REGULATORY REGIMEN FOR GENETICALLY MODIFIED FOODS
THE WAY AHEAD

April 2004

Indian Council of Medical Research
New Delhi

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I. Introduction:

During recent years there has been considerable advancement of Science and Technology for using Modern Biotechnology tools for the production of foods, feeds and drugs. These include the cultivation of genetically modified (GM) crops, use of genetically modified organisms (GMO), specially recombinant bacteria and development of transgenic animal models especially using dairy cattle as bioreactors for producing pharmaceuticals to alter composition of cows milk to resemble human milk. Research is also helping in developing plants such as banana with vaccine against cholera and tomato and muskmelon with vaccine against rabies. Cures even for diabetes and cancer have been attempted with encouraging results through the production of immune proteins in plants. However, among these global developments, the cultivation of GM crops developed for both food and industrial purposes are most important in the Indian context.

In the year 2003 genetically modified crops were cultivated in 67.7 million hectares (167 million acres) which involved 7 million farmers in 18 countries. There has been a 40-fold increase in the global area of transgenic crops form 1996 to 2003. Around 20 million hectares in developing countries were used for GM crops. The following six countries grew 99% of the global transgenic crops:

Country	Area in million hectares	% of Global total
USA	42.8	63
Argentina	13.9	21
Canada	4.4	6
Brazil	3.0	4

China	2.8	4
South Africa	0.4	1

The rest of the countries like Australia, Mexico, India and EU countries like Spain, France and Germany, contribute remaining 1%. India grew *Bt* cotton in around 0.1 million hectares in 2003 which was double of 2002. Brazil and Philippines initiated planting of GM crops (herbicide tolerant soybean and *Bt* maize respectively) in 2003.

The genetically engineered crops commercially cultivated include cotton, soyabean, maize, canola, tomatoes, potatoes and squash. Among these, four crops dominate the GMO markets of the world with soyabean being the most important (61%-41.4 million hectares), followed by maize (23%-15.5 million hectares), cotton (11%-7.2 million hectares) and canola (5%-3.6 milllion hectares). The rest of the crops constituted 0.1% of the total acreage under GM crops. Seventy three percent of the GM crops raised were for herbicide tolerance, 18% were aimed at resistance to insects and 8% were varieties containing both traits. Only less than 0.1% of the crop was aimed at other characteristics like yield improvement, vitamin enrichment, etc. Although the cultivation of GM crops have been claimed to be profitable to farmers, the impact varies by year, location, crop, etc. The global market in transgenic plants is estimated to grow rapidly to $6 billion by the year 2005.

From the Indian view point, more than herbicide resistance, stress resistance to drought, temperature and poor soils, nutritional enrichment, increased productivity and pest resistance are important. Also GM varieties which will eliminate the problem of naturally occurring toxins like the unusual toxic amino acid in *Lathyrus sativus* are important for us.

II. Concerns

Although GM plants have the potential to improve agriculture production, food quality, nutrition and health, various uncertainties exist regarding safety of these foods because there is limited scientific evidence regarding their toxicity or health risks, the methodology used for assessing the risks is not robust enough or sensitive enough, and the molecular and genetic effects of the technology are unpredictable in nature. Widespread concerns have been expressed by the public and scientists about effect of GM foods on the environment, lack of consumer benefits, ethical issues and the perception that a few large multinational corporations will be the prime beneficiaries and would dictate world markets.

(a) Environmental concerns

Emergence of resistance: Many crops have been engineered for pest disease and herbicide resistance. There could be a potential for development of resistance in the target organism. This has been particularly observed in crops developed for insect resistance like cotton. This has resulted in the use of a 'refugia' while cultivating *Bt* crops. Similarly in the case of herbicide resistance crops like soyabean, a potential for development of superweeds due to spread of herbicide resistance from GM crops to weeds exists.

