Draft Establishment Plan for the National Biotechnology Regulatory Authority

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May 28, 2008

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1 INTRODUCTION

1.1 BACKGROUND

India's biotechnology regulatory system has experienced a number of changes since the *Rules for the Manufacture, Use, Import, Export and Storage of Hazardous Microorganisms/Genetically Engineered Organisms or Cells 1989* (*Rules*, 1989) were first notified under the Environment (Protection) Act, 1986, including the elaboration of a series of guidance documents published by the Department of Biotechnology (DBT) in 1990, 1998 and 1999. The extraordinary growth of the Indian biotechnology sector has significant implications for policy in the area of regulation, and two specific reports were commissioned by the Ministry of Agriculture and the Ministry of Environment and Forests to evaluate the regulatory framework for products of agricultural biotechnology and recombinant pharmaceuticals, respectively.

The 2004 Report of the Task Force on the Application of Agricultural Biotechnology chaired by Prof. M.S. Swaminathan (the Swaminathan Report) recommended the establishment of an "autonomous, statutory and professionally-led National Biotechnology Regulatory Authority" (NBRA) that would have "two separate wings – one dealing with food and agricultural biotechnology, and the other with medical and pharmaceutical biotechnology." The Report recommended that the "NBRA is essential for generating the necessary public, political, professional and commercial confidence in the science based regulatory mechanism in place in the country."

The 2005 Report of the Task Force on Recombinant Pharma chaired by Dr. R.A. Mashelkar (the Mashelkar Report) similarly supported the establishment of a National Biotechnology Regulatory Authority/Commission "providing a professionally managed single window mechanism for giving various clearances including biosafety issues." A model for the NBRA was proposed that "would comprise of four wings namely: a) Agricultural products / Transgenic Crops; b) Pharmaceutical/ Drugs and Industrial Products; c) Transgenic Foods/Feed; and d) Transgenic Animals/ Aquaculture" and that "alternate models of how a National Biotechnology Regulatory Authority can be created also needs to be examined." The Mashelkar Report additionally provided a series of recommendations to streamline the existing regulatory system for recombinant pharmaceuticals until the feasibility of establishing a NBRA could be evaluated.

In 2005, DBT published a draft National Biotechnology Development Strategy which elaborated a ten year vision for the future of biotechnology in India. Key policy recommendations and approaches to implement these were established through a process of multi-stakeholder consultations that focussed on cross-cutting issues of relevance to all sub-sectors of the biotechnology community. Under the topic of regulatory mechanisms, the National Biotechnology Strategy recommended "a competent single National Biotechnology Regulatory Authority be established with separate divisions for agriculture products/transgenic crops, pharmaceuticals/drugs and industrial products; and transgenic

food/feed and transgenic animal/aqua culture. The authority is to be governed by an independent administrative structure with common chairman. The inter-ministerial group will evolve suitable proposals for consideration of the government."

The National Biotechnology Development Strategy was approved by the Government of India in November, 2007 after a two year consultation period with multiple stakeholders including concerned ministries, universities, research institutes, private sector, civil society, consumer groups, non-government and voluntary organizations and international bodies[1]. As regards the regulation of biotechnology, the Strategy states that the NBRA will be established as an "independent, autonomous and professionally led body to provide a single window mechanism for biosafety clearance of genetically modified products and processes"[2]. DBT has been given the responsibility to set up the NBRA and until such time as the NBRA is fully functional, biotechnology regulation will continue under the existing regulatory framework.

1.2 ESTABLISHMENT PLAN FOR THE NBRA

This establishment plan for NBRA covers the following:

i. Management structure that needs to be created including hierarchy levels, flow and control of information, geographic structure, various divisions, departments etc.

ii. Definition of the appropriate legal framework for NBRA on the basis of global best practices.

iii. Delimitation of the scope of the Authority in terms of products/services vis-à-vis other government and non-government organizations, industry etc.

iv. The potential legislative impact that the defined NBRA portfolio can have.

v. Definition of NBRA scope of operations to include specific areas to be governed in the industry, services to be provided, limitations, areas of synergy etc.

vi. Mechanism to train and re-train regulatory officials on a continuous basis.

vii. Methods on ensuring transparency, efficiency and flexibility to accommodate new developments in the emerging areas of biotechnology.

viii. Mechanism for accreditation/notification of referral labs, institutes, facilities for biosafety assessment.

[1] http://www.dbtindia.nic.in/biotechstrategy/biotech_strategy.htm
[2] http://dbtindia.nic.in/biotechstrategy/National%20Biotechnology%20Development%20Strategy.pdf

2 MANDATE OF THE NBRA

The NBRA will be an independent, autonomous, statutory agency established by the Government of India to safeguard the health and safety of the people of India and to protect the environment by identifying risks posed by, or as a result of, modern biotechnology[3], and managing those risks through regulating the safe development and deployment of biotechnology products and processes.

3 LEGAL FRAMEWORK

In order to establish and empower the NBRA, DBT is considering to promulgate new legislation, "*National Biotechnology Regulatory Act* (*NBR Act*)". Elements of biotechnology regulation are currently spread over multiple acts and some of these would be amended to establish and operationalize the NBRA. Drafting new legislation would provide an opportunity to consolidate and enhance the efficiency and effectiveness of biotechnology regulation, increase collaboration with state governments in this area, promote public confidence in the regulatory system, and facilitate international trade.

The draft *NBR Act* would provides for (but not be limited to): the establishment of the NBRA; the composition of the NBRA including mandate, responsibilities and membership of its councils, committees, branches, offices etc.; rules of conduct and conflict of interest provisions for management, employees and any delegated parties who may act on behalf of the Authority; the structure, function and powers of the NBRA; the policies and provisions of the national biotechnology regulatory framework; and the operations of the NBRA including decision-making authority, mechanism for appeal, powers of inspection, penalties and other actions that may be taken if the provisions of the Act are contravened. The *NBR Act* should be supported by implementing regulations or rules as required to carry out the provisions of the Act.

The scope of the *NBR Act* would extend to the research, manufacture, importation and use of products of modern biotechnology. Sufficiently broad in scope, the Act would function as a "safety net" that ensures all biotechnology products and processes will be subject to regulation as regards their safety. However, there are specific categories of GM products that are already regulated from a safety perspective by other ministries. If there are sufficient benefits and/or efficiencies gained by having the NBRA as the exclusive biotechnology regulatory body versus recognising that continuing with existing regulatory mechanisms for some categories of GM products/processes may be the preferred alternative as indicated below.

