GEF

Islamic Republic of Iran

Draft

National Biosafety Framework

Department of Environment

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PROJECT BACKGROUND

The UNEP-GEF Project Number **GFL/2716-02-4555** (PMS: GF/6010-0189) on the Development of the National Biosafety Framework of the **I. R. of Iran** started in **November 2002** and ended in **September 2004**.

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DESCRIPTION OF THE DRAFT NATIONAL BIOSAFETY FRAMEWORK

FOR THE I. R. OF IRAN

PART ONE: INTRODUCTION, DEFINITIONS, OBJECTIVES

1. Introduction

Modern biotechnology, with an astonishing arrangement, is a combination of diverse related disciplines such as microbiology, biochemistry, immunology, cellular and molecular biology, plant and animal physiology, ecology, paleobotany, genetic engineering, etc. After World War II, other scientific disciplines such as physics, chemistry, chemical engineering, biochemistry and mathematics were applied to biology as well, and recently the addition of other disciplines such as computer sciences complete the picture. In the early 1970's, a revolution occurred in biotechnology methods; with the application of and reliance on these novel advancements, in 1973 scientists achieved the first successful gene transfer from one living organism to another in the United States.

In fact, for the past 30 years, the latest scientific revolution has enabled mankind to change forms of life with the application of modern biotechnology. Scientists have learned how to separate DNA strings or genes, which contain biochemical instructions, or to transfer them from one species to another. Using elaborate techniques, they can manipulate the genetic structure of living cells, the result of such manipulations being a living modified organism or LMO.

This science finds one of its most important and promising application fields in agriculture, and even more specifically in the food industry. By improving food production, modern biotechnology will guarantee food security for the world, the population of which is rapidly increasing. Reducing the need for more land, more irrigation and more pesticides, this science will help the environment as well. Moreover, modern biotechnology will also pave the way for better medical treatments and modern vaccines.

The application of modern biotechnology techniques to agriculture has already made it possible to reduce the time and cost for the production of various agricultural products. Food quality is being improved and new food items are produced in order to reduce the risk of humans being affected by different diseases. Genes resistant to pesticides, insects and pests are transferred to different plants and this will herald new perspectives for food producers. The whole world today believes that the science of modern biotechnology is one of the seven key industries, which will determine the fate of 8 billion people who will be living on earth in the year 2030. So far, more than eight new genetically modified products have been mass produced and have thus reached utilisation stage by agricultural biotechnology.

- **Reasons why biosafety is important**

Modern biotechnology is so novel that as yet many issues regarding the impact of its products on the environment and in relation to other species have not been clearly defined.

Like many other sciences, this modern science has its own opponents who believe that LMOs and their products will disturb the balance and the nature of the environment, disrupt biological survival and evolution, destroy genetic diversity and affect human health. For the opponents of this science there are three main reasons of apprehension. First, they believe that in the long term, the possible side effects of transgenic organisms on the environment are mostly unknown. Second, they apprehend the consequences of the transfer of a modified gene from one generation of the modified organism to another and thus its possibly unknown results on future generations. And last but not least, they apprehend the consequences of modified gene transfer from a transgenic living organism to a non-target organism.

Therefore, although there is no doubt regarding the role that biotechnology and genetic engineering will play in future development and progress of human societies, potential risks, which may arise as a result of neglecting biosafety regulations should not be ignored.

Thus, while emphasising the importance of developing biotechnology and genetic engineering activities, it is necessary to compile regulations based on which the said activities may be monitored and supervised so that they can be carried out safely. The end purpose of such regulations should be to protect the environment and human health.

At the 1992 Earth Summit in Rio de Janeiro, world leaders agreed on a comprehensive strategy for "sustainable development" - meeting our needs while ensuring that we leave a healthy and viable world for future generations. One of the key agreements adopted in Rio was the Convention on Biological Diversity, which establishes three main goals: the conservation of biological diversity, the sustainable use of its components, and the fair and equitable sharing of the benefits from the use of genetic resources. Later, in January 2000 the Cartagena Protocol on Biosafety was ratified by 101 countries in order to control the international transport of LMOs.

This protocol emphasises the precautionary approach of the fifteenth article of the Convention on Biological Diversity regarding the protection of environment, and emphasises compliance with suitable biosafety criteria and risk assessment measures for the preservation of the environment and human health.

At the same time, many developed countries have made attempts to compile internal rules and regulations in order to monitor and supervise the production, transfer and release of living modified organisms into the environment. Their aim is to decrease the possibility of environmental pollution as much as possible through adequate risk assessment and risk management.

Thus, benefits as well as risks resulting from modern biotechnology should be studied at the same time. Actually, development of modern biotechnology and the elaboration of biosafety regulations should be carried out concurrently.

The Islamic Republic of Iran proved its commitment to biosafety issues by joining the Convention on Biological Diversity in August 1996. According to Paragraph 8 of this Convention, Iran commits itself to the creation and maintenance of tools necessary for supervising, managing and controlling risks in the use or release of living modified organisms resulting from modern biotechnology with regards to human health and the environment.

In addition, on April 23, 2001, the Islamic Republic of Iran signed the Cartagena Protocol on Biosafety.

Also, it was decided that a specialised committee comprising representatives from the Ministry of Science, Research and Technology, the Ministry of Health and Medical Education, the Ministry of Agricultural Jihad, the Ministry of Commerce, the Ministry of Industry and Mining, and the Department of Environment, should be formed to address the following issues:

1. Debate and decision concerning the country's joining the Biosafety Protocol and other related issues;
2. Compilation of a draft for national biosafety laws and regulations.

In November 2003 the Islamic Consultative Assembly of Iran ratified the Cartagena Protocol on Biosafety. According to the date of registration in the secretariat of the protocol, the protocol came into force in Iran on February 18, 2004 and thereby all its contents turned binding.

Creating a national biosafety framework cannot in reality be a substitute for regulations, which should be created for safe application of modern biotechnology. Compiling and ratifying pertinent laws is needed to provide a comprehensive and stable legal system for biosafety.

The national biosafety framework is in fact the preparatory phase for the creation of sustainable administrative laws for the country. In the present framework, due to deficiencies and defects in the legal system of the country, there are defects and deficiencies in the administrative system as well. This framework does not address details, it rather determines the type of activity and the general regulations which should be covered by research institutes and centres.

The framework of the national biosafety structure is a combination of policy making (determining strategies), laws, technical and executive tools and equipment related to environmental safety and human health with the purpose of expanding modern biotechnology and creating living modified organisms.

This structure, based on the format suggested by UNEP and GEF, has the following features:

1. Government policy on biosafety

Including the country's macro policy regarding modern biotechnology, agricultural products, health, environmental protection and sustainable development.

2. Regulatory regime on biosafety

Including laws, regulations and administrative systems.

3. Creating a suitable system to handle requests for authorisation and issuing certificates

Including the development of a suitable system to deal with requests regarding specific and legal activities such as the release of LMOs in the environment and, if necessary, farm experiments; this system deals with anything related to the assessment of risks, procedures and decision making methods.

4. Creating a suitable system for risk management and follow up

Including the development of a system for the assessment and supervision of possible harmful effects of LMOs on the environment and human health.

5. Developing mechanisms for public awareness, educating and participation

Including application of methods for informing, educating and involving interested individuals, institutes and the public regarding the development and the administration methods of the National Biosafety Framework.

1.1. Definitions

National Biosafety Framework (NBF): a framework developed according to UNEP and GEF capacity building project and based on the country's internal needs and requirements with regard to biosafety.

Living Modified Organism (LMO): any living organism containing a new combination of genetic material obtained through the use of modern biotechnology application.

Modern Biotechnology:

a) the application of nucleic acid techniques including recombinant DNA, and direct injection of nucleic acid into cells or organelles;

b) fusion of cells beyond the taxonomic family, that overcome natural physiological reproductive or recombinant barriers, and that are not techniques used in traditional breeding and selection.

Living Organism: any biological entity which has the ability to reproduce and to transfer genetic material, including bacteria, viruses and viroids.

Biosafety: activities which are carried out with the purpose of reducing or eliminating risks resulting from modern biotechnology and its products.

Contained Use: using LMOs in a contained environment or physical structure in which, according to specific criteria, their contacts and effects with the external environment is effectively controlled.

Release: any non-contained application of LMOs.

Introduction into the Market: making LMOs available to the public.

Risk Assessment: assessing any risk that working with LMOs and their resulting products may cause to human health and the environment directly or indirectly in the short or long term;

Monitoring: tracing and follow up to assess probable harmful effects of LMOs on the environment and human health.

Request: a signed written document lodged by any applicant along with necessary forms and backups with relevant authorities.

Import and Export: international transfer, or transfer from one country to another.

Exporter: any legal or real entity who, within the boundaries of the exporting member country, takes step towards exporting living modified organisms.

Importer: any legal or real entity who, within the boundaries of the importing member country, takes step towards importing living modified organisms.

Transit: a situation whereby a foreign product solely passes through a country, entering at one border and exiting at another.

Risk Management: control, supervision and extensive management of probable risks of LMOs on human health and the environment in the short and long run, as well as during international transfer of LMOs.

1.2. Objectives

1. Developing an embracing framework with a scientific, efficient, predictable and transparent foundation to ensure responsible and safe application of modern biotechnology so that, one can benefit from its application, while avoiding or minimising risks associated with it.
2. Ensuring effective control on the use, transfer and transdoundary movement of Living Modified Organisms and products thereof.
3. Developing the necessary mechanisms for the assessment, management and control of probable risks hidden in the use, release, transfer and transdoundary movement of Living Modified Organisms and products thereof, which may have harmful effects on the environment, human health and genetic resources.

1.3. Scope

NBF is a structure for the development and exercise of policies and a guideline for the compilation of biosafety rules and regulations in the I.R. of Iran.

PART TWO: GOVERNMENT POLICY ON BIOSAFETY

2. General Biosafety Policy Making in the Country

The fundamental and strategic policies of the Islamic Republic of Iran, while emphasising the development of systematic biosafety management in the country, insist upon protecting the environment from any harmful effect due to any process, factor and measure which result in polluting and disturbing the balance of the environment, and may end in environmental destruction. In the National Biotechnology strategy (the country's eleven-year plan for the development of biotechnology), which includes the development of biotechnology in environment, botany, medicine, livestock and marine life, industry and mining, and bioethics, it is emphasized that "the development of biotechnology should not be against environmental regulations" and that "the development of biotechnology should be in accordance with the observation of biosafety regulations." This clearly shows that the tendency of the national document towards biosafety is obvious. The cabinet ratified this document on May 5, 2004.

Basically, the development of biotechnology should be in accordance with the environmental regulations of the country, aiming at the protection of genetic reserves and accompanied by the observance of biosafety laws within the framework of global protocols as acceptable to the country. However, and at the same time, biosafety policies, as one of the five pivots of NBF, specifically are:

- Developing a systematic management for biosafety in the country;
- Protecting genetic diversity and the genetic reserves of the country while moving towards sustainable biotechnology;
- Protecting the environment and human health from probable effects of living modified organisms;
- Observing biosafety regulations within the framework of acceptable agreements.

2.1. Structural Frameworks

In order to make the structures leading to the formation of the framework more tangible, and in order to document all the material presented in this discussion, the following figure 1 represents organisational and structural relations for the workable implementation of the framework.

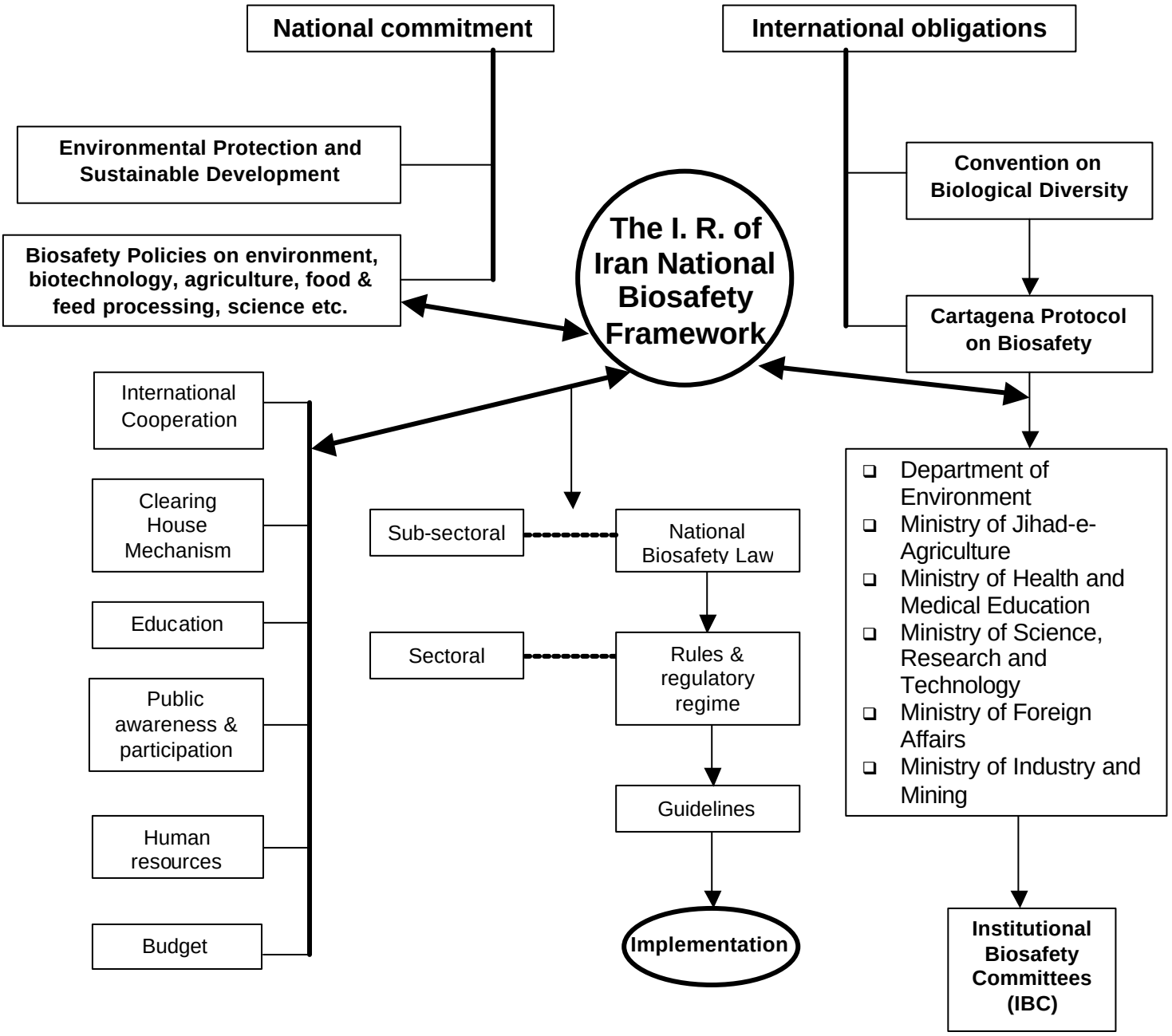

Figure 1: Organisational and structural relations for the workable implementation of the NBF

PART THREE: REGULATORY REGIME ON BIOSAFETY

3. Laws and Enforcement systems

3.1. Introduction

As it was mentioned earlier, the I. R. of Iran ratified the Cartagena Protocol on Biosafety in November 2003. The provisions of the protocol may be enforced in Iran in two ways.

1. Through direct implementation of the regulations and provisions of the protocol.

   In this case, there is a need to define a national legislation that would ensure such an implementation. In addition to the legislation enabling the I. R. of Iran to join the Cartagena Protocol, which was ratified by the Parliament in August 2003, and which is in fact the most important regulation providing the possibility of relating national organisations and legislation with international agreements, thus providing the basis for the enforcement of other biosafety rules and regulations, Article 9 of Iranian Civil Code makes possible, to a certain extent, direct implementation of international regulations, including those of the Cartagena Protocol on Biosafety. Article 9 states that:

   "The provisions of an international treaty signed according to the Constitution between the I.R. of Iran and other governments are binding in Iran."

   In other terms, Article 9 of the Civil Code stipulates that if the government of the I.R. of Iran joins an international treaty through ratification by its parliament, it can enforce the regulations of that treaty as national law.

   Actually, in order to avoid the difficulties of enforcing international legislation in the I. R. of Iran, experience has shown that in addition to the provisions of an international agreement, it is necessary to ratify one or several national laws so as to empower the legislative framework enabling the enforcement of an international or regional treaty in Iran.

   Therefore, the second way is the surest and most appropriate one for the implementation of the Cartagena Protocol on Biosafety in this country.

2. Implementation of the Protocol through national rules and regulations related to the Protocol.

In this case, there are several possibilities:

- first, applicable rules and regulations are complete enough to enable enforcement of the protocol's provisions,
- second, adequate national regulations are non-existent,
- third, national regulations exist but do not correspond exactly to the requirements of the protocol and need to be amended accordingly.

Thus, taking into consideration the above mentioned issues, applicable laws and regulations have been studied, gaps and shortcomings have been identified in order to specify the cases in which

new biosafety rules need to be ratified. In the frame of the national biosafety framework, the kind of regulations that need to be ratified and enforced for capacity building also have to be determined.

There are three classes of applicable rules and regulations:

- First, laws which are at the highest level of legislation and have been ratified by the Parliament;
- Second, enforceable codes ratified by the Cabinet that characterise a sound regulatory framework;
- Third, either applicable standards and principles ratified by the Supreme Council consisting of several ministers, such as the Supreme Council for Environmental Protection, or applicable guidelines and resolutions approved by ministers or heads of governmental organisations such as the Department of Environment.

In this report, rules and regulations pertaining to the two first classes will be discussed.
In addition, it is worth reminding that some regulations are qualifying in nature: they determine and assign the limits of authority and responsibility of an organisation with regard to biosafety. Whereas, other regulations are prescriptive: they actually administer and control biosafety activities that may have an effect on the environment.

3.2. Existing Laws and Regulations in the Islamic Republic of Iran related to biosafety

- *Article 1, of the Environmental protection and enhancement act approved in 1974*, acknowledges the necessity to protect and improve the environment and considers any destructive measure which ends in a disturbance of the balance of the environment, a responsibility of the Department of the Environment, affiliated with the president. According to the same article, this department is also responsible for carrying out scientific and economic researches and surveys regarding the disturbance of balance in the environment and for suggesting regulations, criteria and standards for the purpose of protecting and supervising the factors affecting the environment.
- *Articles 1, 6 and 9 of the Environmental Protection and Enhancement Act* provide general frameworks for the protection of the environment; however, more detailed laws, regulations and criteria need to be compiled and adopted for administration.
  In the Note of Article 9 of the said act, if the application of agricultural pesticides is against environmental protection, the organisation has the responsibility to recommend other substitutes.
- In *Article 114 of the third economical, social and cultural development plan of the Islamic Republic of Iran*, ratified in 2000, the protection of genetic reserves assumes a high degree of importance and priority, so much that it has been exempted from issuing facilities in order to adjust the domestic market.

- *Article 1 of the Game and Fish Law (1967)* emphasises on endangered species and the necessity to protect these species as genetic reserves.
- According to the *Plants Protection Act* ratified in (1967) and its relevant directives, importing any plant or plant part requires obtaining permits from the Ministry of Agriculture. To this end, in 1999 an independent department titled the Department of Biosafety, Gene Reserves, Plasmids and Micro-organisms was established in the Research Institute for Agricultural Biotechnology, a part of the Research and Training Organization of the Ministry of Agricultural Jihad.
- The regulation on waste management was ratified by the Parliament of the I. R. of Iran in June 2004 and entered into force fifteen days later. According to this law, all matters related to wastes - divided into five groups (domestic and town wastes, agricultural wastes, hospital and medical wastes, industrial wastes, hazardous wastes) - are regulated through special legal provisions and management systems, which must cover all stages of production, storage, transportation, destruction and recycling.
- *Article 14 of Medical and Pharmaceutical Affairs and Food and Beverages Act*, approved on 1965, and its amendment on 1988;

  and: 2nd Note of, Article 14 of the above act states that:

  "Production or import of any material or ingredients, medical and dental equipment and the raw material for their packaging, the list of which will be announced by the Ministry of Health and Medical Education, should be with prior permission and agreement from the Ministry of Health and Medical Education."
- *Article 15 of Medical and Pharmaceutical Affairs and Food and Beverages Act*, ratified on (1956), states:

  "Individuals who import or manufacture pharmaceutical materials and biological products included in Article 14 without permission from the Ministry of Health and Medical Education will be sentenced by court to a fine, payable to the Ministry of Health and Medical Education; based on their circumstances, the number and degree of offence and required punishment, the said material will be confiscated and, if necessary, destroyed. The fine for first time offenders starts at 500,000 Rls.
- *In accordance with Article 9 and 24 of the rule for the Production and Import of Medicine*:

  "Permit for the production or import of medication, where production or import of medication is necessary for certain cases or for a short period of time, or where the production or import of pharmaceuticals by one source is not possible or advisable, is allowed after confirmation and permission from the legal commission for the production and import of pharmaceuticals, which will be announced case by case or in general."

  "Individuals who discover or make a new medicine should submit required documents and information in form or forms which they are given and which they should fill in. Their

request will be referred for assessment to the commission for the production and import of medication under article 20 of the Act. In case the medication is approved and the necessity for its production and introduction into the market is confirmed, permit will be issued according to necessary regulations"

- *Import-export regulations* define as follows:

  "By this act, regulations pertaining the import and export of goods and provision of related services are considered binding for all exporters, importers and all those for which the coverage of the law requires mentioning their names; all contradictory regulations are hereby cancelled."

  "Imported and exported goods are divided into the following three groups:

  1. Allowed goods: goods whose import or export requires no permit provided that regulations are observed;

  2. Conditional goods: goods whose import or export is possible after obtaining permits;

  3. Forbidden goods: goods whose import or export is forbidden by the law according to the holly Shari'a of Islam (purchase, sale or consumption)."

  "Importers of various goods, whether governmental or non-governmental, in order to obtain permit to import and register an order, should apply only to the Ministry of Commerce."

  1st Amendment: Approving import of goods is considered as permit for release and there is no need to obtain a separate permit.

- With regard to liability, *Article 14 of the Environmental Protection and Enhancement Act* enables the Department of Environment, as a representative of the government, to claim compensation before Iranian courts for any recorded damage caused to the environment and/or ecological balance in the country.

  More generally, in accordance with *Iran's Civil Code and Civil Liability Act*, each individual has a right to claim compensation before Iranian courts for any prejudice caused to his/her person and/or health. The courts are bound to file their suit and to deliver a verdict compensating the plaintiff.

- In accordance with *Article 9 of the Executive By-Law* on sanitary supervision and control of poisonous and chemical materials approved in 1999 by the Council of Ministers, producers of chemicals and poisonous materials are bound to use special labels, and provide adequate warning with regard to the utilisation of used chemicals and containers. In addition, sellers/dealers of poisonous and chemical materials are bound to avoid the sale of such materials that do not bear an adequate label on their package.

- **International Biosafety Laws**
  - *Ramsar Convention*, Chapter 2, Article 3;
  - *Biosafety Convention*, Articles 1, 3, 6, 7, 8, 9, 10, 11, 14, 15, 16, 17, and 19;

- *Cartagena Protocol on Biosafety*.

- **Executive rules**
  - In the table of the regulations of import-export laws, import or export of any animal or plant species or agricultural products, whether natural or genetically modified, are subject to specific regulations.
  - In the By- law of the Plant Protection Act, the import, production, formulation and application of agricultural pesticides and chemical fertilizers are subject to inspection and approval by Pesticide Supervision Board. This board has the authority to provide certain instructions for the application of chemical pesticides and fertilizers or those cases affecting agricultural products.

