*First Foundation Day Lecture*

*on*

# REGULATORY MEASURES FOR UTILIZING BIOTECHNOLOGICAL DEVELOPMENTS IN DIFFERENT COUNTRIES

**October 17, 2003**

*By*

***Dr Manju Sharma***

*Secretary, Department of Biotechnology, Government of India*


TRUST FOR ADVANCEMENT OF AGRICULTURAL SCIENCES
Indian Agricultural Research Institute
New Delhi-110 012

## TRUST FOR ADVANCEMENT OF AGRICULTURAL SCIENCES (TAAS)

### GOAL

An accelerated movement for harnessing agricultural sciences for the welfare of the people.

### MISSION

To promote growth and advancement of agriculture through scientific interactions and partnerships.

### OBJECTIVES

- ★ Sponsoring seminars and special lectures on emerging issues and new developments in agricultural sciences in different regions of India.
- ★ Promoting local lecture tours and visits to institutions within country of the eminent scientists from international organizations abroad and of the academicians of foreign agricultural academies visiting India.
- ★ Facilitating the partnership with non-resident Indian agricultural scientists visiting India on sabbatical or short leave.
- ★ Instituting awards for outstanding contributions to Indian agriculture by the scientists of Indian origin abroad.
- ★ Arranging special lectures of eminent agricultural scientists in various schools in different parts of the country.
- ★ Providing support to agricultural scientists for participation in conferences/ seminars, in India and abroad, for oral presentation of their research work.
- ★ To act as think tank on key policy issues relating to agricultural research for development (ARD).

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# PREFACE

The Trust for Advancement of Agricultural Sciences (TAAS) was founded on 17th October, 2002 with the main goal of harnessing agricultural sciences for the welfare of the people. Success of "Green Revolution" revealed that our society could reap enormous benefits through faster adoption of technological advancements. In the recent past, developments in agricultural biotechnology have offered several uncommon opportunities for accelerated growth and development, while ensuring benefits to both the farmers and consumers.

In order to harness the fruits of new sciences of biotechnology, it is necessary that we have the needed regulatory measures in place, so that all concerns relating to biosafety are properly addressed before release and use of new biotech products. Obviously, therefore, it is necessary to have the required understanding of global developments concerning regulatory measures. To address this important subject, TAAS was privileged to have Dr Manju Sharma, an eminent scientist and presently the Secretary, Department of Biotechnology, Government of India, to deliver the First Foundation Day Lecture on 17th October, 2003 at the Indian Agricultural Research Institute, New Delhi.

It is our expectation that this lecture would provide useful update on existing regulatory measures for utilizing biotechnological developments in different countries and would clear all related concerns that the public has with regard to both the risks and benefits. We profoundly thank Dr Manju Sharma to have agreed to deliver this lecture.

(R.S. Paroda)
*President, TAAS*

Dr R.S. Paroda, President, Trust for Advancement of Agricultural Sciences (TAAS); Dr S. Nagarajan, Director, Indian Agricultural Research Institute; Prof Anupam Varma, Vice President, TAAS, Dr N.N. Singh, Secretary, TAAS; Ladies and Gentlemen, I feel honoured for being invited to deliver the First Foundation Day Lecture of TAAS, which has been formed to promote growth and advancement of agriculture through scientific interactions and partnerships. I am also happy that TAAS is also organizing a brain storming session on Enabling Mechanisms for Release of Transgenic Crops. It is a very important aspect for successful utilization of biotechnological products.

There is a world-wide recognition of the enormous potential of biotechnology research across the spectrum leading to most powerful tools, which offer limitless opportunities to fight against hunger, diseases, environmental disasters and problems of livelihood security. The focus of my talk today is on agriculture, where biotechnology research is crucial for enhancing its productivity and quality including value addition. In fact, nutritional enhancement of the crop in biotechnology is becoming a major thrust. In the present context of large population growth, one third of the world's population suffers from deficiency in micronutrients, and malnutrition contributing almost to half of the child deaths in developing countries. We are aware that even mild deficiency can damage cognitive and physical developments and reduce the resistance in the child's body. Ian Johnson, World Bank Vice President on sustainable development and Chairman, CGIAR says: "Agriculture can be a vehicle for public health gains in a very low cost and easy way to deliver."

Since the early 1970s, recombinant DNA technology has enabled scientists to genetically modify plants, animals, and microorganisms rapidly. Modern genetic engineering techniques can facilitate introduction of a greater diversity of genes into organisms – including those from unrelated species – than traditional methods of breeding and selection.