[3] Note that is a working definition only, derived from the Convention on Biological Diversity. "Modern biotechnology" means the application of *in vitro* nucleic acid techniques, including recombinant deoxyribonucleic acid (DNA) and direct injection of nucleic acid into cells or organelles, or fusion of cells beyond the taxonomic family, that overcome natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection. It excludes: *in vitro fertilisation*; natural processes such as conjugation, transduction, transformation; polyploidy induction; and accelerated mutagenesis

Regulation of GM foods and recombinant pharmaceuticals

GM foods are regulated by the Food Safety and Standards Authority under the *Food Safety and Standards Act, 2006* (*FSSA, 2006*). Product safety, efficacy, clinical trials and market authorization of recombinant drugs are regulated by the Drug Controller General of India (DCGI) under the authority of the *Drugs and Cosmetics Rules 1945* (*Rules, 1945*) of the *Drugs and Cosmetic Act 1940*. From an operational standpoint, there are opportunities to coordinate the safety assessment of GM foods between the FSSA and the NBRA. The science-based environmental and food safety assessment of GM plants share many common elements (*e.g*., molecular and protein characterization) and redundancies in risk assessment can be avoided if the FSSA refers the regulatory packages it receives for GM food approvals to the NBRA RAU. The RAU could undertake all or part of the safety assessment of GM foods on behalf of the FSSA and submit its report to the Chairperson, FSSA for product approval. Alternatively, GM food safety assessment can remain in the exclusive purview of the FSSA or the regulation of GM foods can be vested with the NBRA. In the latter case, while the NBRA would be responsible for the GM food safety assessment and any subsequent authorization of the GM food as safe, all other rules and regulations that pertain to food (*e.g*., conventional safety provisions related to adulterants, extraneous matter and unhygienic/unsanitary processing or manufacturing of food) would still apply to the GM food as regulated by the FSSA and any other authority in India.

The NBRA will also be responsible for regulating genetically modified organisms with applications in human and veterinary health and a sub-set of products derived from these. This will include the regulation of recombinant biologics such as DNA vaccines, recombinant gene therapy products, recombinant and transgenic plasma derived products like clotting factors, and veterinary biologics but will exclude all other therapeutic proteins derived from recombinant organisms. These will continue to be regulated by the DCGI.

Any provisions in the *NBR Act* related to confidential commercial information must be consistent with other related acts, most notably the *Right to Information Act, 2005*.

4 LEGISLATIVE IMPACT

Products and processes of modern biotechnology are currently regulated in India through a number of acts and their supporting rules and are additionally the subject of various national policies. The legislative impact of the *NBR Act* will only be determined when the Act has been finalized, however, it is anticipated that amendments to the acts and rules listed below may be required.

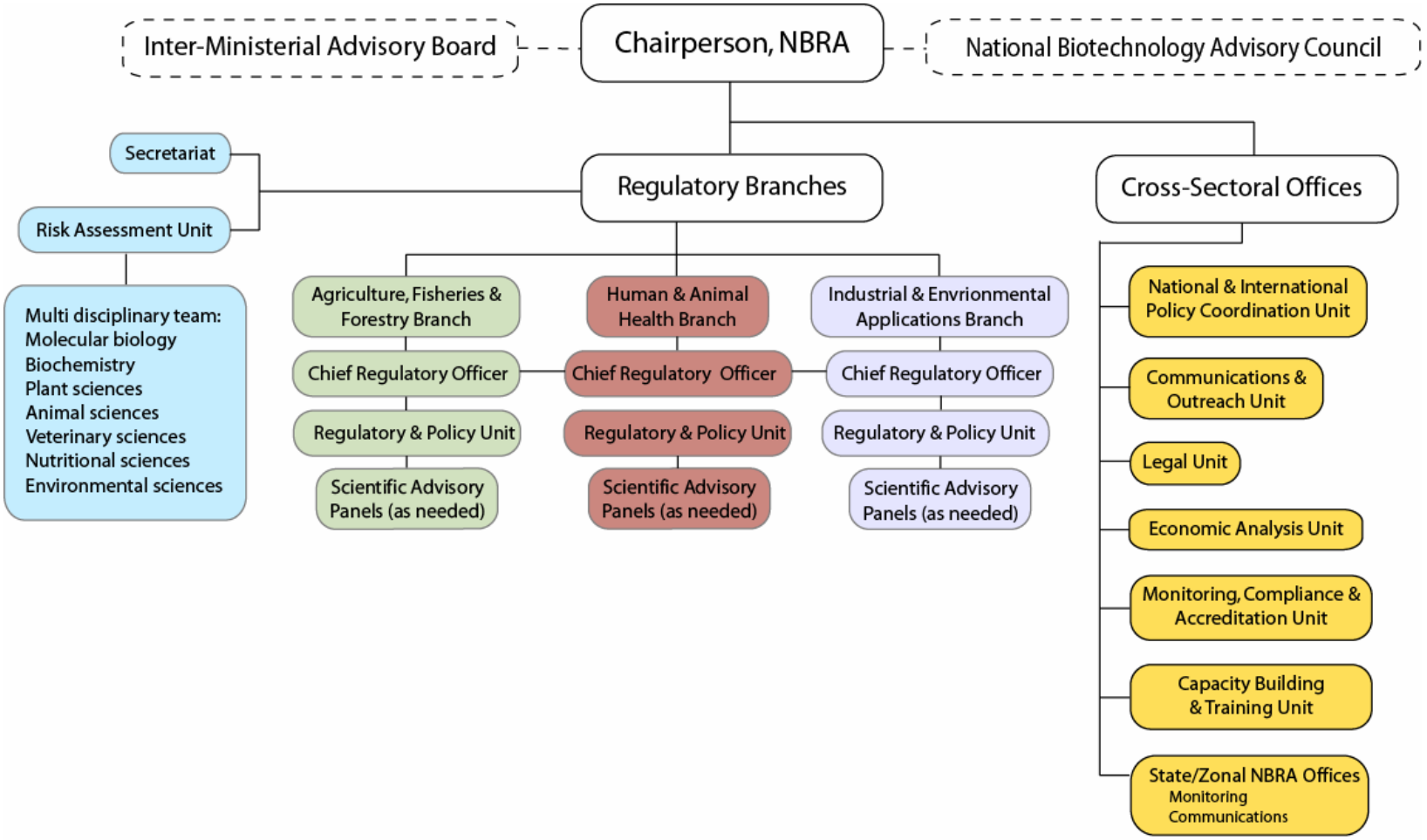
- Rules for the Manufacture, Use, Import, Export and Storage of Hazardous Micro-organisms/ Genetically Engineered Organisms or Cells, 1989 issued under Environment (Protection) Act, 1986
- Drugs and Cosmetics Rules (8th Amendment), 1988
- Plant Quarantine (Regulation for Import into India) Order 2003
- Seeds Bill, 2004
- Food Safety and Standards Act, 2006

Present status of activities regulated under various Acts and Rules and key features of national policies is given in Annexure 1.

5 MANAGEMENT, STRUCTURE AND OPERATIONS

The organizational structure proposed for the NBRA was developed based on best practices identified from analytical studies of other regulatory authorities/systems in India and international approaches to biotechnology regulation. A draft model for the NBRA has been prepared and further refined based on preliminary feedback through consultations with a representative group of key stakeholders. The proposed management structure for the NBRA is described below and the organizational chart is presented in Figure 1.

