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BIOSAFETY, BIOSECURITY AND CODE OF ETHICS

Dr. B.M. Gandhi

The dual use research in life sciences has raised serious concerns for bio-safety and bio-security today as there exists possibilities of misuse of knowledge, information, products and technologies to promote bio-terrorism or bio-warfare activities. Misuse may pose consequential threat to public health and safety, agricultural crops and other plants, animals, the environment, material or national security. India has strict and robust regulations on bio-safety and bio-security policies that provide adequate safeguards for responsible conduct and oversight of life sciences research. However, safety measures are far from satisfactory and the implementation agencies are weak. There is an acute shortage of technically-trained manpower and machinery to strictly enforce the regulatory system.

This paper thus highlights the strength of the existing regulations, but points at the urgent need for: a) coordinated approach by various government agencies and b) capacity building for speedy implementation of existing regulations in order to promote good bio-safety and bio-security practices in India.

Modern biology and bio-technology offers noble ways of manipulating basic life processes. Genetic research involving humans has provided immense benefits to humankind in the form of drugs, vaccines, diagnostics and other knowledge for better management of health and diseases. Genetic research in agriculture has resulted in increased crop production and healthy livestock. However, genetic modification of microorganisms can be used to create other organisms that are more virulent, are antibiotic-resistant, or can destabilize the environment.

Despite a greater awareness of bio-safety and containment practices, handling infectious microorganisms remains a source of infection, and even mortality, among laboratory workers. Incidents of secondary transmission of disease to the public at large, which may be due to possible contamination of the environment or personnel, are also being reported. Accidental mishandling of dangerous biological agents and toxins is attributed to inadequacy in following the prescribed guidelines, poor understanding of the prescribed laboratory procedures, poor training of laboratory personnel, inadequate preparations of dangerous pathogens with reduced bio-security levels and disposal of infected materials without proper disinfection.

In recent years, we have witnessed a series of accidents and security breaches reported at bio-containment facilities in the US (Anthrax, West Nile Virus, and Tuberculosis), UK (FMD), USSR (Anthrax), Singapore (SARS) and China (SARS). Recent episodes in the US of several vials of smallpox left in a cardboard box in an unused storage room; export of potentially infectious live anthrax bacteria samples to laboratories unequipped to handle them; and accidental contamination of a relatively benign flu sample with a dangerous H5N1 bird flu strain have exposed the slackness and casual attitude of the researchers in following bio-safety and bio-security measures. A study by the University of Minnesota has cited about 400 incidences involving potential release of select agents in the US laboratories between 2003 and 2009 mainly due to containment problems, spills and needle sticks and/or other sharp injuries.

These episodes have raised serious issues regarding implementation of legislations at international level as those are taking place even in a developed country like the US where many public and private agencies concentrate on various critical aspects of bio-safety, bio-security, and bio-containment. If such mismanagement can take place in USA, there is every possibility that researchers elsewhere may be indiscreet in following the guidelines, thereby posing a potential risk to the environment and human welfare. Managing the risks require effective policies and globally ratified system of controls and regulations implementable at the international level to ensure that only legitimate scientists can access deadly organisms and oversee potentially dangerous research having dual use implication.

Dual use Research

The r-DNA technology is widely being used in pharmaceutical sector, especially in the use of modern biotechnology derived biopharmaceuticals. The technology is also widely used in the areas of agricultural sciences in terms of transgenic crops, tissue-culture, biofertilisers, biopesticides and bio-control agents. However, it is well recognized now that the advances in S&T can have dual use -- for peaceful and hostile purposes. Dual Use Research in life sciences raise concerns for bio-safety and bio-security as the generated knowledge, information, products or technologies could be misused to pose significant threat. The cutting edge technologies are posing serious concerns since the ability to enhance public health and agriculture can also be used to create bioterror agents, which can unleash destructive forces.

The chemical synthesis of poliovirus has raised the possibilities of research scientists attempting to synthesize other deadly human viruses like Ebola or the Smallpox having more complicated genome or development of a particularly potent toxin. Scientists are attempting to re-create lethal viral strains like pandemic strain of influenza from RNA fragments isolated from frozen lungs of a victim from Alaska. New pathogens pose new challenges, which require new paradigms for effective detection and control. Scientists have developed capabilities for screening microbial targets and drug candidates in chip-scale biomimetic systems. Various groups are developing organ-on-a-chip systems to study infections of organs in a micro-scale device as a new approach to tissue engineering. The US Army is developing an artificial human immune system-on-a-chip, which consists of human immune cells and micro-scale immune structures that facilitate rapid screening of candidate vaccines within weeks.

International Regulations

International efforts have been made by the UN and WHO to highlight biological challenges and raise awareness. Specific guidelines are formulated by each member country for laboratory bio-security and effort is being made to adhere to these guidelines.