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*First Foundation Day Lecture of Trust for Advancement of Agricultural Sciences (TAAS) delivered by Dr Manju Sharma, on 17th October, 2003 at Auditorium of Virology Centre, Division of Plant Pathology, Indian Agricultural Research Institute, New Delhi 110 012*

Thus, plant biotechnology is an extension of traditional plant breeding with one important difference. Instead of mixing thousands of genes to improve a crop plant, modern breeders can use biotechnology to select a specific trait from any plant or microbe and move it into the genetic code of another plant. After the gene has been transferred, the newly modified plant exhibits specific modifications rather than the extensive changes that occur with traditional breeding. This is the precision tool introducing novel and desired characters for plant improvement.

Recombinant DNA (r-DNA) technology has tremendously helped in areas of healthcare, agriculture, process industry and environmental management. However, there are also concerns regarding possible risks and hazards arising from the use of GMOs and products therefrom. The two main areas of concern are the impact on environment and ecosystem and the effects on human health.

As early as in 1975, immediately after the advent of rDNA technology, discussions began within the scientific community about the risks emanating from recombinant DNA experiments. This became even more significant as it was becoming clear that biotechnology research was set to grow very fast in view of the increasing interest by research laboratories and industry. In 1975, at an international gathering of scientists in Asilomar, California, the first set of recommendations to manage the safety of recombinant DNA experiments were formulated which formed the basis of subsequent biosafety regulations in USA followed by other countries like UK, Canada and Australia and for international agreements. These are now commonly referred to as biosafety regulations with the term biosafety covering policies and procedures adopted to ensure environmentally safe application of biotechnology.

To begin with, biosafety concerns were primarily focused on safety procedures within the laboratory. To contain organisms that possibly posed risks to themselves or human health generally. However, this narrow definition of biosafety began to change as rDNA technology began to produce organisms that were useful as commercial products. Novel recombinant products as well as microorganisms, plants and animals have been developed that could be used in industry, agriculture, healthcare and environment through biotechnology. In view of the fact that these

organisms and products would be released into the market and would be widely used, the scope of evaluation of possible risks widened. Today, we are classifying these risks as follows:

***For animal and human health:*** Toxicity & allergenicity; food quality; emergence of resistant pathogens to drugs; and ethical issues.

***For environment:*** Horizontal gene transfer (transgene or promoter dispersion); transfer of foreign gene to microorganisms (DNA uptake); generation of new live viruses by recombination (trans-capsidation, complementation, etc.); persistence of the gene or gene products; genetic pollution through pollen or seed dispersal and loss of biodiversity.

***For agriculture:*** Resistance/tolerance of target organisms; alteration of nutritional value; susceptibility to non target organisms (attractiveness of the organism to pests); formation of weeds or super-weeds (volunteers, increased fitness, invasiveness); increased use of chemicals in agriculture; unpredictable gene expression; instability of transgene; loss of familiarity; higher cost of agriculture; field trials not planned for risk assessment; risks of interaction with non target organisms; etc.

The intended use of GMOs falls into two categories i.e. contained use and field release. Organisms intended for contained use are usually research material and are subject to well-defined risk management techniques involving laboratory containment. Those developed for agricultural biotechnology are intended for field release. Risks in the use of GMOs can be carefully contained in research, healthcare and some industrial applications by well-defined risk management techniques. Their actual use in the field as in agriculture involves exposure of the ecosystem. This continues to raise questions such as unintended changes in characteristics of the exposed species, the possibility of adverse impact on non-target species, the potential for weediness in genetically modified crops and the stability of the inserted gene.

To address the above concerns, biosafety regulations have been developed by many countries, involved in transgenic research and commercialization. There were initiatives to harmonize biosafety regulations by international organizations. The most ambitious attempt to produce a globally harmonized regime for the biosafety has been under the Convention

on Biological Diversity (CBD). Article 19 of the CBD committed members to a protocol on biosafety specifically addressing transboundary movement of GMOs. The Cartagena Protocol on Biosafety was negotiated and adopted under the aegis of CBD on January 29, 2000 and came into force from 11th September, 2003. The protocol seeks to protect biological diversity from the potential risks posed by living modified organisms. India is a party to the CBD and a signatory to Cartagena Protocol on biosafety.

To ensure safety of consumers, producers, farm animals and environment from the use of GMOs, Governments all over the world are following regulatory mechanisms and guidelines. Stringent procedures are in place in some countries. In the European countries, the overall policy and political environments are prohibitive or preventive for even pilot scale experiments and commercial use of GMOs. There are, however, Latin American, African and South East Asian countries where the biosafety measures are not yet adequate. The expertise to implement the guidelines on scientific principles of technology assessment are also lacking. These disparities in overall policy and capacities amongst countries have profound cross border influence in terms of trade and commerce.

