SALK INSTITUTE
FOR BIOLOGICAL STUDIES

David Schubert, Professor
Cellular Neurobiology Laboratory CNB-S
Tel 858-453-4100 Ext. 1528
e-mail: schubert@salk.edu

November 18, 2009

Mr Jairam Ramesh
Hon'ble Minister of Environment and Forests
Government of India
425 Paryavaran Bhavan
CGO Complex, Lodhi Road
New Delhi 110003, India

Email: jairam@vsnl.com

Dear Mr. Jayaram Ramesh:

My name is Dr. David Schubert. I have a PhD in immunology and am a professor at the Salk Institute for Biological Studies in San Diego, California. The Salk Institute is considered one of the best medical research institutes in the world. I am writing this text because of my concern about the introduction of brinjal genetically modified with bacterial Bt toxin into the food supply of India. There are several reasons that the introduction of this genetically engineered (GE) food plant should not be allowed. They include:

1) The lack of need. Brinjal is not a crop threatened by an overwhelming insect infestation.
2) Environmental risk. Brinjal is native to India and the GE genes will unquestionably contaminate the native population.
3) Higher costs. The purchase of seeds on an annual basis as opposed to saving seed from year to year will increase costs at all levels of the food chain.
4) Social and political dependence. Once a foreign company controls the seed market of any single food plant, seed for more GE plants will follow, and the company will have tremendous power over both the farmers, which constitute a major segment of the Indian population, as well as the political process. This has clearly happened in the United States (US), where Monsanto is a major financial supporter of both political parties, and therefore has political appointees who dictate both national and international agricultural policy.
5) Finally, GE brinjal expressing Bt protein poses a serious health risk to those who consume it. This is the issue that I wish to address. First, however, I would like to debunk some myths that are used by the proponents of GE brinjal to claim that it is safe.

Bt cotton (I will use the term Bt throughout to mean a family of Cry 1 insecticidal endotoxins produced by the bacterium Bacillus thuringiensis) is grown in India, and it is claimed that there have been no serious human health problems due to its cultivation. This statement is irrelevant since cotton is not consumed by people, but as you must be aware there is very good evidence that the consumption of Bt cotton plants by farm animals leads to serious health problems and sometimes death. Bt maize is grown in the US and it is claimed that because there has been no documented Bt maize-associated disease, Bt brinjal is therefore safe to eat. This conclusion is invalid for several reasons.

First, only a small fraction of the Bt maize produced in the US is eaten directly. The vast majority in used as animal food and to make oil, high fructose syrup, and ethanol, none of which would contain the Bt

protein. The maize containing the Bt protein that is consumed is largely in the form of highly processed corn chips and related snack foods that are not major components of the diet. In contrast, the Bt protein in brinjal will be directly consumed in massive quantities because the vegetable is a significant component of the Indian diet. In addition, it will be prepared in an infinite number of ways, leading to potential chemical changes in the protein causing unknown toxicology and immunogenicity. Cooking can readily change the structure and antigenicity of a protein. Did the feeding studies done with Bt brinjal include cooked product?

Second, it is logically false to claim that because there is no evidence of illness following the introduction of a GE product, therefore the product is safe to eat. In fact, perhaps my major concern with the introduction of any GE food is that even if it did cause an illness, it would not be detected because of the lack of epidemiological studies and the technical limitations for detecting such an illness. For example, to detect an epidemic of a disease, an incidence of at least of two fold above the background rate of the disease is required. Therefore, if Bt brinjal were to cause a disease like Parkinson's, which has an incidence of about 20 new cases per year per 100,000 people, then in India 200,000 new cases per year would have to be diagnosed and tabulated in order to identify a significant increase, and there would still be no way to associate the disease directly with a Bt crop. In addition, many environmentally caused diseases take many decades of exposure to develop symptoms. Clearly, once Bt brinjal is commercially released, there will be no way to monitor adverse health effects caused by the product.

There are at least four mechanisms by which the introduction of the Bt toxin gene into the Brinjal genome can cause harm. These include (1) the random insertion of the Bt gene into the plant DNA and the resulting unintended consequences[1], (2) alterations in crop metabolism by the Bt protein that results in new, equally unintended and potentially toxic products, (3) the direct toxicity of the Bt protein, and (4) an immune response elicited by the Bt protein. There are scientifically documented examples of all four toxic mechanisms for Bt crops.

An example of the first is the discovery of unintended alterations in the synthesis of nine known carcinogens caused by the GE modification of tobacco, a crop in the same plant family as brinjal[2]. An example of the second is the abnormally high levels of the fiber molecule lignin produced in Bt maize[3]. This trait was discovered because of dramatic changes in the stiffness of the corn stalk. Since multiple strains of Bt maize have this trait, it is most likely that increased lignin production is associated with the expression of the Bt protein itself, not due to mutations caused by the GE process itself (item one above)[4]. Importantly, the synthetic route to lignin in plants is shared with that of rotenone, a plant metabolite known to cause Parkinson's-like disease in animals. It is very likely that there are many other unintentional changes in Bt crops, and a few more have recently been documented[5].

