Minutes of the 25th meeting of GEAC held on 27th March, 2001 at 11.00 a.m. in the Ministry of Environment and Forests

The twenty-fifth meeting of Genetic Engineering Approval Committee (GEAC) was held on 27th March, 2001 under the chairmanship of Shri A.M. Gokhale, Additional Secretary, Ministry of Environment and Forests. List of participants is annexed.

At the outset, the Chairman, welcoming the members informed about the renomination of Dr. Sushil Kumar as the Co-Chairman of the GEAC.

The Chairman referred to the minutes of the twenty-fourth meeting of GEAC held on 12th October 2000, which were circulated to all the members. As there were no comments from the members, the minutes were confirmed. Therefore, the agenda items were taken up for discussion.

Agenda item No. 3.1 (File No. 13/3/2000-CS)

Import of non-hazardous microbial products from M/s Micro-Bac International Round Rock, TX-78681, U.S.A., and trading in these products by M/s Netal Chromatographs, Mumbai.

M/s Netal Chromatographs, Mumbai had submitted a proposal for import of non-hazardous microbial products from M/s Micro Bac International Round Rock, USA, and trading these products.

Since the products to be imported are non hazardous and non-genetically engineered, a view was expressed as to whether the proposal could be considered by the GEAC. However, interpreting the provisions of Sections 2(2) and 3(v) of the 1989 Rules, the Committee agreed to consider the proposal.

As the proposal does not clearly specify the microorganisms to be imported, the Committee was of the view that the suitability of these micro-organisms from environmental angle is difficult to ascertain. The proposal was therefore not approved by Committee.

Agenda Item 3.2 (File No. 10/10/2000-CS)

Manufacture and marketing of r-Hepatitis B vaccine produced in *Pichia pastoris* by M/s Bharat Biotech International, Hyderabad

M/s Bharat Biotech International, Hyderabad had submitted a proposal for manufacture and marketing of r-Hepatitis B vaccine produced in *Pichia pastoris*. The comments of DCGI on the proposal have not yet been received, and the representative of DCGI informed that the proposal is under examination. The Committee decided to approve the proposal in principle, subject to DCGI's approval. It was further decided that upon receipt of DCGI's comments, the Chairman will finally approve the proposal.

Agenda Item 3.3 (File No. 10/12/2000-CS)

Phase III clinical trials of r-Streptokinase by M/s Bharat Biotech International Ltd., Hyderabad

M/s Bharat Biotech International, Hyderabad had submitted a proposal for conducting Phase III clinical trials of r-Streptokinase. The RCGM in its meeting on 7th September 2000 examined the data submitted by the applicant and requested the applicant for carrying out experiments for establishing the non-immunogenicity of the product. Further the DCGI informed that the proposal is under examination in consultation with the experts. The Committee was therefore of the view that the proposal is premature and decided to defer the proposal.

Agenda Item No. 3.4 (F.No. 10/22/2000-CS)

Import and marketing of r-Human erythropoietin (finished form) by M/s Kee Pharma Ltd., New Delhi from Research Institute of Highly Pure Biopreparation, Russia.

M/s Kee Pharma Ltd., New Delhi had submitted a proposal for import and marketing of r-Human erythropoietin (finished form) from Research Institute of Highly Pure Biopreparation, Russia.

Since the Committee has earlier approved import and marketing of r-human erythropoietin, it was decided to approve the proposal subject to the following conditions.

a) The applicant should generate Post Market Surveillance data on not less than 100 subjects within a period of 2 years and submit the same to the Government for evaluation.
b) Each consignment should be accompanied with a certificate from concerned authorities indicating that the product is free from mycoplasmas and adventitious viruses like HIV, HBV, HCV etc. tested by scientifically valid methods.
c) The applicant be encouraged to obtain a certificate for environmental clearance from the exporting company.

Agenda Item no. 3.5 (File No. 10/21/2000-CS)

Import and marketing of interferon alpha 2b submitted by M/s Cadilla Healthcare Ltd., Ahmedabad from Biosidus Argentina.

M/s Cadilla Healthcare Ltd., Ahmedabad had submitted a proposal for import and marketing of interferon alpha 2b from Biosidus Argentina.