Biosafety regulations have drawn the attention from several segments of the society, which is unprecedented in the history of science regulations. Transparency, clarity, competency, impartiality, timely decision making, science based assessment, effective monitoring, publication of data before taking decisions, assessment of national/international priorities, trade, cost effectiveness, single window processing, coordination among concerned ministries/departments and public participation are some of the desirable attributes often suggested by various stakeholders for an ideal regulatory framework. What are the current trends and amendments to accommodate these attributes in the existing framework? It is important for us to understand the regulatory systems for recombinant DNA research and commercialization of products in selected countries.

***United States of America:*** At the Asilomar Conference in February 1975, in California, scientists working with recombinant DNA technology tried to reach a consensus to self-regulate research involving rDNA technology until its safety could be assured. In 1976, the National Institutes of Health

(NIH) published research guidelines for using rDNA techniques. Till 1984, the NIH Recombinant DNA Advisory Committee was the primary federal entity that reviewed and monitored DNA research. However, a legal challenge forced the US Administration to consider and propose policies, to guide the federal agencies responsible for reviewing biotechnology research and its products. In 1984, the White House Office of Science and Technology Policy (OSTP) published the "Coordinated Framework for Regulation of Biotechnology," a framework proposing that genetically engineered products would continue to be regulated according to their characteristics and novel features and not by their methods of production. It also proposed that new biotechnology products be regulated under the existing Federal Statutory Authority and Regulation. In 1986, OSTP finalized this framework. The framework identified lead agencies to coordinate activities. The US regulatory system operates in a coordinated framework involving three government agencies: (1) Environmental Protection Agency (EPA), (2) United States Department of Agriculture (USDA), and (3) Federal Drug Administration (FDA). EPA takes the lead role in the commercialization process when the transgenic product is pesticidal. The transgenic products along with conventional pesticides are regulated under existing Federal Insecticide, Fungicide and Rodenticide Act and no new laws have been enacted for such products derived from biotechnology. If the transgenic product is herbicide tolerant, then EPA regulates the herbicide but not the transgenic for which the USDA is the lead agency. An Inter Agency Working Group (EPA and USDA) has been constituted to deal with this type of situation. USDA grants import permits, and field trial authorization (under 10 acres for transgenic crops) whereas for field trials over 10 acres, EPA is the responsible agency. Regardless of whether the transgene is herbicide tolerant or pesticidal, a submission to FDA has to be made. FDA's focus is on whether or not the introduced transgenic has in any way made the new food substantially different and whether it is safe for consumption. FDA is also the regulatory agency for approvals in case of recombinant DNA products having applications in healthcare.

The agencies involved in regulating genetically modified foods (FDA, USDA, and EPA) are implementing policies based upon a 1986 framework document that coordinates their regulatory activities for biotechnology

products. This framework applies the same set of regulations to all food products and does not differentiate between foods that are produced with r-DNA technologies and those that are produced by traditional methods.

***European Union:*** The EU introduced community biotechnology legislation in the 1990s as part of an effort to address the issues of GMOs and genetically modified microorganisms (GMMs). The EU framework is implemented by the EU institutions (the European Commission, the European Parliament and the Council of Ministers) and the member countries (National Competent Authorities).

The main instrument for giving consent to experimental releases and for placing on the market of GMOs in the community is Directive 90/220/EEC on the deliberate release of GMOs into the environment. Essentially, approval for commercialization requires: i) case-by-case environmental and health risk assessment (to be completed before notification to a national authority), and ii) a step-by-step authorization procedure after notification has been received. The EU system requires mandatory labeling of GM foods containing novel DNA/protein.

***United Kingdom:*** Laboratory experiments are regulated by an EU directive which is implemented in UK. Clearance to grow GM crops commercially for food consumption has not yet been granted in the UK. Considering criticism of current system, in 1998, a ministerial group on biotechnology and genetic modification was set up to consider wide ranging issues arising from genetic modification. It has reviewed the regulatory controls and recommended setting up two new commissions. One of this commission, "Agriculture and Environment Biotechnology Commission" works alongside the Food Standard Agency (FSA) which is the strategic advisory body for the safety of GM food.

***Canada:*** Biotechnology products are regulated nationally by the federal government under authority derived from at least 10 pre-existing legislations (Seeds Act, Feeds Act, Fertilizers Act, Health of Animals Act, Food and Drug Act, Canadian Environmental Protection Act, Plant Protection Act, Consumer Packaging and Labelling Act, Patent Act, and the Pest Control Products Act) that have been amended over time to deal with these new products.