Genetic pollution and pollen movement: The potential for transfer of pollen from GM crops to other plant species has been an issue of much concern. For example, the transgenic material from a GM maize cultivated by a farmer can be transferred without

the farmer's knowledge to a non-GM maize cultivated in the neighbouring field. Such kind of pollen transfer varies with different environmental conditions.

Loss of biodiversity: Contamination of non-GM varieties of plants through pollen drift can cause loss of biodiversity.

(b) Health and Safety Concerns

The use of recombinant DNA (rDNA) technology in the production of GM foods involves transfer of genes from different species into the food producing organism. Such a transfer is facilitated along with various regulatory elements obtained from bacterial or viral sources that are required to empower to produce the trait in the host organism. The safety of these components of the genetic construct is not clearly known as they have the potential to induce toxicity, transfer to gut flora or produce unintended effects leading to changes that are relevant from toxicological/nutritional perspective. Specific safety issues associated with GM foods include direct or indirect consequences of new gene product or altered levels of existing gene product due to GM, possibility of gene transfer from ingested GM food and potential adverse effect like allergenicity and toxic effects. Depending on the modified component, the GM food may contain or consist of GMO or be produced from GMO but not contain GMO. The safety concerns are centered around potential toxicological and nutritional changes that could be harmful to human health.

Toxicity Potential: Various toxicants are known to be inherently present in different plants. Genetic engineering has the potential to alter such constituents or produce newer toxicants. Crops developed for pest resistance and herbicide resistance are particularly focussed for toxicity concern. The case of GM potatoes experiencing *Galanthus nivalis* lectin gene for insecticidal properties is an example of the potential of GM foods to cause

toxicity. In a group of rats fed with GM potato damage to immune systems and stunted growth was observed and the experiment had generated considerable controversy.

Nutritional composition: Genetic modification of plants may result in alteration in nutritional composition which in turn may affect the nutritional status of the consumer or population groups. Currently developed plants with improved nutritive value include GM rice with enriched vitamin A and GM soyabean and rapeseed with modified fatty acid. The impact of such intended modification in nutrient level in crop plants can affect nutritional status of the individual. There is also the potential for unexpected alteration in nutrients as it was observed in the case of GM rice (accumulation of xanthophylls, increase in prolamines). Such changes can affect nutrient profiles resulting in nutritional imbalances in the consumer.

Allergenicity: The allergenicity potential of the new protein expressed on the transgene inserted into the plant is a major food safety concern. Most traits introduced into GM crops result from the expression of one or more protein that may possess allergenic properties. Crops modified for insect resistance have been shown to have the potential for allergic responses. This has been highlighted in the recent findings of Starlink variety of GM maize which has been shown to possess allergic properties in the food chain in USA, EU and Japan. The allergenicity potential of GM food has often been difficult to establish with existing methods as the transgenes transferred are frequently from sources not eaten before, many have unknown allergenicity or there may be a potential for genetic modification process to result in increase of an allergen already present in the food.

Antibiotic Resistance - Potential for Gene transfer: Concern has been expressed on the possibility of transfer of GM DNA from the plant to gut microflora of humans and animals. Of importance have been the antibiotic resistant genes that are frequently used as selection markers, in the genetic modification process. Such genes have the potential to adversely affect the therapeutic efficacy of orally administered antibiotics.

It is significant to point out that there has been no report of any adverse health effects of GM foods and there are no peer reviewed publications on the health effects of GM foods in humans.

© Ethical Concerns

Many persons feel that gene transplantation processes to the germ plasm of crops violates the natural order, but it is not clear how this technique of genetic modification is distinct from plant hybridization, chemically or radioactively induced mutations, cell fusions or synthetic foods? Concerns have also been raised by vegetarian groups on using animal genes in plants.

