Overview of National Implementation Measures for Use of Micro-organisms - BTWC Concerns

Dr. B M Gandhi

The author was Advisor, Department of Biotechnology, Ministry of Science and Technology and is currently the Chief Executive Officer, Neo Biomed Services.

Summary

The bio-medical scientists are restrained to maintain voluntary code to ensure that activities involving microbial or other biological agents, or toxins whatever their origin or method of production, are only of types and in quantities that have justification for prophylactic, protective or other peaceful purposes. A legal network of Rules and Acts by the Government of India provides guidelines to the researchers and the policy makers to enforce prohibitions against biological weapons and govern the transfer of select agents.

It is well recognized that modern technologies have dual use applications both for peaceful purposes as well as hostile use. Modern biology and bio-technology offer novel ways of manipulating basic life processes. Purposefully or unintentionally, genetic modification of microorganisms could be used to create organisms that are more virulent, are antibiotic-resistant, or have greater stability in the environment. In such conditions the scientists shoulder ethical responsibilities in wider applications of such technologies keeping in view the potential risks and concerns of misuse and in compliance with the requirements of international conventions and treaties relevant to their research work.

The managers and the agencies involved in funding, conducting, administering and regulating biomedical sciences research and development share ethical and social responsibility to assure that use of knowledge and skill for the advancement of human welfare is conducted in a way that the use of micro-organisms, toxins or other biological agents is not for hostile purposes.

The use in armed conflicts of biological weapons, as well as of chemical weapons, was prohibited by the Geneva Protocol in 1925. The Biological and Toxin Weapons Convention (BTWC) of 1972, which entered into force in 1976, is comprehensive and prohibits the development, production, stockpiling, transfer or acquisition of biological agents and equipment for hostile purposes. Under the Convention the design, construction or possession, for any purpose, of delivery mechanisms designed to use biological agents or toxins for hostile purposes or in armed conflict is prohibited. More than 160 States have already ratified or acceded to it.

The States Parties to the BTWC have undertaken to facilitate and have the right to participate in, the fullest possible exchange of equipment, materials and scientific and technological information for the use of bacteriological (biological) agents and toxins for peaceful purposes including prevention of diseases without hampering the economic or the technological development of State Parties.

International efforts to regulate the potential environmental damage of man made microorganisms have centered on agreement, reached at the Earth Summit in Rio de Janeiro in 1992, on a set of principles intended to achieve sustainable development while protecting the environment. These principles include: increasing the availability of food, feed and renewable raw materials improving human health; enhancing the protection of the environment' establishing enabling mechanisms for the development and environmentally sound application of biotechnology; and enhancing safety and developing international mechanisms for cooperation. This principle explicitly requires further development of internationally agreed principles on risk assessment and management of all aspects of biotechnology.

Under the circumstances, the bio-medical scientists are restrained to maintain voluntary code to ensure that activities involving microbial or other biological agents, or toxins whatever their origin or method of production, are only of types and in quantities that have justification for prophylactic, protective or other peaceful purposes. A legal network of Rules and Acts by the Government of India provides guidelines to the researchers and the policy makers to enforce prohibitions against biological weapons and govern the transfer of select agents.

Guiding Principles

Several international agencies and professional bodies have drafted ethical codes of conduct for scientists engaged in life sciences. In order to prevent the use of bio-medical sciences for purposes of bio-terrorism or bio-warfare, all persons and institutions engaged in all aspects of bio-medical sciences need to abide by ethical code of conduct. Some of the guiding principles applicable to use of microorganisms for research and development are:

Principles of non-malfeasance, whereby it is ensured that the discoveries of biomedical research scientists and knowledge generated are not likely to facilitate, bio-terrorism or bio-warfare.

Principles of beneficence, whereby it is ensured that legitimate benefits would out-weigh the risks and harms.

Principles of institutional arrangements, whereby reasonable care is taken to ensure that all procedures are complied and all institutional arrangements assure bio-security. Access of biological agents is allowed to bonafide scientists in a transparent manner who, there are reasonable grounds to believe, will not misuse them.

