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GEAC in the eye of another storm

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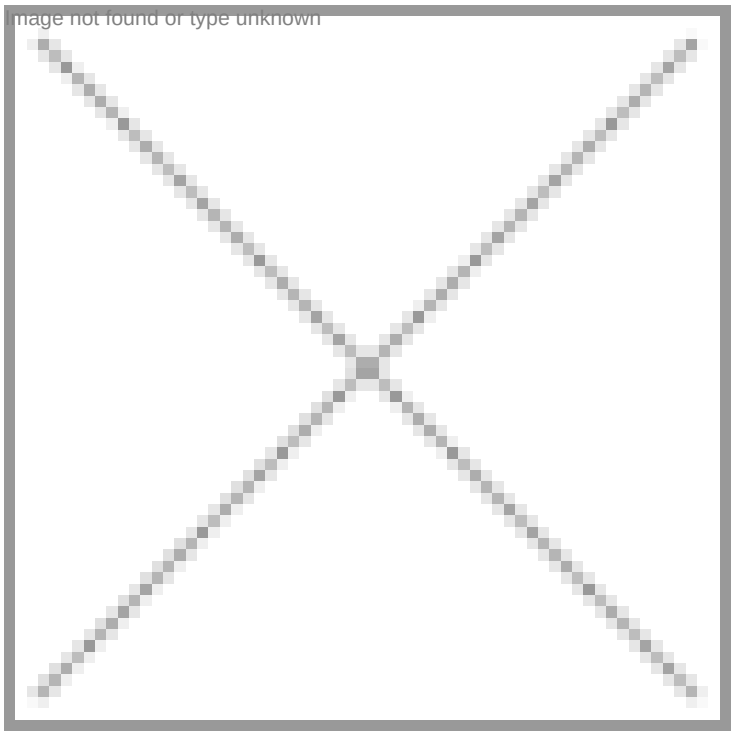
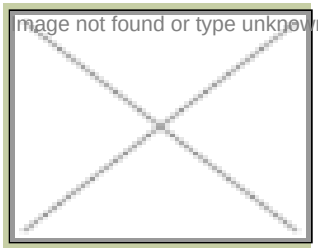


It looks like India's leading biotech regulator, the Genetic Engineering Approval Committee (GEAC), can't avoid controversiesâ€”whether for not doing enough for the industry or for whatever decision it takes once in a few months.

The latest issue is the controversial decision of GEAC on 27 November to ask the pharma regulator, the Drug Controller General of India (DCGI) to inquire how Hyderabad-based Shantha Biotechnics has started "illegal" manufacture of the biotech drug Shankinase.



According to DBT protocol, GEAC has no role to play in granting approvals for clinical trials. All clinical trials are approved by DCGI Advisory Committee, after it has been duly approved by Institutional Biosafety Committee (IBSC) and Review Committee on Genetic Manipulation (RCGM)," Varaprasad Reddy, MD, Shantha.

More damaging to Shantha Biotechnics, a torch bearer of modern biotechnology which has won universal acclaim for its pioneering drugs, was the GEAC's prompt press release the same day which said it has "requested DCGI to conduct a full inquiry into the incident (manufacture of recombinant Streptokinase branded Shankinase without its prior approval) and the reported deaths of some patients during the trials."

"Final view on what action needs to be initiated against the erring company will be decided after getting all reports," the GEAC press release added. GEAC is the regulator for genetically modified products and is part of the ministry of environment and forests. It is chaired by additional secretary rank official, Meena Gupta and has ex-officio members drawn from other wings and scientific agencies of the government.

Ironically, the GEAC decision was taken on a day, when just 500 meters away from its office, some of the country's top biotech experts, NGO activists, industry representatives and scientists were debating the very relevance of GEAC as a bureaucratic regulator whose decisions were far removed from reality. The meeting was organized by leading genetic activist Dr. Suman Sahai to celebrate the 10th anniversary of her organization, Gene Campaign. In fact, a few hours after the GEAC meeting, two senior officials of the regulatory agency put up a spirited defence of the organization for nearly two hours at the NGO meeting and unveiled the roadmap to a transparent regulatory regime.