Figure 1: Proposed organizational structure for the NBRA.



5.1 GOVERNANCE

The NBRA would be led by an eminent biotechnologist in the full-time position of Chairperson and who will hold the rank of Secretary to the Government of India. The Chairperson will be supported by two advisory bodies:

1. The Inter-Ministerial Advisory Board (IMAB) which will promote inter-ministerial and departmental coordination and cooperation as regards the implementation of India's national biotechnology regulatory system including any international impacts that may arise from, or potentially impact, biotechnology regulation in India.

   The IMAB will provide a forum for early discussion of policy options and issues of mutual concern and to develop recommendations on these policy issues for consideration by the Chairperson of the NBRA. It will meet as required to ensure coordination at the senior management level. The IMAB will include representation from concerned government ministries/departments/agencies including:

   - Ministry of Commerce and Industry;
   - Ministry of Food Processing Industries;
   - Ministry of Agriculture;
   - Ministry of Environment and Forests;
   - Ministry of Health and Family Welfare;
   - Ministry of External Affairs;
   - Department of Biotechnology;
   - Department of Science and Technology;
   - Indian Council Agricultural Research;
   - Indian Council of Medical Research;
   - Council of Scientific and Industrial Research;
   - Drug Controller General of India (or proposed Central Drug Regulatory Authority);
   - Directorate of Plant Protection, Quarantine and Storage (or proposed Plant Quarantine Authority); and
   - Food Safety and Standards Authority.
   - Any other to be specified.

2. The National Biotechnology Advisory Council (NBAC) will address overarching policy-related issues that may affect the regulation of biotechnology in India. The NBAC will provide the Chairperson with independent strategic advice on developments in biotechnology and their implications for Indian society. The Council will include representatives from the scientific community, private sector and civil society in diverse fields such as science, business, law,

nutrition, environment, human health and public advocacy. The committee will consist of a Chair and up to 20 members with a range of expertise:

- Crop scientists (one each from public and private sectors)
- Animal/Veterinary scientists (one each from public and private sectors)
- Industrial/Environmental scientists (one each from the public and private sectors)
- Medical/pharmaceutical scientists (one each from the public and private sectors)
- Nutritionist/community health specialist
- Representative from consumer affairs organization
- Representative from farmer organization
- Social scientist (*e.g.*, economist)
- Legal expert
- Others to be specified

Example: Role of the NBAC

The use of plants as production platforms for the expression of pharmaceuticals and industrial molecules (*i.e.*, plant molecular farming) may provide advantages relative to bulk production of the natural source of the corresponding protein such as overall economy of production, lack of need for major capital investment (*e.g.* in fermentation bioreactors), ease and economy of scale-up, lack of risk of contamination with human pathogens, etc. However, concerns have been raised as to whether food crops should be used for such a purpose because of the potential for accidental contamination of the food/feed chains. The NBAC could be asked to develop a national policy on whether some or any food crops can be used for plant molecular farming and what mitigation measures (*e.g.*, geographical limitations on where plant molecular farming can take place) may be required to safeguard the Indian food supply.

5.2 ORGANIZATIONAL STRUCTURE

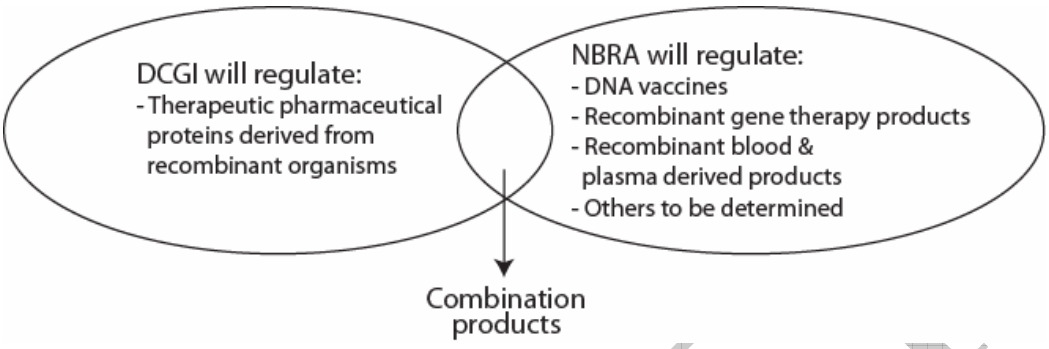
5.2.1 Regulatory Branches

In order to encompass the breadth of biotechnology processes and products that it must regulate, it is proposed that the NBRA should initially have three regulatory branches: 1. Agriculture, Forest and Fisheries Branch (AFFB); 2. Human and Animal Health Branch (HAHB); and 3. Industrial and Environmental Applications Branch (IEAB). Each branch should be headed by a Chief Regulatory Officer (CRO), an eminent scientist with subject matter expertise relevant to the Branch, appointed at the rank of Additional Secretary to the Government of India.

The AFFB will regulate GM plants, animals and micro-organisms used in agriculture, forestry or fisheries, including aquaculture.

The HAHB will regulate genetically modified organisms with applications in human and veterinary health (see figure below). This will include the regulation (*i.e.*, clinical trials, pre-commercial safety assessment, product approval, post-release monitoring) of recombinant biologics (*e.g.*, DNA vaccines, recombinant gene therapy products, recombinant and transgenic plasma derived products like clotting

factors) and veterinary biologics. The DCGI will regulate all other therapeutic proteins derived from recombinant organisms. Where there are combination products comprised of a biological product component with a device and/or drug component they will be assigned to an authority for review and regulation in accordance with the products' primary mode of action. When a product's primary mode of action is attributable to a type of biological product assigned to NBRA, the product will be assigned to NBRA. Similarly, when a product's primary mode of action is attributable to a type of recombinant product assigned to DCGI, the product will be assigned to DCGI.



The IEAB will regulate GMOs used in industrial manufacturing and in environmental applications, such as the use of GMOs for bioremediation of contaminated sites or oil spills.

Each Branch should be supported by the NBRA Secretariat which will function to receive applications, coordinate reviews, communicate with applicants, and maintain all relevant records. Initially, the Secretariat should be one office that provides administrative support to all three Branches (with specific officers assigned to a Branch) however, over time and if warranted, each Branch could have its own Secretariat. This decision will be dependent on the number of submissions to the NBRA and any additional duties prescribed for the Secretariat.

Each Branch will have a Regulatory Policy Unit (RPU) that will be permanently staffed by professionals and will be responsible for developing and implementing Branch specific policies, rules and guidance (*e.g.*, standard operating procedures which would be prepared in conjunction with the Risk Assessment Unit, below). The RPU will also have a communications and outreach function and will be responsible for undertaking stakeholder consultations when new policies, rules and/or guidelines are developed. This is essential to promote transparency and public participation in NBRA programs and operations.