Principles of risk minimization, whereby due care and caution is taken to restrict the dissemination of dual use information and knowledge in cases where there are reasonable grounds to believe that there are serious risks that information or knowledge could be readily misused to inflict serious harm through bio-terrorism or bio-warfare.

Principle of ethical review, whereby research activities are subjected to ethics and safety reviews and monitoring to establish their ethical acceptability.

Principles of transmission of ethical values, whereby the duties and obligations embodied in the code are transmitted faithfully to all who are, or may become, engaged in the conduct of biomedical research.

Principles of voluntariness, whereby researchers are fully apprised of the research and the impact and risk of such research but retain the right to abstain from further participation in research that they consider ethically or morally objectionable.

Principles of compliance, whereby scientists abide by laws and regulations that apply to the conduct of scientists, duties and obligations embodied in this code, and disseminate the same to all concerned.

Code of Conduct for Bio-Medical Scientists

In 1982, the World Health Organisation (WHO) and the Council for International

Organisations of Medical Sciences (CIOMS) issued the 'Proposed International Guidelines for Biomedical Research involving Human Subjects.' Subsequently the CIOMS brought out the 'International Guidelines for Ethical Review in Epidemiological studies' in 1991 and 'International Ethical Guidelines for Biomedical Research involving Human subjects' in 1993.

In India, the Indian Council of Medical Research released a 'Policy Statement on Ethical Considerations involved in Research on Human Subjects'. In February 1980 for the benefit of all those involved in clinical research in India. Ethical Guidelines for Biomedical Research on Human Subjects were released by ICMR in 2000 setting up code of conduct for scientists engaged in biomedical research.

Ethical Guidelines for Genetic Research

Genetic research involving humans has already provided benefits to humankind in the form of drugs, vaccines, diagnostics and other knowledge for better management of health and disease. New vistas for molecular medicine have opened for human welfare especially in the areas of improved diagnosis of diseases, early detection of genetic predisposition to diseases, rational drug design, new drug targets and pharmacogenomics etc. At the same time it is also raising questions of social consequences such as privacy, confidentiality and individual rights to access personal records. There are potential risks in collection of information or principles.

The Ethical Policies on the Human Genome, Genetic Research and Services, 2002 drafted by the Department of Biotechnology of the Government of India provides guidance to the researchers, ethical committees, institutions, organisations and the public on the conduct of research based on recognized ethical principles and values. Issues related to Integrity, Respect and Beneficence; Justice; Consent; Dissemination of Research Results; Gene Therapy and Human Cloning; Genetic Testing and counseling, Genetic Privacy and Discrimination; Intellectual property Rights and Benefit Sharing; DNA and Cell-line Banking; and International Collaboration have been addressed. Even though these guidelines relates to the ethical policies for genetic engineering research and services per se, any such research need to obtain approvals of the competent authorities, including ethical clearances of the institutions, animal and human concerns, biosafety issues etc., which in turn provides guidance and also directly exerts a control over the conduct of the life science experiments.

Due regard must be shown to these principles, embodies in the Convention, in drafting any code of conduct or practice so that it is not misused to restrict or deny access to bio-technologies and to hamper exchange of knowledge and research works amongst the scientists both nationally as well as internationally.

Indian Legal Network

The Government of India, keeping in view potential risks to human and to environment, enacted regulatory mechanism for import, export, use, and research on microorganisms including genetically modified organisms. These are guidelines for the researchers involved with research and developments related to microorganisms and toxins and their genetic modifications, if any and have direct relevance to the provisions of BTWC. Some of the Legislations and Rules by the Government of India of direct relevance to BTWC include:

The Indian Environment (Protection) Act, No. 29 of 1986 dated May 23, 1986 was enacted for protection and improvement of environment and prevention of hazards to human beings, other living creatures, plants and property. Subject to provisions of this act, the government has the powers to take all such measures as it deems necessary or expedient for the purpose of protecting and improving the quality of the environment and preventing, controlling and abating environmental protection, including laying down procedures and safeguards for the handling of hazardous substances and carrying out and sponsoring investigations and research relating to problems of environmental pollution.

