may have no objection to its manufacture if other provisions of the Drugs & Cosmetics Act are fulfilled.

Import of recombinant-streptokinase Injection manufactured by Hyber Biotech Cuba submitted by M/s Kee Pharma Ltd., (Agenda Item No. 13)

13. M/s Kee Pharma Ltd., New Delhi have informed the Ministry that r-streptokinase injection is already being marketed by U.S. Vitamins, Mumbai based on the GEAC clearance to M/s CIMMCO International in 1993. Members felt that since the product was allowed to be imported by M/s CIMMCO based on certain conditions, it would be appropriate to know the results of the experience gained. The Committee felt that a time has come when we should get a survey done as to whether such conditions are being fulfilled by respective applicants. Such a survey could be undertaken with the help of DCGI. Keeping in view the life saving nature of the product, it was decided that the above product may be cleared from the environmental angle subject to generation of post market surveillance (PMS) data on 100 patients for a period of two years.

Policy Matters concerning Streamlining the Procedure for GEAC Clearance

14. Members felt that there is a need to streamline the existing procedures followed by GEAC and to shorten the time-limit so as to encourage healthy competition among various applicants and availability of good quality recombinant products in the market. Such

streamlining of the procedure can result in shortening processing time in following type of situations.

i) Proposals of repetitive nature where the applicant intends to import the same drug/vaccine from the same source.
ii) Applicants seeking permission for Phase III clinical trials from DCGI and DCGI in turn asking MoEF to issue NOC.

15. In both the above situations, it was suggested that intending firms may submit the vital information to MOEF which may be referred to DBT/DCGI for their comments. Based on the inputs received from DBT/DCGI, Chairman, GEAC may take a decision in both the above types of proposals. Details of such cases, where the decision is taken by the Chairman, GEAC, would be put up for the information of the members of GEAC in the next meeting. However, such fast-track procedure will only apply to import/export cases. The proposals concerning manufacture of recombinant products or other products based on hazardous micro-organisms would continue to be examined by GEAC on a case-by-case basis.

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

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