***Australia:*** Research, manufacture, production, commercial release and import of GMOs are regulated under the Gene Technology Act 2000 by the Gene Technology Regulator (GTR). Dealings with GMOs and GM products are also regulated by a number of other regulatory agencies where they are to be used for specific purposes. These include the National Registration Authority for Agricultural and Veterinary Chemicals (NRA) for agricultural and veterinary chemicals; the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) for industrial chemicals; the Food Standards of Australia and New Zealand for foods intended for human consumption; the Therapeutic Goods Administration (TGA) for therapeutic goods; and the Australian Quarantine and Inspection Service (AQIS) for the import of plants, animals and biologicals. The Environment Risk Management Authority is responsible for regulating the environmental release of GMOs in New Zealand.

## REGULATORY FRAMEWORK IN INDIA

Keeping in view the accelerated growth of biotechnology and its potential application, Government of India has evolved a regulatory mechanism for development, evaluation and release of biotechnology products.

The Ministry of Environment & Forests (MoE&F) had enacted Environment and Protection Act in 1986 to provide for the protection and improvement of environment and the related matters. Under this act, the rules and procedures for the manufacture, import, use and release of GMOs as well as products made by the use of such organisms were notified by MoE&F through their Notification No. 621 in Official Gazette of Govt. of India on 5th December 1989. These rules and regulations cover all the areas of research as well as large-scale applications and release of GMOs and products thereof throughout India. The rules also cover the application of hazardous microorganisms which may not be genetically modified.

The rules also define the competent authorities, composition of such authorities and their responsibilities for handling of various aspects of the rules. They are The Recombinant DNA Advisory Committee (RDAC); Institutional Biosafety Committee (IBSC); Review Committee on Genetic Manipulation (RCGM); Genetic Engineering Approval Committee (GEAC);

State Biotechnology Coordination Committee (SBCC); and District Level Committee (DLC). Among these competent authorities, the GEAC is the apex committee for authorizing release of GMOs and products there of into the environment. RCGM regulates the research work at lab level and also at small-scale field trials of transgenic crops and directs generation of data on biosafety. IBSC is responsible for compliance of guidelines at institutional level.

To facilitate adherence of Rules, the Department of Biotechnology has evolved Recombinant DNA Safety Guidelines (1990); Revised Guidelines for Research in Transgenic Plants and guidelines for testing toxicity and allergenicity of transgenic seeds, plants and plant parts (1998); guidelines for preclinical and clinical evaluation of rDNA vaccines, diagnostics and other biologicals (1999).

Apart from the above guidelines, the Government of India has also amended relevant Acts & Rules to facilitate the manufacture and release of GMOs and products thereof into the environment. These include: Drugs and Cosmetics Rules (8$^{th}$ Amendment) (1988); Plant Variety Protection and Farmer's Rights, (2001); Drug Policy (2002) and Seed Policy (2002). The existing regulatory procedures approved production and marketing of Hepatitis B vaccine, EPO, interferon, G-CSF, insulin and streptokinase in health care sector and three *Bt* cotton hybrids in agriculture sector.

International agencies and conventions like CBD, The United Nation Environmental Programme/Global Environment Fund (UNEP/GEF), Organization for Economic Co-operation and Development (OECD), European Union (EU), Food and Agricultural Organization (FAO) and International Service for National Agricultural Research (ISNAR) have been active in harmonization of biosafety regulations in different regions. As stated earlier, Cartagena Protocol on Biosafety is the outcome of the efforts of CBD.

In general, diverse groups of stakeholders have shown interest in biosafety policy and procedures. The decisions taken by the biosafety system are subject to local, national and even international examination. There have been many suggestions for the involvement of all stakeholders in the biosafety decision-making process. In fact, in Egypt, the biosafety

committees include non-governmental organizations as well as non-technical members representing community interest. To build public acceptance of GM products, information access to latest scientific regulatory and biosafety information along with relevant safety data that can be easily understood could be a better option for informed decision and building public acceptance.

Most of the regulatory systems are relatively open and transparent with precautionary approach, and are in general, compliance friendly. All the regulations and guidelines are evolved by the concerned states to protect the environment and also human and animal health. Variations in the regulatory framework, in the present situation, represent the strengths in the science, necessity of the technology, and willingness of the State to adopt goods and services developed through modern biotechnology. A review of different regulatory systems and procedures in selected countries as briefly given above exposes similarities and also differences. It is also important to continuously update mechanisms to meet the current challenges of the society based on the scientific knowledge which is growing phenomenally world over.