- **Gaps and conclusions**

  Taking into consideration what has been presented in section 3.1, it is clear that despite the existence of applicable rules and regulations on the protection of the environment, and control in the production and use of products with a harmful effect on the environment - such as LMOs and products thereof, including their transfer, which is the main concern of the Cartagena Protocol on Biosafety - some legal gaps and shortcoming have been identified and are presented in the following. The identification of such deficiencies proves the definite and urgent need for the definition of a thorough and enforceable National Biosafety Framework in the I. R. of Iran.

  The most important gaps and shortcomings that have been identified in the national legislation with regard to biosafety are the following:

  - Terms and expressions specialised in the field of biosafety, with a specific meaning in the frame of biosafety regulations, such as: "Living Modified Organisms (LMO)", "Release into the environment", or "Risk assessment", which have been determined in the frame of the National Biosafety Framework, need to be defined in the national legislation.
  - The lack of a concerted executive system, and more generally of a national biosafety council or committee in the current legislation has to be taken into consideration in the national legislation.
  - Risk assessment and more especially risk management related to biosafety activities have not been utterly defined in the current national legislation.
  - In case of damage caused to the environment by any activity in relation to LMO or products thereof, liability and redress still need to be specifically defined in the national legislation.
  - And last, in relation with the transfer and transboundary movement of Living Modified Organisms, the national legislation on biosafety needs to specifically stipulate that, the provisions of the Cartagena Protocol are enforceable, wherever necessary.

3.3. Suggested biosafety related laws

3.3.1. Liability and redress

- Applicants who carry out any activity in relation to LMO(s) or products thereof shall be strictly liable for any harm injury or loss caused directly or indirectly by such LMO(s) or products thereof any activity in relation to them. The harm injury or loss includes personal injury damage to property financial loss and damage to the environment or to biological diversity.

- Liability shall attach to the applicant, the person responsible for the activity which results in the damage injury or loss as well as to the provider, supplier or developer of the LMO(s) or products thereof.

- If there is more than one person responsible for the damage, injury or loss then the liability shall be joint and several.

- In the case of harm to the environment or to biological diversity, redress shall include the costs of reinstatement, rehabilitation or clean – up measures actually incurred or to be incurred and, where applicable, the costs of preventive measures and any loss or damage caused by the taking of the preventive measures; provided that the person responsible may be required to carry out the reinstatement or rehabilitation at its own cost and to the satisfaction of the National Biosafety Committee.

More details on this section are in appendix 9.

3.3.2. A Draft of the National Biosafety Law

Laws and regulations which are compiled, ratified and executed in the country regarding biosafety include, on the one hand, controlling and preventive regulations; and on the other hand, within the structure and system of the law, they have a certain classification which starts from the laws ratified by Parliament (after the Constitution) and ends in technical and administrative instructions and regulations which are at the bottommost level of this classification.

In order to compile controlling and preventive regulations, a general framework and certain principals have been included in the national law, executive methods and details of which will be included in instructions and directives.

Pivotal and general issues which have to be included and considered in the draft of the National Biosafety Law (at present, necessary measures are being taken for the ratification of this draft in a governmental commission) are:

- Specific definitions, phrases and terms which are included in the law and have specific meanings and should be defined from the outset; in certain cases definitions will also be included in the directive.
- The range of the execution of the law, or its coverage, should be made clear. It should be made clear which activities and affairs the biosafety law covers. Sometimes the coverage includes time and place conditions but this must be made clear by the law. For example, will the National Biosafety Law include research, or is any biotechnology related research activity outside the coverage of the law?
- The macro administrative system and structure which specifies administrators and executors of the law and even, if necessary, their duties, responsibilities and authorities, will in general be made clear in the form of the national structure and organisation.
- As the main objective is to control activities and affairs which can be potentially dangerous for humans, environment, etc, there should be specific regulations within the law for the assessment and control of potential risks.
- The ranges of supervision on activities which are potentially risk creating and the range and limit of control on these activities will be included in one or more articles of the law.
- As this law will be effective only when binding and enforceable, guarantee for the execution of the law and accountability to respond to possible offences and the punishment for not observing controlling laws should be included in the draft of the law.
- Any event resulting from carelessness or lack of caution or from ignoring governmental rules and regulations can potentially be considered an offence; in addition, in certain cases, such events can damage the environment and human health. That is why a particular chapter or article should be included in the law dealing with compensation of possible damages.
- Finally, as general laws need to determine their administrative structure, it should be made clear which organisations will compile the administrative directive of the national law and then have it ratified by the cabinet.

3.3.3. A Draft of Biosafety Regulations and Criteria

Cases which have to be anticipated in the draft of biosafety regulations and directives are:

- Determining and defining different degrees of biosafety;
- Classifying microorganisms;
- Clarifying conditions and methods of laboratory work;
- Determining regulations related to laboratory work on transgenic plants and animals;
- Determining regulations for greenhouse work (including facilities and design of greenhouses);
- Determining regulations for field research;

- Clarifying conditions and methods necessary for the submission of requests for laboratory or field experiments;
- Clarifying regulations for inter and intra-organisational transfer of biological material and genetically modified microorganisms;
- Determining regulations for the packaging and transfer of LMOs.

Dealing with requests for permits to be issued for field experiments and release and introduction of a product into the market are the responsibility of the National Biosafety Committee (authorized national authority).

3.4. The National Biosafety Committee

As mentioned earlier, the National Biosafety Committee (NBC) is responsible for the compilation of laws and development of a system for biosafety control. The NBC will be supported by a secretariat and will receive expert input from various government agencies.

The following figure 2 represents the organisational structure of the NBC and its related organisations and departments, including Ministerial Biosafety Committees (MBC)and Institutional Biosafety Committees (IBC):

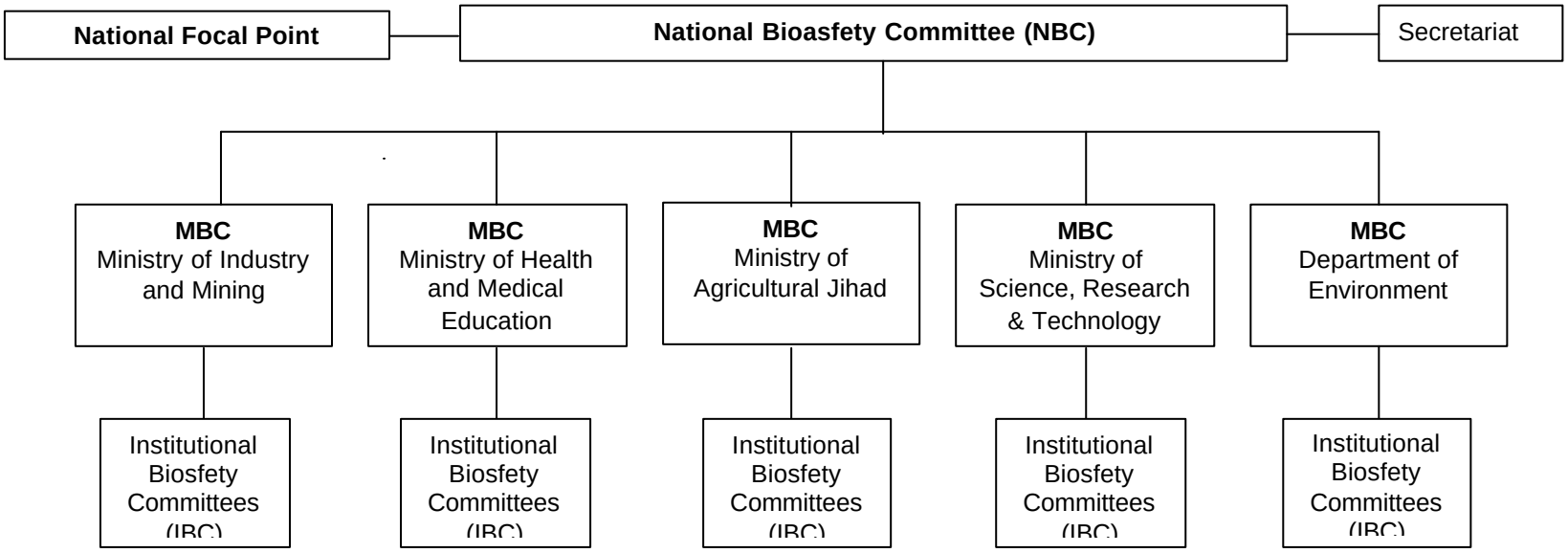

Figure 2: Organisational structure of the NBC

3.4.1. Major Components of the Iranian National Biosafety Committee

Members of the National Committee

1. The Minister of Science, Research and Technology;
2. The Minister of Health and Medical Education;
3. The Minister of Agricultural Jihad;
4. The director of the Department of Environment;
5. The Minister of Industry and Mining;
6. The Minister of Commerce;
7. Four specialists, each from medical biotechnology, agriculture, environment and basic sciences, with an introduction from their relevant organisation;
8. Representatives of the network of NGOs and private organisations;
9. Fully authorised representative from the Strategic Council of Biotechnology.

3.4.2. Duties of the Committee

1. Determination of biosafety macro policy;
2. Ratification of regulations and directives regarding biosafety measures in relation to modern biotechnology activities;
3. Approval of biosafety standards and criteria;
4. High supervision on activities related to the Cartagena Protocol on Biosafety and other related international treaties;
5. Supervision on activities related to biotechnology in relation to biosafety;
6. In cooperation with the MBC, certification of higher-level laboratories and containment facilities (biosafety level risk 2 & 3);
7. Discussion and expansion of instructions for assessing the risks of those microorganisms which have been designated for contained use;
8. Encouragement to relevant centres for the compilation and development of methods and instructions for assessing the risks of those microorganisms designated for field trials and commercial release;
9. Appointment of members of departmental biosafety committees with the help of centres involved in genetic engineering and foreign species under the supervision of relevant heads of organisations.

3.5. Ministerial Biosafety Committees (MBC)

3.5.1. Composition of MBC

1. Joint secretary of the respective ministry or fully authorized representative of the respective ministry who shall be its chairman;

2. Fully authorized representative from each ministry and the department of environment;
3. Three experts or heads of three IBCs under the administrative control of the respective ministry;
4. Two experts on biodiversity and genetic erosion (plant/animal breeders, microbial geneticist etc.);
5. One expert for the evaluation of social impacts (social scientist or economist etc.);
6. Representatives of the network of NGOs and private organisations;
7. One expert for the evaluation of environmental impacts (ecologist or environmentalist).

3.5.2. Powers of MBC

Working in close cooperation with the NBC, the MBC will have the power to enforce all measures necessary to eliminate any threats resulting from modern biotechnology activities which may have harmful effects on human health, biodiversity and environment. Therefore, upon recommendations of the relevant IBC, the MBC will have complete powers to stop any project under its jurisdiction and has the obligation to report any such initiative to NBC.

3.5.3. Functions of MBC

The MBC will function under the administrative authority of the concerned ministry and under the supervision of the NBC. It will be in charge of examining issues and granting clearance on a case by case basis and according to the ministry's mandate. The scope of functions and responsibilities of an MBC will be limited to organisations, public as well as private institutions and industries under the administrative control of the concerned ministry. Main MBC tasks are defined in the following:

1. Assisting NBC activities;
2. Evaluating applications for research and development projects of LMOs, import of LMOs, field tests, and release of LMOs and products thereof and prepare a report for the approval of the NBC;
3. Evaluating proposals requesting deregulation of Living Modified Organisms and products thereof, on the basis of experimental/field trial data and prepare a report for the approval of NBC;
4. Supervising the production, sale, import or use of substances and products including additives or Living Modified Organisms, cells or microorganisms in areas relevant to the concerned ministry and submit a report to the NBC;
5. Liaising with NBC on research, manufacture, process, use, import, export, transport, or sale activities concerning any Living Modified Organisms/substances or cells and products thereof in areas relevant to the concerned ministry;
6. Monitoring scale up or pilot operations for facilities using Living Modified Organisms/microorganisms in areas relevant to the concerned ministry;

7. Giving feed back to the NBC to determine or take measures concerning the discharge of microorganisms or cells from the laboratory/industry and laying down measures to be taken to prevent such releases.

3.5.4. Responsibilities of MBC

MBCs will be established in the controlling ministries and they will be assigned the responsibilities to control measures in organizations under their administrative control as well as those public or private institutions, organization, industries relevant to the concerned ministry. Their responsibilities include:

1. To ensure that all relevant IBCs function properly;
2. To ensure compliance of import, export, transport, manufacture, process, use or sale of any Living Modified Organisms/substances or cells and products thereof with national guidelines and regulations, and under the supervision of the NBC;
3. Working in close cooperation with the NBC, to certify higher-level laboratories and containment facilities (biosafety risk level 2 & 3);
4. Provide funds to add facilities as prescribed by IBC or other regulatory bodies;
5. Ensure that no organization, public or private, relevant to the ministry concerned, initiates any project without prior clearance/permission or authorization by NBC;
6. Finally, withhold funds and/or use administrative authority to immediately stop programmes if national guidelines are violated.

3.5.5. Postal address of MBCs

- **Dr. Soleimanpour**

  Deputy of Natural Environment and Biodiversity
  Department of Environment
  Pardisan Park, Shahid Hemat freeway
  Tehran - Iran

- **Dr. Akbari**

  Deputy of Health
  Ministry of Health and Medical Education
  Enghelab Av.
  Tehran - Iran

- **Dr. Sanati**

  Head of the National Research Organisation for Genetic Engineering & Biotechnology
  Enghelab Av., Ghods Str., No. 19 Shahid Shafiei alley
  Tehran - Iran

- **Dr. Ghareyazi**

  Director General of Agricultural Biotechnolgy Research Institute of Iran

  Ministry of Agricultural Jihad

  Mahdasht Road

  Seed and plant improvement institute campus

  Karaj - Iran

  P.O. Box - 31535-1897
- A representative from the Ministry of Industry and Mining to be appointed.

3.6. Institutional Biosafety Committees (IBC)

Institutions and organizations, public or private, engaged, or with the intent to engage, in research, production, process, import, export, transfer, propagation, or release of Living Modified Organisms, their components, or products thereof must each arrange for the establishment of an Institutional Biosafety Committee (IBC) to serve as the administrative authority on matters of biosafety and on compliance with attached guidelines. In order for the IBC to be able to exercise the full extent of its authority and undertake all of its functions and responsibilities, the pertinent institutions and organizations must appoint appropriate and skilled individuals to the IBC, and support the needs and demands of the committee. In addition to the IBC, institutions and organizations are encouraged to recruit a Bio-Safety Officer (BSO) to work in conjunction with various biosafety committees.

Small research institutions which may encounter difficulties in establishing an IBC may alternatively request other IBCs or the relevant MBC to bear the responsibility for monitoring and supervising the biosafety aspects of their work. Such agreements must be formally formulated between the parties involved and the NBC must be notified of the proceedings. In order to work in close cooperation with the appointed IBC, it is recommended that a representative of the smaller institution serve as an acting or even as an honorary member of the committee.

3.6.1. NBC Certification

In order for the IBC to become operational, it must receive formal endorsement from the NBC, through MBC. Therefore, the pertinent institution will submit to the NBC, and through the concerned MBC, a completed notification form for information and record, as well as approval by NBC. This form will detail:

1. Name and contact details of institution:
2. List of IBC membership:

3. Name and contact details of each committee member:
4. Professional history of each committee member: 5. Faculty history of each committee member: 6. Qualifications of each committee member: **For fields 4, 5, and 6 a CV may be provided for each committee member**
7. Suggested function/terms of reference in IBC for each committee member:
Designated Bio-Safety Officer, if applicable:
A list of institution's current projects, indicating risk assessment category:
A list of laboratories approved for recombinant DNA work (indicating category of containment):
A list of the institution's plant glass houses and animal houses, certified and intended for work with transgenic species (indicating category of containment).

3.6.2. IBC composition

The head of the institution will appoint this committee. Although the content of this guideline should always be respected and provide a useful framework, the primary responsibility for maintaining various standards and ensuring biosafety rest with the institutions and the researchers concerned and should never be wholly dependent upon national guidelines or upon the NBC.

The IBC represents the most important element in biosafety for an institution/organization covering issues related to supervising genetic manipulation work, attending to the health of personnel etc. It should therefore comprise members with considerable expertise and experience in order to assume IBC functions and responsibilities. Moreover it is highly recommended that the chairperson of the IBC retain a senior position under the relevant institution - possibly the Director himself/herself - to ensure swift adoption of the committee recommendations.

In order to supervise laboratory genetic manipulation work, the IBC shall comprise no less than three members, with the following suggested distinctions:

- An individual with the abilities to evaluate, assess and advise genetic-manipulation work in the particular field of research supported by the institution (e.g. plant genetics; virus life history, etc.);
- An engineer with the necessary expertise and practice to inspect the integrity of facilities, instruments and tools governing biosafety conditions in the institution,
- A Bio-Safety Officer, where applicable;
- A subject expert from the institution,
- A representative/member of MBC or NBC or a public representative.

In addition, recognizing that biosafety issues evoke many varied disciplines, it is highly recommended that the IBC establish working arrangements with different individuals knowledgeable in relevant areas.

3.6.3. Powers of IBC

The institution should grant principal authority on biosafety concerns to the supervising IBC enabling it to exercise its powers in undertaking all of its responsibilities and offer criticism and advice without contest.

Working in close cooperation with the MBC, the IBC should have the power to enforce all regulations, report infractions to the institutional head, MBC and/or NBC as the case may be. Moreover, it should recommend, as early as possible, the relevant authority to stop a project if its continuation under the existing circumstances is a threat to laboratory personnel or public environment and health.

3.6.4. Functions of IBC

The IBC has the main following functions:

1. Harmonizing experimental conditions with national guidelines;
2. Assisting researchers in undertaking risk assessment organizing training programs;
3. Determining additional bio-safeguards and drafting supplementary operating instructions for work at the institution, in line with and addressing the specific risks and concerns uncovered during risk assessment;
4. Evaluating the qualifications of researchers involved in biotechnological projects;
5. Assessing whether the institution's researchers retain a thorough understanding of good microbiological practices necessary for the supervising of students, assistants and junior personnel;
6. Monitoring and supervising all regulated work under progress within the institution;
7. Counselling proponents on biosafety issues and on compliance with national guidelines on a regular basis or as requested. The IBC should set apart time for researchers, laboratory and field personnel to approach the committee with questions, disputes or concerns;
8. Where appropriate serving as a gateway for the flow of information ideas and opinions between the MBC/NBC and the research teams;
9. Maintaining and updating a directory of all personnel engaged in activities at every biosafety level;
10. Instructing new personnel on correct laboratory and/or field practices, emergency procedures and equipment operation at the relevant level;

11. Keeping updated records of national as well as international biosafety standards and regulations for laboratory as well as field experiments, and proposing the upgrading of institutional biosafety facilities and/or practices;
12. Attending to the health of laboratory and field personnel.

3.6.5. Responsibilities

To ensure that laboratory genetic manipulation work within the institution conforms to the regulation proposed in this framework, the IBC must address the following tasks:

1. Assess all projects referred to the committee and on the basis of the information provided and the risks forecast determine whether to endorse the work proposed, and if so, under which category of work the proposals fall;
2. Maintain records of approved project proposals for laboratory genetic manipulation work (including notification for project exemption) and the committee's assessments;
3. Forward summaries of all project proposals submitted for IBC notification and the committee's assessments to the MBC&NBC for record and information or for review and recommendation in the case of proposals Risk Category 2&3 work.
4. Undertake risk assessment, in cooperation with research teams as necessary, to determine the appropriate containment and biosafety conditions operating procedures and emergency safeguards for Risk Category 2 and 3 genetic manipulation work;
5. Undertake risk assessment, in cooperation with research teams as necessary, to determine the appropriate containment and biosafety conditions operating procedures and emergency safeguards for the housing storage and/or movement of regulated material and also the management of waste;
6. Prepare; in conjunction with research teams specific contingency plans after undertaking risk assessment and reviewing project proposals;
7. With particular emphasis on Risk Category 3 work, enforce all recommendations and ensure that NBC and committee comments have been acknowledged and promptly addressed;
8. Inspect and certify before use in genetic manipulation work, first biosafety level laboratory facilities, conventional animal houses, first biosafety level plant glass houses and quarantine and medical facilities for infected animals. The MBC&NBC will be responsible for certification of higher-level laboratories and containment facilities only;
9. Recommend, as early as possible, the relevant authority to stop a project if its continuation under the existing circumstances is a threat to laboratory personnel or public environment and health;
10. Monitor and inspect containment features of and working conditions within all laboratories, plant glass houses and animal houses supporting the institution's work, to

ensure that the various facilities are maintained at the relevant standards and requirements, addressed in the following appendixes.

PART FOUR: CREATING A SUITABLE SYSTEM TO HANDLE REQUESTS FOR AUTHORISATION AND ISSUING APPROVAL

4. Creating a Suitable System to Handle Requests for Permits and Approval

A. The secretariat of the National Biosafety Committee (NBC) will put on its web site the list of required documents and necessary forms (such as forms of risk assessment) for permits and certificates for the import, export and release of LMOs.

B. In addition to the documents, necessary information will be presented in such a way that all applicants can identify the relevant national authority, namely the NBC. Full address, contact numbers and the name of the official directly responsible for the said authority will become available to the public on the web site.

C. Members of the NBC are as follows:

- Department of Environment
- Ministry of Agricultural Jihad
- Ministry of Science, Research and Technology
- Ministry of Health and Medical Education
- Ministry of Industry and Mining

D. After filling the necessary forms, along with complete paper work, necessary documents, the applicants will submit them to the relevant Ministerial Biosafety Committee (competent authority) through the NBC.

E. The secretariat of the NBC, after receiving the paper work, will issue a receipt and register the time of paper work submission; the said authority must return the paper work to the applicant within 10 working days, if the paper work is not complete.

The applicant is also to make sure that the submitted paper work is completed within 3 days and must obtain a "Complete Paper Work Received" receipt.

F. In case the paper work is incomplete, documents will be returned to the applicant; this process will be repeated until all necessary papers are submitted.

G. In case the applicant is asking for a certificate for activities which do not need a permit, or in case a certificate has already been issued for a particular LMO, the NBC must fax the applicant a written "**No Need for a Certificate**" or a "**Certificate Already Issued**" within 10 days.

H. When the documentation is completed and the NBC decides that a certificate can be issued for the particular activity applied for, the NBC will carry out a preliminary evaluation.

Moreover, the NBC has the responsibility to publicly notify those applications related to import of LMO, field experimentation of LMO and release of LMO and products thereof.

At this stage, the authorised official will decide upon one of the following three courses to his discretion:

- This application is under the jurisdiction of another competent authority (MBC). In this case, the paper work will be submitted to the said relevant authority along with a letter. A copy of the letter will be sent to the applicant.
- This particular request should be assessed by other competent authorities as well. In this case, documents will immediately be sent along with a letter to other authorised official(s). The first authority will then continue with other stages of assessment such as risk assessment.
- The application is exclusively related to the authorised competent authority. In this case other stages such as risk assessment and the issuing of a permit will be carried out.

I. After the said stages, those competent authorities, which have acknowledged their authority for the assessment of the application, will take measures to assess possible risks.

J. Risk assessment will be performed by a team composed of 7 people with different specialities. This team, whose leader will be appointed by the head of the relevant competent authority (MBC) with approval of the NBC, will be as follows:
   - Three members appointed by the head of the relevant authority;
   - Four members appointed by the heads of other competent authorities (one member each).

K. Risk assessment involves a study of the applicant's documents and claims.

L. All risk assessment teams must submit the latest decision making related information to the focal point and BCH.

M. On the web site of the NBC, measures should be taken to make it possible for those people who wish to introduce themselves as risk assessors to provide a CV, and records of academic experience, education and specialisation. If they are confirmed and accepted as risk assessors, their names and particulars will be registered on the Biosafety Roster of Experts on the web site. Authorities must appoint at least two of the four members from among these people.