The Biological and Toxins Weapons Convention (BTWC) provides for facilitating the fullest possible exchange of equipment, materials and scientific and technological information for the use of bacteriological (biological) agents and toxins for peaceful purposes. Moreover, the Convention is to be implemented in a manner designed to avoid hampering of the economic or technological development of States Parties to the Convention or international cooperation in the field of peaceful bacteriological (biological) activities, including the international exchange of bacteriological (biological) and toxins and equipment for the processing, use or production of bacteriological (biological) agents and toxins for peaceful purposes in accordance with the provisions of the Convention. Due regard must be shown to these principles while drafting any code of conduct to avoid misuse.

Regulatory mechanisms for import, export, use and research on microorganisms, including genetically modified organisms (GMOs) have been developed with guidelines for scientists conducting research, which deal with microorganisms and toxins and genetic modifications, if any, and are of direct relevance to the provisions of BTWC.

WHO, FAO, OIE and other bio-safety agencies promote safe use of biological agents and toxins. WHO guidelines on health regulations and various UN formulated guidelines directly or indirectly deal with the management of crops and livestock. National initiatives are based on obligations of States under the BTWC and UN Security Council Resolution 1540-2004 to pursue and achieve common objectives of non-proliferation and prohibition to prevent use of bio-sciences for bio-terrorism or bio-warfare.

USA has taken steps to define “Research Standards and Practices to Prevent the Destructive Application of Biotechnology”. In this regard, an expert group under Prof. Gerald Fink of the Massachusetts Institute of Technology made recommendations to address the problem of dual-use and bio-security advocating for self-governance by the life sciences community, creation of a comprehensive system, both nationally and internationally, and international guidelines to minimize misuse of biotechnology. Specific recommendations include:

- Educating scientists about dual-use and risk mitigation.
- Stronger review processes to be established by government agency for experiments involving potential misuse.
- Voluntary self-regulation by scientists who should review the submissions for publication to assess potential risks to public health and national security.
- Creation of a National Science Advisory Board for Biodefense (NSABB) for advice, guidance and oversight with the authority to periodically review existing laws on biological materials and personnel.
- Develop communication channels between the life sciences community and security officials.
- Create an International Forum on Biosecurity to "harmonize national, regional and international measures" with those of the US.

Biosafety in India

Bio-safety measures ensure that such research is conducted in accordance with the highest standards to protect the health of researchers, the public and the environment. Laboratory bio-safety generally focuses on prevention of accidental or unintentional exposure to or release of pathogens and toxins so as to protect workers, public, animals and the environment from accidents. The bio-safety market includes biotechnology and manufacturing; control testing, food and agricultural and veterinary testing, environmental testing, and response to known or suspected acts of biological warfare, bioterrorism or other related criminal activity.

Bio-safety also refers to promoting safe laboratory practices, procedures, proper use of containment equipment and facilities, risk assessment and management, evaluation of GMOs, etc.

In India the concept of bio-security and bio-safety is well conceived with the advances in S&T and the progress is viewed against emerging concerns around bio-security. The bio-security regulatory regime of India stems from the Environment (Protection) Act, 1986 (Rules of 1989) that stipulates rules and procedures for manufacture, import, use, research and release of genetically engineered organisms and their products. The GMOs are placed as hazardous microorganisms and their regulation under the EP Act is justified by their alleged potential to be hazardous substances or environmental pollutants. The regulatory regime is jointly implemented by the Ministry of Environment and Forests (MoEF) and the Department of Biotechnology (Ministry of Science and Technology), with appropriate interventions from the Ministries of Agriculture and of Health and Family Welfare.

The National Health Research Policy (2007) of Indian Council of Medical Research ensures the requirements of the National Health Policy (2002) that the results of health research are translated through inter-sectoral coordination amongst the government, private sector and the academia and that research is carried out with adequate levels of bio-safety so that new, exotic and dangerous organisms could be handled without posing any threat.

Research in Genetic Engineering

India's bio-security regulations for genetically engineered products are among the most stringent in the world. The institutional framework of the bio-security system is a coordinated activity of the following:

Recombinant DNA Advisory Committee (RDAC): RDAC under the Department of Biotechnology recommends, from time to time, suitable and appropriate safety regulations for recombinant research, its use and applications. The Committee reviews national and international developments in biotechnology to advise the Government on policy issues.

Institute of Bio-safety Committee (IBSC): ISBCs are most crucial in designing, evaluating and monitoring bio-security regime. Constitution of IBSC for an area of research is mandatory for all research institutions / universities / industries handling microorganism / genetically engineered organisms to oversee preparation of an up-to-date site emergency plan according to the manuals/guidelines of the Review Committee on Genetic Manipulation **(**RCGM). This committee looks into all the bio-safety aspects, including experimentation and containment issues. There are about 320 IBSCs in the country currently.