5.2.2 Risk Assessment

Scientific risk assessment is a cornerstone of biotechnology regulatory systems and public policy decisions related to the safety and acceptability of GMOs. A strong scientific capacity and knowledge base is widely viewed as key to assessing risk; which entails identifying hazards, assessing their magnitude and duration, and estimating their likelihood of occurrence while recognizing the nature and importance of the attendant uncertainty in each phase. Risk assessment of biotechnology products and processes is an intensive and scientifically demanding activity. In order to ensure that the NBRA secures the best science advice possible, it is proposed that both internal and external scientific bodies be used as described below.

The case-by-case assessment of products and processes should be undertaken by a Risk Assessment Unit (RAU) permanently staffed by a multi-disciplinary team of scientists responsible for undertaking science-based risk assessments, including but not limited to those required to approve field (or similar) and clinical trials of experimental GMOs and commercial release of GMOs in India (*i.e*., product-specific risk assessments). The use of in-house scientists will: permit the development of considerable expertise within the NBRA; provide for a degree of consistency not afforded by the ever-changing membership of advisory and *ad hoc* committees; and can address the real or perceived conflict of interest that arises if product developers are also product assessors. Crucially, senior management must be committed to ensuring that the RAU is properly and appropriately staffed and that resources are made available on an on-going basis to promote and access training and the recruitment of new knowledge. In absence of this commitment, the RAU will not be able to maintain its scientific credibility and public confidence in decision-making by the NBRA will be compromised.

The RAU will be comprised of cells such as: Core Characterization; Animal Biotechnology; Plant Biotechnology; Human Health Biotechnology, and Industrial and Environmental Biotechnology (for examples of indicative expertise see Table 3). Wherever possible, scientists who themselves have multidisciplinary training and experience should be employed. For example, an ecologist or environmental biologist assigned to the Industrial and Environmental cell may also be able to provide support to the Animal, Plant and/or Human Health cells. As new applications of biotechnology arise, additional expertise may be added to the Units (*e.g*., aquaculture, silvaculture).

Table 1: Possible expertise for RAU cells.

Core Characterization Cell	**Animal Biotechnology Cell**	**Plant Biotechnology Cell**	**Human Health Biotechnology Cell**	**Industrial and Environmental Biotechnology Cell**
Molecular biologist	Animal physiologist	Plant physiologist	Immunologist	Ecologist
Toxicologist	Animal pathologist	Plant pathologist	Epidemiologist	Environmental biologist
Microbiologist	Animal nutritionist	Entomologist	Pharmacologist	Industrial microbiologist
Biochemist	Animal breeder	Agronomist		Analytical Chemist
	Veterinary scientist	Plant breeder		

When an application is received by the NBRA and deemed administratively complete by the Secretariat (*e.g*., each section of a regulatory package has been completed) it will be forwarded to the CRO of the appropriate Branch. This will be facilitated by the fact that guidelines will be published clearly indicating the format, information and data required by each Branch for trial and commercial approval applications. The CRO will then submit the application to the RAU and the assessment process will begin. Given the multi-disciplinary nature of the RAU and the fact that its scientists will be well trained and experienced risk assessors, it is anticipated that all product-specific safety assessments will be completed by RAU scientists and only under exceptional circumstances will it be necessary to solicit external science advice.

It is important for the NBRA to have some foresight mechanism in place to identify and address potential knowledge gaps that may affect risk assessment and decision making. To that end, each Branch CRO will have the authority to convene Scientific Advisory Panels on an as-needed basis to provide additional science advice so that the CRO, supported by the RAU, can address current and emerging issues. SAPs will be structured to provide scientific advice, information and recommendations to the CRO on biotechnology and related issues that may result from regulatory actions that could impact on human and animal health and the environment. It is not anticipated that the SAPs will be involved in product-specific risk assessment or decision making but will instead be used on an as needed basis to revisit old issues in light of new scientific information (*e.g*., the utility of insect resistant management plans for stacked *vs*. single trait insect resistant cotton events) and to provide scientific advice about safety-related concerns that may arise with new or different applications of biotechnology (*e.g.*, the use of plants as production platforms for the expression of pharmaceutical compounds).

To facilitate the selection of members for a SAP, the each CRO will establish a roster of qualified scientific experts. To this end, the NBRA will publish a notice requesting nominations for scientists to be included in each of the three rosters of experts. The notice will detail the Terms of Reference and qualifications for roster membership. The Branch CROs, in consultation with the RAU and RPUs, will then select scientists with relevant expertise and who meet conflict of interest provisions. The rosters of experts will be made public.

An example of the complementary functions of the RAU and a SAP is presented below.

Hypothetical issue: The NBRA receives an application for approval to evaluate genetically engineered tilapia (*Oreochromis niloticus*) transformed with a growth hormone gene isolated from another fish species. The objective of the transformation is to significantly improve gross food conversion efficiency so that the fish achieve marketable weight sooner than their non-transgenic counterparts in aquaculture operations. The application is for a trial that will be conducted in large, in-land tanks with no possibility of release of the fish into natural aquatic systems.

Role of the RAU

The CRO/AFFB receives the completed application for the tank trial from the NBRA Secretariat and initiates a review process by the members of the animal biotechnology cell of the RAU. Because the trial will be conducted under contained conditions (in-land fish tanks), all of the biological waste will be incinerated (*e.g*., fish carcasses) and the waste water will be chemically treated, filtered and recycled, the RAU does not have any significant concerns about the trial progressing.

However, this application is a trigger for the RAU to notify the CRO/AFFB that there may be an application for commercial approval of the transgenic tilapia in the near future, the first such application for a transgenic fish. In consultation with the RAU, the CRO determines it is appropriate to convene a SAP to address issues associated with the commercial release of transgenic fish as there is no detailed and specific guidance currently in place. This is necessary as the product developer and the RAU must know what information and data will be required by the NBRA to support a safety assessment of a specific product as a prerequisite to its commercial release.

Role of the SAP

The CRO/AFFB charges the SAP with the following:

- To provide objective, scientific information on potential environmental risks and benefits of transgenic fish for scrutiny by the scientific community and the public;
- To help identify any potential risks that may be associated with introducing transgenic fish into Indian aquaculture, so these can be avoided/managed as appropriate;
- To assess the strengths and weaknesses of current regulations and guidelines in India, compile and analyze international approaches to regulating transgenic fish, and provide recommendations to improve the risk assessment framework for transgenic fish;
- To evaluate if additional scientific capacity may need to be developed within the NBRA to support future safety assessments of transgenic fish by the RAU.

The SAP prepares a comprehensive report that addresses the above and submits this to the CRO/AFFB for action.

5.2.3 Cross-Sectoral Offices

There are a number of very important activities that must be undertaken by any biotechnology regulatory agency in support of and in addition to its risk assessment and decision making functions. Recognising this, it is proposed that the NBRA will have seven cross-sectoral offices that will function on an Authority-wide basis. These will include:

1. **National and International Policy Coordination Unit** to serve as the point of coordination for national biotechnology policy formulation and issues management. The Unit will ensure there is strategic alignment and policy coherence on priority issues by interacting with other central government and state ministries/agencies to coordinate biotechnology policy formulation throughout the public sector and will flag significant policy issues for consideration by the IMAB and/or NBAC as required. The Unit will also act as the national point of contact for international activities related to establishing and implementing policies that impact the regulation of biotechnology and will monitor, review and analyse national and international policies that may affect Government of India priorities for the biotechnology sector.