N. After risk assessment, the result will be submitted by a letter to the head of the relevant MBC. The result of risk assessment as well as assessment and response from other authorities will be then submitted to NBC. The secretariat of NBC will send a suitable answer to the applicant as follows:
   - Approval of the application;
   - Rejection of the application and giving detailed reasons for rejection in writing;
   - Approval of the application conditionally. This condition could be geographically limited release or other factors.

O. All the stages of risk assessment and the submission of a written response to the applicant should be completed within 70 days (starting from the day of submission of paper work).

Amendment: If NBC do not submit a response within 90 days of receiving and registering completed paper work, an "Approved" response will be assumed. The applicants can then take measures regarding their application according to an "Approved" response.

P. The applicant must, during the stages of risk assessment, offer full cooperation and submit all information if necessary. The risk assessment team has the right to invite the applicant to attend risk assessment sessions (without the right to vote).

Q. In case applicants have objections to their response, they can submit a written appeal within 30 days, mentioning reasons and presenting complementary supporting documents and evidence to the NBC.

R. The NBC must, after careful examination, inform the applicant of the final decision within 6 months.

   Amendment: If within 6 months after submitting a written appeal to the NBC no response is received, the applicant has the right to assume an "Approved" response and act accordingly.

S. Having approved an application, the MBCs are responsible for supervision and evaluation, and must obtain 6-month or yearly reports from the applicant.

T. In case the MBC receives new information related to submitted applications, it has an obligation to inform the NBC and ask for a revision/cancellation of the issued permit or certificate.

U. The NBC can suspend or cancel issued permits and certificates, providing reasons in writing, for a limited time (in any case no longer than one year).

The process and the timelines presented above, are summarised in the following figure 3:

Pre applications process that allows for interaction with the NBC to establish that the applicant understands the required information and the process and costs (if any) involved. During this process appropriate forms and guidance is provided to the applicant.

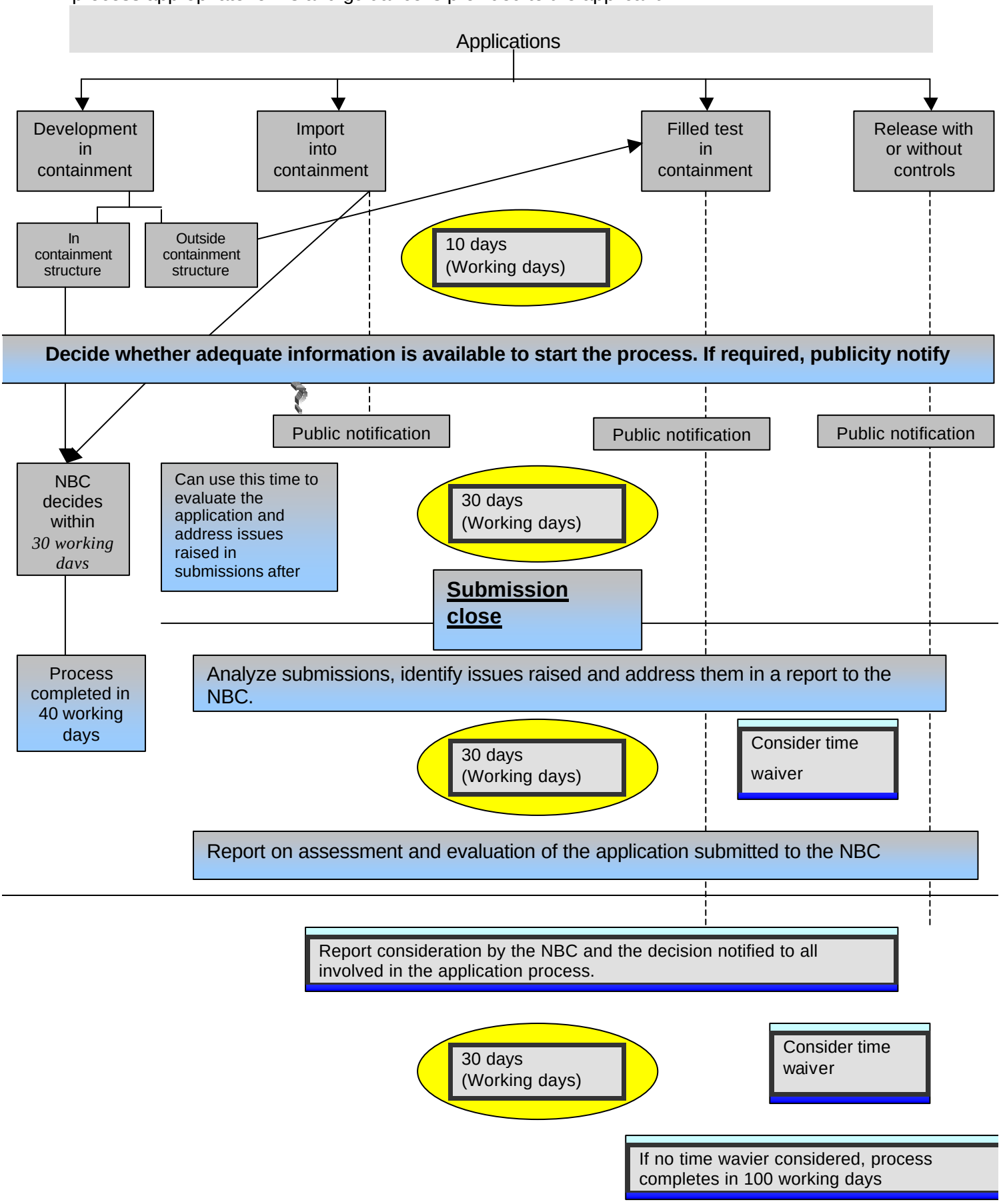

Figure 3: System to Handle Requests for Permits and Approval

4.1. Risk Assessment

The purpose of the said assessment is to identify and assess potential harmful effects of more than 1% LMOs on the conservation and sustainable use of biological diversity, taking also into account risk to human health. Risk assessment is performed by the MBC and NBC, and adequate decisions will be made with respect to said LMOs.

The assumption of proper risk assessment is that a set of general experimental principles can be identified under which laboratory, small-scale field research of low or negligible risk can be conducted with a specific Living Modified Organism.

- The *first* working assumption is that certain general scientific principles related to the organism, the research site, and experimental conditions have varied relative importance in determining whether an experiment is of low or negligible risk.
- The *second* assumption is that a conclusion regarding that risk of an experiment can be reached by evaluating the relevant factors and their interaction under the conditions of the experiment including, when available, existing data from greenhouse and laboratory studies.
- The *third* assumption is that the interaction of these factors is easier to address in small-scale field experiments than in large-scale experiments because of their limited scope, which permits closer monitoring, generally easier assessment and analysis and the possibility of more effective containment measures in the event of unforeseen and potentially damaging occurrences.

  A number of assumptions are also made concerning the key factors which determine the safety of any specific experiment (see following figure 4).

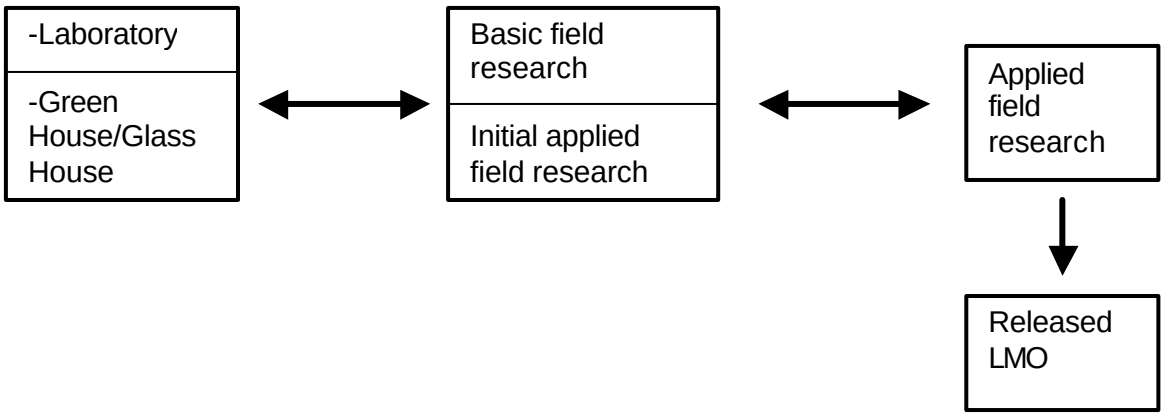

Figure 4: Different stages in risk assessment

4.1.1. General Principles

1. Risk assessment should be carried out with sound scientific standards, and if necessary, it can take into account expert advice of, and guidelines developed by, relevant international organisations.
2. Lack of scientific knowledge and scientific agreement should not necessarily be considered as existence or non-existence of a risk.
3. Risks related to LMOs and products thereof on non-modified organisms or parent organisms in the environment should be considered.
4. Risk assessment should be performed on a case by case basis. Necessary information can make a difference in the nature and level of details from one case to another, depending on the importance of the living modified organism, its purposeful application and probably the receiving environment.
5. The risk assessment process can, on the one hand, lead to the need for more information regarding specific cases, which may be needed and identified during the assessment process; and on the other hand, information regarding other cases may not be relevant in certain situations and under certain circumstances.
6. To be thorough, the purpose of the said assessment, when applicable, will involve the following stages:
   A. Identification of new phenotypic and genotypic characteristics in relation to living modified organism - which may have harmful effects on genetic diversity and presumably the receiving environment - according to possible risks to human health;
   B. Possible assessment of realised harmful effects of LMOs, according to the level and type of their release into the receiving environment.
      a) Assessment of the said consequences should determine harmful effects.
      b) General evaluation and examination of the risks of LMOs should be done based on an assessment of harmful effects and results.
      c) Recommendations should be included regarding whether the risks are manageable or acceptable and, if necessary, strategies for the management of such risks should be identified.
      d) When there is uncertainty regarding the level of risk, more information should be asked for in particular cases for the necessary risk management, strategies or supervision on LMO in the environment.

4.1.2. Points to Consider

Depending on the case, risk assessment will address related scientific and technological details according to the following particulars (ref. text of the Cartagena Protocol on Biosafety, Annex III):

A. *Recipient organism or parental organisms.* The biological characteristics of the recipient organism or parental organisms, including information on taxonomic status, common name, origin, centres of origin and centres of genetic diversity, if known, and a description of the habitat where the organisms may persist or proliferate;
B. *Donor organism or organisms.* Taxonomic status and common name, source, and the relevant biological characteristics of the donor organisms;
C. *Vector.* Characteristics of the vector, including its identity, if any, and its source or origin and its host range;
D. *Insert or inserts and/or characteristics of modification.* Genetic characteristics of the inserted nucleic acid and the function it specifies, and/or characteristics of the modification introduced;
E. *Living Modified Organism.* Identity of the living modified organism, and the differences between the biological characteristics of the living modified organism and those of the recipient organism or parental organisms;
F. *Detection and identification of the living modified organism.* Suggested detection and identification methods and their specificity, sensitivity and reliability.
G. *Information related to the intended use.* Information relating to the intended use of the living modified organism, including new or changed use compared to the recipient organism or parental organisms; and
H. *Receiving environment*. Information on the location, geographical, climatic and ecological characteristics, including relevant information on biological diversity and centres or origin of the likely potential receiving environment.

4.1.3. Guidelines for risk assessment

At the international level, a number of developed and developing countries have prepared or adopted biosafety guidelines for both laboratory investigation and field applications of research and development experiments involving r-DNA.

The main objective of applying such guidelines is to ensure safety and minimize all the possible risks which are likely to occur, encountered or subsequently generated beyond expectation. Such guidelines may differ from one country to another. However the principles are essentially more or less similar. In many cases, acceptable guidelines in developed countries are used as references, subjected to consideration and then modified or amended to be appropriate and in compliance with the existing related laws and regulations within respective countries. At the international level, efforts have been made by UNIDO, FAO, WHO, OECD and other international agencies to prepare biosafety guidelines with contributions from international experts to help assist developing countries to formulate their own biosafety guidelines.

As far as the I.R. of Iran is concerned, there is an urgent need to develop and implement national biosafety guidelines to help the development of r-DNA technology in the country. These guidelines are important and essential, not merely for researchers within the country, but also for various cooperative and collaborative ventures between national institutions and overseas research partners interested in laboratory testing or additional field trials of GMOs in I.R. Iran.

In order to provide a comprehensive biosafety framework for the I. R. of Iran, risk assessment guidelines in genetic engineering and biotechnology for laboratory work, field work and planned release are proposed in appendices 2 to 9 of the current NBF.

The Committee welcomes all advice, suggestions, comments and criticism from all concerned in order to incorporate them and render the present guidelines more feasible and supportive of the overall development of r-DNA technology in the country.

***** To complement the material in this chapter, Appendixes 2 to 9 have been included as follows:
Appendix 2: Laboratory instructions for LMOs;
Appendix 3: Specific needs for work in certain genetic experiments;
Appendix 4: Strategies and responsibilities in laboratories and research centres;
Appendix 5: General levels of plant biosafety;
Appendix 6: Biosafety levels for laboratory animals;
Appendix 7: Guidelines for Field Experiments;
Appendix 8: Regulations and restrictions for field experiments;
Appendix 9: Transfer and transboundary movements of LMO (export, import and labelling).

4.2. Confidential business information

The competent authority shall protect information which it determines as being confidential after a claim for confidentiality is made by the applicant.

In no case may the following information supplied by the applicant be kept confidential:

a) description of the LMO(s) or products thereof, names and addresses of the applicant, purpose and location of the import, deliberate release (including the location and scale of the release), contained use or placing on the market of the LMO(s) or products thereof;
b) methods and plans for monitoring of the LMO(s) or products thereof and for emergency response;
c) the evaluation of foreseeable effects, in particular any pathogenic and/or ecologically disruptive effects;

d) the fact that the LMO(s) or products thereof have been banned or subject to stringent conditions.

Any person carrying out any activity under this Act shall supply information necessary for the competent authority to carry out its supervisory, monitoring or enforcement tasks or to deal with any emergency measures in relation to the activity and there shall be no claim of confidentiality in relation to such information.

Further information on this section is in appendix 9.

PART FIVE: CREATING A SUITABLE SYSTEM FOR RISK MANAGEMENT AND FOLLOW UP

5. Creating a Suitable System for Risk Management and Follow Up

Once an activity has been issued with a permit, inspection, monitoring and follow up mechanisms start. Supervision and inspection is carried out by a team comprising inspectors from the National Biosafety Committee and organisational inspectors. The number of inspectors will be different depending on the case under supervision. Specific experiences and inspecting methods related to the activities of the LMOs should be clearly defined by biosafety committees of relevant organisations. Based on the outcome of risk assessments, general and specific supervision systems should be enforced.

5.1. Purpose of the Follow Up

- Ensuring that the release of LMOs has no possible side effects on the environment and human health.

5.2. Administrative Procedures

- Assessing the results of prior experiments and assessing possible risks;
- Collecting data and analysing it in order to predict possible risks;
- Studying unintentional effects on the environment and on human health;
- Applying continuous supervision mechanisms for LMOs released in the environment;
- Supervising and controlling continuous environmental effects of LMOs;
- Training experts and inspectors (with different specializations such as environmental, agricultural, commercial, medical, etc.) and providing supervision and control instructions for biosafety experts;
- Developing a reference laboratory network for experiments on the assessment and control of environmental effects.

5.3. Risk Management

The national structure of biosafety should comprise, according to the case, a committee comprising experts from different fields of specialisation such as biotechnology, genetic engineering, molecular biology, agriculture, biochemistry, toxicology, microbiology, immunology, environment, veterinary medicine and other specialists. Therefore, in case there are any environmental, agricultural or health damages resulting from LMOs, the level of the damages incurred can be assessed (by the committee) and, according to the type of risk, necessary measures can be suggested to relevant authorities.

Instructions pertaining to the transfer of LMOs are included in Appendix 9.

5.4. Identification and labelling

Any LMO or products thereof shall be clearly identified and labelled as such, and such identification shall specify the relevant traits and characteristics in sufficient detail for purposes of traceability.

Products containing, or consisting of, LMOs shall be clearly labelled and packaged in accordance with the following information, and comply with further requirements, if any, imposed by the National Biosafety Committee, to indicate that it is, or has been derived from LMOs; and where applicable, whether it may cause reactions, allergies or other side-effects.

Labelling and packaging information:

1. The words "**This product contains LMO(s)**" whenever there is evidence of the presence of more than 1% LMO(s) in the products.
2. The words "**This product may contain LMO(s)**" where the presence of LMO(s) in a product cannot be excluded but there is no evidence of any presence of LMO(s).
3. The words "**This product may cause.... [specify the particular reactions, allergies or other side effects]**" where it is known that a particular reaction, allergy or other side-effect may be caused by the product.
4. Where applicable, the words "**This product contains genetic material (nucleic acids) from LMO(s)**" or "**This product is base on raw materials from LMO(s)**".

Additional information on this section is in appendix 9.

PART SIX: PUBLIC AWARENESS AND PARTICIPATION MECHANISMS

6. Public Awareness, Training and Participation Mechanisms

6.1. Objective

The purpose is to encourage public participation and training using NBF measures in order to establish a participatory and informing system regarding the advantages and disadvantages of the application of LMOs for the people and eventually collecting feedback from the people regarding harmful and continuous side effects of LMOs.

6.2. Informing and Public Awareness

Informing is necessary for public awareness. Public awareness will result in public participation. The National Biosafety Committee is responsible for the planning needed to reach these goals. Informing is an endless process and cannot be considered as a limited duty.

Documentation

- According to Article 3 of the Constitution, in order to reach the goals of the system, the government of the Islamic Republic of Iran must apply all its facilities to the following affairs:
  Paragraph 2 – (Article 3) elevating the level of public awareness in all respects through correct application of the press and the media and other means;
  Paragraph 8 – encourage participation of the masses of people in determining their own political, economical, social and cultural destiny.
- According to paragraphs 2-4 on the country's biotechnology policies in the social dimension as included in the National Biotechnology Document:
  "Development of biotechnology should be accompanied by increasing public awareness towards this technology."

6.2.1. Public Information and Awareness Mechanism

Information must be up to date, precise, useful, scientifically valid, serious, appropriate, relevant, simple and easy to understand.

- People involved in the act of informing should be well informed as well as honest in speech and act.
- Information should be given by authorised people.
- Materials should be made available to the public in a comprehensible form, avoiding unnecessary technical information, and in adequate quantity.
- Informing should be in accordance with the Iranian culture.
- To choose better methods, experts in teaching and training, psychologists and sociologists must be involved.

- In certain cases, to ensure the confidentiality of information on organisations and institutes, it is possible to ask them to make their information directly available to involved institutes.
  The following information is not considered confidential under any circumstances:
  - Name and address of applicants;
  - General descriptions of the LMO(s);
  - Areas covered by such activities;
  - A full risk assessment report by the applicant;
  - Any method or planning for necessary measures.
- Individuals and interested institutes should have access to all biosafety decisions and the information based on which such decisions have been made.
- Information on biosafety issues should be performed under the supervision of the secretariat of the National Biosafety Committee.

6.2.2. Information and Training Tools

These tools are applied to inform the public on modern biotechnology, its advantages and risks, and they include:

- Using the media and the press (radio, television, newspapers, magazines);
  - Interviews with experts;
  - Publication of articles;
  - Films;
  - Other.
- Developing, expanding and updating a national biosafety information centre;
- Informing through labels (in particular on GMF food items);
- Holding conventions suitable for different groups;
- Holding training workshops suitable for different groups;
- Preparing bulletins, pamphlets and posters for different groups of people;
- Creating biosafety courses for different biotechnology majors;
- Preparing information compact disks for the use of the public;
- Creating an MS biosafety major in the educational system of the country. It should be mentioned that key courses related to biosafety for PhD students in biotechnology and genetics are being taught in the country's major universities.
- Including several general training sessions in high schools and universities.

6.3. Public Participation

Public participation in self-determination is one of the requisites of the Constitution of the Islamic Republic of Iran, originating from Islam and the government has an obligation to encourage and

make its realisation possible through relevant organisations. Participation will be made possible after informing, training and gaining the trust of the public, and it should be planned and executed at different stages and levels. Different types of participation can be considered for different groups of people. Public masses mainly participate by "sharing information". Other groups would participate as consultants. Groups of specialists and national authorities would be involved in decision making, and higher level authorities in policy making, normally based on a bottom-up approach.

Public Participation Mechanism and Tools:

- Legislating participation;
- Empowering the civic society and NGOs in order to reinforce the foundations of hierarchical participation;
- Elaborating the participation of religious representatives;
- Holding opinion poll conventions and workshops;
- Creating suitable methods for public opinion polls (such as preparing questioners for different groups of people);
- Creating independent consultative committees;
- Creating and expanding a biosafety information centre to help achieving goals and to facilitate information exchange between decision makers, managers, experts and the public.

APPENDICES

Appendix 1

Applicable rules and regulations

1.1. Article 14, medical and pharmaceutical affairs and food and beverages act, ratified on 13/12/1965, and related amendments ratified by the Islamic Consultative Assembly on 11/3/1988

"Importing any kind of biological products (such as vaccines and serums), laboratory material, baby food items, any kind of medicine and medical raw material, medical packaging and related machinery and spare parts in any form by the private or governmental sector, and also clearing of the said items from the customs as well as the production of any kind of medicine or biological product, their supply and sale inside the country or their export requires prior permission from the Ministry of Health and Medical Education and obtaining the necessary permit or certificate."

Article 14, medical and pharmaceutical affairs and food and beverages act, ratified on 13/12/1965, and related amendments ratified by the Islamic Consultative Assembly on 11/3/1988, 2nd amendment

"Production or import of any material or ingredients, medical and dental equipment as well as raw material for their packaging, the list of which will be announced by the Ministry of Health and Medical Education, should occur with prior permission and agreement from the Ministry of health and Medical Education."

Article 15, medical and pharmaceutical affairs and food and beverages act, ratified on 13/12/1965, and related amendments ratified by the Islamic Consultative Assembly on 11/3/1988 (crimes)

"Individuals who import or manufacture pharmaceutical materials and biological products included in Article 14 without permission from the Ministry of Health and Medical Education will be sentenced by court to a fine, payable to the Ministry of Health and Medical Education; based on their circumstances, the number and degree of crimes and required punishment, the said material will be confiscated and, if necessary, destroyed. First time offenders will be fined from 500,000 Rls. to 5,000,000 Rls. and second time offenders from 5,000,000 Rls. to 10,000,000 Rls. If the offence is repeated, in addition to maximum financial fines, a jail sentence of three to six months will be added."

1.2. Article 9, regulation for the production and import of medicine

"Permit for the production or import of medicine, where production or import of medicine is necessary for certain cases or for a short period of time, or where the production or import of pharmaceuticals by one source is not possible or advisable, is allowed after confirmation and permission from the legal commission for the production and import of pharmaceuticals, which will be announced on a case by case basis or in general."

1.3. Article 24, regulation for the production and import of medicine

"Individuals who discover or make a new medicine should submit required documents and information in forms they are supplied with. Their application will be assessed by the commission for the production and import of medicine under article 20 of the Act: in case the medicine is approved and the necessity for its production and supply into the market is confirmed, permit will be issued according to necessary regulations."

1.4. Article 1, import – export act

"By this Act, regulations pertaining the import and export of goods and provision of related services are considered binding for all exporters, importers and all those for which the coverage of the law requires mentioning their names; all contradictory regulations are hereby cancelled."