In Hyderabad, Shantha Biotech-nics was quick to challenge the GEAC decision. Within 24 hours, Shantha released its side of the story at a media conference and reaffirmed that its manufacturing and trials of the blood-clot busting drug were perfectly in order as it followed all the regulatory processes in the country. The tenor of Shantha's managing director Varaprasad Reddy was that GEAC had no business to poke its nose into something which was not in its mandate.

"According to the Department of Biotechnology protocol, GEAC has no role to play in granting approvals for clinical trials. All clinical trials are approved by DCGI Advisory Committee, after it has been duly approved by Institutional Biosafety Committee (IBSC) and Review Committee on Genetic Manipulation (RCGM)," Reddy asserted.

Shantha's argument that GEAC had no business in this issue has found widespread support in the industry. "It is evident that the roles of GEAC, DCGI and RCGM are not clearly defined. I am in agreement with Shantha's view on the matter: i.e., GEAC does not come into the picture when it comes to granting permission for pre-clinical and clinical trials. This is the role of RCGM and DCGI. Hence Shantha has certainly not deviated from the norms," asserted industry leader and president of the Association of Biotechnology-Led Enteprises (ABLE) Kiran Mazumdar-Shaw."

According to the current regulations, GEAC's role is confined to approving the use of the recombinant drug as it uses an altered genetic material and GEAC has given this approval a few months back. Then the drug goes through the normal regulatory approval, proves as prescribed by the DCGI which involves a host of clinical trials, and the data is vetted by the drug controller. After this process is over, being a gene-based drug, it will have to go to the GEAC for final approval for manufacturing and commercial release. This is clearly stated in the approval letter issued by the DCGI.

"I understand that Shantha has provided all the data pertaining to the trials along withinvestigators' report and I am inclined to accept Shantha's contention that Streptokinase which is used as a clot buster for myocardial infarctions does carry the risk of fatality and statistically the current information does not indicate any fault in the product," Mazumdar-Shaw added.

Shankinase too was approved by DCGI for Phase III clinical trials in various centers across India. Randomized multi-centric double-blind comparative trials were conducted in Hyderabad, Bangalore, Pune, Lucknow and Mumbai, in which the safety and efficacy of Shankinase was compared with the international innovator brand of Streptokinase. The conclusion of the investigators, which is signed and submitted to the DCGI, states that the product generated results that were "absolutely satisfactory and safety was comparable" with the international brand, according to the company. The trials' data was submitted to the DCGI as per the correct procedure and found satisfactory and approval was granted for manufacturing stated Reddy.

A Hyderabad-based NGO had reportedly complained to the GEAC that some deaths had occurred during the clinical trials. The GEAC decision to ask for an inquiry by the DCGI was based on this complaint.

Shantha chief clarified that there were a total of six deaths reported in the Double Blind Comparative Clinical Trial of Shankinase vs Best Known International Brand.

In the Double Blind trials, vials of both the brands are masked and the identity is not known to the investigator, the patient and

the company. A total of 134 patients with myocardial infarction were administered both these products, across six hospitals in five cities in India. When the results were decoded, it was found that three deaths occurred in the group administered with Shankinase and an equal number (three) of deaths occurred in the group which was administered the international brand.

"It has to be noted with responsibility that the patients who are administered Streptokinase are patients with acute myocardial infarction (heart attack) and there is an acceptable efficacy benchmark (60-70 percent) seen throughout the world with this product. Since this is a drug for an emergency situation for seriously unhealthy patients, some deaths are bound to occur in any large-scale trial," stated Reddy.

In fact, Reddy said, it was for this very purpose that the ethical committee of the principal investigators chose to conduct a Comparative Double Blind Clinical Trial so that all biases could be eliminated. Thankfully, because of this decision by the investigator, the results submitted by the principal investigators have been accepted by the DCGI.