It is expected that Unit staff will represent the NBRA in meetings/negotiations related to international conventions that impact biotechnology regulation and risk assessment (*e.g.*, Cartagena Protocol on Biosafety, the International Plant Protection Convention) and subject-relevant committees and task forces of the Codex Alimentarius Commission, the World Organization for Animal Health, World Health Organization, the Food and Agriculture Organization etc.

Example: This Unit could facilitate a policy dialogue between the NBRA and the FSSA related to the commercial release of transgenic animals where products derived from these animals may enter into the Indian food supply. This would be done to ensure that there is consistency in national policies related to animal biotechnology and additionally evaluate any international consequences that may be associated with such policies.

2. **Communications and Outreach Unit** to liaise with NBRA stakeholders and the public to ensure that information about NBRA programs and activities are communicated in a transparent and accessible fashion. The NBRA will be committed to ensuring that its programs and operations are reported in an open and accessible fashion. This Unit will:

- Ensure that the processes and criteria for risk assessment and risk management are easily accessible so that product developers, stakeholders, and the public can be confident that the biotechnology regulatory system is both credible and predictable.

- Be responsible for notifying the public of all applications for field and clinical trials and the commercial release of GMOs and of all regulatory decisions that are made.

- Develop public outreach programs to inform the public about the mandate and programs of the NBRA.

- Coordinate stakeholder consultations, opportunities for public participation in the regulatory system, and will be the primary point of contact for public, media or other enquiries to the NBRA.

- Be responsible for systems administration, preparation and maintenance of information databases and the NBRA website.

Example: This Unit will develop and maintain the authoritative NBRA website which will provide detailed and current information about all NBRA programs, activities and publications. It will also develop and maintain a password protected database to log, track and retrieve pertinent information from applications received by the NBRA.

3. **Legal Unit** to provide advice and interpretation of legal instruments used to regulate biotechnology in India and their international implications, provide legal counsel to the Chairman, CROs and other NBRA personnel as required, and coordinate with other departments and ministries to ensure that the regulatory responsibilities of the NBRA are harmonized with other central and state level ministries/departments where there may be regulatory overlaps or gaps.

Example: It will be the responsibility of this Unit to ensure that any proposed amendments to regulations and/or guidance as regards biotechnology are carefully evaluated for impacts before they are implemented. As the *NBR Act* is implemented, this Unit will work with other regulatory authorities to ensure that rules that are currently in place (*e.g.*, *Rules, 1989*) are not repealed until the corresponding rules are notified under the *NBR Act*. This will avoid the situation that occurred recently when a decision was made that processed foods would no longer attract the provision of Rule 11 of *Rules, 1989* before a similar rule was notified under the *FSSA, 2006*.

4. **Economic Analysis Unit** to coordinate the provision of expert advice on the possible economic implications of biotechnologies on the Indian economy, including but not limited to impacts on rural

development. The Unit will also be responsible for undertaking *ex ante* studies of the economic impact of commercial release of specific products. The Unit will subsequently prepare a report for the Branch CRO indicating the results of these studies and a recommendation to approve or not approve the subject product. The Product Rulings Committee (see 5.3 below) will consider the Unit's recommendation as well as the recommendation prepared by the RAU and will issue a draft decision for public comment after which a final decision will be published. **Note that this Unit will not be required if a decision is made to exclude non-safety considerations from product specific decision making**.

5. **Monitoring, Compliance and Accreditation Unit** to ensure that activities related to the manufacture, production, commercial release and import of GMOs comply with regulatory requirements.

The Unit will be the NBRA's operational point of contact with Institutional Biosafety Committees (IBSCs). The Unit will maintain an accurate registry of all IBSCs to ensure that they are active and are meeting their reporting obligations. IBSCs will be responsible for reviewing and approving recombinant DNA research at the institutional level to ensure that it is compliant with the NBR Act, regulations and guidelines. The responsibilities of IBSCs under the NBRA will remain largely consistent with details provided in DBT's IBSC Handbook (http://dbtbiosafety.nic.in/Files/Handbook.htm). This includes: ensuring that facilities are adequate to maintain containment of recombinant organisms; adequate training is provided for all principal investigators and laboratory staff; institutional procedures and practices meet all regulatory requirements; and that reporting requirements are in accordance with NBRA guidance. The NBRA may consider having an NBRA nominee on each ISBC. If so, the nominee should provide a report of each ISBC meeting to the NBRA.

The Unit will work with the NBRA's State/Zonal Offices that are tasked by the NBRA with the responsibility for monitoring, audits, inspections and investigations of permitted or accredited parties to ensure that regulatory compliance is addressed in a consistent and transparent fashion.

The Unit will additionally coordinate the accreditation of referral laboratories used by product developers to provide safety-related data (see also Chapter 7).

Example: This Unit will work with State/Zonal Offices to ensure that confined field trials of GM plants are conducted in accordance with the requisite Guidelines and Standard Operating Procedures. The Unit will coordinate training and evaluation of field trial inspectors to ensure that inspections are conducted in a consistent and professional manner. The Unit will provide the State/Zonal Office with a schedule for each trial site inspection and will remain vigilant to ensure the inspections are completed in a timely fashion. In situations where a compliance infraction is identified during the field trial inspection, the Unit will determine the appropriate remedial action and will coordinate a follow up inspection as required.

6. **Capacity Building and Training Unit** will coordinate the human resource development programs of the NBRA which will include training opportunities for NBRA personnel as well as other interested and affected stakeholders (see Chapter 6 below).

7. **State or Zonal NBRA Offices** will work to facilitate state-level operations on behalf of NBRA headquarters. These operations could include: inspection of permitted or accredited research and/or manufacturing establishments; monitoring of field or other trials; and liaising with relevant state departments. NBRA state/zonal offices will work with the concerned state government departments, research institutions and organisations to ensure that inspection and monitoring activities are undertaken according to NBRA best practices. This will include convening, on an as needed basis, *ad hoc* committees consisting largely of state personnel with training provided by the NBRA to undertake these activities. The provision for setting up state (or zonal) level committees will permit each committee to be established to respond to actual state/zonal needs, providing more flexibility to ensure that the membership has the expertise and experience needed to respond to particular situations or issues. The NBRA state/zonal offices will be under the administration of the NBRA and will have no product-specific decision making authority as the decision to approve or not approve a product of modern biotechnology on the basis of its safety assessment should remain an exclusive regulatory function of the NBRA. Case specific state participation in NBRA activities is illustrated as under:

- Monitoring of confined field trials of transgenic crops will be undertaken with the participation of State Agriculture Departments and State Agriculture Universities (SAUs). The financial and capacity building (*i.e*., training) support for undertaking all such activities shall be provided by the NBRA through its state offices. NBRA-supported Coordinating Cells may be established in SAUs to facilitate the coordination of communications about confined field trials within the state. For example, a Coordinating Cell could work cooperatively with state extension personnel and SAUs to address the information needs of concerned local bodies *e.g*., village Panchayats.