With a view to protecting the environment, nature and health, in connection with the application of gene technology and micro-organisms, the Central Government, Ministry of Environment & Forests enacted the **Rules for the Manufacture, Use/ Import/ Export and Storage of Hazardous Microorganisms/GeneticallyEngineered Organisms or Cells through notification of December 5, 1989.** These rules are applicable to the manufacture, import, export and storage of micro-organisms and gene-technological products; genetically engineered organisms/micro-organisms and cells and correspondingly to any substance and products and food stuff etc. of which such cells, organisms or tissues hereof form part; new gene technologies and organisms/ micro-organisms and cells generated by the utilization of such or other gene-technologies and to substances and products of which such organism and cell form part.

Competent authorities have been identified, which ensures implementation of the provisions of the Act. **Recombinant DNA Advisory Committee (RDAC)** recommends suitable and appropriate safety regulations for India in recombinant research, use and applications from time to time. **Institute Bio-safety Committee (IBSC)** is mandatory to be constituted by an occupier including research institutions / university / industry handling microorganism / genetically engineered organisms. IBSC prepares an up-to-date site emergency plan according to the manuals/ guidelines of the Review Committee on Genetic Manipulation (RCGM). This committee also looks into the biosafety aspects including experimentation and containment issues. **Over 350** such committees are already functional in various research institutions / universities / industries handling microorganism / genetically engineered organisms. **Review Committee on Genetic Manipulation** based in the Department of Biotechnology monitors the safety related aspects in respect of on-going research projects involving genetically engineered organisms/hazardous microorganisms. The Committee also brings out Manuals of guidelines specifying procedure for regulatory process with respect to activities involving high-risk category and controlled field experiments and reviews to ensure that adequate precautions and containment conditions are followed as per the guidelines. **Genetic Engineering Approval Committee (GEAC)** under the Ministry of Environment, Forest and Wildlife approves activities involving large-scale use of hazardous microorganisms and recombinants in research and industrial production related to release of genetically engineered organisms and products into the environment including experimental field trials.

Department of Biotechnology formulated **Recombinant DNA Guidelines in 1990,** which were further revised in 1994 and again in 1998 addressed issues related to large-scale production and deliberate release of GMOs, plants, animals and products into the environment, shipment and importation of GMOs for laboratory research. It also deals with genetic transformation of green plants, rDNA technology in vaccine development and on large-scale production and deliberate/ accidental release of organisms, plants, animals and products derived by rDNA technology into the environment. Research under the guidelines has been classified into categories based on the level of the associated risk and requirement for the approval of competent authority. The guideline gives principles of occupational safety and hygiene for large-scale practice and containment, safety criteria and physical containment conditions depending on the type of organisms handled and potential risks involved and various quality control methods needed to establish the safety, purity and efficacy of rDNA products.

Revised guidelines for research in transgenic plants & guidelines for toxicity and allergenicity evaluation of transgenic seeds, plants and plant parts, were enacted by the Department of Biotechnology in 1998 to include complete design of a contained green house for transgenic plants. Besides, it provides the basis for generating food safety information on transgenic plants and plant parts.

A set of **Guidelines were developed** on

safety, purity, potency and effectiveness of the project. **By the Department of Biotechnology for generating pre-clinical and clinical data for rDNA vaccines, diagnostics and other biological, 1999** to help in the production of relevant data for submission to Drug Controller General of India.

Notification of the **Task Force on Recombinant Pharma (2006)** suggested a regulatory mechanism and process related to use of living Modified Organisms (LMOs) in the pharmaceutical industry during the various stages of R & D, testing, manufacture, import and marketing of LMOs as drugs/Pharmaceuticals. These recommendations shall be applicable in respect of recombinant Pharma products under Rules for the Manufacture, Use, Import, And Export and Storage of Hazardous Micro Organisms Genetically Engineered Organisms or Cells, 1989' of EPA, 1986.

National Seeds Policy, 2002 ensures that all genetically engineered crops/varieties are tested for environment and bio-safety before their commercial release as per the regulations on guidelines of the EPA, 1986.