(d) Socioeconomic Concerns

The perspective on the use of modern biotechnology for food and agriculture differs not only among the developed countries and developing countries but also differs among high income countries. While most EU countries are not enthusiastic about GM food, it is more acceptable for countries like Australia, Canada and USA because of the importance of export of agriculture to their countries. Developing countries such as Argentina and China are promoting GM foods in a big way. Some developing countries considering commercialization of GM crops are hesitant to do so because of the fear of losing access to the European market not only for commodities that have been genetically

modified but also for those that have not been modified. Practically it would be difficult to keep GM and non-GM commodities separate and often they could get mixed.

Modern agriculture biotechnology is increasingly subjected to Intellectual Property protection, and is generally developed by Private Sector companies. This could also lead to reduced competition, monopoly of profits and exploitation of small farmers. It is also felt that GM crop production may harm small farmers in the developing countries as imported GM commodities will undercut local production. Agriculture biotechnology could lead to increased inequality of income and wealth because large farmers may capture most of the benefits.

The potential benefits could include the productivity gains needed to feed the increasing population, lesser expenditure on pesticides/herbicides, improved nutritive value, durability of products during post harvest stage, etc.

III. Current Status of Safety Assessment of GM foods - International

The safety assessment of GM food has been addressed by several international organizations like the Organization for Economic Cooperation and Development (OECD), Food and Agriculture Organization (FAO), World Health Organization (WHO) and Codex Alimentarius Commission (CAC). The general consensus of these organizations has been that the safety assessment of GM foods requires an integrated and stepwise case-by-case approach. Various strategies have been designed to assess the safety of GM crops and these have been evaluated in a series of workshops and meetings.

Joint FAO/WHO Expert Consultations on foods derived from biotechnology

Various consultations have been convened by WHO and FAO to address the safety issues concerning GM foods. The concept of Substantial Equivalence (SE), initially formulated

by OECD and evaluated in these consultations, became a key element in the safety assessment procedures for GM foods. Substantial Equivalence involves a comparative approach where the relative safety of GM food or food component to an existing food or food component is established. Factors taken into account in the safety assessment include phenotypic, agronomic and functional characteristics as well as potential intake and dietary impact of the introduction of GM foods. The outcome of such comparison will be that the food is (i)SE and thus no further testing is required, (ii)SE except for the inserted trait such that the focus of safety testing is on this trait or (iii)not SE and a case-by-case assessment is carried out according to the characteristics of the new product. Depending on the type of outcome the food is subjected to further nutritional and toxicological studies. A decision-tree approach has also been prepared by some authorities for determining the extent of testing required in specific cases. SE determinations have been carried out for a variety of GM crops.

Codex Alimentarius Commission

The Codex Alimentarius Commission of the FAO/WHO set up an Ad-hoc intergovernmental task force on foods derived from biotechnology to develop standards, guidelines and recommendations for foods derived from biotechnology. The task force identified that the risk assessment of GM foods requires scientific data which addresses the current safety concerns of GM foods like the effect of the genetic modification process including the function and properties of newly inserted genes, the safety and nutritional properties of newly expressed substances in the food and their impact on diet, potential for allergenicity, potential for gene transfer to human and animal cells, and unexpected changes in the composition of the modified product due to insertion of novel

genes or suppression of constituent genes. A draft guideline for the conduct of safety assessment of foods derived from genetically modified plants has been brought out by the task force.

Cartagena Protocol on Biosafety :

The Cartagena Protocol was negotiated under the auspices of the Convention of Biological Diversity (CBD) in 1992. The Protocol provides rules for safe transfer, handling and disposal of Living Modified Organisms (LMOs) or Genetically Modified Organisms (GMOs). Its aim is to address the threats posed by LMOs to biological diversity, also taking into account the risks to human health. The Protocol takes into account the general principles of risk assessment developed by international bodies. Two features of the protocol, the Advance Information Agreement (AIA) and the Precautionary Approach are being incorporated in risk/safety assessment procedures in many countries particularly in the context of trade in GMOs. The AIA provides for a prior assessment by importing country of GMOs intentionally introduced into the environment like seeds for plantation, live fish for release etc. This agreement calls for documentation and identification of LMOs which include the relevant trait, information handling, storage, transport and use along with a full report or risk assessment. In making the decision to import, the Protocol allows a precautionary approach to be used to restrict or ban the GMO if there is a lack of scientific certainty due to insufficient information on the potential risks that LMOs can have on biodiversity and human health.