- The Communications and Outreach Unit of the NBRA will work with state government and other state-level stakeholders (*e.g*., farmers/growers organizations, SAUs, KVKs in the area of agricultural biotechnology) to ensure that information about NBRA programs and activities are communicated in a transparent and accessible fashion.

- Inspection mechanisms to ensure the containment of recombinant organisms in research as well as manufacturing facilities will be implemented in close association with state authorities. The state functionaries may also be empowered suitably in this regard to ensure compliance with NBRA rules and guidance.

A State or Zonal Office will be established and staffed as required to meet the workload for that state/zone.

5.3 DECISION MAKING

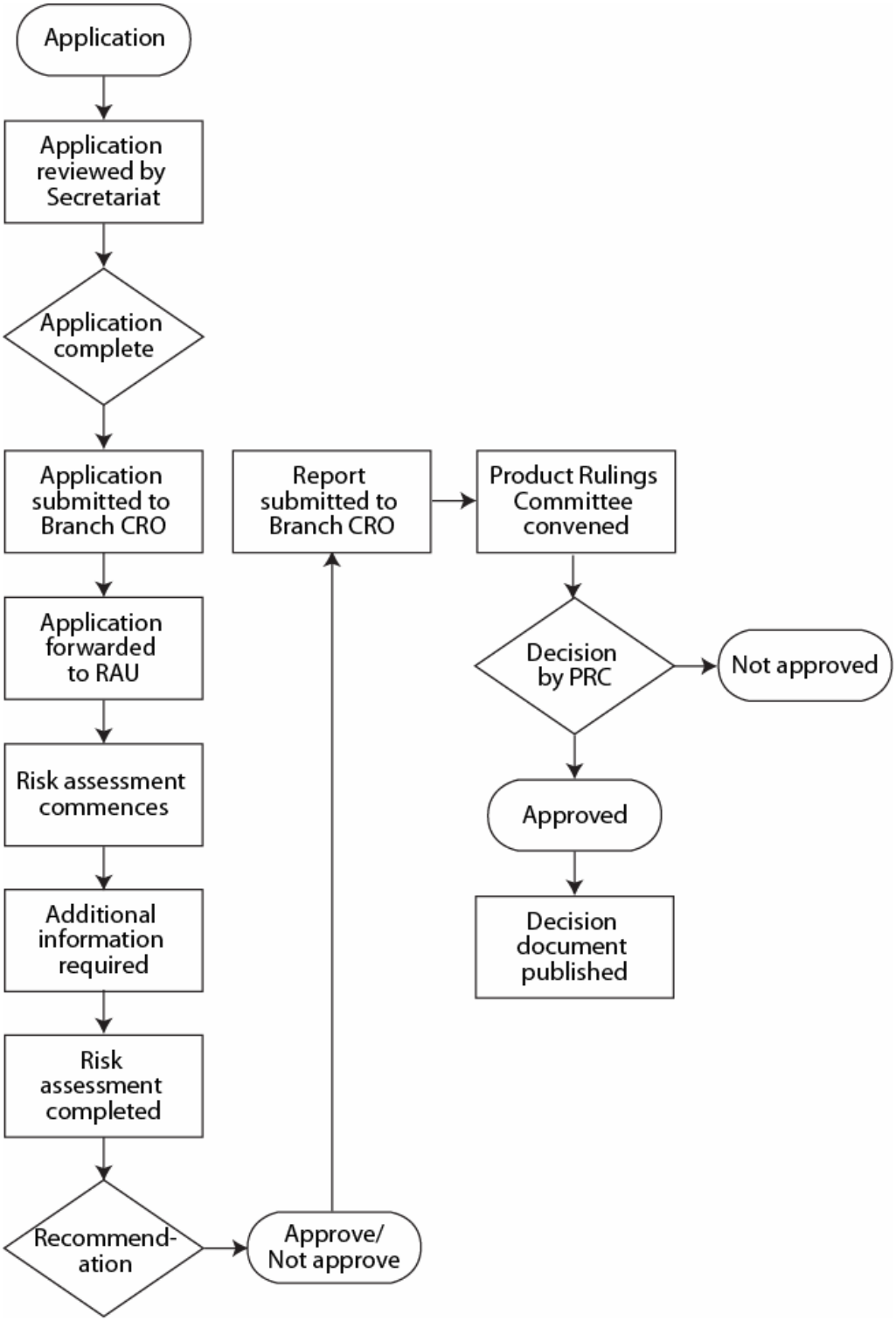
Final decision making authority will be vested with the Product Rulings Committee which will be comprised of the NBRA Chairperson and the CROs of the three regulatory branches. For applications related to field or clinical trials, or commercial release of biotechnology products, the Product Rulings Committee will additionally include three scientists selected from the roster of experts (see 5.2.2) of the appropriate regulatory branch.

Applications for imports, field or other experimental trials, or commercial release of GMOs will be received by the Secretariat and referred to the appropriate Branch CRO when deemed complete from an administrative standpoint. The CRO will then forward the application to the RAU. For trial applications, the RAU will ensure that all requirements for the safe management of the trial have been addressed and then will make a recommendation to the concerned Branch CRO to approve or not approve the trial. As regards the commercial release of a GMO, the RAU will provide a report to the Branch CRO as to whether all required safety considerations have been addressed by a product developer and will make a recommendation to approve or not approve the subject product.

The CRO will consider the RAU's recommendation as well as any other non-safety considerations as required by legislation and prepare a draft decision. The NBRA Chairperson will convene a meeting of the Product Rulings Committee bi-weekly and each CRO will present the draft decisions for applications received. The Product Rulings Committee will review each file to ensure all steps in the risk assessment and decision making process were correctly applied and will then take the final decision to approve or not approve the trial or product in question. This decision will be communicated in writing to the applicant and will be published on the NBRA web page (see Figure 2).

The *NBR Act* rules will indicate time standards for each step in the review of an application up to an including the decision to approve/disapprove a product for commercial release. This provides for transparency and predictability in regulatory decision making that is important for product developers as well as the public.

Figure 2: Work flow diagram representing how the application and decision making processes will function in the NBRA.



6 HUMAN RESOURCE DEVELOPMENT

The human resource environment that both enables and limits effective regulation is shaped by the scope and quality of competency in the disciplines of biological science; expertise in information acquisition, communications, and management; and experience in critical thinking, analysis, and decision making. Skills must be developed for biotechnology product evaluation and to maintain parity between risk assessors and their counterparts working to develop products. This requires constant updating on new scientific advances, without which the knowledge base of regulators and risk assessors has a limited expectancy.