Firing a salvo at the GEAC for not sticking to its mandate, Reddy asked: "It would be interesting to know whether GEAC has ever taken any cognizance of the deaths in the clinical trials of Streptokinase or any other product, conducted recently or in the past by Indian manufacturers or foreign companies. It is an irony that the GEAC gives environmental clearance to imported products even before clinical trials are conducted, whereas it expects products developed in India to go through it seeking their approval for clinical trials as well as final clearance for manufacturing."

Ironically, the 27 November GEAC statement also contains the information that it had approved the introduction of many imported biotech drugs in the country. The GEAC has not clarified whether the rigorous trials of these drugs had been conducted within India.

As a process, GEAC relies on the Department of Biotechnology (DBT) for scientific inputs. The Review Committee on Genetic Manipulation (RCGM), constituted by the DBT and chaired by a scientist, and the Institutional Biosafety Committees in all organizations conducting experiments on genetically modified products are the key agencies in this sector. All pharma products are first vetted by the DCGI which uses medical experts drawn from the Indian Council of Medical Research (ICMR).

The November issue of BioSpectrum had reported the extensive use of illegal Bt cotton seeds, the country's first officially approved product, in many parts of Gujarat. A GEAC inquiry which tested 10 randomly drawn samples of these spurious seed brands had confirmed the use of "unapproved" Bt genes. Yet the GEAC is not in a position to take any action. GEAC officials have admitted that a stringent action may create a "socio-economic" crisis in the state. The Gujarat state government which has to take action against these practices is reportedly supporting the use of these illegal seeds to benefit its farmers.

It indeed is a strange regulatory system we have for genetically modified products in India.

N Suresh

India, US shake hands in biotech

The renewed friendship between India and the US after September 2001 is manifesting itself in many areas. Biotechnology and life sciences is certainly a top priority area for both countries. This was amply demonstrated by the dialogue between both countries under the Indo-US High Technology Cooperation Group (HTCG) involving top policy makers, industry organizations and captains of India's industry on November 19, 2003 in Bangalore.

"High technology is key to the cooperation between both the countries in fostering bilateral trade," remarked Kenneth I Juster, under secretary of commerce, Bureau of Industry and Security of the US Department of Commerce and the key American interlocutor.

HTCG was set up in November 2002 to take forward the discussions between Prime Minister AB Vajpayee and US President George W Bush a year earlier in Washington. The first meeting of the group was held in July 2003 in Washington D.C. The second in the series was the one in Bangalore. Both the governments have identified three key areas for cooperation in high technology. These are: 1) Defense 2) Information technology and nanotechnology, 3) Biotechnology and life sciences.

The new found friendship and cooperation has resulted in improving high tech exchanges between India and the US which were suspended following India's nuclear tests in May 1998. "Now less than one percent of India's exports to the US involve higher scrutiny and licensing. There were some 700 applications for technology export/import licenses from India compared

proval rate for Indian applications was over 90 percent," informed Juster.

the cooperation, said leading Indian technocrat and DG, Council of Scientific and Industrial ashelkar. Dr Mashelkar is the key Indian interlocutor in the Indo-US high tech dialogue. "India's real advantage is not just cost but the value offered. That is why over 100 of the Fortune 500 companies have set up their research and development centers in India in recent years," he told the Bangalore gathering.

The American cooperation in life sciences was reiterated by former US ambassador to India, Thomas Pickering, a vice president of Boeing Corp. and the private sector chairman of HTCG. "India's proven capabilities in biotechnology makes the country a promising future destination. India should be quick in integrating into the global drug production and new drug discovery networks," Pickering advised.

Top policy makers, industry representatives and CEOs of Indian and American companies participated in three parallel sessions on the priority areas. They thrashed out the various issues in the smooth transfer of technologies between India and the US. The dialogue process has gained momentum in 2003, indicated by the active involvement of the key movers from both sides, two times this years. Industry leaders from both sides expect the removal of various irritants on priority basis so that they could look forward to a bumps-free ride on the Indo-US High Tech Corridor.

N Suresh