World Trade Organization (WTO) agreements :

The WTO is mainly involved in establishing rules for international trade in GM foods. Two agreements in the WTO apply to risk assessment and labeling of GM foods. These

are the Agreements on Sanitary and Phytosanitary Measures (SPS) and Technical Barriers to Trade (TBT). The risk assessment of GM foods for trade requirements is addressed under the agreement on Sanitary and Phytosanitary Measures (SPS). This agreement deals with application of food safety and animal and plant health regulations. By imposing science-based disciplines and requiring risk assessment based on science and applied only to the extent necessary to protect human, animal or plant life or health, it aims to prevent governments from using health and safety laws to limit international trade. The TBT agreement assists to ensure that WTO members do not use domestic regulations, standards, testing and certification procedures to create unnecessary obstacles to trade. It encourages countries to use international standards where appropriate.

IV. Regulatory System for GM foods in Selected Countries

(a) USA:

Regulation: Coordinated framework for regulation in biotechnology.

Agency for environmental safety assessment: USDA, EPA

Agency for food safety evaluation: FDA.

Highlights:

- Sectoral approach regulation
- Procedures for notification, performance standards, safety standards.
- Labeling policies: no mandatory labeling.
- Mandatory pre-market approval (under consideration).

(b) European Union (EU):

Regulation: Environmental release and marketing, contained use, safety review and labeling.

Agency: Directives for deliberate release into environment and placing on the market.

Highlights:

- Procedures for authorization and notification.
- Procedures for risk assessment.
- Mandatory monitoring, labeling and traceability, consultation of scientific committees, consultation of public
- Establishment of 1% threshold for adventitious contamination of non-GM with GMO.

(c) Australia:

Regulation: National Gene Technology Regulatory System.

Agency: Office of the Gene Technology Regulatory

Highlights:

- Whole of government approach
- Labeling of foods containing GM protein or DNA in final product
- Minor ingredients and highly refined oils exempt from labeling
- 1% tolerance for unintended mixture

(d) China:

Agency: Safety Administration Office for Agricultural Biological Genetic Engineering (Ministry of Agriculture)

Highlights:

- Procedure for administration of registration of imported feed and food additives

- Labeling requirements for all imported GM soyabean, corn, rapeseed, cottonseed and tomatoes
- Approval procedure for release into environment

5. Current regulatory system in India:

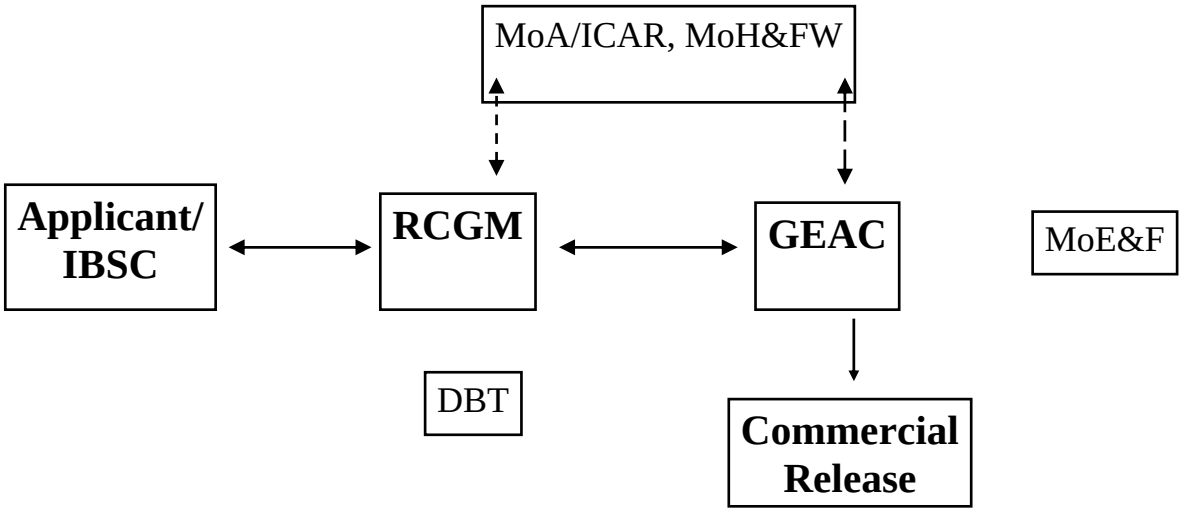
The following are the existing guidelines in India for transgenic crops:

A. The EPA Act 1986 and Rules1989 of **Ministry of Environment and Forests**, namely which deals with rules and procedures for handling GMOs and hazardous organisms. The Genetic Engineering Approval Committee (GEAC) established by the Ministry acts as a statutory body for review and approval from environmental angle of activities involving large scale use of GMOs and their products in R&D, industrial production, environmental release and field application. The Ministries of Environment and Forests has issued a draft notification in July 2001 as an amendment regarding the permission and approval of foodstuffs. This notification restricts a person from importing, manufacture transport, store, distribute or sale of any food, feed, raw or processed or any ingredient of food, food additives or any food product that contains GM material, without the approval of the GEAC. A Biotechnology Coordination Committee under the GEAC functions as the legal and statutory body with judicial powers to inspect, investigate and take punitive action in case of violation of statutory provision under EPA. Issues for action include review and control, and monitoring of large scale use of GMOs in R&D and industrial production, environmental release and experimental field trials.

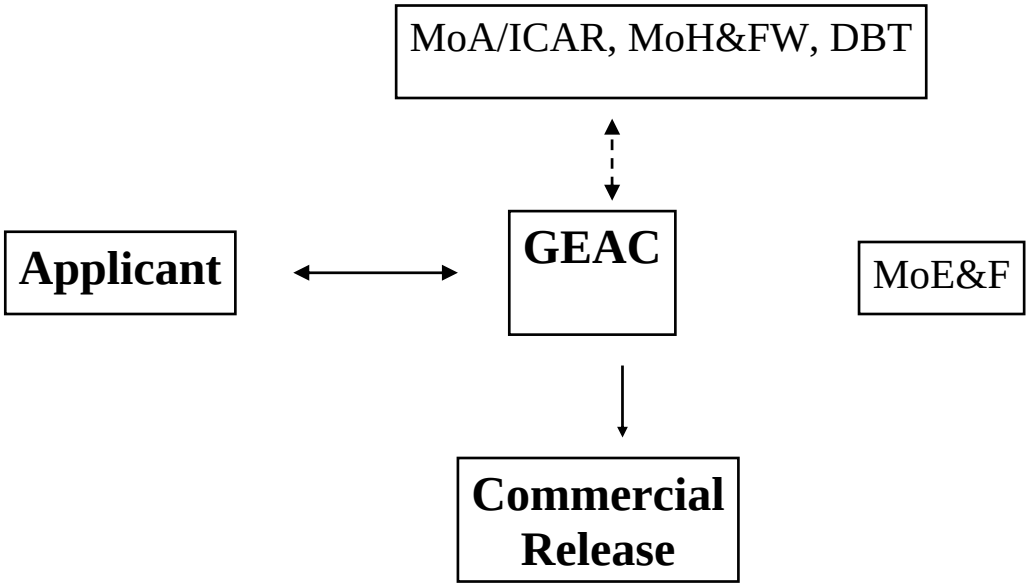
B. The Review Committee on Genetic Manipulation (RCGM) under the **Department of Biotechnology** (DBT), Ministry of Science and Technology, monitors the safety related aspects of ongoing research projects involving GMOs. It brings out manuals of guidelines specifying procedures for regulatory process, activities involving GMOs in research, use and application from environmental safety angle (Recombinant DNA Safety Guidelines 1992 and Revised Guidelines for Research in Transgenic Plants 1998). The mechanism of implementation of guidelines is through the Recombinant DNA Advisory Committee (RDAC) and Institutional Biosafety Committee (IBSC). The RDAC takes note of development at national and international levels in biotechnology on recombinant research, use and application while the IBSC is the nodal point for interaction within an Institute, University, Commercial Organization included in rDNA research or implementation of rDNA guidelines. The IBSC is constituted in all centres engaged in genetic engineering research and production activities. Such committee should also include a representative from the health sector. In addition there is a provision of State Biotechnology Coordination Committee (SBCC) and District Level Committee (DLC).