1.5. Article 2, import – export act

"Imported and exported goods are categorised into the following three groups:

1. Authorised goods: goods for which no permit is required as long as regulations are observed for their import or export;
2. Conditional goods: goods for which import or export is possible after obtaining permits (this provision may serve as a basis for regulating the import/export of LMOs);
3. Forbidden goods: goods for which import or export (as well as purchase, sale or consumption) is forbidden by law and the holy Shari'a of Islam."

1.6. Article 8, import – export act

"Importers of various goods, whether governmental or non-governmental, in order to obtain permit to import and register an order, should apply only to the Ministry of Commerce."

1st Amendment: Approving import of goods is considered as permit for clearing and there is no need to obtain a separate permit.

1.7. Article 3, Paragraph 2, Ramsar Convention

“Any of the parties of the agreement will take necessary measures in order to gather information, as fast as possible, regarding changes in ecological conditions which have happened or are about to happen, or the happening of which is possible due to pollution resulting from technological advances or other human activities in the bodies of water in their own land and as included in the list.

Information related to such changes will immediately be put at the disposal of the organization or department indefinitely responsible for the affairs of the said office as mentioned in Article 8.”

1.8. Convention on Biological Diversity, Articles 1, 3, 6, 7, 8, 9, 10, 11, 14, 15, 16, 17 and 19:

1.8.1. Article 1: Objectives

The objectives of this convention, whose regulations must be observed, include the protection of biodiversity, continuous use of species and fair and equal sharing of the benefits resulting from the application of genetic reserves, including proper access to genetic reserves and the correct transfer of related technologies, while respecting the rights related to those reserves and technologies, and also provision of necessary budgets.

1.8.2. Article 3: Principle

Governments, based on the United Nations charter and the principles of international rights, have the right to control the use of their own resources according to their own environmental policies. They must ensure that activities carried out in their territory or in regions under their control will not damage the environment of other countries or of regions which are outside their national territory.

1.8.3. Article 6: General Measures for Sustainable Protection and Utilization

According to its own particular conditions and capacities, each member country must:

A. Develop strategies, projects and plans for sustainable protection and utilization of biodiversity, or reform the existing strategies, plans and projects in a way that reflects the measures determined in this convention in relation to member countries and,
B. As much as possible and in a suitable way, include protection and utilization of biodiversity in their plans, projects and departmental and interdepartmental strategies.

1.8.4. Diagnosis and Supervision

Each member country, as much as possible and in particular according to the objectives related to Articles 8 to 10, must:

A. Determine those elements of biodiversity which are important for sustainable protection and utilization according to the classified list in Appendix 1;

B. Through sampling and other techniques, monitor those biodiversity elements clarified in Paragraph A above and pay special attention to those which require specific measures to be protected and also those with higher potentials for sustainable use;
C. Determine processes and prepare a list of activities which have important effects on the sustainable protection and use of biodiversity and also determine the degree of their effect through sampling and other technologies and,
D. Organise and protect at any cost information resulting from diagnosis and supervision measures mentioned in A, B and C above.

1.8.5. Article 8: Internal Protection

As much as possible and in an appropriate way, each member country must:

A. Create a network of protected regions or those regions which require particular measures for the protection of biodiversity;
B. If necessary, prepare guidelines for the selection, creation or control of protected regions or those regions which require particular measures for the protection of biodiversity;
C. Organise and manage biological resources which are important for the protection of biodiversity, whether inside or outside protected regions, in order to provide sustainable protection and use;
D. Support ecosystems and natural habitats and protect last populations of species in their natural environments;
E. Encourage sustainable development compatible with the environment of those regions close to protected areas in order to protect these regions even more;
F. Revive and rebuild damaged and destroyed ecosystems and encourage the revival of endangered species in different ways, such as organising and executing projects or other management strategies;
G. Create, or continue the application of, tools necessary to organise, manage or control the potential dangers of using biotechnologically modified living organisms and their release which might have harmful environmental effects and which can affect sustainable protection and use of biodiversity; special attention must be paid to risks endangering human health;
H. Prevent importation of foreign species which endanger the ecosystems and habitats of other species; otherwise, control or destroy them;
I. Based on internal laws, respect and protect the knowledge, innovation and customs of local and native communities which include methods of traditional life-style suitable for the protection and correct use of biodiversity, or expand a more extensive application of these by involving and encouraging possessors of such knowledge, innovation or customs; fair

sharing of benefits resulting from the utilisation of such knowledge, innovation or custom must be encouraged;

J. Compile rules and regulations necessary for the protection of endangered species and populations;
K. Legalise or manage related procedures or activities wherever the existence of important harmful effects is apparent according to Article 7;
L. Participate and cooperate in the provision of financial resources and other supports for internal protection as discussed in Paragraphs A to K above, specifically where developing countries are concerned.

1.8.6. Article 9: International Protection:

Each member country, as much as possible and in a suitable way, and in the first place in order to complete measures related to internal protection must:

A. Take measures for the international protection of elements of biodiversity, preferably in the country of origin;
B. Create and maintain facilities for international protection of and research on plants, animals and microorganisms, preferably in the country of origin of the genetic matter;
C. Take measures for the revival and improvement of endangered species and try to return them to their natural habitats under suitable conditions;
D. In order to regulate international protection, organise and manage the collection of biological resources from their natural habitats, in a way that won't endanger internal ecosystems and populations of natural species, except in cases where part B is applicable, and where specific and temporary external measures are necessary.
E. Cooperate in the provision of financial resources and other support measures for international protection as mentioned in parts A and B above, and also create and maintain facilities related to international support in developing countries.

1.8.7. Article 10: For sustainable use of the elements of biodiversity of each member country as much as possible and in a suitable way they must:

A. Consider regulations related to the sustainable protection and use of genetic reserves in their internal policy makings.
B. Take measures in order to prevent or reduce harmful effects on biodiversity.
C. Encourage and support the conventional use of biological reserves according to the traditional and cultural customs which are compatible with the conditions of their sustainable use and protection.
D. Support local populations in the development and execution of optimisation measures in damaged areas whose biodiversity has been reduced.

E. Encourage cooperation between government officials and the private sector in order to develop methods of sustainable use for biological reserves.

1.8.8. Article 11: Encouraging measures

Each member country, as much as possible and in an appropriate manner, must take reasonable economical and social measures which can be considered as motivations for the sustainable use and protection of biodiversity.

1.8.9. Article 14: Assessing and reducing harmful effects

1. Each member country, as much as possible and in an appropriate manner must:

A. Employ suitable methods for the assessment of considerable harmful environmental effects which their projects might have on biodiversity in order to prevent such effects, and consider appropriate popular contribution in the application of these methods.

B. Take necessary measures to guarantee that the environmental consequences of those groups of plans and policies which have harmful effects on biodiversity are taken into consideration.

C. Encourage information exchange and consultation regarding those activities under its authority or control which may have considerable harmful effects on the biodiversity of other countries or regions beyond their territory by signing suitable mutual, local or many sided agreements of reciprocal behavior.

D. In case of danger or immediate and fatal damage to biodiversity in regions under the authority or control of other governments or for regions outside their national authority, immediately inform the governments which have been potentially endangered and take necessary measures to prevent or reduce the said risks and damages.

E. Increase national measures for immediate reactions to events or activities which happened either by natural or other causes and which indicate fatal and immediate risks for diversity, and encourage international cooperation in order to complement the said national efforts which are agreed upon by governments or organisations of the related regional economical unity in order to create common cautionary projects.

2. Based on adequate studies, member countries must address the issues of damage acceptation and compensation, including revivals and payment of compensation money for damage to biodiversity, except in those cases where the acceptance of damage is completely an internal issue.

1.8.10. Article 15: Rewarding measures

1. Bearing in mind the right of governments to rule over their natural resources, the right to make decisions regarding access to genetic reserves is that of the national governments and subject to internal laws.
2. Each member must try to create conditions whereby access to genetic reserves is facilitated for other member countries in a way suitable from the environmental point of view; there should be no restrictions that are against the goals of this convention.
3. In this convention, genetic resources supplied by one of the member countries, according to this article and articles 16 and 19, are exclusively those resources which have been supplied by those countries which are the origin of those resources or, according to the content of this convention, those countries which have had access to them.
4. Access to genetic resources, in case it is granted, may occur based on conditions agreed upon by both parties and must be subject to the conditions of this article.
5. Access to genetic resources may occur with the prior information and agreement of the member country supplying those resources, unless the said country has appointed another member.
6. In order to carry out scientific research projects based on the genetic resources supplied by other member countries, each member country must fully cooperate in participation of and if necessary in those countries.
7. In order to make the utilisation of research and development results and benefits from commercial application of genetic resources, fair and equal, each member country must take legislative or administrative measures or make policies for cases 16 and 19 as well as through financial arrangements mentioned in cases 20 and 21, if necessary, so that countries supplying those resources obtain their share of benefits as well. Such participation must be based on mutual agreement.

1.8.11. Article 16: Access to technology, and its transfer

1. Each member country, confirming that technology includes biotechnology, and that access to technology and its transfer among member countries are the principal elements of achieving the goals of this convention, based on the contents of this article, must create necessary facilities for other member countries for access to and transfer of those technologies related to sustainable use of biodiversity or the application of genetic reserves which do not damage the environment considerably.
2. Access to technology as mentioned in paragraph 1 above, and its transfer to developing countries, must be provided or facilitated in completely just and highly desirable circumstances, including conditions preferred and granted by both parties and, if necessary, based on financial arrangements in cases 20 and 21. In cases where the technology is under patent or other rights of

intellectual property, access and transfer will be according to conditions compatible with proper and effective support of the said rights of intellectual property. Application of this paragraph will be compatible with paragraphs 3, 4 and 5 below.

3. Each member country must, in an appropriate manner, take administrative or policy making measures in order to give access to member countries, in particular developing countries which are supplying genetic reserves, to technology and its transfer based on conditions mutually agreed upon by both parties, including the fact that technology must be protected according to patent and other laws of intellectual property or, if necessary, through the exercise of regulations in articles 20 and 21 and according to international laws and in accordance with paragraphs 4 and 5 below.

4. Each member country must, in an appropriate way, take administrative and policy making measures for the private sector to facilitate access to technology, its common development and transfer as mentioned in paragraph 1 above so that governmental departments and private organisations of developing countries can benefit as well. Such cases must observe requirements in paragraphs 1, 2 and 3 above.

5. Member countries must, acknowledging that patent and other rights of intellectual property can influence the execution of the conditions of the convention, ensure that such rights support the convention and that they are not against its objectives by cooperating according to national laws and international rights.

1.8.13. Article 17: Information Exchange

1. Member countries must facilitate exchange of information from all existing public sources related to sustainable protection and use of biodiversity while taking specific needs of developing countries into consideration.

2. Information exchange must include exchange of results of technical, scientific, social and economical research and also information related to training, assessing and evaluating plans, specialised knowledge, native and traditional knowledge and also in combination with technologies mentioned in paragraph 1 of article 16. Information exchange should also, if possible, include returning information to its origin.

1.8.14. Article 19: Application of biotechnology and distribution of its advantages

1. Each member country must, in an appropriate way, take legislative, administrative or policy making measures to provide effective participation in research activities related to biotechnology by that group of member countries, especially developing countries which are supplying genetic reserves for these researches and, if possible, the countries themselves.

2. Each member country must take every scientific measure to encourage and promote equal and fair access for member countries, in particular developing countries, to results and advantages of

biotechnology based on genetic reserves which have been supplied by member countries. This access must be based on conditions mutually agreed upon.

3. Member countries must debate and make clear the need for a protocol and its form so that suitable methods and measures for the safe and healthy transfer and utilisation of LMOs, which are the result of biotechnology and may leave undesirable effects on sustainable use and protection of biotechnology, are defined.

4. Each member country, directly or through a legal or real entity under its authority which presents organisms as mentioned in paragraph 3 above, must make available any existing information regarding the application of those organisms and safety regulations for their application by member countries. Also, member countries should make available any existing information on the potential effects of specific organisms which those organisms can have in relation with the member country importing them.

Appendices 2 to 9 are related to
biosafety risk assessment guidelines

Appendix 2

Laboratory instructions for LMOs

2.1. Good laboratory practices

- Never do direct mouth pipetting of infectious or toxic fluid;use a pipettor.
- Plug glass and other pipettes with cotton .
- Do not blow infectious materials out of pipettes .
- Do not prepare mixtures of infectious materials by bobbling expiratory air through the liquid with the pipette .
- Use an alcohol moistened pledget around the stupper and needle when removing a syringe and needle from a rubber stoppered vaccine bottle .
- Use only needle-locking hypodermic syringes .Avoid using syringes whenever possible .
- Dispose excess fluid bubbles from a syringe vertically into a cotton pledget moistened with disinfectant ,or into a small bottle with a cotton pad .
- Before and after infecting an animal ,swab the site or injection with disinfectant .
- Sterilize discarded pipettes and syringes after use .
- Before centrifuging ,in spect tubs for cracks .
- Use centrifuge bottles with tight lids .
- Wrap a alyophilized colture with disinfectant-wetted cotton before brakeing . Always wear gloves and lab cote .
- Never live a discarded tray of infected material on unattended .
- Sterilize whole contaminated discarded materials .
- Periodically ,clean up deep-freezes and refrigerators in which cultures and stored to removed broken ampoules or tubes .Use rubber gloves and respiratory protection during the cleaning .
- Handle diagnostic serum specimens carrying a risk of infectious hepatitis with rubber gloves .
- Develop the habit of keeping your hands away from your mouth, nose ,eyes and face .This may prevent self in inoculation.
- Avoid smoking ,eating and drinking in the laboratory .
- Make special precautionary arrangements for respiratory ,oral ,intranasal ,and intratrachael inoculation of infections material.
- Give preference to operating room gouuns that fasten at the back .
- Evaluate the extent to which the hands may become contaminated with some agents and operations ,forceps or rubber gloves are available .
- Laboratory clothing should not be worn taken to the dining room , library and other non-laboratory areas .

- Decontamination of work surface is a must .
- Shake broth cultures in a manner that avoids wetting the pug or cap .

Aerosol Minimization

Because of their entrapping nature , pose special problems in that the laboratory worker maybe unwillingly exposed .Procedures which produces aerosol include :

- Grinding
- Blending
- Sonicating
- Resuspending Packed cells or viruses
- Inserting a hot loop into a culture
- Centrifugation
- Flaming an inoculation loop so that it break.
- Forcefull rejection of fluid from a pipette or syringe .
- Releasing the vacuum on a freeze dryer .
- Opening a tube within which the air pressure may differ from that of the room such as may occur when the tube is opened at a temperature different from which it was sealed .

2.2. Laboratory instructions for LMOs (Living Modified Micro-organisms)

Laboratory instructions are divided into the three levels of laboratory risks as follows:

2.2.1. First level, laboratory risks

2.2.1.1. Biosafety

Laboratory risks of the first level or degree are applied to experiments with the least amount of risk. Such experiments must be carried out thoroughly according to practical standards compiled for experiments involving conventional microorganisms. Pathogenic microorganisms must be experimented according to appropriate restrictions and necessary precautions, including training for people and strict observation of instructions. Laboratory staff should be completely familiar with all pathogenic microorganisms under experiment and also with different classifications of biosafety.

2.2.1.2. Contact with IBC

All laboratories, which are considered as least risky, must at first be referred to IBC for approval in accordance with appropriate containment standards for plants, microorganisms, and animals. In the absence of IBC, for organisational support of experiments, responsible staff must approach related institutions (section A) After conducting the necessary examinations, IBC makes the final

decision regarding which category the said experiments fall into. No experiment covered by this directive shall start before the suggested project has been approved by IBC.
For those experiments which are considered as belonging to the first category of laboratory risks (section B), additional changes in their sequences in any part of the system under experiment, which might endanger it, must be referred to IBC for renewed approval because of a potential change in the level of risk.
In the second stage, the corrected project proposal must be presented to IBC along with the preliminary project proposal, whereupon amendments are reviewed and decisions are made to see whether the amendments would put the experiment in a higher level of risk or not. Related institutions must be informed about recent decision makings by IBC.

2.2.1.3. Experimental features of the first category of laboratory risks

1. In experiments involving those microorganisms which naturally exchange genetic material and in which the donor and the recipient both belong to the same species, or in which the donor is capable of transferring genetic material under natural conditions. A list of such combinations is found in Section E.

Work with previously approved host/vector systems (Section F) and in which the donor DNA exhibits all of the following properties:
It must not be one of those microorganism which are pathogenic for humans, animals or plants;

- It must not contain more than 2/3 of the total viral gene, and the experiment must not end in the reproduction of live viruses;
- Experiments should be conducted on a gene which causes the coding of a protein which regulates growth in cells of mammals; the protein should not be cytotoxic or contain toxic protein for vertebrate per LD50 < 100µg/kg (Section G)

2. Protoplast fusion among non-pathogenic microorganisms or between plant cells;
3. Fusion of cells derived from animals which do not lead to the formation of living microorganisms hybrodima without viral induction (such as EBV in the production of monoclonal antibodies).

2.3. Second category of laboratory risks

2.3.1. Biosafety

The second category of laboratory risks includes a lower degree of risk as compared with level 3 for society and environment. All experiments on organisms are carried out according to this level of restriction, which is presented in section C. Although it is possible to apply more safety precautions or higher levels of physical restriction (especially conditions of restriction in places designed for manipulated animals) related to the DNA or its segments, which might create risks or illness, all stages of experiment will be conducted under the supervision of IBC.

2.3.2. Contact with the Institutional Biosafety Committee (IBC)

The project manager or the official responsible for its research has the primary responsibility to determine the degree of the potential risks of the experiment and related appropriate precautions according to the levels of risk. The project proposal should be sent to IBC by the project manager for decision making. IBC must assess the proposed working conditions, methods, degrees of restriction, and the capacity of the project. Seeing the results of risk assessment, IBC may determine other specific requirements for the work. Experiment will start only after IBC approval. IBC will then send the proposed projects and their assessment to NBC to obtain permits.

2.3.3. Experiment features for the second degree of laboratory risks

1. Work with previously approved host/vector systems but in which the genetic material inserted exhibits one or more of the following properties (Section – F, NBC Authorized Host/Vector Systems):

Protein codes which are responsible for the regulation of metabolism, growth and cell division;

- ❖ It is pathogenic;
- ❖ It is a sequence of DNA or DNA derived from microorganisms which are pathogenic for humans, plants or animals.

2. Work with unfixed host/carrier (host/vector) systems;

3. Complete genetic changes in the plant;

4. Substitution of the genome of ovocysts, zygotes and young germ cells in any way which results in the creation of new microorganisms;

5. Genetic manipulation on a living animal which results in the creation of new organisms.

2.4. The third category of laboratory risks

2.4.1. Biosafety

The third category of laboratory risks is a considerable class of risks for the laboratory staff, the society and the environment. Gene therapy and experiments whose risks are as yet unknown fall into this category. Suitable levels of restriction depend considerably on the innate nature of the experiments and the results of risk assessment.

2.4.2. Contact with IBC

IBC carries information from researchers to NBC. In addition, it will send proposals, assessments and necessary recommendations. Work cannot start without approval from IBC and NBC.

2.4.3. Experimental characteristics of the third category of laboratory risks

Application of pathogenic genes to microorganisms; (Section F)

1. Transfer of the total viral genome, viroids or genetic particles, which have been identified as generating infections in humans, plants and animals. In general, application of gene sequences less than 2/3 of each complete viral gene, and work on cases where the genetic matter involved lacks a vital part suitable for the action of oprons for cloning, or the packaging of new viruses fall into this category. In such laboratory conditions, the revival of living pathogenic viruses is rejected.
2. Recombination of complete viroid or viral genome or genetic particles which result in infection or pathogenicity in nature;
3. Changing the range of the host in order to create infection or pathogenecity;
4. Work with viral vectors which can cause infection in human cells;
5. Work with microbial hosts or vectors which can cause diseases in humans, animals and plants, except for those which have been included in Section F as approved hosts and carriers;
6. Application of genetically manipulated DNA sequences which are proteins responsible for growth or toxic for human cells;
7. Work which involves the following toxic and dangerous processes:

    - DNA encoding for toxins with LD50 < 100μg/kg which indicate a high level of gene expression regardless of how much of the patein toxin protein is coded (Section G);
    - Undefined DNA from microorganisms producing toxins, which can possibly have a sequences producing undefined toxin;
8. Use of a helping vector combination - incomplete virus, which has a high tendency to produce complete recombinant viruses.
9. Injection of genetic matter to the embryo of genetically modified animals for the production of virus.
10. Promotion through cloning:
    - Gene therapy through genetic modifications.

2.5. Undefined experiments

Certain experiments do not fall into categories 1, 2 and 3 because the type of the matter with which the experiment is carried out is unclear; therefore, to determine the level of such combinations under this directive they should be treated at least as risk category 3.

Sustainability of any kind of research work depends on commitment regarding a change in the direction of research, in the direction of new information or in the direction of observing reviewed directives. The project manager must present projects to IBC for more consideration and recommendations before final approval, or when informed of any change in a considerable factor

(in particular physical and biological restrictions) which may in turn introduce new risks that may fall into other classes of biosafety categorisation.

Those researchers who wish to restrict access to specific information for several committees must attach “commercial confidential” labels on related files.

Appendix 2 - Section A

2.A.1. Duties of IBC

One of the major duties of IBC is studying research projects from the point of view of biosafety. IBC must assess any project within a maximum of 40 days. Regarding the percentage of damage, points of 1, 2 or 3 are given. In order for research forms to be identical and in order to facilitate the stages of their assessment by different biological committees, a particular pattern has been developed to prepare research projects proposals, which everyone must follow.

2.A.2. Preparing research project proposals, and how they are approved based on biosafety regulations

For the execution of the following activities, corresponding permits are obtained through different ways: genetic modification of plants or animals on a laboratory scale, release of LMOs and related products (efforts on field scale) which are a result of level 1 activities, and commercialisation of GMOs products.

Before starting a project, the proposal should be presented to IBC. If the said project is to be executed in more than one organisation, the IBC of those organisations must receive a draft of the project, which also mentions the multi-organisational nature of the project. The project manager should prepare three copies of the proposal. IBC refers one copy to NBC, a copy remains for assessment in IBC and a copy remains as reference in the files.

If IBC ranks the project 1 or 2 (weak or average in the categorisation of harmful biological factors), work can start after approval from IBC; however, if the designated number is 3 (includes dangerous harmful biological factors), whether the project starts depends on approval from NBC. IBC and NBC must also control required physical restrictions while the project is being implemented.

2.A.3. Project Title and Objectives

Notable and exceptional intents should be indicated in the title or under objectives.

Short and long term objectives should be stated separately if the research work proposed is likely to continue for several years.

Distinguishing immediate from remote aims, together with providing a timetable of activities (under the Methodology and Protocol section), will permit the IBC to assess the proposal in sequence. As such, where the entire proposal does not merit endorsement (or where endorsement of later stages depends on the results of early work), the IBC may approve particular initial stages rather than having to reject the proposal as a whole, allowing preliminary work to begin as the proposal is

revised (or as results are compiled). Researchers should clearly indicate which parameters of the work require primary endorsement.

Ideally, the objectives should communicate, to some considerable extent, a service to the welfare of the community or the environment, local or global. Justify hazardous or high-risk work by relating why the ends cannot be attained through conventional or alternative practices that offer less risk.

2.A.4. Methodology and Protocol

Only a concise--but thorough--description of the main experimental procedures is required. A timetable of activities should be included to allow the IBC liberty in assessing the proposal in sequence. Detail any special precautions/safeguards to be adopted, with references to the specific risks and concerns identified in initial risk assessments.

2.A.5. Materials

For work with multiple donor DNA, hosts and/or vectors, indicate when and how each shall be used. As with providing a time table of activities and distinguishing short and long term aims, clarifying these points will allow the IBC to assess the project in stages or modules.