RCGM: RCGM managed by the Department of Biotechnology monitors the safety related aspects of on-going research projects involving genetically engineered organisms /

1hazardous microorganisms. The Committee also brings out manuals consisting guidelines specifying procedure for regulatory process with respect to activities involving high-risk category and controlled field experiments. The Indian Council of Agricultural Research conducts bio-security evaluation of the agricultural products while the Drug Controller General of India as the Central Drug Regulatory Authority provides bio-security clearance of medical products.

Genetic Engineering Approval Committee (GEAC): GEAC functions under the MoEF and approves activities involving large-scale use of hazardous microorganisms and recombinants in research and industrial production and proposals related to release of GMOs and products into the environment. Since June 2006, an event-based approval system has been put into place to speed up the process. An "event" refers to a specific gene construct that can be incorporated in a number of existing hybrids or varieties.

State Biotechnology Coordination Committee (SBCC): The Committees inspects, investigates and takes punitive action in case of violation of statutory provisions.

District Level Committee (DLC): This Committee **i**nspects, investigates and report to SBCC or the GEAC about compliance or non- compliance of r-DNA guidelines or violations under EPA. It also acts as nodal agency at District level to assess the damage, if any, due to release of GMOs.

Monitoring- cum-Evaluation Committee (MEC): MEC undertakes field visits to review the experiments / trials and the collection of data during the limited open field trials. MEC also collects information on the comparative agronomic advantages of transgenic crop; assess and advise on the risks and benefits from the use of transgenic plants; assist in collecting, consolidating and analyzing field data for evaluating the environmental risks emanating from the transgenic plants; and recommend those transgenic crops which would be found to be environmentally safe and economically viable to RCGM and GEAC.

M.S. Swaminathan Task Force, 2003 recommended setting up of an independent and professional watchdog, namely the National Biotechnology Regulatory Authority (NBRA), to generate public confidence in the use of GMOs. The task force also suggested that the role of the GEAC may be confined to bio-safety and environmental safety till the formation of NBRA. It has suggested that the MEC should report to the GEAC.

Biosafety Regulations

Several countries have also formulated bio-safety regulations and guidelines on modern biotechnology. The MoEF and the Department of Biotechnology (DBT), under the Ministry of Science and Technology of India, are responsible for implementation of rules 1989 under the EPI Act

The prevailing bio-safety laws in the country include:

The Indian Environment (Protection) Act of 1986 provided the government all the power 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 damage to the environment, including laying down procedures and safeguards for handling of hazardous substances and carrying out and sponsoring investigations and research relating to problems of environmental pollution.

The Rules were enacted under the EPA in 1989 for the Manufacture, Use/ Import/ Export and Storage of Hazardous Microorganisms/ Genetically Engineered Organisms or Cells. The Act also provides guidelines on ethical and social responsibilities of scientists, institutions, and industries.

Recombinant DNA Guidelines by DBT (1990) provided principles of occupational safety and hygiene for large-scale practice and containment, safety criteria and physical containment conditions. It specified appropriate containment facilities depending on the type of organisms handled, potential risks involved and various quality control methods needed to establish the safety, purity and efficacy of rDNA products.

The **Guidelines developed in 1999 for generating pre-clinical and clinical data for rDNA vaccines, diagnostics and other biologicals,** address issues of safety, purity, potency and effectiveness of the project.

Guidelines for Research in Transgenic Plants & Guidelines for Toxicity and Allergenicity Evaluation of Transgenic Seeds, Plants and Plant Parts, 1998 by DBT covered rDNA research on development of transgenic plants and field evaluation, imports and shipment, design of a contained green house and generating food safety information on transgenic plants and plant parts.

Mashelkar Committee, a Task Force on r-pharma, 2006 recommended Procedure for Regulation of Recombinant Pharma Products derived from Living Modified Organisms (LMOs). Recommendations were made for (i) products derived from LMOs but the end product is not a LMO and (ii) product derived from LMO where the end product is a LMO. The product where the end product is a LMO has the potential for propagating / replicating in the environment and therefore needs a higher level of regulation as compared to products derived from LMOs where the end product is not a LMO. Further, the magnitude and probability of environmental risk depends on the extent of use of LMOs within the R&D and production units. In case of imports this risk is not there, especially in cases of therapeutic proteins in finished form.

Import of GM products: The Directorate General of Foreign Trade notified new regulations for import of GM products by amending Schedule I (Imports) of the ITC (HS) Classification of Export and Import Items under Section 5 of the Foreign Trade (Development and Regulation) Act, 1992. The import of GMOs/LMOs for the purpose of (i)

R&D; (ii) food; (iii) feed; (iv) processing in bulk; and (v) for environmental release is governed by the provisions of the Environment Protection Act, 1986, and Rules, 1989. Application for import of GM material for R&D is processed by RCGM and approval is given by GEAC.