The NBRA requires the development of a strategic human resource development plan to provide a framework for the identification of corporate skill needs, both current and for the future, and for the identification and incorporation of the learning needs of individuals. While the preparation of such a plan is outside the scope of the current project, the following is offered as a framework that could be used to stimulate discussion on this issue.

6.1 RECRUITMENT

The NBRA will be committed to implementing a recruitment and selection process that is open, transparent and applies the principle of merit selection. In order to launch the NBRA, the professional core of NBRA headquarters' staff would include, but not be limited to:

Position	***Minimum qualifications***
Chairperson	*Eminent biotechnologist (Ph.D.) appointed at the rank of Secretary to the Government of India.*
CRO	*Eminent scientist (Ph.D.) with subject matter expertise relevant to the Branch, appointed at the rank of Additional Secretary to the Government of India.*
RAU	*Ph.Ds with a minimum of 5-10 years of active research in their field.*
RPU	*M.Sc/Ph.D. with MBA/legal or other relevant policy-related post-graduate qualifications.*
NIPC Unit	*M.Sc/Ph.D. with international affairs/legal or other relevant policy-related post-graduate qualifications.*
Comm. Unit	*Science/agriculture graduates with post-graduate training in journalism/media/mass communication/agricultural extension.*
EA Unit	*Ph.D. in economics, minimum 7-10 years experience in economic risk/benefit analysis.*
Legal Unit	*LLB with minimum 10 years regulatory or legislative affairs experience*
MCA Unit	*M.Sc. or M.D. with post-graduate diploma in compliance management/accreditation/auditing/clinical research.*

6.2 TRAINING OPPORTUNITIES

The establishment of the NBRA provides an exciting opportunity to develop a new model for a regulatory authority in India and human resource development within the Authority should move beyond the traditional concepts of training and development through coursework. It should look at the methods that are most appropriate for achieving the desired knowledge and skills acquisitions and should encompass and include, but not be limited to, on-the-job training, placements, rotations, research, seminars, mentoring, coaching and study.

The upper management of the NBRA will be committed to a process of continual quality improvement in both programs and operations. Professional development and training opportunities will be made available for all NBRA professional staff to ensure that the scientific, risk assessment and risk management capacity of the Authority remains current and consistent with international standards. The Capacity Building and Training Unit, in collaboration with the other six cross-sectoral offices, the RAU and RPUs, will additionally provide training opportunities for state-level personnel who are tasked with responsibilities related to the regulation of biotechnology as well as other stakeholders where capacity building needs have been identified.

Training of professional NBRA staff should promote national and international technical cooperation including active participation in regional and international programs and fora dealing with biotechnology regulation, risk analysis (assessment, management and communication), accreditation and auditing etc.

While there are many qualified scientists with expertise in the subject areas pertinent to the NBRA mandate, there are considerably fewer experienced in the areas of risk assessment and regulatory policy development. Substantive training should be provided to the NBRA's scientific staff to assist them in making the paradigm shift from bench or field scientists to regulatory risk assessors. This may be best facilitated by arranging for 6-12 month terms in other biotechnology regulatory authorities. For example, RAU scientists that will be assessing recombinant human health care products could be placed with the Center for Biologics, Evaluation and Research, U.S. FDA and those responsible for transgenic animals and recombinant veterinary products could be placed with the Center for Veterinary Medicine, U.S. FDA. Other regulatory agencies that could be approached include the Canadian Food Inspection Agency, Environment Canada, U.S. Environmental Protection Agency, Biotechnology Regulatory Services of the U.S. Department of Agriculture, Australia's Office of the Gene Technology Regulator, and the European Food Safety Authority. These placements should begin as soon as recruitment has been completed.

Example: Possible topics for training of RAU scientists involved in the risk assessment of genetically modified trees and plants

- Understanding and separating risk assessment, risk communication and risk management
- The role of the risk assessor
- Standards for information and data requirements
- Concepts and principles of environmental assessment
- The host plant: taxonomy; reproductive biology; cultivation; ecology in managed and unmanaged ecosystems
- The donor organism: the donor genes; potential pathogenicity of the donor organism
- Molecular characterization of transgenic plants
- Protein characterization of the expressed traits: stability and expression of the novel protein(s)
- Gene transfer to related plants
- Gene transfer to unrelated organisms: Probability of plant-bacteria horizontal gene transfer (HGT); consequences and environmental impact of HGT
- Assessing weediness potential
- Secondary and non-target adverse effects: non-target test organisms (eco-toxicology); other non-target effects
- Insect resistance management and other post-commercial monitoring requirements

Additional training opportunities can be provided through:

- **Scholarships** to provide graduate and post-graduate training for young professionals to ensure that there is a pool of new candidates for NBRA employment. These may be provided for Ph.D. or post-doctoral training in India or in other countries.

- **Fellowships** for NBRA professionals to promote continued knowledge acquisition and to ensure that RAU and other NBRA scientists maintain their scientific currency and credibility. For example, a fellowship may be provided to a professional staff of the Monitoring, Evaluation and Compliance Unit to permit him/her to become a certified GLP auditor or participate in ISO 9000:2000 Series Auditor / Lead Auditor Training.

- **Research grants** to scientists to support research that will strengthen science-based regulatory decision making. For example, financial support could be directed to identify a panel of sentinel organisms that may be the best predictors

of non-target effects of insecticidal proteins expressed in genetically engineered, insect-resistant plants.

- **Mentoring programs** to ensure that young professionals are able to understand and appreciate biotechnology regulation so that they may consider employment directly with the NBRA or involvement in research programs that will support the mandate of the NBRA.

- **Web-based outreach programmes** to provide continuing education opportunities to NBRA and other personnel in the regulatory and regulated communities. For example, the NBRA could develop an e-learning program for those who will be tasked with monitoring confined field trials of experimental, genetically engineered crops. The course could include a progressive series of modules that individually address topics such as transport, storage, management of the trial during the growing season, harvest, and post-harvest trial site management. The "student" would take a test at the end of each module and would only be able to pass the course when all modules have been successfully completed. The NBRA may consider making such a course mandatory for anyone involved in monitoring field trials under the auspices of the NBRA and require annual or bi-annual re-certification.

- **Networks** to promote knowledge sharing and stimulate collaborative research. For example, a multidisciplinary network of plant breeders, entomologists, population geneticists and integrated pest management specialists could be established to ongoing inputs to the RAU about insect resistant management.

- **In-house seminars and journal clubs** used to keep up to date with developments in fields of study pertinent to the NBRA. The NBRA could build participation in such activities into staff work plans to recognise that these are a valid part of learning and so of importance to the Authority. A monthly or semi-monthly seminar series, targeting developments in issues relevant to NBRA will allow for the greater dissemination of information and increase the effectiveness of communication channels. These seminars may be delivered by NBRA staff or by invited speakers.