The toxicity and immunological hazards of the Bt protein are discussed in more detail below. It should be emphasized that the majority of this material has been published in peer-reviewed journals and reproduced in more than one laboratory, therefore ruling out the possibility of an individual investigator's bias.

Allergies are complex responses of the immune system to foreign substances and vary widely between individuals in an unpredictable manner. Bt toxins have long been used as insecticidal sprays on a variety of crops, but the spray is a less toxic form of the protein than that made by GE plants. The spray consists of spores of the Bt toxin that must be activated in the gut of the insect. In contrast, Bt toxin in brinjal is a highly activated form of the Bt protein that does not require modification in the insect gut to become toxic. It is therefore much more potent than that used is sprays. Despite this major difference in Bt form and activity, and even though the spray is not ingested by farm workers, there is solid evidence that the Bt proteins elicit a strong immune response in some workers after a few months exposure, and it is likely that many more workers are affected, but associate their allergic response with the spray and decide to work elsewhere[6]. Since Bt proteins have amino acid sequence homology with known allergens, allergic

reactions in some individuals are not unexpected[7,8]. Most importantly, it should be emphasized that the concentration and amount of Bt toxin protein that people will eat in Bt brinjal will be thousands of times higher than the exposure levels of farm workers.

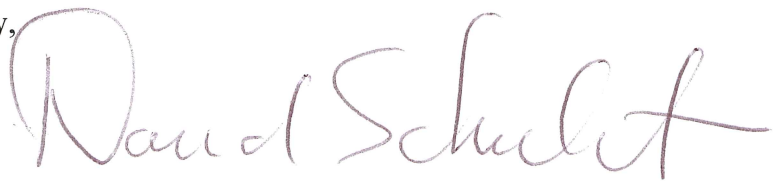
In support of the human data, when animals are exposed to Bt toxins, the toxin also acts as a potent immunogen, eliciting responses from both the blood and gut-based immune systems[9-11]. Based upon these data, the US Environmental Protection Agency (EPA) recommended extensive safety testing of Bt crops for this trait[12], but due to the lack of required safety testing for GE food crops in the US, this was never done[4]. Although I am sure that you are aware of this fact, it should be restated that the US agencies that allowed the introduction of Bt food crops did not require any demonstration that the GE food was safe for human consumption.

Additional animal studies have shown that Bt toxins directly cause tissue damage. For example, Fares and El-Sayed demonstrated that feeding mice Bt potatoes caused the appearance of structurally abnormal cells in the gut[13]. Other studies reported histopathological changes in the kidney and liver of rats feed Bt corn[14], and changes in urea and protein levels in the urine of rats fed Bt rice[15]. While there was no extreme pathology in any of these studies, they were all short term (up to 90 days) and done with healthy animals. The outcome may be quite different if the Bt protein is consumed by infirm, under nourished, aged, or very young individuals, for the body responds quite differently in individuals compromised by any of these conditions, and all groups will be eating Bt brinjal. As far as I know none of the safety testing of Bt brinjal has taken this fact into account.

Since a significant fraction of any population falls within one or more of these categories, it is difficult to believe that the regulatory authorities could overlook this problem. To emphasize this point, it has recently been shown that the immune response to feeding very young and very old mice Bt maize is different from that of the non-GE maize fed control groups. Most interestingly, the immune responses were also very different in the young and old age groups[16]. These very robust data clearly demonstrate how difficult it is to extrapolate negative data from short term feeding studies in healthy adult animals to real world situations. They also further emphasize the need for extreme caution before the irreversible introduction Bt brinjal into the food chain.

The above citations clearly show that the family of Bt proteins can act as allergens in animals and some individuals. Most importantly for the health of the Indian population, if the introduction of Bt brinjal is allowed, an enormous number of individuals are going to consume amounts of Bt toxin that are thousands of times higher than anytime previously in the short history of this GE technology. This population is extremely heterogeneous in genetic makeup, age, and also with respect to underlying health. It is the genetics and health status of the individual that determines his or her response to foreign proteins such as Bt toxin. Less healthy individuals are much more prone to negative immune reactions. Since the ability of Bt toxin to cause an allergic response in some individuals is unambiguous, it is virtually certain that within the vast Indian population a large number of people eating Bt brinjal are going to be or will become allergic to this foreign protein; this number cannot be predicted and some of the immune responses will likely be severe, causing anaphylaxis and possibly fatalities. Since there will be no way of tracking these adverse reactions within the population, and since once Bt brinjal is commercially grown, its genetic presence within a major calorie source for the Indian population is irreversible, a simple decision has to be made. Is the negligible benefit of Bt brinjal worth the clear risk? My conclusion is that it is not worth the risk and that it would be a profound disservice to India if Bt brinjal were allowed to enter her food supply.

Respectfully,



David Schubert, Ph.D.
Professor
Salk Institute for Biological Studies
La Jolla, CA 92037

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