Food Safety

The food quality and safety with regard to genetically modified (GM) food in India is regulated through several central ministries and departments that include the MoEF as Secretariat of the GEAC; Department of Health in the MOHFW for implementation of the PFA Act; Indian Council of Medical Research (ICMR) on various issues including GM foods; Ministry of Agriculture through Department of Agricultural Research and Education/Indian Council of Agricultural Research (ICAR) and Department of Animal Husbandry and Dairying; Ministry of Food Processing and Industry for licensing of processed fruits and vegetable industries; and Ministry of Commerce and Industry (MOCI) for formulation of export policy of the country. The Government through its various departments like Health, Revenue, Commerce and the Directorate General of Foreign Trade has initiated several steps to streamline the safety and quality of imported food.

Food Safety and Standards Act, 2006 established the Food Safety and Standards Authority of India (FSSAI) to lay down science-based standards for food items. It seeks to regulate manufacture, import, storage, distribution and sale, to ensure availability of safe and wholesome food for human consumption. The Food Safety Management System has been defined under Good Manufacturing Practices (GMP), Good Hygienic Practices (GHP), Hazard Analysis and Critical Control Point (HACCP) and such other practices as may be specified by regulation, for food businesses. The food standards include specifications for ingredients, contaminants, pesticide residues, biological hazards and labels. The Commissioner of Food Safety (CFS) of each state, through food safety officers (FSOs), enforces the standards. Food items such as irradiated food, genetically modified food, organic food, health supplements and proprietary food cannot be manufactured, processed or sold without adhering to specific regulations. The act provides for a graded penalty structure as well.

Prevention of Food Adulteration (PFA) Act, 1954, and Rules, 1955 were enacted with the objective of assuring the quality and safety of food as well as encouraging fair trade practices. Under the rules, no person shall manufacture, sell, store or distribute adulterated or misbranded food products, whether imported or domestically produced, not conforming to the prescribed standards. The state governments and the union territories are responsible for monitoring and implementation of the provisions of the PFA Act and Rules.

Essential Commodities Act, 1955 has been enacted to protect the interests of the general public through control of the production, supply and distribution of and the trade and commerce in certain commodities. The act empowers the central and state governments to issue control orders for regulating production, distribution, quality, movement and licensing of essential commodities.

Export (Quality Control and Inspections) Act, 1963 provides for establishment of the Export Inspection Council of India that advices the central government regarding measures for the enforcement of quality control and inspection in relation to commodities intended for export.

Bureau of Indian Standards (BIS) Act, 1986 is a statutory autonomous body set up by this enactment. It provides for quality certifications in terms of products and management systems that ensure quality, safety and dependability for consumers. Drinking water, food colors and additives require mandatory certifications. The capability of an organization's management systems is assessed through Quality Management Systems; Environmental Management Systems; Occupational Health and Safety Management Systems; and Food Hygiene – Hazard Analysis and Critical Control Point System.

Animal Health

The MoEF and the Ministry of Agriculture (MOA) are responsible for issues related to protection of animal health, including domesticated animals, wildlife health in sanctuaries and wildlife parks. The MOA also regulates import of livestock and related products and provides export certification. The Department of Animal Husbandry and Dairying has the task of monitoring and coordinating various institutions engaged with animal health. Whereas each state government is responsible to protect the health of animals within its own boundaries, the central government issues notifications and guidelines on epidemic outbreaks and also forms ad hoc monitoring committees.

Wild Life (Protection) Act, 1972 seeks to protect wild animals, birds and plants with a view to ensure ecological and environmental security. According to the Act, use of chemicals, explosives or any other substances is prohibited which may cause injury to or endanger any wildlife. An amendment to the Act in 2000 mandates that the Chief Wildlife Warden shall take measures for immunization against communicable diseases of livestock kept in or within five kms of a sanctuary.

Livestock Importation Act, 1898, amended in 2001 as Livestock (Importation) Amendment Ordinance, provides for the regulation of the import of livestock which is liable to be affected by infections or contagious disorders. The Act empowers the central government to regulate, restrict or prohibit, as it may think fit, the import into the territories to which this Act extends or any livestock product which may be liable to affect human or animal health. It also empowers the state governments to make rule (s) on the detention, inspection, disinfection or destruction of imported livestock.

Plant Agriculture & Quarantine

The Protection of Plant Varieties and Farmers' Right Act, 2001 provides for the establishment of an effective system for protection of plant varieties, the rights of farmers and plant breeders and to encourage the development of new varieties of plants. This legislation allows fair and equitable share of the benefits accruing from the use of and the innovations based on India's genetic resources.

The Biological Diversity Act, 2002 provides for the conservation of biological diversity and sustainable use of its components and equitable sharing of the benefits arising out of the use of biological resources. The Act provides for setting up of an apex National Biodiversity Authority, State Biodiversity Boards and State Biodiversity Management Committees and biodiversity registry to regulate access to the country's plant and animal genetic resources.

The Patents Act and Intellectual Property Rights amendment, 2002 expressly forbids the patenting of traditional knowledge and life forms in order to protect the interest of various stakeholders in India of impact arising out of OECD legislation that allows for the patenting of genetically modified organisms and life-forms.