The current system for in house development and imports is given below:

Agencies Involved in Rules,1989 of EP Act 1986 for Environmental release of transgenic crops for in-house development



Agencies Involved in Rules,1989 of EP Act 1986 for Environmental release of transgenic crops/ food products by imports



C. **Limitations of the Regulatory System in India**

(i) Lack of adequate standards for risk assessment

(ii) The procedure and information required for a full environment risk assessment and appropriate safety and emergency responses not laid down.

(iii) Instructions and conditions for use on labeling and packaging of products containing GMOs yet to be specified.

(iv) Detailed safeguards as embodied in the Cartagena Protocol yet to be incorporated.

(v) Lack of infrastructure for risk assessment.

(vi) Shortage of skilled personnel from laboratory researchers to extension service officers.

(vii) Although food safety studies are fairly rigorous as prescribed by the RCGM, there are always uncertainties in the risk assessment process because this is a novel technology. Also there needs to be special considerations when the food forms a major portion of the diet (for e.g. cereals) and the special sociocultural habits of the population need the consumption of parts of the plant which are unconventional for other civilisations (e.g mustard leaves). In such a scenario special studies may have to be undertaken even on human volunteers.

VI. The Way Ahead:

A good beginning had been made in India with the involvement of Ministry of Environment and Forests as well as Department of Biotechnology along with other Ministries and Departments regarding the regulatory aspects on GM foods specially those pertaining to introduction of GM crops.

There is an urgent need to **strengthen the coordinating mechanism** concerning the area of GM foods in the country. Currently the Ministry of Environment and Forests as well the Department of Biotechnology, both of whom were pioneers in regulating GM foods in India as well as the Ministries of Agriculture, Health, and Commerce have considerable stake in the field. A whole of government approach rather than sector by sector approach is essential. A 'National Gene Technology Regulatory System' which will have the overall mandate of regulating the use of biotechnology products, be they plants, microbes, animals or drugs, needs to be established with the Office of the Gene Technology Regulator to protect the health and safety of the people and to protect the

environment by identifying and managing risks posed by the gene technology. Perhaps this could be achieved by designating one of the ministries for this purpose.

However, the **mechanism of implementation** of the Ministry of Environment and Forests notification needs to be developed specially with those concerned with Food Control activities. The various factors pertaining to food safety to be looked into by the Ministry of Health both at the application stage, commercial release stage, import and post market surveillance are:

(a) Genetic modification process

(b) Safety of new proteins

(c) Occurrence and implications of unintended gene transfer between the GM plant food and the gut microflora of humans or animals.

(d) Potential allergenicity of new proteins (either on consumption or occupationally exposed)

(e) Role of new food in the diet and dietary intakes.

(f) Effect of processing and cooking.

(g) Experimental studies in animals and eventually controlled human trials.

(h) Finding out long term or rare effects through targeted epidemiological techniques beyond any normal post marketing data collection.