The DCGI has not yet given its comments on the proposal as they are awaiting the results of Phase III clinical trials from the applicant. The Committee therefore decided to defer the proposal. The proposal will be considered by the Committee on receipt of comments from DCGI.

Agenda Item no. 3.6 (File No. 10/19/2000-CS)

Import and marketing interferon alpha injection (3, 6, 9 MIU) from M/s L.G. Chemicals Ltd., Korea by M/s L.G. Chemicals Pvt. Ltd., New Delhi.

M/s L.G. Chemicals Pvt. Ltd., New Delhi had submitted a proposal for import and marketing interferon alpha 2a injection (3,6,9 MIU) from M/s L.G. Chemicals Ltd., Korea.

The representative of DCGI informed that they have sought some more details from the applicant, and are awaiting the same. The Committee therefore decided to defer the proposal and to consider the same on receipt of DCGI's comments.

It was also agreed that in all such cases where DCGI seeks further details/clarifications from the applicant, the DCGI will keep the MoEF informed by endorsing a copy of their communication to MoEF, so that MoEF too could follow up with the applicant.

Agenda Item no. 3.7 (File No. 18/2/2000-CS)

Manufacture and marketing of Ecovac-4 by M/s Panacea Biotech Ltd., New Delhi in two strengths: (1) Diptheria, Tetanus, W-Petussis with Hepatitis B-10 ug vaccine; and (ii) Diptheria, Tetanus, W-Petussis with Hepatitis B-5 ug vaccine.

M/s Panacea Biotech Ltd., New Delhi had submitted a proposal for manufacture and marketing of Ecovac-4 in two strengths DTP-HB-10 ug and DTP-NB-5 ug. The applicant has not provided information on the source of procuring the DPT components of the vaccine, as well as the status of approvals for manufacture and marketing of these individual vaccines or their combinations. The representative of DCGI informed that they too have sought some more details and information from the applicant. It was decided that the applicant would be asked to provide information on the source of procuring the DPT components of the vaccine, as well as the status of approvals for manufacture and marketing of these individual vaccines or their combinations. The Committee decided to defer the proposal and consider on receipt of this information.

Agenda Item no. 3.8 (File No. 10/4/2000-CS)

Manufacture and marketing of Hepatitis B Antigen/Vaccine using r-DNA Technology by M/s Serum Institute of India, Pune.

M/s Serum Institute of India Ltd., Hadapsar, Pune had submitted a proposal for manufacture and marketing of Hepatitis B Antigen/Vaccine using r-DNA technology.

The representative of DBT informed the Committee about the shifting of the manufacturing unit of this firm from Hyderabad to Pune. The Committee was of the view that even though shifting of the manufacturing unit per se does not require approval of GEAC, thus shifting does entail some other implications which require compliance under the 1989 Rules. These requirements inter alia include setting up of IBSC, necessary approval from concerned State Government etc. It was therefore decided that the applicant may be asked to resubmit the proposal indicating all necessary compliance under the Rules. The Committee rejected the proposal at this juncture for want of information on compliance of statutory requirements.

Agenda Item no. 3.9 (File No. 10/1/2000-CS)

Import and marketing of highly purified rhu TNFR:FC Protein from M/s Boehringer Iugelheim Pharma K.G. (B) Pharma, Biberach, Germany by M/s Wyeth Lederle Ltd., Mumbai.

M/s Wyeth Lederle Ltd., Mumbai had submitted a proposal for import and marketing of highly purified rhu TNFR:FC Protein from M/s Boehringer Iugelheim Pharma K.G. (B) Pharma, Biberach, Germany.

The representative of DCGI informed that the applicant has been asked to submit results of clinical trials by the ICMR. The DCGI will furnish their comments on receipt of this information from the applicant. The Committee accorded in principle approval to the proposal and agreed that the Chairman will give final approval on receipt of comments from DCGI.

Agenda Item no. 3.10 (File No. 13/4/98-CS)

Permission for large scale field trials for Hybrid MECH-915 in Northern in Kharif 2001 seasons States by MAHYCO Mumbai.