Destructive Insects and Pests Act, 1914 regulates the introduction and movement of any insect, fungus or pest which could be destructive.

Plant Quarantine (Regulation of Import into India) Order, 2003 of the MoA provides guidelines for prohibiting and regulating the import into India of agricultural articles and products, which are likely to raise bio-safety concerns. The order regulates the agricultural imports into India based on classification of plants into three categories: prohibited plant species; restricted species; species requiring additional declarations and special conditions: and plant material imported for consumption or industrial processing. Procedures of imports have been defined for these categories, including requirements of phytosanitary certificate, requirement of permit, requirements for GMOs of plant origin, and compliance requirements to harmonize with International Plant Protection Convention (IPPC).

Plant Quarantine Bill, 2004 mandates establishing the Plant Quarantine Authority of India (PQAI) to meet India's obligation under the IPPC to establish a central regulatory agency for plant protection. The bill seeks to bring about a comprehensive regulatory framework for prevention of the spread of quarantine pests both domestically and internationally.

Pesticide Legislations

Pesticide legislations are implemented under the MOA as the nodal ministry through the Central Insecticides Board and Registration Committee and the Directorate of Plant Protection, Quarantine and Storage.

Insecticides Act, 1968 ensures the availability of quality, safe and efficacious pesticides to the farming community and to manage risks to human health and the environment. The act seeks to regulate the import, manufacture, sale, distribution, use and transport of insecticides, including herbicides, fungicides, rodenticides, etc.

Seed Legislation

Seeds Act, 1966 provides for the regulation of the quality of certain seeds. Central Seeds Committee constituted by the central government advises the centre and states

on matters arising out of the administration of this act. The seeds used for human consumption, however, are regulated under the Essential Commodities Act, 1955.

National Seeds Policy, 2002 ensures that all genetically engineered crops/varieties are tested for environment and bio-safety.

Seeds Bill, 2004 has a mandatory requirement of registration of all kinds and varieties of seeds with the National Register of Seeds under the Central Seeds Committee. The registrations of transgenic seeds under the bill require following the existing bio-safety regulations. For biosecurity purposes, the bill has a provision to exclude certain varieties of seeds from registration to prevent their commercial exploitation.

Biosecurity

Bio-security Program involves development of policies addressing life sciences research that yields information or technologies with the potential to be misused to threaten public health or national security. Laboratory bio-security addresses the measures of protection against intentional theft, misuse, or release of biological materials among other things. The Biosecurity Program ensures developing policies for responsible conduct and oversight of life sciences research. The prevalent bio-security laws include:

The **Prevention of Terrorism Act, 2002** applicable to the terrorist acts with intent to threaten the unity, integrity, security or sovereignty of India or to strike terror in the people or any section of the people, does any act or thing by using bombs, explosives or inflammable substances or firearms and lethal weapons or poisons or noxious gases or other chemicals, biologicals or otherwise of a hazardous nature or by any other means whatsoever, in such a manner as to cause, or likely to cause, death of, or injuries to any person or persons or loss of, or damage to, or destruction of, property.

The Weapons of Mass Destruction and their Delivery Systems (Prohibition of Unlawful Activities) Bill, 2005 prohibits unlawful activities in relation to weapons of mass destruction and their means of delivery and to build upon the regulatory framework related to controls over the export of WMD-usable materials, chemicals, organisms, equipment and technologies.

India has been exercising **control over the export of Special Chemicals, Organisms, Materials, Equipment and Technologies (SCOMET)**, which include microorganisms / toxins, including bacteria, fungi, parasites, viruses, rickettsials, plant pathogens, and GMOs. Export of these SCOMET items requires a license under the Foreign Trade (Development and Regulation) Act, 1992.

Director General Foreign Trade under **Foreign Trade Policy** issue notifications, which provide classification to the Export and Import of Genetically Modified Food, Feed, GMOs

and LMOs to be governed under Environment Protection Act, 1986 and Rules 1989, RCGM, GEAC)based on their intended use.

Drugs and Cosmetics Rules 1988 notification vide GSR No. 944 (E) dated September 21, 1988 by Ministry of Health and Family Welfare detailed the requirement of the activities for enabling the import or manufacture of biological and biotechnological products, the manner of conducting clinical trials in India and their presentation, or the method of presentation of clinical trials data generated elsewhere. All new drugs to be imported or to be produced locally for marketing purposes require the permission of the Drug Control Authorities.

Drug Policy 2002 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 and approvals for foreign investments as well as foreign technology agreements.

Water (Prevention and Control of Pollution) Act (1974) provides for the prevention and control of water pollution and the maintaining or restoring of wholesomeness of water, for the establishment of Boards for the prevention and control of water pollution, for conferring on and assigning to such Boards powers and functions relating to prevention of water pollution..

Air (Prevention and Control of Pollution) Act, 1981, and Rules (1983) provide for the prevention, control and abatement of air pollution, for the establishment of Boards for conferring on and assigning to such Boards powers and functions relating thereto and for matters connected therewith.