For GM foods that are imported into the country and GM foods that are marketed in the country after import or even GM foods clandestinely grown without undergoing the proper approval process, the food control mechanism to oversee such activity needs to be developed. The Health Ministry with its vast network of Food

Control infrastructure currently in place along with the State Governments and Union Territories could very effectively be utilized for the control of GM foods also. The role envisaged for the Health Ministry should include supervision of sale of GM foods in the domestic market, their inspection, testing, legal action to be taken for non-compliance, consumer awareness activity, etc. For this purpose, adequate infrastructure needs to be built up in terms of modern laboratory facilities, training of food inspectors and laboratory personnel, etc.

It is likely that in the near future a large quantity of GM foods will be moving in the international market and India would be both importing and exporting GM foods. Under the WTO regime there **cannot be separate regulation** on GM foods meant for domestic consumption and export. As far as the imported foods are concerned there need to be legislation on providing obligatory information.

A comprehensive **safety assessment of GM foods** needs to be carried in harmonization with the Codex Alimentarius Comission. The existing mechanism needs to be strengthened while the basic data needed for the safety assessment needs to be generated by the applicant in any of the recognized laboratories. The Health Ministry needs to have a Special Committee on Novel Foods as part of the Central Committee for Food Standards (CCFS) to be chaired by the Director General, ICMR (or his nominee). All applications including for labeling received by the RCGM/GEAC need to be referred and cleared by this committee. The Committee needs to have well laid out set of criteria. This has to be done at every stage namely application for in-house development, environmental release, imports and commercial cultivation after trials. In case, special

studies are needed to conclusively prove the safety or otherwise of the GM food, they should be carried out in the laboratories designated for the purpose by the ICMR.

Post marketing surveillance of GM foods is meant to see health effects if any among the population groups consuming these products need to be carried out. The Health Ministry/ICMR needs to monitor health status both on a short term and long term basis by involving respective State Governments. The existing State Level food control systems need to be linked up with the State Biotechnology Coordination Committee (SBCC) and the district level health officials involved in food control activities need to be associated with the District Level Committee (DLC).

The risks and uncertainties surrounding the process of genetic engineering and the resulting GM products had resulted in considerable public debate and consumer groups have been vociferous in demanding **labeling** of GM products. Policies on labeling of GM foods differs from country to country but consumers' right to know to enable them to make informed choice is generally recognized. Labeling is compulsory in EU countries, Japan, Switzerland and Australia while in USA there is no obligation to label GM foods unless there are substantial changes in composition. In India there is a need to compulsorily label a food if it contains novel DNA/protein or has altered characteristics. However, it need not cover some foods like refined edible oils and the food ingredients added in minor quantities. The imported foods too should be subjected to label regulations. It should have certificate of origin indicating GMO status and proof of analysis from certified laboratories.

Proper information regarding GM food need to be **communicated to the public** so that the average consumer is rightly informed and misinformation is minimized.

Regulatory Officials like the Food and Custom Inspectors and Agricultural Extension Officials need to be adequately trained to carry out the task related to GM foods.

Transparency in decision making process is essential not only at the international level in the post WTO era but also at the domestic level to satisfy the concerns raised by the Civil Society groups. For this purpose, access to information about process, and applications as well as decisions taken need to be in the public domain. At the same time, business information needs to be kept confidential. The public needs to have adequate opportunity to provide comments with adequate response from the official side where required. However, the representatives of Civil Societies need not be involved in decision making process. Only a limited number of voluntary agencies are active in the area and they have very strong opinions. They should not be involved in the regulatory process. However, to be transparent, the information generated, reports, etc., which are not of classified in nature including confidential business information about companies, can be shared with the **Civil Societies**. Suggestions and criticisms from them should be welcome.

In a huge country like India, involving the general public in the form of public consultations may be difficult on a case by case approach. Only the vociferous minority sponsored by vested interested groups, either industry sponsored or selective active voluntary agencies, would be vocal. On the other hand, public criticisms and concerns referred directly or through the media need to be addressed. However information on new GM varieties/products and the decisions made on the applications need to be made public through gazette notification/website/press release.

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