Some details of the relevant history of prior work with components of the biological system should be provided, including track records of safety and biological containment. Indicate whether the DNA, hosts and vectors concerned are commonly or rarely subjected in regulated work. Above all, identify any problem DNA, host or vector with a history of unsafe use (e.g. often realizing the hazards determined in initial risk assessments). If related host/vector systems have been field tested or released, a summary of the results/analysis would be appropriate.

2.A.6. Donor DNA

The origin of all donor DNA should be specified - scientific name and strain of the biological source(s), whether procured or constructed by the research team, and if procured, who made it. Researchers must account for how donor DNA was or will be constructed/cloned and should make clear as to whether several genes or species are involved. Some details of the biological source(s) are appropriate, for instance, whether a local or exotic strain and patterns of local distribution, particularly if imported.

All important characteristics of donor DNA should be listed. Uncharacterized donor DNA should be so indicated, otherwise the IBC shall expect a review of the known functions of target genes through to the known functions of the proteins encoded.

2.A.7. Host Organisms or Tissues

The scientific name and strain of all host organisms and biological sources of host tissues need to be specified. In addition, regarding host tissues, researchers should briefly account for how the

tissue cultures were or will be prepared/grown. For work using as hosts, genetically modified or constructed organisms also include a review of the genetic manipulation work involved.
List all substantial hazards conveyed by host organisms or tissues, particularly, regarding pathogenicity and infectivity. Other details of the hosts may be appropriate, for instance, geographic distribution and biologically active compounds secreted.

2.A.8. Vectors

Work with biological vectors requires a concise description of the known vector properties (e.g. host range) in addition to nomenclature or identification. As with host organisms/tissues, list all substantial hazards borne, particularly, regarding pathogenicity and infectivity. For vectors which are genetically modified or constructed (e.g. retroviral vectors), provide some details of the construct and methodology involved. A genetic map would also be appropriate.
In the case of electroporation, and other electrical or mechanical methods for transfer of donor DNA into hosts, only a brief statement is expected.

2.A.9. Host/Vector System(s)

Researchers should elaborate, somewhat, on the predicted stability of introduced genetic traits (including, the localization and copy number of target genes, introduced gene expression, frequency of reversion to wild type characteristics) and the form of heredity of the target phenotype(s). Where applicable, also assess the likely stability of plasmids, phages, viruses, etc. in host organisms/tissues.
Identification characteristics or markers should be detailed for IBC and NBC references.
A concise - but thorough - risk assessment for the host/vector system(s) proposed is required. Specify whether the level of biological containment provided classifies each system as **'NBC Authorized'** or **'Not Authorized'**.

2.A.10. Auto-Ecology

Under 'Ecological Context', substantiate the level of biological containment provided by each host/vector system involved. Researchers need to briefly assess the viability of host/vector systems in the open environment (particularly, the natural tendency for invading wild populations, and for developing into pests or weeds) and indicate any factors (including genetic modifications) which might limit growth, reproduction and survival. Additionally, the IBC shall expect a review of the natural crossing possibilities to, or possibilities for exchange of genetic material with related species/natural variants.
Any details of the evolutionary potential should be presented under this heading.

2.A.11. Laboratories and Facilities

Clarify which phases of the work will be conducted in each of the laboratories and facilities identified, specify the certified containment level and describe any special containment/safety features offered. Researchers must indicate whether permission has already been obtained for use, and if so, indicate the period of time awarded and attach written confirmation.

2.A.12. Details of Personnel

Attach a CV for each personnel involved in the proposed work, covering personal qualifications (e.g. education, training, professional history) and relevant research experience. Ideally, the general responsibilities of each individual should also be noted, so that the IBC may assess, on a case-by-case basis, whether personnel are adequately prepared and capable to handle the duties assigned.

It is essential that brief medical histories of all personnel at risk be included.

2.A.13. Commercial-in-Confidence

Researchers who wish to restrict access to information of commercial significance (e.g. trade secrets or confidential business reports) provided to the IBC and NBC in projects proposals, should mark relevant material or portions **"Commercial-in-Confidence"**.

2.A.14. Draft of research proposal on laboratory scale

Research proposals include several parts. In the beginning, the following form must be filled in:

1. Project name:
2. Name of principal institution/research centre/laboratory where project is conducted Address: Phone: Fax: Email: Web site:
3. Full name of project manager: Address: Phone: Fax: Email:
4. Full names of project staff: Address: Telephone: Fax: Email: Staff details: Staff name and experience: Duties and responsibilities of the staff in detail:
5. Project description
6. Date of commencement:

7. Expected date of completion: 8. Which category of biological harmful groups does this project belong to? Group 1 ? Group 2 ? Group 3
9. Materials and methods:
10. Details of biological systems applied to this project: • The origin of the considered DNA • The geographical distribution of the organism giving DNA • Characteristics of the considered DNA • Type of organism • Type of host • Applied carriers • Methods of transferring DNA to the host • Characteristics of the host / carrier system and their continuous study • Autoecology of each host / carrier system and the study of their possible combination with related species • Level of physical restriction
11. A history of previous research done on the applied biological system
12. Name of other institutions/research centres/laboratories involved in the project For each institution: Address: Phone: Fax: Email: Web site:
12. Permit for using laboratory facilities 13. Full name of laboratory head: 14. Signature of laboratory head:
Signature of project manager: Date:

2.A.15. In case of work on plant systems the following form must be added to the first form described in this section

1. Details of the considered biological system to be used: A. Is the plant to be used harmful and dangerous? Yes ? No If the answer is yes, please answer the following ecological questions: ✓ The plant reproductive cycle and its evolutionary potential ✓ Distribution, reproduction and protection of the plant in open environments related to the cultivation of the plant ✓ Factors limiting the growth, reproduction and survival of the plant ✓ The possibility of its natural combining with wild populations of the same species ✓ Harmful characteristics of the species B. Are microorganisms used in this study? Yes ? No ? C. Is the above microorganism harmful to humans, animals or plants? Yes ? No ? If the answer is positive: ✓ Pathogenic and infectious characteristics or potential for the production of

certain toxins in the microorganism ✓ The type of the method of transfer
2. More details on work methods in this plant section A. Materials used to culture that microorganism and an explanation of the stages of sterilization; B. Design of project manager for the cultivation of the genetically modifies plant C. Design for containing these plants D. Design for containing materials related to these plants and also: Spores Seeds Pollens Edible parts of the plant
3. Design for the conditions of disposing of the waste parts of the plant (including some side plant products)
4. Details regarding equipment and facilities needed for assessment
5. Any additional necessary information

2.A.16. In case of work on animals the following form must be added to the first form described in this section

1. Details of the particular laboratory animal for this project ▪ Scientific name of the animal - Rank of the animal - Classification of the animal ▪ Is this a local or native animal? If the answer is no, please specify the original place of the organism. ▪ The number of laboratory animals needed for each experiment ▪ The number of animals needed for the whole project
2. Details of genetically modified microorganisms ▪ Is genetic manipulation on somatic cells or on germinal cells? ▪ Characteristic of the DNA under experiment ✓ What is its origin? (Which biological resource has it been provided from?) ✓ Used carrier ▪ History of prior application of the genetically modified sample ▪ Methods of DNA transfer Electrical Mechanical Application of a biological carrier ▪ History of prior research projects in which this biological carrier has been used. ▪ Suggested sources related to the level of containment ▪ A study of the method of the suggested genetic modification to that animal ✓ Reproductive potential of the animals under experiment ✓ Assessment of the potential and ways of heredity in that living modified organism
3. Place of keeping genetically modified animals 4. Choice of a suitable level of containment for work on that animal
5. Number and type of other animals existing in that place
6. The nature of other research going on in that place/laboratory, whether it is work on infectious diseases of animals or research on another genetic modification.

2.A.17. IBC Assessment of Proposal for Laboratory work of LMO

1. Name and full professional address of Project manager submitting proposal.	**2. Name(s) of other project managers responsible for the project. please give their professional addresses if different from that in'1'**
Tel: **Fax:** **E.mail:**	**Tel:** **Fax:** **E.mail**

3.	**Title of project.**	
4.	**Intended date of commencement**	
	Expected date of completion.	
5	**Assessment of the Project Proposal**	
5.1	**Project Objectives & Methodology:**	**Approved [ ] Not Approved [ ] Inconclusive [ ]**
5.2	**Biological System:**	**Approved [ ] Not Approved [ ] Inconclusive [ ]**
5.3	**Site or Location:**	**Approved [ ] Not Approved [ ] Inconclusive [ ]**
5.4	**Safeguards and Contingency Plans:**	**Approved [ ] Not Approved [ ] Inconclusive [ ]**
5.5	**Timing and Period of Work:**	**Approved [ ] Not Approved [ ] Inconclusive [ ]**
5.6	**Details of Personnel :**	
	• **Experience and expertise**	**Approved [ ] Not Approved [ ] Inconclusive [ ]**
	• **Training and instruction**	**Approved [ ] Not Approved [ ] Inconclusive [ ]**
	• **Health**	**Approved [ ] Not Approved [ ] Inconclusive [ ]**
	Other (please specify)	**Approved [ ] Not Approved [ ] Inconclusive [ ]**

6. Assessment of supplementary information on Plant Work	
7. Assessment of supplementary information on Animals	
8. Risk category as assigned by the IBC	**Category 1 [ ] Category 2 [ ] Category 3 [ ]**
9. Laboratory Containment	**C1 [ ] C2 [ ] C3 [ ]**
10. Animal Houses Containment	**C1A [ ] C2A [ ]**
11. Plant Glasshouse Containment	**PH1 [ ] PH2 [ ] PH3 [ ]**

SECTION B –IBC RECOMMDATION

12. The project has been reviewed by the IBC as assessed above and the Committee does not endorse [ ] the work as proposed; does not endorse [ ] the work with the following provisos.
i) Provide additional information/documents on **ii) Follow conditions/amendment in your research as follows**
13. The following special provisions must be adopted

SECTION C – IBC REQUESTS MBC

14. The project proposal has been reviewed by the IBC and as assessed above, the Committee requires and requests MBC specific advice/action regarding the following
15. Signature of IBC Chairperson
Date / /

Appendix 2 - Section-B
Requirements for Containment Level C1

2.B.1. A Note on Physical Containment

Containment Levels C1, C2 and C3 are the different classes or grades of physical containment which may be afforded by genetic manipulation laboratories/facilities. The fundamental objective of physical containment* is to prevent undue exposure of the laboratory worker, the community or the environment to regulated material and as such, is achieved primarily through the adoption of proper laboratory procedures and containment equipment. Special laboratory design provides a secondary means of protection and figures prominently in the containment of the more hazardous, genetically manipulated agents.

Three standard combinations of laboratory procedures, containment equipment and laboratory design give rise to the three basic levels of physical containment, detailed hereinafter. Where alternative combinations or supplementary precautions may better address the concerns of research work at hand, the project supervisors and the IBCs involved shall be primarily responsible for the preparation of specific and varied provisions, as is appropriate (e.g. immunization requirements, microwaving of infectious wastes, provisions for a central vacuum system).

* Biological containment is a rather different matter but may often supplement physical containment.

2.B.2. Laboratory Procedures

1. When work is in progress, laboratory doors are closed and entrance is restricted at the discretion of the project supervisor.
2. Personnel wear, over street clothes, laboratory coats or gowns which are removed before leaving the laboratory.
3. Eating, drinking, smoking and applying cosmetics are all prohibited.
4. Food and drinks may not be stored in the work area at any time.
5. Mouth pipetting is prohibited; mechanical pipetting instruments are used instead.
6. All procedures are performed cautiously to minimize the creation of aerosols. Use of sonication or vortex machines, and other procedures which tend to generate aerosols, should be done in biological safety cabinets.
7. Personnel wash their hands with liquid soap and warm water after handling experimental organisms and cultures, and before leaving the laboratory.
8. Instruments used in culture work or with contaminated material are to be disinfected after use, if the instruments are not readily steam sterilized. For glassware, a hypochlorite solution made up

with 5000 ppm of chlorine (dilute household bleach 1:8 and allow to react for at least 30 minutes), prepared daily, provides a suitable disinfectant.

9. Floors, work benches and surfaces are decontaminated with a suitable disinfectant after each session and immediately after any spill of viable material. Other than the basic hypochlorite solution, disinfectants must be prepared and used according to the manufacturer's instructions.

10. All microbiological wastes are decontaminated (preferably, autoclaved) before disposal.

11. Regulated materials are packaged within securely- sealed double containment units (section 5.1) before being removed from the laboratory to autoclaves or rooms and facilities elsewhere. These units must be opened to allow for thorough penetration of steam during autoclaving.

12. An appropriate pest control program is in effect, as supervised by a licensed pest control operator.

Please Note: All work to be performed in a C1-level laboratory must observe C1-level procedures regardless of whether the work involves genetic manipulation.

2.B.3. Containment Equipment

1. Biological Safety Cabinets are provided (particularly, where laboratory operations tend to generate considerable amounts of aerosol). As terms of reference, specifications for and use of biological safety cabinets shall comply with the standards:

- Biological Safety Cabinets (Class I) for Personnel Protection;
- Laminar Flow Biological Safety Cabinets (Class II) for Personnel and Product Protection;
- Biological Safety Cabinets - Installation and Use (which also addresses the problem of frontal airflow disturbances and details protocols for decontamination);
- There is close access to a steam steriliser.

2.B.4. Laboratory Design

1. A closet, for laboratory coats and gowns, is provided next to the exit.

2. Room and work surfaces are smooth, impervious and resistant to attack by standard acids, alkalis, organic solvents and moderate heat.

3. The laboratory can be easily cleaned and thoroughly decontaminated; gaps and spaces between room surfaces, benches, furniture and equipment are accessible for wipe down. Ideally, benches, furniture and equipment should be anchored and sealed to room surfaces. False ceilings should be avoided.

4. Laboratory windows that open are fitted with fly-screens.

5. The laboratory entrance is labeled with an official sign designating the certified level of containment (available from the IBC, pending certification), with the universal biohazard symbol and, when work is in progress, with a notice detailing the entry requirements and procedures.

Names and contacts (e.g. postal address, telephone and pager number) of the responsible authorities should be clearly indicated.

6. Signs are posted within the laboratory, outlining the appropriate operating procedures, contingency plans and instructions for upkeep and maintenance.

7. Freezers, refrigerators, liquid nitrogen tanks and other appliances for the storage of recombinant DNA or of manipulated genetic material, are labeled with the universal biohazard symbol.

Appendix 2 - Section C
Requirements for Containment Level C2

Containment level C2 provides a moderate level of physical containment through an even blend of proper laboratory procedures, suitable containment equipment and special laboratory design.

2.C.1. Laboratory Procedures (all of containment level C1, and the following...)

1. Persons enter the laboratory for cleaning, audits, repairs and other activities at the discretion of the project supervisor (or the biological safety officer) and only after laboratory surfaces have been properly disinfected.
2. Laboratory coats, gowns and protective clothing are placed in sealed bags or boxes (which may be readily steam sterilized), and brought to an autoclave for decontamination after each session and before laundering. Laboratory clothing shall not be worn outside the laboratory.
3. Sonication, Vortex and other machines/instruments that generate aerosols are kept and used only in biological safety cabinets.
4. Work surfaces and biological safety cabinets are decontaminated with formaldehyde gas after each session and after major spills of viable material.
5. Laboratories are inspected and serviced periodically. Screens, filters, ventilation and drainage systems are cleaned regularly.

Please Note: No other work must be done simultaneously with work requiring C2 levels of physical containment.

2.C.2. Containment Equipment (all of containment level C1, and the following...)

1. Independent room exhaust fans are installed to achieve room pressure control. Exhaust fans must be equipped with a variable-speed drive and should be able to maintain a minimum air pressure differential of 50 pascals. Discharge should be through a high-efficiency exhaust filter.
2. Exhaust filters are HEPA class, outfitted with a metal separator and rigged to a supplementary prefilter, of the same specifications as replacement air filters (#3). Exhaust filters will have a modular, metal framework and will not make use of fluid or grease seals. As the norm, unit specifications must comply with Australian Standards 1324 clause 4.3.1 (b) and performance audits must observe A.S. 1807.6 testing guidelines.
3. Channels to draw in replacement air are engineered with contractible apertures and high-efficiency filters that prevent back-flow. As the norm, filter specifications must comply with Australian Standards 1324 for Type 1, Class A or Class B models, and have at least a 90% arrestant efficiency against Test Dust No. 2 under A.S. 1132.5 testing guidelines.

4. An airlock is provided at each access, to maintain a reduced laboratory air pressure during entry and exit. The basic design incorporates a pair of outward-opening doors, arranged in sequence so that a small chamber rests in-between. Each door must be self-closing and fitted with a viewing panel. The outer door requires a security lock.

5. Manometers are installed to monitor air pressure drop across exhaust prefilters and a Magnehelic type differential pressure gauge is outfitted to measure room negative pressure. Ideally, climate-control switches, exhaust fan speed dials and replacement air aperture-adjustment controls should be affixed next to the gauge to support manual room pressure control.

6. Special protective clothing, head covers, overshoes, gloves, molded surgical masks and respirators are provided as required.

2.C.3. Laboratory Design (all of containment level C1, and the following...)

1. The laboratory is isolated from and does not open onto public walkways.

2. Laboratory windows are closed and sealed; walls, ceilings and floors are substantially airtight.

3. Access to roof spaces above the laboratory, and to other enclosing or contiguous voids, is restricted so as not to unwittingly compromise structural integrity.

4. Room and work surfaces are resistant to attack by disinfectants, gases and other agents used in the laboratory.

5. Ventilation designs allow the laboratory to operate at a requisite room pressure of 50 pascals below external air pressure, when all doors are closed; during entry and exit through airlocks, internal air pressure shall remain at least 25 pascals below external pressure.

6. Fans, filters and ventilation shafts are positioned to facilitate inspection and performance audits.

7. Architectural and structural requirements accommodate the need for laboratory pressure to be maintained below external air pressure. An airlock is provided at each access. Laboratory surfaces and windows can withstand the variable air pressure loads imposed by ventilation fans during all modes of operation.

8. The various sensing devices set off or sound an alarm to indicate loss of room pressure control.

9. A fan coil cooling system, using chilled water or a refrigerant as the cooling medium, is in place, where exhaust ventilation rates alone cannot sufficiently offset room heat loads. Care must be observed in setting up the system to avoid airflow disturbances in front of biological safety cabinets.

10. The laboratory can be sealed-off to allow for decontamination of the entire room with formaldehyde gas. Ventilation shafts, exhaust ducts and replacement air apertures can be closed-off (e.g. by way of dampers and cover plates). Ideally, provisions for remote power switches should be made to allow for the safe generation of fumes. Systems are in place to treat formaldehyde gas, generated for decontamination of work surfaces and biological safety cabinets, to allow for safe discharge into atmosphere.

Appendix 2 - Section D
Requirements for Containment Level C3

Containment level C3 offers a higher level of physical containment and necessitates much more rigorous conditions than does containment level C2. A medley of additional engineering and architectural requirements is warranted —ranging from the installation of various and duplicate items of machinery inside the work area, to the special design of laboratory ventilation and drainage systems, to be separate from those servicing the rest of the complex. Heightened laboratory performance would likely be extended to include directional airflow and emergency life-support. Further provisions for personnel safety might involve advanced protective clothing (e.g. one-piece positive pressure suits) and chemical showers. Additional operating procedures must be adopted as well, complementing the equipage and construct of C3-level facilities.

Institutions, with plans to support C3-level laboratories, must confer with the NBC to determine and fulfill the relevant and extensive requirements, as dictated by the nature of existing risks and concerns. No discrete criteria are given.

Appendix2 - Section E
Biological Containment

2.E.1. Organisms recognized to exchange DNA through known physiological processes

Members of any of the following sub-lists are recognized to exchange DNA through known physiological processes, unless otherwise specified. Researchers should keep in mind that these lists are not exhaustive and feel free to suggest to the National Biosafety Committee, for consideration, other pairs of organisms which have been shown or observed to exhibit natural exchange of genetic material, and merit inclusion to this list.

Unless otherwise specified, work with organisms that naturally exchange genetic material is considered 'exempt' under Category 1, if the donor and the recipient species are members of any of the following sub-lists, and provided that the vector(s) do not incorporate DNA from organisms outside that particular sub-list.

Sub-list A
Alcaligenes (2)
Campylobacter jejuni (2)
Campylobacter coli (2)
Campylobacter fetus (2)
Citrobacter (including Levinea)
Enterobacter
Erwinia
Escherichia
Klebsiella
Pseudomonas aeruginosa
Pseudomonas fluorescens
Pseudomonas mendocina (3)
Pseudomonas putida
Rhizobium (2)
Salmonella (including Arizona)
Shigella
Serratia marcescens
Yersinia enterocolitica

Sub-list B
Bacillus amyloliquefaciens
Bacillus aterrimus
Bacillus globigii
Bacillus licheniformis
Bacillus nato
Bacillus niger
Bacillus pumilus
Bacillus subtilis
sub-list C
the following:

Streptomyces aureofaciens
Streptomyces coelicolor
Streptomyces rimosus
into Streptomyces sanguis

Sub-list D
Streptomyces cyaneus
Streptomyces griseuss
Streptomyces venezuelae

Sub-list E
one-way transfer of:
Streptococcus mutans or
Streptococcus lactis DNA
into *Streptococcus sanguis*

Sub-list F
Streptococcus faecalis
Streptococcus mutans
Streptococcus pneumoniae
Streptococcus pyogenes
Streptococcus sanguis

Sub-list G
Bacillus cereus
Bacillus thuringiensis

Appendix 2 - Section F

NBC Authorized Host/Vector Systems

The National Biosafety Committee regards and evaluates host/vector systems primarily on the basis of the potential for the aggregate to survive and to multiply in the open environment or generally, the viability of the system in conditions that may be encountered beyond that of the source laboratory. These biological containment and general biosafety concerns also take into consideration the natural tendency for the vector(s) to be transferred to non-target hosts, whether the conditions be, among others, the laboratory setting, field test plots or the immediate surroundings. An index of currently approved host/vector systems, patterned after the 1993 Australian GMAC list, follows.

Host/Vector Systems approved by the National Biosafety Committee on the basis of biological containment provided:

Class	**Host**	**Vector**
Bacteria	*Escherichia Coli* K12 or a derivative thereof which does not contain conjugative plasmids or generalised transducing phages.	1. Non-conjugative plasmids 2. Bacteriophage - lambda - lambdoid - F1 (e.g. M13)
	Bacillus Subtilis or *Bacillus licheniformis*; Asporogenic strains with a reversion frequency of less than 10^{-7}	Indigenous Bacillus plasmids and phages with host ranges not inclusive of *B. cereus* or *B. anthracis*
	Pseudomonas putida stain KT 2440	Certified plasmids: pKT262, pKT263 and pKT264
	Certified Streptomyces species: *S. coelicolor* *S. lividans* *S. parvulus* *S. griseus*	1. Certified plasmids: SCP21, SLP1, SLP2, PIJ101, and derivatives thereof 2. Actinophage phi C31 and derivatives thereof
Fungi	Specified strains of Neurospora crassa modified to prevent aerial dispersion	No restriction
Tissue culture	Mammalian, including human cells	Non viral or defective viral vectors (including retrovirus or retroviral/helper combination) that cannot infect mammalian cells.
	Plant cell culture	Disarmed non-tumorigenic Ti plasmid vectors in *Agrobacterium* tumefaciens and non-pathogenic viral vectors.

Source: Guidelines for Small Scale Genetic Manipulation Work, January 1993, GMAC, Department of Administrative Services, Australia.