Biomedical Waste Management & Handling) Rules, 1998 provide for the management and handling of biomedical wastes generated from hospitals, clinics, other institutions for scientific management of biomedical waste. Such activities are governed by legislation through State Pollution Control Boards.

Agricultural Biosecurity Bill, 2013, introduced in Lok Sabha in 2013 aims to establish an integrated national bio-security system covering plant, animal and marine issues to combat threats of bioterrorism from pests and weeds. The Bill repeals the Destructive Insects and Pests Act, 1914 and the Livestock Importation Act, 1898. An Agricultural Biosecurity Authority of India (Authority) is recommended to oversee regulation of import and export of plants, animals and related products; (ii) preventing introduction of quarantine pests from outside India; and (iii) implementing post-entry quarantine measures.

The **National Disaster Management Authority (NDMA)** has been constituted under the Disaster Management Act, 2005. The National Guidelines for Biological Disaster Management (NGBDM) (2008) released by NDMA deals with natural and manmade

biological threats and emergencies. The Central and State governments are required to set up appropriate Biological Disaster Management Authorities.

Ethics and Code of Conduct

To prevent misuse of bio-medical sciences, persons and institutions engaged in all aspects of advanced biological research need to abide by a voluntary code of conduct. Scientists should be made aware of the potential risks and their ethical responsibilities. They should also comply with the international conventions and treaties.

India has drafted codes of conduct or principles of ethics for scientists to ensure that activities involving microbial or other biological agents or toxins are of types and in quantities that have justification for prophylactic, protective or other peaceful purposes.

The Ethical Guidelines developed in 2000 for biomedical researchers are consistence with the Helsinki Declaration, adopted by the World Medical Assembly in 1964. It was amended in October 2000 based on principles of autonomy, privacy, justice and equity.

Ethical Guidelines for Biomedical Research on Human Participants (2006) released by ICMR defines codes on general principles on research using human participants. While medical research must not violate any universally applicable ethical standards, a researcher needs to adhere to safety concerns and ethical principles. The Ethical Committees have also developed mechanisms for enforcing accountability and transparency by the research institutions.

The code of conduct for research scientists is governed by the principles of:

- **Non-malfeasance whereby it is** ensured that the discoveries of biomedical research scientists and knowledge generated do no harm and that the bio-science and biotechnology discoveries do not facilitate bio-terror/bio-warfare;
- **Beneficence whereby it is ensured that** the **scientific knowledge** gained through advanced life sciences research genuinely benefits the society that outweigh the risks & 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.
- **Principles of risk minimization,** whereby due care and caution is taken to restrict the disseminations 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 b**e** readily misused to inflict serious harm through bioterrorism 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.

In 2002, the Department of Biotechnology developed the **Ethical Policies on Human Genome, Genetic Research and Services** to provide guidance to researchers, ethical committees, institutions, organizations and the public on the conduct of research, based on the recognized ethical principles and values. It addresses issues ranging from consent and dissemination of results to human cloning, intellectual property rights and international collaborations.

Mitigation Strategies

Mitigation strategies may aim at preserving benefits of life sciences research while minimizing its risk of misuse. The objectives for which can be achieved through:

- Promoting safe, secure and responsible use of dangerous biological agents and toxins;
- Creation of national mechanism to establish and maintain security and oversight of pathogenic microorganism and toxins;
- Ensuring Code of Conduct/Principles/Guidelines are followed voluntarily;
- Establishment of legal and institutional procedures and mechanisms for monitoring and regulation;
- Strengthening awareness programs and requirements for bioterrorism preparedness to all stakeholders;
- Focus on education and outreach.

A scientific, rigorous, transparent, efficient, predictable and consistent regulatory mechanism and protocol for bio-safety and bio-security evaluation and related system need to be followed to meet these objectives. That may include:

- Adequate safeguards are employed to contain biological agents or materials and therefore prevent the exposure of workers, other people, or the environment to agents that may adversely harm them;
- Ensure biosafety measures so that research is conducted in accordance with the highest standards;

- Ensure that Good Microbiological Practices (GMP) are followed to enhance worker safety, environmental protection, and address the risk of handling agents requiring increasing levels of containment;
- Develop policies for responsible conduct and oversight of life sciences research
- Scientists are made aware of risks, international conventions and treaties relevant to their research work;
- Government's oversight is required.

Magnitude of the Problem

Implementation of bio-security regime in India naturally faces many challenges given the vastness of the country that stems from the fact that research is funded by both governmental and non-governmental sectors; there is acute lack of trained manpower and shortage of resources; and multiple agencies' involvement in this sector.