The GEAC in its 23rd meeting had accorded approval to MAHYCO for undertaking large scale field trials of Bt Cotton in some Southern States in the Kharif season 2000 and in Northern States in Kharif 2001. This sanction was for field trials of MECH-12, MECH-162, MECH-184 only, which suits the climate of the southern India. The MAHYCO now proposes to undertake the large scale field trials of Bt Cotton in Punjab, Haryana and Rajasthan using Hybrid MECH-915 which is suitable for the northern States. The RCGM has earlier permitted small scale field trials using MECH-915 hybrid in Northern States. In view of this, the Committee decided to approve the proposal with the same terms and conditions as were communicated to MAHYCO with the earlier approval for field trials in Southern States.

Agenda Item no. 3.11 (File No. 10/7/2000-CS)

Import and marketing of r-Human Leucostin Injection (Filgrastin) r-Human Granulate Colony Stimulating factor from M/s Dong – A Pharmaceuticals Ltd., Korea by M/s Emcure Pharmaceuticals Ltd., Pune.

The GEAC in its 24th meeting had considered the proposal, but did not accord approval as Phase III clinical trials were not conducted in Korea where the product is manufactured. The applicant has now submitted reports of Phase III clinical trials received from the Parent Company. It was decided that this will be communicated to DBT and DCGI for their comments. Upon receipt of their comments, the proposal will be referred to the Committee. Thus, at this juncture, the proposal was deferred.

Agenda Item no. 3.12 (File No. 17/12/98-CS)

Import and marketing of PEG Interferon alpha 2b from M/s Sehring Plough Corporation, Brinny, Ireland by M/s Fulford (India) Ltd.

M/s Fulford (India) Ltd. had submitted a proposal for import and marketing of PEG Interferon alpha 2b. The proposal was considered in the 24th meeting of GEAC. As the proponent had not submitted data on immunogenicity, the proposal was deferred. The immunogenicity data submitted thereafter by the applicant was referred to DBT/DCGI for comments. The representative of DCGI informed that the proposal is under examination. The Committee decided that on receiving DCGI's comments, the Chairman may approve small scale import of the product for limited Phase III clinical trials, as per the standards earlier laid down by the Committee for generating data as suggested by the DBT.

Agenda Item no. 3.13 (File No. 16/23/93-CS)

Revalidation of approval for manufacturing of Human Insulin injection by M/s M.J. Pharmaceuticals Ltd., Mumbai.

M/s M.J. Pharmaceuticals Ltd., Mumbai had requested for revalidation of the approval granted earlier by GEAC in 1994 for manufacturing of Human Insulin injection. The firm manufactured the product upto 1997, and thereafter discontinued it due to some management problems. As per Rule 13(a) of the 1989 Rules, the approval of GEAC is valid for four years at the first instance and renewable for two years at a time.

It was decided that detailed information may be obtained from the firm with respect to interalia:

- any adverse incident that might have occurred during manufacturing
- details of management problems for which the manufacturing was discontinued.

The Committee also decided that Dr. S.K. Mahajan, BARC, will prepare a proforma for monitoring, taking into account the proforma developed by the DBT.

Agenda item No. 3.14 (File No. 10/25/2000-CS)

Import and marketing of CLONEPO r-Human erythropoietin (EPO) from Shenghai Clonbiotech Co. Ltd. China by M/s Dr. Reddy's Laboratories Ltd., Hyderabad.

M/s Dr. Reddy's Laboratories Ltd., Hyderabad had submitted a proposal for import and marketing of CLONEPO r-Human erythropoietin (EPO) from Shenghai Clonbiotech Co. Ltd., China.

As Phase III clinical trials for this product have been conducted only in China, the Committee felt that there is a need to conduct such trials on Indian population before approving their large scale import and marketing. The Committee therefore decided to approve limited import of the drug as per the norms of DCGI for conducting Phase II clinical trials on Indian subjects, with the following conditions:

(a) Applicant to generate clinical trials data on not less than 100 human subjects and submit the same to the Government for further evaluation. The clinical trials should generate the following information:

(i) Immunogenicity status
(ii) Change in efficacy status as measured by suitable scientifically valid output parameters for EPO and
(iii) Measurement of contaminants levels in staring materials in India

(b) Each consignment of the limited import should be accompanied by a certificate from the concerned exporting authorities that the product is free from mycoplasmas and adventitious viruses like HIV, HBV, HCV, SV40 etc. tested by scientific valid methods.