Special Provision:

Situations in which the donor DNA is introduced into the host through electrical, mechanical or any other means without the use of biological vectors, shall be regarded and treated, by the IBC and the NBC, as approved host/vector systems provided that all of the following conditions are realized:

- The host represents any of the above approved host organisms or tissue cultures;
- The donor DNA is not derived from microorganisms which are root causes of diseases in humans, plants or animals;
- The donor DNA represents or comprises no more than 2/3 of any complete viral genome and is employed in such a manner as to disallow the possible regeneration of live viruses (as opposed to such work wherein the hosts carry the missing segments of viral genomes or whereby regeneration is made possible under the context of ensuing propagation sequences);
- The donor DNA does not code for proteins, which regulate the growth of mammalian cells (e.g. product of oncogenes), for cytotoxic proteins, or for toxins, to vertebrates, with an LD50 of less than 100 µg/kg.

Such systems may be considered for an exempt status under Category 1 work.

Appendix 2 - Section G
High-Risk, Virulent Toxins

Laboratory genetic manipulation work which entails the cloning of gene sequences (or the breeding and propagation of microorganisms carrying such sequences) coding for toxins, to vertebrates, with an LD50 of less than 100 µg/kg must be authorized by the National Biosafety Committee before any work is allowed under way. A list of some such lethal toxins follows.

- Abrin
- *Bacillus anthracis* lethal factor
- *Bordetella pertussis* toxin
- Cholera - see *Vibrio cholerae*
- *Clostridium perfringens* epsilon toxin
- *Clostridium tetani* toxin
- *Corynebacterium diptheriae* toxins
- *Escherichia coli* heat labile (LT) enterotoxin and LT-like toxin
- Oxygen-labile haemolysins such as streptolysin O
- *Pasteurella pestis* murine toxins
- *Pseudomonas aeruginosa* exotoxin A
- Ricin
- *Shigella dysenteriae* toxin
- *Staphylococcus aureus* determinants A, B and F, alpha and beta toxin, and exfoliative toxin
- *Vibrio cholerae* (comma) toxin and toxins neutralised by antiserum monospecific for cholera toxin (e.g. heat labile toxins of E. coli, Klebsiella and other related enterotoxins)
- Yersinia enterocolitica heat stable toxin

The NBC would appreciate any notices from researchers of other virulent toxins determined to have an LD50 of less than 100 µg/kg. The NBC requests supporting data on such toxins in order to confirm and accredit the findings.

Appendix 3
Specific needs for work in certain genetic experiments

3. Specific needs for work in certain genetic experiments

3.1. Experiment and work with dangerous genetic particles

Separation of genetic parts to use in experiments on carrier-host systems can involve many risks and hazards, depending on the type of genetic matter being used. The following cases can be particularly dangerous while under experiment:

- DNA which codes various proteins, directly or indirectly, to regulate metabolism, growth and cell division;
- Gene which codes cell death or pathogenic toxins death;
- Oncogenes, in particular those which show a high degree of gene expression or attach themselves to gene promoters which have a high level of activity in human cells;
- All viral genomes;
- Parts of viral genomes which have the potential to reproduce live viruses.

The important thing to consider while working with genetic parts is the risk to have them penetrate the body through cuts, skin lesions or contaminated needles. Therefore, wearing gloves and avoiding contact with the skin and paying special attention while working with sharp instruments in the laboratory is mandatory.

3.2. Requirements and precautions while working with live viral carriers

A variety of live viral carriers are used for the effective transfer of genetic matter into cells.
Hazards of such carriers depend on:

1. The host range of the virus;
2. Methods of contagion (airborne, or through body fluids);
3. Degree of infectiousness and the possibility of infection repetition;
4. The possibility for the genetic matter of the virus to insert the genome of the host;
5. The nature of the foreign genetic matter inserting the genome of the host.

What is presented hereafter are issues that must be born in mind while working with retroviral carriers, as well as other live viral vectors. Most experiments in which infectious viruses are used as carriers fall in group 3 of hazards and must be approved by the National Biosafety Committee before they can begin.

3.3. Retroviral carriers

Retroviral carriers are used for the effective transfer of genes into various animal cells. Like other ucarion carriers, they have regulatory sequences which regulate the expression of inserted genes.

Most carriers lack the ability to produce cloning viruses because the inserted gene replaces that part of the virus genome which codes the proteins needed for the reproduction of the original virus. Therefore, along with these incomplete viral vectors, supplementary vectors are used which contain cloning or structural proteins.

A number of packaging cell lines also plays a supplementary role for the cloning and packaging of the virus. Selection of such lines is important because they can produce an infectious virus which has no cloning power; as a result, there is no possibility for transfer from one cell to another or to the host cell (according to the definition of host-carrier systems). Based on what system is used for cloning the virus (supplementary viruses or packaging cell lines of the virus), it is possible to determine the type of cells needed.

There are various methods for the packaging of retroviruses, but according to the purpose of this protocol they are classified based on their potential for contaminating specialized types of cells (classified according to the range of the host).

A. Ecotropic Viruses

These are that group of retroviruses which are able to grow in the cells of the species from which they have been derived, in limited amounts, or at an undistinguishable level in cells of other species.

B. Xenotropic Viruses

Although this group of viruses exists inside a species, generally such viruses cannot clone well within the cells of the same species as they lack a receiver; therefore, they insert ranging cells from heterologs and clone.

C. Amphotropic Viruses

These viruses are not only able to grow in the cells of the species from which they have been separated but they can be cloned in the cells of a vast range of other species as well.

All viruses described above show high levels of risk and danger. It should be born in mind that if the genetic matter inserted into the viral carrier is itself dangerous, risks will become multiplied. In cases where retroviral carriers, which have the capacity to infect or reproduce in a human cell, are used, the hazards of the inserted genetic matter should be born in mind according to the following points:

1. Known viral oncogenes with cell origin;
2. Genes coding proteins which regulate or change growth patterns in mammal cells or which are characteristic patterns (like growth factors, their hormones and receivers);
3. Genes coding molecules whose activity or expression are regulated as a result of growth factors being stimulated;
4. Genes coding known or probable toxins (such as cytotoxic proteins).

The principle which has to be born in mind while working with retroviruses is the possibility of the accidental insertion of the virus into the cells and tissues of the operator as a result of lesions or abrasions on the surface of the skin. Most of these dangers are considered when an individual or individuals are in direct contact with a retrovirus because this virus has a short life and changes gradually.

Preparations for the production of recombinant viruses must be carried out according to practical biosafety guidelines for genetic modification in a laboratory. Once produced, these viruses must be transferred and applied while observing approved methods.

3.4. Cases to observe while working with non-human ecotropic retroviruses

Non-human ecotropic retroviruses, due to a completely limited hosting range, do not grow in human cells in any considerable level. As a result, they are not considered as a too dangerous factor for people. In most cases, observing biosafety standards while culturing the tissue is enough.

3.5. Request form to be filled before transferring LMOs or their products

The applicant must clarify considered species and the varieties derived from them. If there are multiple species, each species must be treated as an individual and included in the application. For virus resistant plants, an additional part should be added, which includes the nature of the virus that creates the resistant phenotypic coding sequences.

1. Taxonomic name of the virus: - Family: - Virus traits: - Names and synonyms of the virus:
2. Type of the nucleic acid of the virus:
3. Does the virus contaminate systems or tissues?
4. Satellites or supplementary viruses:
5. Range of the virus host:
6. Method of transfer:
7. If the virus is transferred by a carrier, clarify the characteristics of the carrier and also method of transfer:
8. Clarify transcapsidation or synergism with other viruses:

The collected data can be presented in the form of a table. The following sources can also be added:

- Range of host;
- Carrier insects, etc.

In transgenic instruction of the plant while using agrobactrium, the applicant must indicate the way of disarming the agrobacterium. The applicant must provide details of the transgenic method.

For other transgenic methods the applicant can:

- Explain the sources of different components of the plasmid and the transgenic method.
- Explain any meaningful change in the transgenic method, tissue reproduction and other cases.
- Prepare a precise restrictive map of the plasmid; this map is used to assess Southern data.
- If possible, study the data statistically; in case there is unpublished information, or when a scientific expert makes comments, those comments must be recorded in the declaration.
- If the unpublished data is related to a scientific research, these data can be attached to the application in the form of a letter.
- In any case, materials and methods, data analysis and related discussions must be prepared in detail.
- Positive comments regarding the results of the experiment which cannot be predicted are not acceptable.
- The applicant must mention every discrepancy between the modified and non-transgenic organism, which is not directly related to the particular phenotype. This discrepancy should include discrepancy in the morphology of the rate of growth, resistance to disease and degree of the product sensitivity to insects. If the particular organism is a plant, the viability of the pollen seed, the growth of the seed and related agricultural operations must be mentioned.
- Applicants must mention the characteristics of the modified and non-modified organisms and compare them with each other.
- Explain whether the presented data is related to hybrid or non-hybrid plants. If it is related to hybrid plants, the condition of the plant growth must be made clear.
- If the organism is a plant, the following points must be taken into consideration:
  - Are the presented data related to greenhouse operations or field trials? If it is a filed trial operation, sites of the experiment, different manners and years of experiment must be clarified.
  - In this case, the manner of seed growth, seed dormancy, seed yield, growth rate and other behavior are needed.

- Southern study must include information related to DNA derived from the living organism, selected transform ranks and carriers.
- To prove whether or not only sequences related to the carrier plasmid have been inserted into the genome, the plasmid DNA without genes is marked and is sent for Southern analysis.
- In case of agrobacterium, the applicant must clarify whether genes outside LB/RB have been inserted in the genome of the plant or not. If there is a complete copy of each gene, the applicant must make it clear whether the gene has been expressed in the plant or not. To prove the insertion of the target DNA it is possible to use PCR analysis. It is not necessary to sequence the transgenic plant and the sequences of the adjacent gene. It is not necessary to determine the number of transgenic copies, but the number of insertions can be used in studying the heredity of the considered gene.
- In case of those plants which have become transgenic directly, the applicant must summarily mention the data related to the genes.
- It must be clarified whether the gene is under control of bacterial or plant promoters.
- Has a complete copy of the gene inserted into the plant? Has protein been expressed in the plant? What from is the expression?
- A table must be prepared, and the related data must be included in this table.
- Manner of Mendelian heredity and the Chi square analysis of 2 transgenic genes must be detailed.
- RNA-Northern analysis is necessary in case of plants made resistant to virus.
- Levels of protein expression related to the particular gene and marker genes in different tissues, manners of plant growth and experiment conditions (inductive and non-inductive conditions) are necessary and should be measured, studies must cover the level of enzyme activity.
- Serology and Western blots and Elisa tests may also be useful.
- The distribution of the immunogenic source is necessary for serological study.
- In case of plants resistant to viruses, the transgenic RNA of the viral gene must be determined and compared with the amount of RNA produced by the non-transformed contaminated plant.
- Applicants should make it clear whether transgenic DNA (or protein) is present in tissues similar to non-transgenic contaminated plant.
- Applicant must clarify the amount of protein cover of the virus in both types of the plant.

In case of disease

- Name of disease, scientific name;
- Factor causing the disease must be provided;

- If information concerning pests and diseases has been obtained from other countries, the applicant must mention the manner of distribution of the pests, diseases and pathogens present in those countries. Manners of diseases spread and sensitivity must be added;
- Various types of wild and transgenic plants must be clarified;
- If the plant contains known toxic material, the applicant must declare the level of these materials after transgenecity.

Appendix 4

Strategies and responsibilities in laboratories and research centres

4. Strategies and responsibilities in laboratories and research centres

The aim of universities and research centres, which deal with dangerous biological material, is to procure safety and secure the health of the people. The responsibilities of the laboratory supervising manager, the Biological Safety Officer (inspector), and the laboratory staff are described in the following. However, all the people involved in research activities in laboratories/research centres are responsible for securing safe conditions in their work environment and for themselves, as well as for the external environment and the whole community, by strictly complying to safety measures and standards.

4.1. Project Manager

Project Manager is the individual who supervises research activities. The PM is responsible for all operations and methods which fall into his/her domain. This responsibility is vast and covers cases such as biological safety. Individuals who work in a laboratory must be confident that all measures in their work environment have been taken so as to guarantee their safety.

Of course, the PM must provide biological safety plans for laboratory staffs.

The PM is responsible for all activities conducted in a laboratory. Methods and operations applied there must be documented in writing. The PM has the ultimate responsibility for the laboratory and is defined as follows:

1. The PM must be a member of faculty.
2. A laboratory PM is a person who has a laboratory space.
3. The PM is the individual responsible for the work done in the laboratory.

Generally speaking, the project manager must clarify the following issues:

- Necessary plans;
- The places where every stage of work should be carried out;
- Researchers, laboratory staff and other co-workers;
- Before creating any change which may increase biological hazards, the manager must get the approval of IBC;
- Before starting any activity, the following cases must be studied:
  - New viruses, new carrier systems;
  - Work with modified systems which can be applied to human systems;
  - Work with new cell lines;
  - Increase in the rate of reproduction or the degree of infection;

- Emphasis on toxic material;
- Small genomes which have been increased to more than 2/3 of total genomes;
- New plans and procedures which increase the danger of aerocell.

Therefore before any change in the combination of dangerous biological material occurs, the manager must obtain written approval from IBC. As the head of the staff, the manager must evaluate whether new factors or protocols increase or create new hazards (meaning: created risks are more than what is mentioned in the approved protocol).

If hazards increase (or if there is any doubt and uncertainty in this regard), assessments must be made and changes carried out before research can be approved.

4.2. General Responsibilities

(1) If the project manager has recently been introduced to research projects, he/she must attend related courses and become familiar with dangerous biological material. Courses are flexible according to the need of the manager.

(2) The project manager must develop and complete features of laboratory projects with regards to biosafety. He/She must provide the necessary biosafety information and knowledge needed by laboratory staff and experts. He/She should as well plan the ways in which research projects and laboratory facilities must expand.

(3) Disposal of dangerous biological materials with which people deal in laboratories needs the approval of IBC.

(4) Those research projects needing directing criteria must be approved before they are put into application and they must be approved by IBC before getting approval from the organisation.

(5) Laboratory personnel and technicians fixing the equipment that may come into contact with dangerous biological material must be made aware of the risks involved and of the ways to reduce such risks. It is necessary for anyone coming into contact with such material to become familiar with safety principles and regulations.

(6) It must be made sure that the environment in which staff and employees work and the equipment with which they work are free from any kind of contamination.

(7) Any considerable problem related to the above mentioned activities or methods in research regulations regarding biosafety diseases must be reported within 24 hours to the centre.

(8) Whenever a limited or suspicious case is observed, it must be reported immediately to biological safety officers (BSO).

(9) Continuous training should be organised with regard to techniques applied to microbiology.

(10) It must be made sure that all the personnel of research departments have received necessary training regarding biosafety and medical aids.

(11) Develop and expand emergency safety measures while transporting contaminated material or when they are accidentally spilled.
(12) Create an atmosphere in the lab allowing free discussions on biosafety issues where problems and safety cases can be easily debated. The manager should not show unreasonable reactions towards people who may criticise existing shortcomings or problems.
(13) The laboratory should be provided with the necessary equipment needed for work on dangerous biological material. Training should be provided to relevant people accordingly.

In experiments a list should be prepared of various materials which are applied in the experiment. The project manager must clarify and use different combinations of various cases which involve quantitative parameters.

4.3. Duties and responsibilities of BSOs

Bio-Safety Officers are independent experts in all fields related to biotechnology and biosafety. They are nominated by the IBC and put in charge of conducting inspections as well as training on biotechnology research & development projects with regards to safety issues and laboratory procedures.

4.3.1. Duties of BSOs

1. Creating a series of basic characteristics regarding physical and biological contamination according to the principles included appendix 2B to 2G.
2. Selecting suitable microbiological experiments and activities and applying useful laboratory techniques for scientific research.
3. Report to IBC and MBC any change for them to inspect and approve.

Example:

1) If the objective of an experiment is to change the cells of a specie into the cells of another specie through genetic manipulation, the results of the experiment should be reported to IBC and NBC;
2) Work on cells containing infectious organisms;
3) Work with a small part of a genome factor more than 2/3 of which has been modified/incorporated;
4) Modification in animal species.

4.3.2. Duties of BSO

1. If necessary, the BSO may assist the project manager in his duties (see sections 4.1. and 4.2. in appendix 4).

2. Supervise the safety of activities conducted by laboratory workers and make sure that all applied techniques and methods are safe.
3. Report in writing to IBC and MBC any problems seen in experiments, safety issues, and activities related to contamination.
4. Immediately notify IBC and MBC of any accidental spilling of contaminating material or any error in experiments which endangers the personnel.
5. Make sure that all conditions of risk assessment and precautions of the project have been applied.
6. As approved by IBC and as mentioned in laboratory methods, check access to material in biosafety laboratories which must be limited to the personnel directly involved in the experiment.

4.4. Laboratory staff

Those individuals who work in a laboratory, such as researchers and technicians, are considered as laboratory staff. It is possible to consider lecturers, students, and interns as occasional lab workers as well.

The laboratory staff plays an important role in creating a suitable work atmosphere. Every individual must take care of his/her own safety and that of their coworkers. If an individual does not observe the rules and regulations of the research centre, or the plans related to biosafety, it is impossible to create a suitable work atmosphere.

Access to laboratory facilities by lab staff depends on biosafety risk levels and authorisation from IBC.

4.4.1. Responsibility of laboratory staff

1. They must carefully observe regulations and plans specified for laboratories.
2. They must report any problem or any violation in ongoing projects or any accident to the project director or supervising manager.
3. If they witness any important violation of biosafety strategies or administrative plans and methods, they must report to biosafety officials quickly. In case the manager cannot solve these problems within a specific time period, no measures can be taken against those individuals who have informed biosafety officials or the administrative biosafety committee.

Appendix 5
General levels of plant biosafety

5. General levels of plant biosafety

The main objective of containing a plant is to avoid unintentional transfer of viable and heritable material, that is a plant genome containing recombinant DNA, including nucleic or organelle heredity material or the release of organisms resulting from recombinant DNA along with plants.

The principles of containment are based on the assumption that organisms being used do not have any effects on human health or that of other animals (unless they have been modified specifically for this purpose). The application of biosafety containment conditions must reduce to a considerable extent the possibility of unpredictable harmful effects on organisms and the environment outside the laboratory. Examples of such effects are the unintentional spread of a severe pathogenic organism from a greenhouse to the local agricultural products or the unintentional entrance and settlement of an organism in a new biological environment.

There are four biosafety levels for plants, namely BL1-P (Biosafety Level 1-Plants), BL2-P, BL3-P and BL4-P. The choice of containment level needed for research activities related to molecules of recombinant plant DNA along with plants is specifically discussed under the title of “Biological Containment Practices”. This part describes greenhouse procedures and special greenhouse facilities for physical containment.

BL1-P to BL4-P have been designed to present different biosafety levels for plants which contain recombinant DNA, in the presence or absence of other laboratory animals. These levels of biosafety, along with conditions of physical containment described as physical containment procedures, present flexible methods to ensure safe conduct of research.

For those experiments in which plants are bred under BL1-P to BL4-P conditions, containment procedures have to be observed exactly as described in the physical containment section. These containment methods include using plant tissue culture rooms, growth rooms with laboratory facilities or experiments conducted on open counters.

If reproductive structures, which can be released into the environment, are produced, additional physical containment must be exercised by the greenhouse supervisor or the institutional biosafety committee as necessary.

5.1. Biosafety level 1 – plants (BL1-P)

5.1.1. Standard methods

A. Access to greenhouse

- While experiments are being conducted, the greenhouse supervisor will make decisions regarding access limitation.
- Staff must study BL1-P procedures before entering the greenhouse and must then follow these procedures. Suitable methods will be applied to the organism under experiment and carried out according to the procedures decided upon for that greenhouse.

B. Recording experiments

- All experiments conducted in the greenhouse must be recorded and filed.

C. Decontamination and deactivation

- Organisms under experiment must be deactivated with methods complying with biosafety measures before disposal outside greenhouse facilities.

D. Controlling undesirable species and moving microorganisms

- In order to control undesirable species (including weeds, rodents, pests or pathogenic factors), a plan is prepared following methods suitable for these organisms and according to administrable regulations and conditions.
- Arthropods and other moving organisms will be kept in suitable containers. If certain microorganisms (such as flying arthropods or nematodes) are released within the greenhouse, precautionary measures will be taken to prevent their escape from the laboratory.

E. Simultaneous experiments in a greenhouse

- Experiments related to organisms which require a lower level containment than BL1-P can be conducted at the same time as BL1-P experiments, provided that all activities are carried out according to BL1-P greenhouse procedures.

5.1.2. Facilities

A. Definitions

- The term “greenhouse” applies to a building with walls, ceiling and floor, which is basically used to breed plants in a controlled and protected environment. Walls and the ceiling are normally made of transparent or semi-transparent material to allow the passage of light necessary for plant growth.
- The term “greenhouse facilities” includes actual greenhouse rooms, parts for breeding plants, including all passages and adjacent parts, and is considered part of the containment area.

B. Greenhouse design

- The greenhouse floor may contain sand or other porous material. A minimum of non-porous passages (such as concrete) is suggested for middle sections.
- Windows and other openings in the walls or ceiling might be opened for ventilation, and there is no need for specific obstacles to prevent the escape of pollens, microorganisms or small organisms (such as arthropods and flying organisms); in any case, the use of curtains is suggested.

5.2. Biosafety level 2 – plants (BL2-P)

5.2.1. Standard procedures

A. Access to the greenhouse

- At the time of an experiment, the greenhouse supervisor makes decisions regarding limited access for individuals directly involved in the experiment.
- Staff is asked to study and follow BL2-P instructions. Suitable methods are applied according to instructions acceptable for the greenhouse and for organisms under experiment.

B. Recording experiments and events

- Experimental plants, microorganisms or small organisms, which enter or leave greenhouse facilities, must be recorded.
- All experiments going on in greenhouse facilities must be recorded and filed.
- The main researcher must immediately report to the greenhouse supervisor, institutional biosafety committee or any other related authority any accident that would result in the unintentional release or spilling of microorganisms. Reports of such accidents are prepared and filed along with related documents.

C. Decontamination and deactivation

- Organisms under experiment must be deactivated with methods complying with biosafety measures (e.g. sterilisation by autoclaves, incineration) before disposal outside greenhouse facilities.
- Purification of exiting water is not necessary. If part of the greenhouse is made of sand or similar material, suitable treatments will be applied periodically in order to deactivate any organism which has the capacity to survive unnoticed in sand.

D. Controlling undesirable species and moving living organisms

- A plan will be prepared and executed in order to control undesirable species (such as weeds, rodents, pests or pathogenic factors) with suitable methods and according to administrable regulations and conditions.

- Arthropods and other moving living organisms will be kept in suitable containers. If certain microorganisms (such as flying arthropods or nematodes) are released in the greenhouse, precautionary measures will be taken to prevent their escape from greenhouse facilities.

E. Simultaneous experiments in a greenhouse

- Experiments related to other organisms, which require levels of containment lower than BL2-P, can be carried out simultaneously with those requiring BL2-P, provided that all work is done according to BL2-P greenhouse procedures.

F. Signs

- Signs indicating ongoing experiments will be raised. These signs will include:
    a. Name of the person responsible;
    b. Plants being used;
    c. Any specific need to use this area.
- If organisms being used have a definite potential for creating serious harmful effects on natural or arranged ecosystems, their presence will be recorded on the sign raised on the greenhouse door.
- If there is danger to human health, a sign will be raised which bears the global biosafety logo.

G. Transfer of material

- Material containing experimental microorganisms which enter or leave greenhouse facilities in an untouched or living condition will be carried in a closed unbreakable container complying with international standards.

H. Instructions for greenhouse procedures

- Instructions for greenhouse procedures will be prepared and adopted. These instructions will:
    a. Inform the staff of the consequences of not following procedures;
    b. Explain probable strategies to be used in case of unintentional release of organisms.