In governmental sector, research is financed by the Department of Health Research, Ministry of Health and Family Welfare, under the aegis of the ICMR through its National Research Institutes and Regional Medical Research Centers. Three departments under the Ministry of Science and Technology (i.e. Department of Biotechnology, Department of Science and Technology; and the Council of Scientific and Industrial Research under the Department of Scientific and Industrial Research) are involved in medical research. Besides, the Defense Research and Development Organization (DRDO) and the University Grants Commission through a large number of Central or State Universities, autonomous research institutions, medical colleges and other academic institutions are equally involved in advanced medical research. The research projects on animal health are supported by the Indian Council of Agricultural Research in its several specialist institutions and the State agricultural/veterinary universities.

In such a scenario, ensuring bio-safety and bio-security in all public and private institutions becomes difficult. There are more than 800 medical and healthcare R&D institutions; 375 medical colleges, 575 universities, more than 10,000 pharmaceutical and biopharmaceutical industries and unlimited number of healthcare entities and diagnostic laboratories handling biomedical wastes. Similarly, there is a huge number of people involved with advanced research in agriculture, food safety, animal husbandry, aquaculture and environment and industry and other life science areas dealing with biological agents. The concept of bio-safety and bio-security needs to be extended to each and every establishment handling infectious pathogens.

A cross sectional study carried out by Mustafa (2008) on safety measures being adopted in clinical laboratories of India showed that only 60% of laboratories had person in-charge of safety; 73% had safety education program regarding hazards; in 91% of laboratories staff was using protective clothing; 78% of laboratories follow hazardous materials regulations; regular health checkups are carried among laboratory staff in 43.4% of laboratories; safety manual is available in 56.5% laboratories and 95.6% of laboratories follow waste disposed off as per bio-medical waste management rules.

Generating widespread awareness requires a holistic and systematic approach that may include:

- Improved understanding and management of the risks associated with accidental and deliberate misuse of biological agents
- Develop strategies for biorisk management for R&D in public and private sectors
- Understand need of large number of academic and research institutions
- Outreach to large number of stakeholders Trained Management and Biological Safety Officer with the support of the Institutional Biosafety Committee can effectively address issues of bio-safety in institutional set ups.

Education and Outreach

The Department of Biotechnology (DBT) has created a dedicated website on bio-safety reflecting National and International Guidelines and National Rules & Procedures in consultation with Institutional Biosafety Committees. DBT also developed a website on Indian GMO Research Information System (IGMORIS) with the aim to provide information on research works. The DBT has issued a detailed handbook on the functions and role of the ISBC as per the Recombinant DNA Safety Guidelines, 1990.

The DBT has supported Bitoech Consortium India Ltd. New Delhi to organize workshops on various aspects of bio-safety related to GMOs to apprise the members of the IBSCs on bio-safety rules, regulations & procedures. The DBT-sponsored programs on capacity building in bio-safety conducted by BCIL include preparation of research documents and reports and organizing national and international conferences,/workshops on key policy issues, state and district level events for stakeholders and farmers' welfare and a newsletter "The South Asia Biosafety Program (SABP)" is published monthly.

Development of policies governing the publication of sensitive research works with the aim to address the bio-security aspect of research is another requirement. Effective steps to ensure bio-security without hampering research and free exchange of information are needed. A system of checks and balances must be put in place. Issues requiring consideration are:

- Increased awareness of threats, prevention, response and risk of bio-terrorism
- Develop training programmes and materials for educating scientists on laboratory bio-risk management
- Establish procedures to monitor research activities and mechanisms to prevent dissemination of information likely to be utilized for bio-terrorism
- A bottom-up approach in formulation and implementation of bio-safety and bio-security policies through direct involvement of scientists
- Adoption of outreach policy towards industry to involve it in the policy formulation process

- Training curriculum in bio-waste management and environment risk management of pharmaceuticals.
- Creation of information and technology infrastructure for effective intraand inter-sectoral communication.

Biorisk Management

The biorisk management approaches adhere to the principles that reduce the risk of unintentional exposure to pathogens and toxins or their accidental release; reducing the risk of unauthorized access, loss, theft, misuse, diversion or intentional release of micro-organisms; and those suitable measures have been adopted and effectively implemented. The framework incorporates continuous awareness-raising, following code of conduct, and training.

Any investigation into the nature of the biological materials and the procedures used to store, handle, transfer and dispose those materials would comprise the process of biorisk assessment. This may include review of research proposals and identify hazards that the biological materials can cause in a lab. Biorisk management procedures determine the control measures (or mitigation strategies) to be used to implement to minimize or eliminate the defined risk. Risk assessment and improvement of biorisk management can efficiently address issues relating to bio-safety and bio-security.

Laboratory biorisk management as defined under CWA 15793:2011 includes the analysis of ways, development of strategies and their implementation to minimize the likelihood of the occurrence of biorisks; methodology used to organize and analyze scientific information in order to estimate the probability and severity of an adverse effect (assessment) and measures to minimize this effect (mitigation); and establishing policies and practices for risk management in the lab.