Drug Policy, 2002 has reference to the recombinant DNA products where Clause 12.1 of the policy states that bulk drugs produced by the use of rDNA technology, bulk drugs requiring in vivo use of nucleic acid as the active principles and specific cell/tissue targeted formulations require an industrial license for production.

The Weapons of Mass Destruction and their Delivery Systems (Prohibitions of Unlawful Activities) Act 2005 ensures punishment under the act for any act of omission contrary to the provisions thereof, of which the person is guilty in India. The act applies to unlawful exports, transfer; re-transfer, transit and trans-shipment, directly and indirectly, of any one biological and chemical weapon by any state or non-state actor, of materials, equipment and technology of any description relating to weapons of Mass Destruction or their means of delivery.

The Foreign Trade (Development and Regulation) Act, 1992 No. 22 of 1992 dated August 7, 1992 and Export Control on Dual Use Technologies.

Our industry is a user of special materials, equipment and dual-use technologies and products. Fully aware of the potential misuse of the uncontrolled proliferation of these technologies and products of direct and indirect application to Weapons of Mass Destruction (WMD) and their means of delivery, India has been exercising a degree of control over the export of these Special Chemicals, Organisms, Materials, Equipment and Technologies SCOMET) items. Export of these SCOMET items requires a license which is regulated under notification No. 5 (RE-2000)/1997-2002, New Delhi, dated March 31, 2000 issued by the Director General of Foreign Trade, Ministry of Commerce, Government of India known as The Foreign Trade (Development and Regulation) Act, 1992 No. 22 of 1992 dated August 7, 1992 commonly know as FTDR Act. Category 2 of the Appendix III of the notification includes list of microorganisms/toxins including bacteria, fungi, parasites, viruses, rickettsials, plant pathogens and genetically modified organisms, which require license and export of these items, are also controlled by other applicable guidelines issued from time to time.

Export or attempt to export in violation of any of the conditions of license to export shall, *inter alia,* and without prejudice to prosecution under any other Act for the time being in force, invite criminal prosecution under the Customs Act, 1962.

Export of SCOMET items is permitted only against a license / permission, in accordance with the Policy contained in Appendix 3 to Schedule 2 of ITC (HS). It is not permitted under an advance license or any other license issued (under a duty exemption or remission scheme) by the DGFT. For obtaining a license or permission for a SCOMET item, the exporter has to apply in the Aayaat Niryaat Form to the Directorate-General of Foreign Trade to be considered by Inter Ministerial Working Group (IMWG) under the Chairmanship of the Export Commissioner and consisting of

representatives of concerned agencies in the Government of India, which include Ministry of External Affairs, Ministry of Defense, Central Board of Excise & Customs, and concerned Ministries/Departments (e.g. Departments of Atomic Energy/Space/DRDO/ Department of Chemicals and Petro-chemicals/ Department of Bio-technology), as required, for technical advice.

Import of biomaterials is free as mentioned in **Schedule-1 of ITC (HS) classification of Export-Import items 2004-2009**.i.e these materials do not require any import license. However, the import duty is paid which is near about 22% for microbiological samples. The permission of regulatory bodies like GEAC, RCGM and DCG(I) {For Substances Mentioned in D&C Act} is necessary for imports.

Transfer of Biological Material

India's current system of controls over exports of special materials, equipments and technologies was instituted in 1995 on the basis of recommendations made by a Small Group set up in Department of Science & Technology in 1993. Transfer of biological material through joint collaborative international projects or industrial ventures related to work with these exotic biological agents and toxins require close scrutiny. The Ministry of Health & F.W. vide Office Memorandum No.L.20025/90-90-F. dated February 27, 1992 permitted the restricted transfer of biological material abroad under certain circumstances for research/ diagnostic purposes. Guidelines for **Exchange of Human Biological Material for Biomedical Research** purposes were issued by the Ministry of Health & F.W vide F. No. L.19015/53/97-IH (Pt.) dated November 19, 1997. Human Material with potential for use in biomedical research included Organs and parts of organs; Cells and tissue; Sub-cellular structures and cell products: Blood; Gametes (sperm and Ova); Embryos and Fetal Tissue; Wastes (urine, feces, sweat, hair, epithelial scales, nail clippings, placenta etc.); Cell lines from human tissues etc.

