*A report by R Prasad with the heading "GM crops' biosafety testing procedure questioned" appeared in the June 25, 2008 issue of "*The Hindu*". It had to do with qualms raised by Dr P M Bhargava regarding the manner in which genetically-modified (GM) crops, especially those expressing the* Bacillus thuringiensis *toxin ("Bt crops"), were being approved for release by the Genetic Engineering Approval Committee (GEAC) of the Ministry of Environment and Forests, Government of India (see* http://www.thehindu.com/2008/06/25/stories/2008062555961400.htm*).*

Because of the significance of the scientific issues involved, a request was made to Dr Bhargava to prepare a summary of the problems as he saw them. He was told that a similar request would be made to a scientist who was acquainted with current procedures for testing and validating the release of genetically modified crops and had a different view. The articles would be exchanged between the two so as to provide both authors with the opportunity to correct errors of fact, re-assess interpretations and revise their respective texts. They would then appear in Journal of Biosciences *as back-to-back opinion pieces. The hope was that this would initiate an informed debate.*

Dr Bhargava agreed to the proposal and sent in his submission on July 14, 2008. Following that, one after the other, three scientists who were well-known for their expertise in plant molecular biology, biotechnology or genetics were invited to respond. The first two declined to take up the invitation for different reasons. The third indicated that a response was about to be sent but it has not been received.

Under the circumstances an abridged version of Dr Bhargava's opinion is being published here as a stand-alone Commentary. Journal of Biosciences *remains open to a reasoned rebuttal of its contents. If it is found suitable for publication, the course of action originally proposed will be followed: the writer and Dr Bhargava will be given an opportunity to examine each other's views, modify their texts accordingly and submit their cases in brief.*

Editor

Commentary

Insufficient regulatory supervision prior to release of genetically modified crops for commercial cultivation in India

(1) Do we need GM crops?

No. We have far better alternatives such as integrated pest management (IPM), biopesticides and appropriate agro-practices including organic farming for almost all crops. IPM is a part of the country's stated national agriculture policy. It has been shown to be effective but is not being used.

(2) Was appropriate risk assessment carried out in the case of the Bt-cotton crops that have been released?

No. For example, our present system of testing for allergenicity does not take into account recent work (e.g., papers in this area – a paper titled "Allergic potential of novel foods" in the *Proceedings of the Nutrition Society*, volume 64, issue No.4, pp 487–490 of November 2005; a paper titled "Allergenicity Assessment of Genetically Modified Crops – What makes sense?" in *Nature Biotechnology* of January 2008, volume 26, pp 73–81; a paper titled "Transgenic expression of bean alpha-amylase inhibitor in peas results in altered structure and immunogenecity" in *Journal of Agricultural Food Chemistry*, 2005, volume 53, pp 9023–9030). The Annexure lists 29 tests relevant to the release of GM crops. Only a few have been done for Bt-cotton and GM crops in the pipeline, and that too inadequately (see item 5 below).

Keywords. Field trials; GM crops; monitoring; regulatory supervision; risk assesment

Abbreviations used: Bt, *Bacillus thuringiensis*; GM, genetically-modified; GMO, genetically-modified organism; IPM, integrated pest management

The "Annexure" pertaining to this article is available on the *Journal of Biosciences* Website at *http://www.ias.ac.in/jbiosci/june2009/pp167–168/annex.pdf*

(3) Were field trials adequately done and appropriately monitored?

No. So far no clear-cut objective and substantive parameters for monitoring have been worked out. (Draft guidelines have been prepared only recently.) There has been no professional training for monitors.

(4) Do certified, professionally reliable and competent facilities exist in the public sector at one place for assessment of risks and validation/cross-validation of data provided by companies seeking release of their genetically modified crops?

No. We badly need such facilities.

(5) Have there been fallacies in existing procedures on the basis of which approvals have been given or are being considered for open release of GMOs?

Yes**.** All the tests carried out so far on the basis of which approvals have been given or are in the pipeline have been done either by the applicants themselves or by organisations to whom samples were supplied by the applicants. No note has been taken of the substantial evidence indicating harmful effects of GM crops, for example, Bt-cotton, the only GM crop approved for open release. Field trials (of, for example, Bt-Okra) have been conducted without appropriate professional approval of the State Government. Inconsistencies between the data and the conclusions drawn by the applicant have been ignored.

(6) Does any system exist for punishment in case of violation of existing laws?

No. We have no law that permits farmers whose fields are contaminated with GM plants from adjoining fields as has happened at places in the country, to claim compensation. (For example, we have in the market Doritus corn chips now, which have been shown to contain GM corn and GM soya.)

(7) What is the international experience with regard to genetically modified organisms (GMOs)?

We should learn a lesson from international experience and new knowledge gathered since the approval of the first Bt-cotton in India. Thus, on 16th May 2008, a 147-Nation Conference in Bonn concluded that GMOs were responsible for damage to other plants. (Understandably the US was not a party to this conclusion.) The above-mentioned UN study says that India faces a huge risk because of safety norms on genetically modified crops not being in force.

(8) What is my recommendation?

What I have said above would favour a moratorium on the sale of any GM seed or open field trials of any GM crop, for a period of 7 to 8 years. During that period research should be carried out up to the stage of contained field trials and a laboratory set up in the public sector, exclusively for risk assessment of GM crops (see point 4). It should be financed by the Central Government but should be managed jointly by the Central Government and civil society in a manner that will ensure public credibility and acceptance. Concurrently, our requirements for release of a GMO in the environment must be revised taking into account what is stated in this note. A system should be set up for identifying violations of the law with regard to GMOs and appropriate penalties imposed for such violations.