5.2.2. Facilities

A. Definitions

- The term “greenhouse” applies to a building with walls, ceiling and floor which is basically used to breed plants in a controlled and protected environment. The walls and the ceiling are normally made of transparent or semi-transparent material to allow the passage of light necessary for plant growth.
- The term “greenhouse facilities” includes actual greenhouse rooms, parts for breeding plants, including all passages and adjacent parts, and is considered part of the containment area.

B. Greenhouse design

- The floor of the greenhouse is probably covered by penetrable material. Concrete is suggested, but sand or other porous material is acceptable for under the tables, unless the microorganisms under experiment can spread easily through soil. Soil beds are acceptable unless organisms under experiment can easily spread through soil.
- Windows and other openings in the walls and the ceiling of greenhouse facilities can be opened for ventilation and there is no need for specific obstacles to prevent the escape of pollens or microorganisms; however, curtains are needed to prevent the entry or exit of small flying creatures (such as arthropods and birds).

C. Autoclaves

- An autoclave will be available for decontamination of contaminated material in the greenhouse.

D. Ventilation systems

- If fans are used, their size will be chosen in a way as to minimise the entry of arthropods. Cooler or fan windows will be manufactured in a way as to open only when the equipment is working.

E. Other issues

- Other requirements for BL2-P containment might be met with a growth chamber or growth room inside the building, whose physical external structure prevents access and escape of microorganisms and macro-organisms in a way that the above conditions are met.

5.3. Biosafety level 3 – plants (BL3-P)

5.3.1. Standard procedures

A. Access to greenhouse

- Permission to enter the greenhouse is limited to those people who work on the project or with the purpose of carrying out supporting activities. The greenhouse supervisor has the responsibility to determine who has permission to enter greenhouse facilities, and to decide how.
- Before entering the greenhouse, staff must read and then observe BL3-P greenhouse instructions. Suitable methods will be followed according to accepted instructions for the greenhouse and the organism under experiment.

B. Recording experiments and events

- Reports on plants, microorganisms or small animals under experiment, which are brought into or leave greenhouse facilities, must be prepared and recorded.
- A detailed account of the experiments going on in the greenhouse must be recorded and filed.

- The chief researcher must immediately report to the biosafety official, greenhouse supervisor or the institutional biosafety committee and other authorities any accident which would result in the unintentional release or spilling of microorganisms. Documents of such accidents will be prepared and filed.

C. Decontamination and deactivation

- Before disposal, all experiment materials will be sterilised in an autoclave or deactivated through methods complying with biosafety measures, including water which has been in contact with microorganisms under experiment or materials subjected to such microorganisms or contaminated equipment, except for those which are kept in a living, untouched condition for experiment purposes.

D. Controlling undesirable species and moving microorganisms

- A plan will be made and executed to control undesirable species (including weeds, rodents, pests or pathogenic factors) with suitable methods and according to administrable regulations and conditions.
- Arthropods and other moving living organisms will be kept in suitable containers. Based on the particular living organism, experiments will be carried out in containers designed for the containment of moving living organisms.

E. Simultaneous experiments in a greenhouse

- Other experiments related to organisms which require a lower level of BL3-P containment can be carried out at the same time as those requiring BL3-P containment, provided that all work is carried out according to BL3-P greenhouse procedures.

F. Signs

- A sign indicating ongoing experiments will be raised. This sign will contain:
    a. Name of the individual responsible;
    b. Plants being used;
    c. Any specific need to use this particular area.
- If the organisms being used have a definite potential to create serious harmful effects on natural or arranged ecosystems, their presence will be declared on the sign raised on the greenhouse door.
- If there is any danger to human health, a sign bearing the global biosafety logo will be raised.

G. Transfer of materials

- Those experiment materials which enter or leave greenhouse facilities in untouched or living condition will be kept in completely tight, unbreakable double paned containers. During transportation, if the same plant species, whether host or carrier, are within effective spreading distance from the experiment organism, the surface of the second pane might be decontaminated. Decontamination might be achieved by passing through a chemical

disinfectant or a fumigation chamber or by a substitute method which effectively deactivates organisms under experiment.

H. Instructions for greenhouse procedures

- Greenhouse instructions will be prepared and adopted. These will:
    a. Inform the staff of the consequences of not observing such methods,
    b. Discuss probable strategies which can be employed in case of an unintentional release of organisms with potential for serious harmful effects.

I. Protective clothing

- Disposable, solid front and wrap around gowns will be worn in greenhouse facilities, if considered necessary by the greenhouse supervisor due to a possible risk of spreading the microorganisms under experiment.
- Protective clothing will be taken off before leaving the greenhouse and will be decontaminated before being washed or disposed of.

J. Other issues

- It is imperative for the staff to wash their hands and disinfect thoroughly before leaving the greenhouse.
- All procedures used to minimise bubbles, excessive splashing of material, the overflow of soil from experimental plant pots, as well as other experiment instructions will be observed.

5.3.2. Facilities

A. Definitions

- The term “greenhouse” applies to a building with walls, a ceiling and a floor which is basically used to breed plants in a controlled and protected environment. The walls and the ceiling are normally made of transparent or semi-transparent material to allow the passage of light necessary for plant growth.
- The term “greenhouse facilities” includes actual greenhouse rooms, parts for breeding plants, including all passages and adjacent parts, and is considered part of the containment area. While building or repairing the greenhouse, the need for negative pressure must be considered.

B. Design of the greenhouse

- The floor of the greenhouse is made of concrete or other impenetrable material; measures will be taken for the collection and decontamination of exiting water.
- Windows are closed and sealed. All windowpanes are unbreakable (for example, double-paned tempered glass).

- The greenhouse is an enclosed building with seamless front, completely separated from open areas for unrestricted traffic. The least level of requirement for entering the greenhouse is passing through two series of doors which close and lock automatically.
- Greenhouse facilities must be surrounded by a safety wall so that equal safety distances are observed.
- The inside cover of walls, ceiling and the floor will be resistant to the penetration of fluids and chemical material in order to facilitate the cleaning and decontamination of the area. Any leak in these structures and surfaces will be sealed.
- Table tops and other surfaces must be seamless, resistant to the penetration of water and resistant to acids, alkali, water solvents and mild heat.
- The greenhouse has a sink close to the exit door which works with food, arm or automatically.

C. Autoclaves

- An autoclave will be available for the decontamination of material inside greenhouse facilities. A double door autoclave is recommended for the decontamination of exiting material from greenhouse facilities.

D. Ventilation systems

- There will be an independent ventilation system. This system will maintain changes in pressure and directed air flow according to need, and will guarantee the outside-in (or zero) air current.
- Air exiting greenhouse facilities will be purified by high efficiency HEPA air filters and then sent out. Filter containers must be designed in a way that they can be decontaminated in place before being removed; they must be tested after they are changed. Air providing fans must have adjustable valves that close when the fans are off. It is possible to substitute ordinary filters and valves with HEPA filters in ventilation systems. The incoming and outgoing air current must be adjusted in a way that at all times the air current is inward (or zero).

E. Others

- It is possible for BL3-P greenhouse requirements to be met by using a growth room or growth chamber inside the building which has the situation, access, patterns of air current and decontamination facilities and which meets the purposes mentioned above.
- Vacuum pipes will be fitted with high efficiency HEPA air filters or equal filters and fluid disinfecting parts.

5.4. Biosafety level 4 – plants (BL4-P)

5.4.1. Standard procedures

A. Access to the greenhouse

- Permission to enter the greenhouse is limited to those people who work on the project or with the purpose of carrying out supporting activities. The greenhouse supervisor is responsible for determining the people who have permission to enter or work in greenhouses during experiments.
- Access will be arranged by the greenhouse supervisor, the biosafety official or other physical safety authority of greenhouse facilities; access will be restricted by security doors and locks.
- Before entering the greenhouse, people will be informed of potential environmental dangers and suitable protective instructions to ensure environmental safety. People permitted to enter greenhouse facilities act according to the instructions and observe all procedures for entering and exiting the premises.
- Staff will only enter the greenhouse through changing rooms and bathrooms, and will take showers every time before leaving greenhouse facilities. Only when necessary will they use airlocks to enter or exit the laboratory. When necessary, every reasonable effort must be made to prevent possible transfer of living organisms from their contained area.
- Staff must read BL4-P instructions before entering the greenhouse, and must then observe them carefully.

B. Recording the experiments and events

- Reports on all experiment material entering or leaving the greenhouse must be made and filed.
- A detailed description of all ongoing experiments in greenhouse facilities will be recorded and filed.
- Reports must be made and filed of all individuals who enter or exit greenhouse facilities, along with time and date for each entry.
- The main researcher must immediately report to the biosafety official, the greenhouse supervisor or other involved authorities any greenhouse accident which would result in the unintentional release or spilling of experimental microorganisms. Documents of such events will be recorded and filed.

C. Decontamination and deactivation

- All material, except for those which must remain living and untouched for experimental purposes, will be autoclaved before leaving the greenhouse. Those equipment or materials which might be destroyed in high heat or steam will be disinfected by substitute methods (such as sterilization by gas) in airlock rooms or chambers designed for this purpose.

- Water, which has been in contact with microorganisms under experiment or materials subjected to experiments with such organisms (such as overflowing water when irrigating plants), will be collected and disinfected before being disposed.

D. Controlling undesirable species and moving microorganisms

- A chemical control plan will be put into action to eliminate undesirable pests and pathogenic material according to administrable regulations and conditions.
- Arthropods and other moving microorganisms used in experiments which need BL4-P containment will be kept in closed suitable containers. Based on the organism under study, experiments will be conducted in containers designed for containing moving living microorganisms, and complying with international standards.

E. Simultaneous experiments in a greenhouse

- Experiments with other organisms which require containment levels lower than BL4-P can be conducted at the same time as those requiring BL4-P, provided that they are conducted according to BL4-P greenhouse procedures. When microorganisms under experiment require lower levels of containment than BL4-P, greenhouse procedures reflect the highest level of containment needed for the microorganism under experiment.

F. Signs

- A sign will be raised containing information regarding experiments being conducted. This sign will have the following information:
    a. Name of the person responsible;
    b. Plants being used;
    c. Any specific requirement for using this area.
- If microorganisms being used have a potential to create serious harmful effects on natural or arranged ecosystems, their presence will be announced on the sign raised on the greenhouse door.
- If there is danger to human health, a sign bearing the global biosafety logo will be raised.

G. Transfer of material

- Experiment material which enter or leave greenhouse facilities in an untouched or living 5condition will be transported to a sealed, unbreakable container, which will in turn be packed into a second sealed unbreakable container. This will leave the greenhouse by going through a disinfectant, fumigation or airlock chamber designed for this purpose.
- Material and equipment will be brought into greenhouse facilities through a double door autoclave, disinfectant or airlock chamber which are carefully decontaminated after each use. After securing the exit door, staff working inside greenhouse facilities can take out the material by opening the inner door of the autoclave, the disinfecting or the airlock chamber. These doors will be secured after material has been brought inside greenhouse facilities.

H. Greenhouse procedures instructions

- Instructions for greenhouse procedures will be prepared and adopted. These instructions include methods to be applied at the time of unintentional release of organisms under experiment.

I. Protective clothing

- Ordinary clothes will be taken off in the outside changing room. All staff will put on full laboratory clothing (possibly disposable) before entering greenhouse facilities.
- Lab clothes will be taken off while leaving greenhouse facilities and prior to entering baths. These clothes will be kept in a locked cabinet in the inside changing room.
- All lab clothes will be autoclaved before being washed or disposed of.

5.4.2. Facilities

A. Greenhouse design

- Containment of greenhouse facilities includes a separate building with clearly defined boundaries and separate area in one building. The need to establish zero pressure must be taken into consideration when building or renovating greenhouse facilities.
- Inside and outside changing rooms, separated by bathrooms, will be available for the staff to enter or leave greenhouse facilities.
- Windows will be closed off and sealed. All glass panes (including double-paned tempered glass or equal) will be unbreakable.
- Greenhouse entry doors must close and lock automatically.
- Greenhouse facilities must be enclosed within a safety wall so that equivalent safety distances might be observed.
- Greenhouse walls, ceiling and floor must be built in a way as to construct a sealed inside protection, facilitate fumigation and prevent animals and arthropods from entering. These inside surfaces must be resistant to the penetration of and destruction by chemical fluids and material in order to facilitate cleaning and disinfecting in this area. All openings into these structures and surfaces (such as pipes and other facilities) must be sealed.
- Table tops and other surfaces must be seamless, waterproof and resistant to acids, alkali, organic solvents and mild heat.
- A double door autoclave, fumigation chamber or ventilated airlock must be provided for the passage of material, machinery or equipment which is not brought into greenhouse facilities through changing rooms.

B. Autoclaves

- A double door autoclave is provided to disinfect materials exiting greenhouse facilities. The outer door of the autoclave opens outside the greenhouse, is sealed to the outside wall and is automatically controlled so that it opens only after sterilization cycle is completed.

C. Ventilation systems

- There will be an independent ventilating system. This stem will maintain pressure difference and directed air current as necessary and will provide outside-in air current (or zero) from outside the greenhouse. Differential pressure transducers will be used to receive pressure differences. If there is a problem in the system, these transducers will set off the alarm. Attention must be paid to power supply source. To ensure constant air flow from outside in (or zero), air passages will be connected at all times. The rate of settling should not exceed 7% per second (pressure against time logarithm) during a 20 minute period in 2 inches of water pressure.
- Air leaving greenhouse facilities will be purified by high efficiency HEPA filters and will then leave the building and the fans, then be dispersed away from the buildings. HEPA filters will be inspected and approved after substitution and filter chambers will be designed. HEPA filters will be provided for the treatment of air entering greenhouse facilities as well. HEPA filters will be examined and approved each year.

D. Other issues

- Sewer vents and other ventilation lines will be equipped with high efficiency HEPA filters. HEPA filters will be inspected and approved each year.
- A pass-through dunk tank, a fumigation chamber or other equivalent methods will be available for decontamination to ensure that those material and equipment which cannot be autoclaved can be disinfected.
- Fluids exiting hand washing sinks, the floor and autoclave chambers will be disinfected by heat and chemicals before they leave contained greenhouse facilities. Fluid deposits from bathrooms and toilets can be disinfected by heat and chemicals. Chemical or autoclave disinfecting applied to fluid deposits will be assessed by standard procedures. Mechanical decontamination and bioremediation will be assessed by a thermometer and microorganism indicator with a definite heat sensitivity pattern. If chemical deposits are decontaminated by chemical disinfectants, their effectiveness must be proved against target and witness organism.
- If a central vacuum system is available, it will not service areas outside greenhouse facilities. High efficiency HEPA filters will be placed as close as possible to the point of application of the vacuum service. Other gas and fluid services to greenhouse facilities will be protected by measures that prevent fluid reversal. HEPA filters will be inspected and approved each year.

Appendix 6

Biosafety levels for laboratory animals

6. Biosafety levels for laboratory animals

6.1. Biosafety level 1 – Animals

Biosafety levels 1 and 2 are the two common categories of physical containment. Although the emphasis to use these containment levels is for laboratory animals, it is possible to extend the application of these levels of biosafety to cases such as donor DNA, biological vectors and tissue cultures. Like physical containment levels in laboratories, levels of physical containment in places where animals are kept are applied by choosing suitable performances and containment equipment and designing suitable rooms.

Biosafety level 1 is suitable for experiments on animals which are well known, do not cause diseases in healthy mature people and also have the least possible danger for the laboratory staff and the environment.

6.1.1. Executive procedures

The project manager for animal biosafety will establish procedures, methods and instructions needed in emergency situations. Before it could begin, each project must be studied by the NBC.

Operational stages and specific procedures:

- A biosafety manual must be prepared and made available in the laboratory. Staff must be familiarized with specific hazards of work with these factors and read and commit to memory the necessary instructions and methods.
- Wearing uniforms, protective clothing and coveralls is recommended. Laboratory uniforms must be left in laboratory animal rooms. Protective clothing and coveralls must not be worn outside places designated to animals.
- Eating, drinking, smoking and wearing lenses and make up are not permitted. Food for human use must be kept in specific places. They are not permitted in areas designated to animals and in related laboratories.
- All recommended methods must be followed carefully in order to minimize the production of airborne particles.
- Work surfaces must be decontaminated after each experiment or after each spilling of living material.
- All the remaining contaminated material left in the laboratory animal room (such as animal tissue, carcases and contaminated surfaces) must be carried in strong and impenetrable

containers, and then disposed of in suitable containers according to the facilities of the laboratory. It is recommended that these wastes be incinerated.

- All staff must wash their hands with soap and warm water after contact with cultures and animals and after taking off their gloves and before leaving the laboratory.
- A preventive and protective plan is needed to control the entrance of insects and rodents into the area designated to animals.
- People in contact with laboratory monkeys should wear protective coveralls in order to protect their face, eyes and mucus surfaces.
- While work is being done, and when animals are free, all doors leading to the area must be closed and entry into the area must be controlled by a supervisor.
- All laboratory equipment, the floor and all used surfaces must be disinfected after the work is finished and also after spilling of any infectious material. Disinfectants must be ready and at hand according to the building instructions.
- Manipulated animals must be kept in separate cages.
- Stimulating laboratory animals must be avoided as much as possible during work.
- Pest control plans must be followed effectively and constantly under the supervision of the supervisor.
- Those laboratory animals which are being used for genetic experiments and their tissues must not be used for other cases under any circumstances.

6.1.2. Suggested safety equipment

- Only authorized people who work on projects have the right to enter the area designated to animals. Before entry, the individual must be aware of the potential biosafety hazards of these factors and prepare suitable safety and protection measures.
- Facilities for keeping animals must be designed in a way as to make it possible to clean and maintain them. Internal surfaces (walls, floors and ceilings) must be waterproof.
- Windows are not recommended for animal rooms. Any window must be unbreakable. Windows must be seamless and closed off. In cases where it is possible to open windows, a system is imperative to control insects' entry.
- If there is a drainage system in the animal room, all surfaces must constantly be disinfected with enough water and a suitable disinfectant.
- Biological safety cabinets must be available for work at biosafety level 1.
- Water tanks, aquariums and other equipment used to keep vertebrate and non-vertebrate marine life must be equipped with mechanisms to protect the water they contain and also to protect laboratory organisms and their gametes.

- The biohazard global sign must be posted at the entrance to the laboratory animal room according to dangerous and pathogenic factors. The biohazard sign indicates infectious agents, name and telephone number of the laboratory supervisor or any other responsible person, and the necessary conditions to enter the animal room.
- Cages must be cleaned, washed and disinfected manually or with special equipment. The minimum washing temperature is 180 degrees Fahrenheit.
- Necessary facilities to work with sharp and cutting instruments must be taken into consideration.
- It is necessary to install automatically closing and opening doors outside the area specific to animals. Doors to animal rooms must open to the inside and be kept closed while working with the animals.
- Other internal facilities such as the lighting system, ventilating canals, electricity lines and connecting pipes must be designed and installed in a way as to create the smallest possible amount of surface in animal rooms.
- Ventilation of laboratory animal rooms must be done according to standard tables found in manuals for keeping and taking care of laboratory animals. It is recommended that the room designated to laboratory animals be under negative pressure as compared to other parts.
- Places where animals are kept must be separated from places where people come and go.
- Lighting must be adequate for all activities; harsh lights and reflections, which might hinder perfect sight, should be avoided.

6.2. Biosafety Level 2 – Animals

This level of biosafety is suitable for work with factors which cause diseases in humans, those pathogenic factors which mostly enter the human body through swallowing, the skin and the mucous.

6.2.1. Executive Procedures

Apart from these procedures, methods and instructions which are established by the project manager and the BSO at the time of emergency, there are specific procedures and methods which must be approved by IBC and MBC according to necessary conditions.

Operational stages and specific procedures:

- A biosafety manual must be prepared and made available in the laboratory. Staff must be familiarized with the specific hazards of work with these factors and study and commit to memory necessary instructions and methods.

- Staff must receive all necessary tests and vaccines required for work with potentially dangerous agents, such ac vaccines for hepatitis B and tuberculosis, etc.
- Eating, drinking, smoking and wearing lenses and applying cosmetics are not permitted. Food for human use must be kept in specific places. These are not permitted in the areas designated to animals or in the laboratory.
- Wearing protective uniforms and coveralls in the laboratory animal room is imperative. Uniforms must be taken off before leaving animal rooms. Protective uniforms and coveralls must be left in the area specific to animals. Wearing gloves while in contact with contaminated animals is imperative in order to prevent the skin from contact with infectious material.
- All recommended methods must be followed carefully in order to minimize the creation of splashes or aerosols.
- Equipment and work surfaces in animal rooms must be regularly disinfected and decontaminated with effective disinfectants after work with infectious agents and especially after a spilling or splashing of these or other infectious material.
- Necessary trainings must be included in plans for this level of biosafety for work in areas and rooms designated to laboratory animals, and provision must be made for necessary and suitable trainings to work with dangerous factors and precautions necessary for preventing hazards of contact with these factors and for assessment of work methods.
- Staff must receive up to date trainings If necessary, old trainings and procedures must be changed. It is necessary to record all trainings.
- People who are at risk of coming into contact with infectious and dangerous factors, specially the said factors are particularly dangerous, must not be allowed to work in animal rooms unless methods and ways are used which can reduce these dangers.
- Only animals related to the experiment are allowed into animal rooms.
- Facilities for washing hands are imperative.
- Spilling of material or accidents, which end in increasing the risk of contact with dangerous factors, must be reported to authorities immediately. It is necessary to record accidents and measures taken to decontaminate.

6.2.2. Recommended Safety Equipment

- Entry into animal rooms is not allowed except for a limited number of people. People who enter laboratory animal rooms must be aware of the potential dangers of the factors with which they work.
- In order to prevent the spread and transfer of infection, all collected infectious samples must be labeled and transported in a way as to prevent such spread and transfer.

- Policies for the safe handling of sharp instruments are instituted.Needles and syringes or other sharp instruments must be used only once. Used disposable needles must not be bent, broken, recapped or removed from disposable syringes. It is better to use syringes with attached needles. Plasticware should be substituted for glassware whenever possible.
- Staff must wash their hands after handling cultures and animals and after removing and before leaving the laboratory.
- The global biosafety sign must be posted on the entrance to the room of laboratory animals according to dangerous and pathogenic factors. The danger sign is there to identify infectious agents and bears the name and telephone number of the laboratory supervisor or other authorized people; conditions necessary for entering animals room must be made clear.
- A preventive and protective plan is needed to control the entry of insects and rodents into the area designated to the animals needed for the project.
- Other protective equipment for staff will be different according to a study and assessment of and change in factors. It is imperative to use eye protectors and respiratory masks, especially while working with monkeys.
- In this level of biosafety it is necessary to use biological safety hoods or other physical containment measures with protective equipment (visors and respiratory masks) in cases where applied methods create airborne particles. These cases include autopsy of contaminated animals, lifting tissues or fluids from contaminated animals and eggs of contaminated hens, or lifting different secretions of these animals.
- When it is necessary to place the animals under experiment in preliminary biosafety containment suitable for that animal species, filtered cages are recommended.
- Areas and rooms designated to laboratory animals must be separated from other spaces in the building where people come and go.
- Access to laboratory animal rooms and areas of related laboratories is limited by doors which have security locks. Outer doors close and open automatically. Doors to the laboratory animal room open to the inside and close automatically and are kept close during experiments.
- Facilities for keeping the animal must be designed in a way as to make it possible to maintain and clean them. Internal surfaces (walls, floors, ceilings) must be waterproof.
- Other internal facilities and installations such as the lighting system, air canals, electricity lines and connecting pipes must be designed and installed in a way as to create the minimum amount of surface.