Dual use items and technologies have potential to be used as weapons in addition to their commercial applications and have growing threat of terrorism to society. Realizing the threat various groups/arrangements were made to track the exports of these dual use materials / agents in various countries. **Australia Group** is one such group. This group formed in 1985 has 41 countries and European commission as its participants. The Australia Group is an informal forum of countries which, through the harmonisation of export controls, seeks to ensure that exports do not contribute to the development of chemical or biological weapons. All states participating in the Australia Group are parties to the Biological Weapons Convention (BWC), and strongly support efforts under those Conventions to rid the world of CBW. India is not a member of this group.

Information Dissemination

In order to identify potential users of the dual-purpose new technologies, baseline information and distribution of disease pattern may be essential. In this regard awareness programmes about the possible threats against biological weapons may give special emphasis to information on various types of biological weapons and the availability of systems to detect and analyze the nature of biological weapons, source of availability of drugs and vaccines, and the laboratory facilities to deal with certain attacks. A strong working relationship between research institutions, scientists and health professionals would improve the capacity to both detect and respond to bio-terror attack. Laboratory diagnostic procedures in common use as improved biotechnologies would help in early response. Emergency distribution and treatment of antibiotics and vaccines would be useful for emergency interventions for naturally occurring epidemics. Policies related to threat perceptions and role of stake holders would need to be examined and additional efforts would be required for development of vaccines and diagnostics for the potential bio-war agents.

Baseline information is required on Indian biotech industries and pharmaceutical industries dealing with production of vaccines/

diagnostics/other products using exotic micro-organisms known to have potential of use as biological weapons. Collaborative programmes involving participation of foreigners' transfer of biological agents and toxins material would require close scrutiny.

Every country is proposed to take necessary action with regard to developing strategies for bio-security against biological weapons without hampering legitimate research and free flow of information in the field of biotechnology. A system of checks and balances needs to be developed to assure that the growing power of the life sciences is only used to protect life and not to destroy it. The following issues require attention of the policy makers as well as researchers;

- There must be an increased awareness of the risk of bio-terrorism among scientists and scientific leaders. In order to augment awareness about the security issues, arrangements would need to be made for training and accreditation of programmes that would increase considerable awareness and stimulate better communications between scientific and national securities communities.

- Bio-security policies must take a bottom up approach by including direct involvement of working scientists. Any such strategy that blocks the publication of certain research materials would impede carriers of scientists in the fields of biotechnology and discourage new incumbents to enter into research in biotechnology. Guidelines would need to be developed to allow the researchers to publish their work without providing information that would be useful to bio-terrorists.

- Universities and other scientific institutions should develop procedures to monitor scientific activities and design fool proof action plan to prevent any strategic information leakage in relation to bio-technology to bio-terrorists who would in return adversely utilize this information for creating bioterrorist activities.

- The whole issue of bio-security would need to be looked into from the view point of bio-safety, bio-security and information dissemination and if need to be necessary SOPs may be prepared.

- Guidelines may be prepared for dissemination of information with regard to publication of sensitive information on the duel use technologies.

- A policy of outreach to industry must be adopted and industry should be fully informed and involved with the process of national polices consideration.

To Conclude

Fully recognizing that modern technologies and related equipment have dual use applications both for peaceful as well as hostile purposes, the scientists shoulder ethical responsibilities in wider applications of such equipment and technologies in compliance with the requirements of international conventions and treaties relevant to their research work. The researchers, managers and the agencies involved in funding, conducting, administering and regulating biomedical sciences share ethical and social responsibility to ensure use of modern knowledge on micro-organisms, toxins or other biological agents for the advancement of human welfare. Government of India is taking all necessary steps to ward against bio-terrorism activities. Various legislations have been enacted to protect the environment of pollutants and any other subversive activity because of the biological agents. However, to ensure bio-safety and bio-security, awareness programmes with active participation of the researchers in the implementation arms of legislations would need to be further strengthened.