Thereafter the applicant may submit the results of Phase III clinical trials for consideration of GEAC for permitting large scale import and marketing.

Agenda Item no. 3.15 (File NO. 10/20/2000-CS)

Import and marketing of r-Human Erythropoietin from M/s L.G. Chemicals Ltd., Korea by M/s L.G. Chemicals Pvt. Ltd., New Delhi

M/s L.G. Chemicals Pvt. Ltd., New Delhi had submitted a proposal for import and marketing of r-Human Erythropoietin from M/s L.G. Chemicals Ltd., Korea. The representative of DCGI informed that the proposal is still under examination. The Committee decided to approve the proposal in principle for limited import for conducting Phase III clinical trials. It was agreed that on receipt of DCGI's comments, the Chairman, GEAC may grant the final approval for this purpose.

Agenda Item no. 3.16 (File No. 10/1/2001-CS)

Manufacture and marketing of r-human Granulocyte Colony Stimulating Factor (r-hG-CSF) by M/s Dr. Reddy's Laboratories, Hyderabad

M/s Dr. Reddy's Laboratories, Hyderabad had submitted a proposal for manufacture and marketing of r-human Granulocyte Colony Stimulating Factor (r-hG-CSF). The representative of DBT informed that RCGM has earlier given approval for this product. The Committee decided to accord approval for manufacturing and marketing of the product.

Agenda Item No. 4: Base paper prepared by DBT on monitoring mechanism for production and use of r-products in the country.

The Committee considered the proforma developed by DBT for prospective monitoring of cases approved by the GEAC. The members underscored the importance and utility of obtaining feedback for retrospective monitoring of cases approved by the GEAC. For this purpose, it was agreed that Dr. S.K. Mahajan, BARC, would develop a monitoring proforma based on the DBT's proforma, for obtaining feedback every two years. The members were invited to provide suggestions/comments to Dr. Mahajan within fifteen days at sk-mahajan@yahoo.com or skmaha@magnum.barc.ernet.in or Tel. 022-5505151.

The Committee emphasised the need for undertaking physical monitoring as well. For this purpose, it was suggested that each of the members of GEAC would build a team/group around him comprising of local experts for monitoring purposes.

5. Any other item

5.1 Permission for Phase III clinical trials

In order to streamline the existing procedures, and shorten the processing time, the GEAC in its 22nd meeting held on 10.4.2000, decided that applicants seeking permission for import of recombinant drugs for Phase III clinical trials, may approach DCGI directly. DCGI in turn may seek NOC from MOEF after examining the matter.

However, since this procedure is not working properly, the Committee decided to go back on this decision and to continue with the present system.

In this connection, it was also agreed that the GEAC will meet four times a year, on the last Friday of March, June, September and December.

5.2 Permission for import of same products from same source

In the 22nd meeting of GEAC held on 10.4.2000, it was also decided that for proposals of a repetitive nature where the applicant intends to import the same drug from the same source, approval may be accorded by the Chairman after referring the matter to DBT/DCGI. Thereafter, the Committee may be informed about such approvals given.

The Committee was informed that since the 24th meeting of the GEAC held on 12.10.2000, approvals have been given for two proposals following this short-cut procedure. These are:

(i) Import and marketing of Biovac B, a recombinant Hepatitis B vaccine from Green Cross Vaccine Corporation, Korea by Wockhardt.
(ii) Import and marketing of interferon alpha 2B injection from Heber Biotech Cuba by Kee Pharma Ltd.

The Committee agreed that henceforth if such a proposal is received within two years of approval for the first proposal, the Chairman may accord approval after referring the matter to DBT/DCGI, as is being done presently. However, if the proposal is received after two years of the approval first granted, then the GEAC will consider the proposal for approval taking into account the feedback received on the case approved earlier.