Based on the phenomenal advances, novel tools and techniques in biology and their application for the welfare of humankind, the field of biotechnology has assumed enormous significance and the 21st Century is being referred to as the "Century of New Biology and Biotechnology". We had a Green Revolution; we had an Industrial Revolution; we are heading towards the Gene Revolution which will transform the social and economic scenario world over. We have witnessed one of the most spectacular technological breakthroughs in the 20th Century that of the decoding of Human Genome Draft Sequence; the excitement of the scientific community moves into the next phase i.e. the post genomic activities. With all these rapid strides, need for improved biosafety and ethical procedures is felt globally.

An article in the recent issue of 'Nature' (September 11, 2003) has a very interesting title "Biotechnology at the bar". It states:

"Science is moving too fast for the legal system to keep up. But lawyers and scientists have a solution – a body that would help courts tackle cases involving the latest research. ..... Nicola Nosengo investigates."

Thus, when we talk of biosafety regulatory mechanisms, obviously the question of ethics also arises. From all the scientific breakthroughs and developments taking place today in the field of modern biology, one has to clearly recognise the need for more and more teamwork of an inter-disciplinary nature, of a synergy between biosafety regulations, bioethics and legal and judiciary systems of delivery. Franklin Zweig has been most active in bringing aspects of science and legal matters on a common platform and has been trying to initiate a dialogue and set up a platform for discussion. He has said: "Biotechnology is pushing society into a new area, where the letter of the law is grey, not black."

We have had concerns, in our society, about both the advantages and risks of this emerging field of biotechnology, particularly in agriculture. However, time and again, with proper scientific explanations, these have been addressed and awareness of the need for the harnessing of research results into development sectors understood.

In the editorial in HINDU dated 15th October, very important issue has been brought out as follows: "Biotechnology will have its greatest impact on two sectors: health and agriculture. So meeting the requirements of foreign companies is not likely to be the engine of growth for Indian biotechnology companies, as in the case of IT." The same editorial concludes with the statement:

"Mass health and food needs can ensure that the Indian biotechnology industry can have an impact that computers and software will not."

In a report on Transgenic Plants and World Agriculture prepared under the auspices of the Royal Society of London, Science Academies of US, Brazil, Mexico, China, INSA and TWAS, it is said: "We conclude that steps must be taken to meet the urgent need for sustainable practices in world agriculture if the demands of an expanding world population are to be met without destroying the environment or natural resource base. In particular, GM technology, coupled with important developments in other areas, should be used to increase the production of main food staples, improve the efficiency of production, reduce the environmental impact of agriculture, and provide access to food for small-scale farmers."

At the end, I again warmly thank Dr R.S. Paroda for giving this opportunity. I also wish the Brainstorming Session on "Enabling Mechanisms for Release of Transgenic Crops' a grand success, and I shall look forward to receiving recommendations of this important meeting. I close my lecture with a quote from Gautam Buddha, who said:

*"Of all diseases, hunger is the greatest, .....*
*there is no other treasure equal to that of rice."*

## DR MANJU SHARMA

Born on 13 February 1940 in Kanpur, India, Educated at Lucknow University, India, M.Sc. (Botany), 1961 and Ph D. (Plant Anatomy and Plant Chemistry), 1965.

Secretary, Department of Biotechnology (DBT), Ministry of Science and Technology, India, 1996 to date; President, Natl. Acad. of Sciences, Allahabad; General President of the Indian Science Congress Association.

Chief of Science and Technology and Environment, Planning Commission, India; Scientific Secretary (OSA-PM); Joint Adviser, Planning Commission; Director, Department of Science and Technology, India.

***Awarded:*** Birbal Sahni Gold Medal for best student in M.Sc., 1961; VASVIK Award for best women scientist, 1991; Norman E. Borlaug Award in the field of Agriculture and Related Sciences, 1995; Distinguished Scientist Award, Indian Science Congress Assn., 1996; Asutosh Mukerjee Memorial Award, 2000; B.P. Pal Memorial Award of Indian Science Congress, 2001; G.M. Modi Science Award, 2002; Conferred Honorary Doctorate by several Universities.

***Fellow:*** National Academy of Agricultural Sciences; Natl. Acad. of Science, India; Third World Academy of Sciences.

***Research Areas:*** Promotion, development, identification and monitoring of all areas of biotechnology, including product development and technology transfer and application. Her research on sclereids and latex has contributed significantly to the knowledge of their structure and function from the viewpoint of phylogenetic evolution and identification of plants.

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