A dedicated human resource is required to implement provisions of biorisk management, which requires:

- Developing training curriculum for stakeholders
- Organise training programs, workshops to train-the-trainers
- Organize training programmes on bio-threats and bio-risk mitigation strategies for law enforcement officials
- Developing training implementation strategies, including regional training centres
- National Coordination Centre /Academy to oversee Implementation of Biorisk Management Programs.

The National Biotechnology Development Strategy (NBDS) 2007 by Department of Biotechnology suggested establishment of the National Biotechnology Regulatory Authority (NBRA). A statutory National Biotechnology Regulatory Bill, 2008, is under consideration. The NBRA will function through interaction with an Inter-Ministerial Advisory Board and a National Biotechnology Advisory Council and would have appropriate regulatory branches, one each for (a) agriculture, fisheries and forestry, (b)

human and animal health, and (c) industrial and environmental applications; and a Risk Assessment Unit that will undertake bio-security evaluation and recommend appropriate action to the NBRA.

Containment Facilities

In India a number of containment laboratories for human and animal health safety are being planned and about 30 bio-safety laboratories of the level of BSL3 or BSL2+ are currently under operation, mostly at the ICMR and the Council of Scientific and Industrial Research laboratories, Defense Research and Development Laboratories, vaccine industries and other research institutes. A High Security Animal Disease Laboratory (HSADL) having state-of-the-art bio-safety was set up in Bhopal in 2000 and the other one at Microbial Containment Complex, Pune is functional since 2012. The premises, materials and workers in these labs however, remain poorly supervised and managed urgently requiring efficient management of premises, materials and personnel.

Important Issues

India has robust and strict regulatory framework that provides for all adequate safeguards and regulations for bio-safety and bio-security policies. However, there is lack of technically trained manpower and adequate machinery to strictly enforce the regulatory system. Thus efforts should be made at meeting the urgent need of technical requirements and capacity building. Biosecurity needs to be viewed more broadly from the perspective of public policy on health, environment and sustainable development. Laboratory safety in India needs to be a part of an overall safety program in hospitals and all this can be achieved by having a quality control program in hospitals in general and laboratories in particular. Accreditation has to be made necessary and all laboratories should be graded as per their performance against a set of predetermined standards.

A debate is currently underway in the country to consider putting restrictions on the funding and publication of research undertaken in areas of dual use concern on grounds of security. Suggestions are floating to develop a mechanism by the funding agencies to identify implications of projects with dual use research concern at the time of the presentation to the IBSCs, peer review by experts at the time of consideration of proposal for funding or by the journal editorial system to identify them at the stage of peer review/publication.

A coherent bio-security strategy for healthcare research and microorganisms and agricultural crops, farm animals, living aquatic resources and agriculturally important micro-organisms involving education and social mobilization of regulatory measures would facilitate scientific partnership between various institutions engaged in bio-monitoring and other bio-security programs. A coordinated effort among the concerned agencies and proper regulation would lead to protection and promotion of bio-security within the delimitations of their respective mandates. Efforts should be made to harmonize regulations with international policies.

A panel discussion at the International Meeting on Host Parasite Interactions held at National Institute of Animal Biotechnology, Hyderabad on July 15, 2014 highlighted the issues involved with bio-safety and bio-security procedures. The group suggested the government to take initiative in drafting uniform guidelines for all laboratories working with BSL 2/3 or 4 microorganisms; technical guidance documents for technical / administrative staff in laboratories working with exotic organisms; establish an agency for Biorisk Management central to academia, industry, civil society and legal fraternity for biological disaster management, international collaboration and risk mitigation strategies. The experts rightly stressed on issues of information and awareness; implementation of regulations and guidelines, education and outreach, capacity building, risk assessment and risk management. Capacity development should aim at strengthening the legislative framework and operational mechanisms.

In line with recommendations by various expert bodies, and to increase awareness and training on safety & security in research institutes, academia & industry, establishing a dedicated centralized autonomous body/centre with a mandate to develop human resource in Biorisk Management may provide India an advantage in the biotechnology sector. It would promote a culture of good bio-safety and bio-security practices through effective monitoring, education and training, information dissemination and knowledge sharing in pursuit of benefits of life sciences research. This will also ultimately foster the culture of responsibility among the researchers.

Such a body may develop specialized courses in bio-risk management; related policies, applicable regulations, audits, inspections, and manage challenges and opportunities associated with facility risk assessment; organize short-term training courses, workshops symposia and conferences.

It is equally important to develop dedicated guidelines for medical surveillance and evaluation system, secure plants, animals, aquatic resources and agriculturally important microorganisms, update safety manuals; bio-security plan; safe practices and standard operating procedures; and emergency response plans and wide dissemination and outreach to large number of beneficiaries through electronic media and periodic newsletters.

It would be important to document occurrences of all biosafety lapse incidents, creation of databases for the agents responsible and documentation of available mitigation measures.

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The Author is Chief Executive Officer at NeoBioMed Services (100, Vasant Enclave, New Delhi), India. He was formerly Advisor to Government of India in the Department of Biotechnology, Ministry of Science and Technology.

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