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Annexure to *Commentary* entitled

Insufficient regulatory supervision prior to release of genetically modified crops for commercial cultivation in India

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Tests that must be done on GM plants intended to be released in the environment

(1) Using controlled field trials and studying the impact on ecology (for example, on populations of bees and other useful insects).
(2) Monitoring gene flow from transgene-carrying organisms to other organisms.
(3) Guarding against dispersal into areas where harm could be done (as happened with water hyacinth and parthenium)
(4) Studying the stability of the transgene product in the whole organism and/or parts thereof under various conditions of storage or handling (e.g. cooking in case of an edible genetically-modified organism [GMO]).
(5) Monitoring the effect on soil microflora.
(6) Testing for allergenicity.
(7) Carrying out acute toxicity studies with native (not "surrogate") protein, genetically-modified (GM) seeds and other GM plant material that is normally ingested by animals, including cattle. These studies should be done both on experimental lab animals and on farm animals such as goat, sheep and cows.
(8) Carrying out chronic toxicity studies (including carcinogenicity) as above.
(9) Studying the effect on microflora harboured by cattle.
(10) Looking for effects on soil micronutrients in regions where the GMO is likely to be released or find its way.
(11) Comparing the growth characteristics of the GMO and the parent organism.
(12) Looking for the emergence of new dangers, for example of 'super weeds', following prolonged use of herbicide-resistant GM crops.
(13) If the GMO is a plant, measuring its biomass productivity in comparison to the parent.
(14) Comparing the inputs required for optimal growth of the GMO relative to the parent organism and comparison of the relative cost: benefit ratio (this should include financial inputs and social costs).
(15) Monitoring the effect on useful insects.
(16) Monitoring the development of resistance to the trait for which the plant is genetically modified.
(17) Studying the increase in requirements for refuge crops.
Refuge crops are usually non-GM crops planted along with GM crops, for example, to provide an environment in which resistant pests might be out-competed by the normal (sensitive) pests.
(18) Studying a possible increase in the susceptibility of GM crop to pests and infectious agents other than those that may be expected to be killed or inactivated by the effects of the transgene.
(19) Studying the effect on the populations of non-susceptible pests following at least five successive plantations in the case of GM plants carrying the *Bacillus thuringiensis* (Bt) toxin gene.
In many cases involving successive plantations of Bt crops, the density of pests that were not originally susceptible to the Bt toxin increases. The number five is used as a guideline on the basis

of published data on the progressive increase in the population of pests that were initially known to be resistant to the Bt toxin.

(20) Carrying out a statistically validated programme involving the karyotyping and gross chromosomal analysis of genetically modified food plants and their consumers.
Chromosome alterations, e.g. translocations, can lead to serious health problems.

(21) Monitoring reproductive interference.
This refers to a change in the reproductive capability of an organism consuming the GMO or a product derived from the GMO.

(22) In the case of GM food material, possible interaction with commonly used drugs.
Drug-drug interaction is today accepted as an important issue in medical practice. A new or altered protein could have a drug-like effect.

(23) DNA fingerprinting and proteomics analysis, and characterisation, both structurally and functionally, of new and altered proteins.
It is established that genetic engineering leads to a higher rate of mutation than conventional breeding. DNA fingerprinting may (of course, not always) pick up some of the mutations. Functions in a cell largely depend on its protein profile. The only way to pick up changes in cellular protein profiles is through a proteome analysis which would identify new, altered or deleted proteins. Sequence comparison with known proteins in the protein data base (coupled with the knowledge we have of structure-relationships in proteins) can give some idea of the possible function of a new or altered protein – for example allergenicity, examples for which exist in the literature.

(24) Sequencing of transgene-flanking regions and the transgene; identification of the site(s) of integration of the transgene in the GMO.
The region that is sequenced should be large enough to identify the nature of the site of integration. For example, if insertion of the transgene takes place at certain invariant sites in the telomeric region, there could be serious problems.

(25) Identifying changes in the glycosylation pattern of proteins, which are known to occur in GMOs (and can affect the function of the protein).

(26) A study of the transcriptome.
Changes in transcription pattern can lead to changes in proteins and thus changes in their functioning. This is related to items 2 and 3 mentioned above and is intended to provide similar information pertinent to safety assessment.

(27) Monitoring changes in the relative concentration of major and important intracellular metabolites and precursors.
Normal ranges are available in many cases or can be easily obtained. For example, the free amino acid profile of a cell is generally reflected in the gross amino acid composition of the total protein in the cell. A major change in the concentration of just one amino acid can lead to translational errors and changes in the protein profile (apart from influencing pathways via feedback etc.). The metabolites and precursors chosen will depend on the particular case.

(28) Monitoring changes in surface properties that may affect normal interactions between species, and with the environment.
This can be studied through techniques such as scanning electron microscopy, atomic force microscopy and fluorescence-activated cell sorting (FACS). The cell types chosen would depend on the GMO and its projected use.

(29) Development in the country (if not already available) of a technique to determine with accuracy, even a 0.01 % contamination with GMO or its product.
0.01% is the level of contamination with a GMO that can be reliably detected with today's technology. It is also the limit of contamination of non-GMOs, by GMOs, permitted by the Government of India.