7 FACILITY ACCREDITATION/NOTIFICATION

DBT has indicated that it would like the NBRA to implement an accreditation system for referral laboratories that provide testing services for the safety assessment of GM crops and foods derived from these. This presupposes that the accreditation system will be for pre-commercial (*i.e.*, pre-approval) testing which is distinctly different from the accreditation of laboratories that may undertake seed testing after a transgenic event has been granted environmental and food safety approvals (*e.g.*, to confirm varietal purity).

The NBRA will establish data quality standards for all of the types of studies submitted to support the safety assessment of GMOs and these specific requirements will be stipulated in rules under the *NBR Act*. In some cases the requirement may be for a specific study to be undertaken in an accredited laboratory. The two systems for laboratory accreditation that are currently in use in India and most applicable to biosafety and food safety testing of GM crops are: the National Accreditation Board for Testing and Calibration Laboratories (NABL) and the National GLP Compliance Monitoring Authority. Importantly, both of these apply internationally recognised accreditation standards which are a necessary prerequisite for laboratory accreditation if international acceptance of Indian studies is to be achieved.

The Monitoring, Compliance and Accreditation Unit of the NBRA will work with these accreditation bodies to develop specific guidelines for referral laboratories that will provide testing services for the safety assessment of genetically engineered crops and foods derived from these. Laboratories that wish to seek NABL and/or National GLP Compliance Monitoring Authority accreditation will follow existing application requirements and then submit proof of accreditation to the NBRA's Monitoring, Compliance and Accreditation Unit. The Unit will maintain and publish a roster of accredited organisations, information of value to both the RAU as well as product developers wishing to use accredited laboratories.

Example: In June 2007, the NABL published "Specific Guidelines for Biological Testing Laboratories" which are a supplement to ISO/IEC 17025 and are applicable to laboratories using techniques in areas related to toxicology, veterinary science, biochemistry, molecular biology and cell culture. These guidelines provide specific guidance for both assessors and for laboratories carrying out biological testing and set out the specific requirements that a biological testing laboratory has to meet. These guidelines provide an example of the type of guidance that the Monitoring, Compliance and Accreditation Unit of the NBRA may wish to prepare.

ANNEXURE 1: PRESENT STATUS OF ACTIVITIES REGULATED UNDER VARIOUS ACTS AND RULES AND KEY FEATURES OF NATIONAL POLICIES

Table 1: Biotechnology activities regulated under Acts and Rules.

S.No.	Act/Rules	Issued by	Activities covered
1.	Rules for the Manufacture, Use, Import, Export and Storage of Hazardous Micro-organisms/ Genetically Engineered Organisms or Cells, 1989 issued under EPA	Ministry of Environment & Forests	Cover entire spectrum of activities involving GMOs and products thereof including sale, storage, exportation, importation, production, manufacturing, packaging, etc. Food stuffs have been moved out of the purview of Rules, 1989 recently.
2.	Drugs And Cosmetics Rules (8th Amendment), 1988	Ministry of Health and Family Welfare (Department of Health)	All recombinant drugs are subjected to approval by DCGI as new drugs, environmental release permitted under EPA. An approved rDNA drug to be considered as new drug if there is a change in the host, the vector, the gene construct or even the process of production and purification.
3.	Plant Quarantine (Regulation For Import Into India) Order 2003	Department of Agriculture & Cooperation	Covers regulation of import of germplasm/ GMOs/transgenic plant material for research purpose.
4.	Biological Diversity Act, 2002 and Biological Diversity Rules, 2004	Ministry of Environment & Forests	Regulates the use of biological resources including genes used for improving crops and livestock through genetic intervention.
5.	The Seed Bill, 2004	Ministry of Agriculture	Mandatory registration of all types of seeds including transgenic seeds.
6.	The Food Safety and Standards Act, 2004	Ministry of Food Processing Industries but will be implemented by the Ministry of Health	Regulates manufacture, storage, distribution, sale and import of food which includes GM food.

Table 2: Key features of national policies addressing or affecting biotechnology regulation.

S. No.	Policies	Issued by	Activities covered
1.	National Seeds Policy, 2002	Department of Agriculture & Cooperation (DAC)	• GM crops/varieties to be tested as per EPA rules, 1986 for environment and bio-safety • Import of Transgenic plant varieties seeds for research purposes only through the NBPGR. • Transgenic crops/varieties to be tested for agronomic value for at least two seasons by ICAR • Commercialization, registration and marketing of released transgenic plant variety seeds as per the provisions of the Seeds Act. • MoEF and Dept of Agriculture to monitor performance of commercially released transgenic plant varieties in field for at least 3 to 5 years. • Crop Protection by PVP legislation similar for commercially released transgenic varieties and non-transgenic varieties. • Certification from Competent Authority of the exporting country for all imported transgenic seeds required • GEAC approval required for the import of all GE varieties • Label for all GE materials for sale indicating their transgenic nature and specific characteristics which helps in testing, identification and evaluation of transgenic planting materials in the country.
2.	Drug Policy, 2002	Ministry of Health and Family Welfare	• rDNA technology based drugs requires industrial licence for production. • All rDNA technology based products need approvals for foreign investments as well as foreign technology agreements.
3.	Foreign Trade Policy (2006-09)	Director General of Foreign Trade	• EPA approval for import of GMOs / LMOs for the purpose of R & D; Food; Feed; Processing in Bulk and Environment release • GEAC approval for Import of any GM product used for Industrial production, Environmental release, or field application. • RCGM approval for import of GM products for R& D purpose and GEAC approval for commercialization of GM products by Companies / Institutes. • All imported GM products must have a declaration of Genetic Modification.
4.	National Environmental Policy, 2006	MoEF	• Review of regulatory processes for LMOs in respect with scientific knowledge, ecological, health, and economic concerns. • Periodically review of National Bio-safety Guidelines and Bio-safety Operations Manual to ensure that these are based on current scientific knowledge. • Ensure Conservation of bio-diversity and human health when dealing with LMOs in a manner consistent with the multilateral Bio-safety Protocol.
5.	National Biotechnology Development	DBT	• Proposal to set up a committee of inter-ministerial group and reputed scientist to address anomalies and issues that arise in various acts related to

	Strategy, 2007		regulation of biotechnology activities in R&D, import, export, releases etc. and to review guidelines, protocols, SOPs and ensure their dissemination to all stakeholders. • Proposal to establish a competent single NBRA with separate divisions for agriculture products/transgenic crops, pharmaceuticals/drugs and industrial products; and transgenic food/feed and transgenic animals/aqua culture. • Awareness generation among students in universities, colleges etc on issues related to biosafety and promoting a genetic literacy movement within government and public schools through 50 genome club nature clubs. • Proposal to create a media resource network to facilitate access to information and empower policy makers by participation in regular training programs.
6.	National Policy For Farmers, 2007	National Commission on Farmers (NCF)	• Training and awareness in agronomic management procedures in respect of GM crop varieties. • Need to assess the risks and benefits associated with GM crops in a credible and transparent manner. • Priority to GM crops that incorporate genes which can help to impart resistance to drought, salinity and other stresses.