- Windows are not recommended for animal rooms. Any kind of window must be unbreakable. Windows must be closed off and seamless. In cases where it is possible to open these windows an insect control system is definitely needed.
- If the animal room has a drainage system, all surfaces must be constantly disinfected with adequate water or a suitable disinfectant.
- Exiting air must be directed out after passage through filters and purification without being circulated in other parts. Ventilation of laboratory animal rooms must be accomplished according to standard tables found in manuals for keeping laboratory animals. In the room designated for a laboratory animal the air must always flow from outside in so that negative pressure is established.
- Cages used to keep animals must be washed, cleaned and disinfected manually or by special equipment. Minimum washing temperature must be 180 degrees Fahrenheit.
- It is necessary to have an autoclave in facilities for keeping laboratory animals for the decontamination of contaminated material.
- All equipment must be suitably decontaminated before leaving laboratory animal room and animal areas.
- Lighting must be adequate for all work, and harsh light and strong reflections, which hinder perfect sight, must be avoided.

6.3. Biosafety Level 3 – Animals

This level of biosafety is suitable for work with animals contaminated with one of the dangerous indigenous or exotic agents whose transfer through airborne particles causes severe and dangerous and/or even fatal diseases. In this level of biosafety, in addition to what is present in biosafety level 2, specific buildings and facilities and physical containment conditions are necessary.

6.3.1. Executive stages

Apart from standard procedures, methods and instructions which are established in emergency cases by the project manager and the BSO, other specific procedures and methods must as well be approved by IBC and MBC.

6.3.2. Operational Stages and Specific Procedures

- Entering the room of a laboratory animal is not allowed except for a limited number of people. People who enter a laboratory animal room must be aware of the potential dangers of the factors with which they work.
- Suitable plans are necessary to monitor the health of the staff.

- All staff must receive necessary vaccines and suitable tests which are needed for work with potentially dangerous factors; examples are hepatitis B vaccine and tuberculosis test. Necessary serums must be available.
- People who are in danger of coming into contact with infectious and dangerous agents, specifically when the said factors are particularly dangerous, must not be allowed to work in animal room unless methods and ways are used which can reduce these dangers.
- A biosafety manual must be prepared and made available in the laboratory. Staff must be familiarized with the specific hazards of work with these factors and study and commit to memory necessary instructions and methods.
- Eating, drinking, smoking and wearing lenses and make up is not permitted. Food for human use must be kept in specific places. These are not permitted in areas designated to animals and in related laboratories.
- All recommended methods must be followed carefully in order to minimize the production of airborne particles.
- Equipment and work surfaces in the animal room must be regularly decontaminated with effective disinfectants after work with infectious factors. Decontamination is especially necessary after spills or splashes or other contamination created by infectious factors.
- All residues from animals room (including animal tissues, carcasses, contaminated beds, used food, sharp instruments or other used animal tissues) must be carried in strong and impenetrable containers and disposed of in containers suitable for the disposal of such material, according to the facilities of the laboratory. It is recommended that these residues be incinerated.
- There must be necessary facilities to work with sharp implements. Needles, syringes and other sharp instruments must be used only once. Do not recap them and do not separate the needle. Syringes with needles attached must be used. Plasticware should be substituted for glassware whenever possible.
- Staff must wash their hands after contact with cultures and animals and after taking off their gloves and before leaving the laboratory.
- The global biosafety sign must be posted on the door of the laboratory animal room according to dangerous and pathogenic factors. This danger sign is there to identify infectious factors and bears the name and telephone number of the laboratory supervisor or other authorized people; conditions and facilities necessary for entering animal rooms (such as immunization of staff against diseases, respiratory masks) must be made clear and attached onto the door.
- In order to prevent the spread and transfer of infection, all collected infectious samples must be labeled and transported in a way as to prevent such spread and transfer.

- Staff must receive necessary training for work with dangerous factors and must observe necessary precautions to prevent risk of contact. Staff must receive up to date training. If necessary, old training and procedures must be changed. It is necessary to record all training.
- A preventive and protective plan is needed to control the entry of insects and rodents.
- Cages in which laboratory animals are kept must be decontaminated in autoclaves before their beds are changed or before they are washed and cleaned. Equipment must be decontaminated according to existing regulations before transfer or change or substitution.
- If infectious material is spilled on a surface, only those staff members which have received correct training and have learned how to work with dangerous factors and materials must attempt cleaning and decontamination. Spillage of materials or accidents which increase the risk of contact with dangerous factors must be reported to the authorized supervisor immediately. Measures taken to decontaminate, medical assessments and received treatments must be recorder in the accident log.
- All residues from laboratory animal rooms must be decontaminated before disposal by incineration or other methods.
- Material, equipment and plants unrelated to the laboratory and permitted experiments are not allowed into animal rooms.

6.3.3. Safety Equipment (Primary Barriers)

- Coveralls and protective clothes must be worn when entering laboratory animal rooms. It is also necessary to wear thick gloves with these clothes. Open front uniforms are not suitable for work at this level of biosafety. Protective clothing must be taken off before leaving laboratory animal rooms, and coveralls must be taken off and put in baskets for decontamination before leaving the building entirely.
- Safety equipment for staff must be determined based on assessments and determination of the type of factors present. Staff must use all safety and protective equipment in all activities which involve contact with infectious material and contaminated animals. Staff must wear gloves while working with animals. Gloves must be taken off with standard and aseptic methods and decontaminated along with other residues from animal rooms before they are thrown away. Boots, shoe covers or other foot covers and disinfecting puddles must be available and used.
- It is possible to minimize the risk of transfer by small airborne particles from contaminated animals or their beds by placing them in cages which are put in air current systems such as biological safety hoods or cabinets, and by covering walls and floors of the cage by filters. Biological safety hoods and other physical containment equipment must be used in

cases where there is risk of producing small airborne particles. These cases include autopsy, lifting of tissues or fluids from contaminated animals or trachea secretions.

6.3.4. Safety Equipment and Facilities (Secondary Barriers)

- The areas and rooms designated to laboratory animals must be separated from areas where people come and go.
- Access to the internal area is limited by doors which open and close automatically. These exit doors might be remote controlled or have magnetic card locks.
- Entry into animal rooms is through entrances with two doors, including a changing room and a bathroom.
- It is also possible to use double door autoclaves to transfer equipment inside and the residue outside. The doors to laboratory animal rooms open inward and are controlled automatically.
- Facilities for keeping animals must be designed in a way as to make it easy to maintain and clean them.
- Internal surfaces (walls, floors, ceilings) must be waterproof. Seams in walls, floors and ceilings must be covered well, and also openings into ducts and spaces between the doors and the hinges in order to facilitate decontamination.
- Automatic hand washing systems must be installed for animal rooms. These had better be installed close to exit doors.
- Other internal equipment and installations such as lighting systems, air canals, electricity lines and connecting pipes must be designed and installed in a way as to create minimum surface in the animal room.
- Windows are not recommended for animal rooms. Any window must be unbreakable. Windows must be seamless and closed off. In cases where it is possible to open these windows, an insect control system is necessary.
- If there is a drainage system in animal rooms, all surfaces must be regularly decontaminated by adequate water or suitable disinfectants.
- Ventilation of the building and of animal rooms must be according to tables found in manuals for keeping animals. The air current supplied for this purpose is always from the clean to the contaminated parts of the building. This air current is not recycled into other parts of the building. Filtration and other air decontamination measures are not necessary for the outgoing air; however, the outgoing air must be directed away from areas and spaces which absorb the air. Otherwise, the outgoing air must pass through HEPA filters. It is imperative to make sure that the correct air current is towards the inside of the room designated for laboratory animals. It is appropriate to use electronic equipment indicating

the direction and intensity of air current into different parts of the building to reach the desirable level. At any rate, laboratory animal rooms must be kept at negative pressure as compared to other parts of the building.

- The outgoing air passing though the HEPA filters of class 2 biological safety filters can be sent into animal rooms again, provided that these hoods are controlled and tested each year for precision and effectiveness. Also, when the air living these hoods is directed outside the building, the exit ducts of the hoods must be connected to exit systems to prevent any interference of the air current with other exit systems.
- In cases where biological safety hoods type 3 are used, it must be made sure that the air leaving the hoods is directly connected to the main system of the exit air.
- Cages used to keep animals must be disinfected with washing equipment in 180 degrees Fahrenheit.
- Autoclaves are necessary in the laboratory and building designated to animals for decontamination of residues before they can be transferred to other parts.
- Lighting must be suitable for all activities; harsh lights and reflections which might hinder perfect sight should be avoided.
- All designs and facilities used in biosafety level 3 must be according to standard. Facilities must be tested so far as design and manufacture are concerned, and the observation of indices must be finalized and approved before they can be used. These tests must be repeated each year.
- Additional facilities and installations such as staff showers and bathrooms, HEPA filters and electricity and water pipes must be taken into consideration and installed if necessary.

6.4. Biosafety Level 4 – Animals

This level of biosafety is suitable for work with external dangerous factors which threaten human health to a high degree. These factors might be transferred through small airborne particles which are unknown and about the transfer of which adequate information is not available. The building used for this level of biosafety is constructed according to working conditions, procedures, instructions and standard containment equipment.

6.4.1. Executive Procedures

Apart from standard procedures, methods and instructions which are established by the project manager and BSO in emergencies, IBC and MBC must approve specific methods and procedures according to circumstances.

6.4.1.1. Operational Stages and Specific Procedures

Entry into laboratory animal rooms is not allowed except for a limited number of people. People who enter laboratory animal rooms must be aware of the potential dangers of the factors with which they work.

- Suitable plans are needed to monitor the health of the people in order to enter level 4. This plan includes suitable immunization, serum samples of the staff and access to measures needed to prevent the outbreak of diseases.
- People who are more likely to be at risk of contact with infectious material and factors, particularly when infectious factors may have dangerous consequences for them, are not permitted to enter laboratory animal rooms unless methods are used which can reduce or eliminate such risks. Specialists must assess the health of the staff.
- A biosafety manual must be prepared and made available in the laboratory. Staff must be familiarized with specific hazards of work with these factors and read and commit to memory the necessary instructions and methods.
- Eating, drinking, smoking and wearing lenses and make up is not permitted. Food for human use must be kept in specific places. These are not permitted in areas designated to animals and in related laboratories.
- All recommended methods must be followed carefully in order to minimize the production of airborne particles.
- Equipment and work surfaces in animal rooms must be regularly disinfected with effective disinfectants after work with infectious factors. Decontamination is especially necessary after a spilling or splashing of such material or other infections created by infectious material.
- Spillage of material or any accident which increases the risks of contact with dangerous factors must be immediately reported to the related supervisor. A log is needed to record accidents and also measures taken to decontaminate. If infectious materials are spilled on a surface, only those people correctly trained who have learned how to work with dangerous factors and materials must attempt to clean and decontaminate.
- All residues from animal rooms (including tissues, bodies, contaminated beds, other waste material, clothing and uniforms) must be disinfected in double door autoclaves before they are sent to the laundry.
- Measures should be taken for work with sharp and cutting implements. Needles and syringes or other sharp implements must be used only once; returning them into their cover and separating the syringes must be avoided. It is better to use syringes with attached needles and plastic instead of glass containers.

- The global biosafety sign must be raised on the door to the room of laboratory animals according to dangerous and pathogenic factors. The danger sign is there to identify infectious factors and bears the name and telephone number of the laboratory supervisor or other authorized people. Conditions necessary for entering animal rooms and facilities needed to enter (such as immunizing the staff against diseases or the use of respiratory masks) must be made clear and raised on the door.
- Staff must receive necessary training regarding the dangerous factors with which they work and observe precautions necessary to prevent the risk of contact. In addition, they must receive up to date training. If necessary, old training and procedures must be changed. It is necessary to record all training.
- Animal cages must be decontaminated and autoclaved before their beds are changed or before they are cleaned and washed. Equipment must be decontaminated before they are transported, fixed or substituted, according to regulations. Equipment and work surfaces in laboratory animal rooms must be regularly washed and decontaminated with effective disinfectants after work with infectious factors and especially after spellings and splattering or other contamination resulting from work with infecting factors.
- Those people who have to work with contaminated animals must work in teams of at least two members. According to the assessment of dangerous factors and needed conditions, suitable procedures are necessary for work with special cages such as isolators and with unconscious animals in order to reduce probable risks of contact.
- Animals and plants unrelated to the experiment are not allowed entry into laboratory animal rooms.
- In order to control and assess these systems and this level of biosafety for animals creating conditions such as 24 hours of quarantines and controlling exit and entry systems are among effective measures.
- In order to enter the building and the room designated to laboratory animals, staff must pass through changing rooms and bathrooms. Staff must take showers whenever they leave the building. Except for emergency cases, staff must not enter the designated area except when they are passing through parts which are under air systems.
- When using class 3 biological safety hoods, staff take off their clothes outside the special changing rooms and leave them there. Full clothing and covering for work at this level of biosafety is underwear and pants along with main protective clothes and special shoes and gloves, which must be put on before entering the designated area. When leaving the laboratory and animal rooms, the above mentioned garments must be taken off before going into changing rooms and bathrooms. All coverings and clothing must be decontaminated in autoclaves.

- In animal biosafety level 4 it is necessary to change all garments. For possible decontamination, it is also necessary for those people who enter the designated area to take showers. All uniforms must be decontaminated in autoclaves.
- All necessary material and equipment which must be taken into the designated area must be decontaminated in fumigation chambers or double door autoclaves. The inside door can be opened after making sure that the outside door of the autoclave or the fumigation chamber has been closed, and only then can the staff take the necessary equipment into the designated area. The doors to double door autoclaves or fumigation chambers are closed and locked from inside, and opening the doors from outside is possible only after decontamination.
- A warning system must be established to announce accidents and dangers due to the contact of factors with the staff and for the staff health. In addition, quarantine systems, isolations and medical treatments are necessary for those people who have suffered an accident.
- At certain intervals, serum samples must be taken from people working in these systems for analysis.

6.4.1.2. Safety Equipment

- Laboratory animals which are used at this level of biosafety must be kept under class 3 biological safety hoods.
- At level 4 of biosafety, staff is in rooms with positive pressure and wear special garments. All laboratory animals must be kept in preliminary containment systems such as cages placed in well ventilated areas. Walls and floors of theses cages must be covered with filters and the spaces containing the cages can be biological safety hoods or laminar flow.
- All equipment and instruments must be used only once so that cleaning them is not necessary. It is also possible to use disposable cages for animals. Disposable instruments must be autoclaved before being disposed, and it is better to incinerate them.

6.4.1.3. Biological Safety Hoods

At different levels of biosafety, especially levels 2, 3 and 4, biological safety hoods are among the most important facilities and equipment to increase the safety of work with infected and danger creating factors and to decrease contact risks for people, environment and the material being used. Biosafety cages have been designed in a way that makes it possible to protect people and the environment from dangerous biological factors and keep experiment material safe from contamination. This is while chemical smoke hoods have been designed in a way that it is only possible to save people from chemical and toxic gases. Therefore, as chemical smoke hoods have

not been fitted with HEPA filters, they should not be used when working with dangerous biological material.

These hoods are small systems of physical containment with high efficiency and precision inside a bigger physical containment system in the laboratory, and that is why they have an important place in the physical containment of the laboratory. That is why biological safety hoods are called preliminary barriers for the manipulation of infectious and danger creating factors in a laboratory whose existence is particularly necessary in biosafety levels 2, 3 and 4. Design and structure of the inner spaces of laboratories are secondary barriers. In the air currents which is established from outside to the inside of the laboratory in these systems, the amount of the air that leaves the laboratory is greater than the amount that enters, and this creates negative pressure in the laboratory. This system is optional for biosafety level 2, but for biosafety levels 3 and 4 this kind of air current system is obligatory; at all times air current is from places clean or with the least amount of contamination towards places contaminated or with the highest degree of contamination.

In biosafety levels 3 and 4 the air current within the system must be considered contaminated, and that is why it must leave the building directly. This means that the exit system for each laboratory and each part of a laboratory must be a separate system. The air exiting the laboratory and the room equipped with biological safety hoods must be filtered in cases where a higher level of physical containment is necessary to control small airborne particles; such filtration system is obligatory for biosafety level 4 but optional for biosafety level 3. In cases where the exit system for the air inside the laboratory building is also responsible to take out the air inside biological safety hoods, the said system must have the capacity to maintain the air current leaving the hoods at a desirable limit when there is a drop or cut in the air current inside the system.

Also, the air exit system must be adjustable both manually from inside the room and from the control center. The amount of air entering the laboratory must be adequate for the appropriate functioning of the exit system. Before biological safety hoods can be installed, necessary studies and surveys must be carried out regarding the engineering design for the installation of a central ventilation system. Avoiding curves and excessive lengths for exit air canals and employing widthwise connection as much as possible increases the efficiency of this ventilating system. The air leaving the building must do so far away from other points so that it cannot reenter other general places or other parts of the laboratory.

Useful facilities which must be taken into consideration for and installed inside biological safety hoods are the vacuum valve and electricity outlets with suitable covers. These hoods must have an independent electrical circuit system.

Outside biological safety hoods there must be provided a gas valve along with emergency and safety valves. There is no need for UV lamps in biological safety hoods. If UV lamps are needed, every week, necessary steps must be taken to clean and dust them to remove any dust particles which might reduce their microbicide potential. These lamps must be constantly tested and

controlled by UV light spread measurement device. UV lamps must be turned off when there are people inside the laboratory, as they cause severe damages to the skin and eyes. Retina burning and skin cancer are among these damages. The place for installing biological safety hoods is among the important points in using these systems. Bearing in mind the developments and advances in the manufacture of these hoods, which protect people, products and the environment from the risk of being contaminated by dangerous and infectious factors, special attention must be paid to ensure maximum application of the advantageous effects of these preliminary barriers. These hoods must be installed at a 12-inch distance from sides and back from other points so that access to air current needed by biological safety hoods can be made easy, and also to prevent the air from reentering the laboratory. A 12- to 14-inch distance is also necessary above biological safety hoods in order to provide adequate space for air to pass with suitable intensity through the exit canal which leaves the hood; a barometer is also necessary. When the exit system of biological safety hoods is connected to the ventilation system of the building, adequate space must be provided so that there is no interference between air currents.

This system can be provided by making the exit air canal of the hood to the main canal of the building ventilating system long. Also, it should be made possible to test or change HEPA filters. The suitable, ideal location for biological safety hoods is away from the points of entry and exit (as far away as possible from places where staff come and go). Staff passing in front of biological safety hoods can disturb air currents inside the hood. The air current forming in front of these hoods is very fragile and its rate of up and down movement is about 1 mile per hour.

Open windows and laboratory equipment which can create air currents (such as centrifuges, vacuum pumps) must not be placed close to biological safety hoods. Also, chemical hoods should not be close to biological safety hoods.

6.4.1.4. High Efficiency Particulate Air Filters (HEPA)

HEPA filters are an important part of the main equipment of laboratory building, especially for biosafety levels 3 and 4, and for cleaning and decontaminating the air leaving the laboratories. Also, biological safety hoods are based on the application of these filters. After a while, because the efficiency of these filters in passing the air current decreases due to heavy loads of contaminating material, these filters must be changed. These filters must be decontaminated before they can be disposed of. Formaldehyde gas is suitable for microbial decontamination, but it is better to consider the filters as a contaminated biological material and therefore incinerate them in special furnaces.

Biological safety hoods can be divided into several groups.

6.4.1.5. Biological Safety Hoods Class 1

These hoods protect people and the environment against danger creating factors but do not constitute protection for material and factors which are worked with inside the hood. These hoods have air currents similar to chemical hoods but also have a HEPA filter for the exiting air current in order to protect the environment. In those group of hoods the unfiltered air blows on the work surface inside the hood. Personal protection is established by creating an air current towards the inside of the hood at 75 feet an hour. With the production of biological safety hoods class 2 the application of these hoods has decreased, but at any rate in certain cases class 1 hoods are used for preliminary activities such as putting lidded centrifuge and small fomenters inside the hood, preparing culture environments and homogenizing tissues, which may create small airborne particles.

The intensity of the air current inside the laboratory or the room where these hoods are installed decreases the efficiency of these hoods.

Rapid hand movements by people working, the place of installing the hood as compared to the exit and entry doors and heat sources are also involved in decreasing the efficiency of these hoods.

These hoods protect the researcher against small airborne particles but create no protection against the work environment inside the hood. Therefore, the air current inside these hoods is not clean and sterile. These hoods cannot be used for chemical works. If necessary, supplementary filters must be used to absorb chemicals.

6.4.1.6. Biological Safety Hoods Class 2

These biological safety hoods protect the researcher, the material and the work environment inside the hood against external contamination. This class of hoods is used for research on animal tissue, cell cultures and especially for work with viruses. In these hoods, the air entering the hood, instead of passing through the internal space of the hood, is directed downward through a series of pores in front of the hood and from there is taken upward through a canal on the back of the hood and after passing through HEPA filters returns to the inside of the hood and another part also passes through another HEPA filter and then leaves the equipment or the hood.

Biological safety hoods class 2 are divided to classes A and B. In class 2A, the air which goes from the pores under the hood towards the HEPA filters in under positive pressure; in this type, 30% of incoming air leaves the hood and 70% returns to the hood. In these hoods the amount of air coming in through the front door of the hood must be equal to the 30% which has left. If the air going out is less than the air coming in, a positive pressure is created, and as a result pathogens and risk creating factors can enter the areas inside the hood. In the same manner, if the air leaving the hood is more than the air coming in, a negative pressure is created and as a result risk creating factors in the laboratory air enter the hood.

This type of biological safety hoods are especially sensitive to anything in the environment which can disturb the air currents in them.

Biological safety hoods class 2 may in turn be divided into several groups. One group is entirely different from biological safety hoods class A2. A major difference with these hoods is the amount of air circling inside them, which is much smaller than A2 class. Another difference is that the incoming air current from the inside of the room to the inside of the hood is filtered first. The amount of air leaving these hoods is 70% and the amount of air which falls into the cycling current is 30%.

In another type of class B hoods which are also known as B2 biological safety hoods, the air current which enters the front of the hood at 100 feet a minute, after passing through a HEPA filter, thoroughly leaves the hood along with part of the air in the hood and has no circling air current. Thus the researcher is safe from pathogens escaping inside the hood. In order for the work environment inside the hood to be clean as well, another canal has been installed on top of the hood for air to enter after passing through a HEPA filter.

6.4.1.7. Biological Safety Hoods Class 3

These hoods have been designed for work in biosafety level 4 and provide the highest level of protection for people, the environment and material inside the hood. Material and equipment which are brought into the hood have been put in containers and then passed through double door autoclaves or double disinfecting tanks. HEPA filters which have been used in these hoods have an absorption index of 99.999% and are known as ultra high efficiency particulate air filters.

Observing the following points is necessary while working with biological safety hoods:

- The environment inside the hood must be decontaminated with 70% alcohol or another disinfectant before starting and after finishing the work.
- If the hood is equipped with UV lamps, they must be turned on for at least 15 minutes; after they have been turned off, the hood must be turned on and left for 10 minutes before work can begin.
- Precise aseptic techniques and methods for preventing contamination and contact with danger creating material are effective only when used with biological safety hoods, and not on their own.
- Hoods must be installed in an isolated place and separate from other parts of the laboratory and away from strong air currents (away from doors, windows, fans, coolers and heaters).
- Based on approved plans, steps should be taken towards the decontamination of biological safety hoods with suitable disinfectants or disinfectant gases such as formaldehyde.
- The surfaces of all the equipment which are to be taken into the hood must be disinfected.
- Actions such as rapid and sudden movements of the hand, and also objects cluttering inside the hoods, which disturb air currents inside the hood, must be avoided; otherwise, there is the danger of creating small airborne particles.

6.1.4.8. Suitbale Application of Biological Safety Hoods

1. Upon entering the room, immediately turn off UV sterilization lamps (if they have been installed).
2. Turn on all the blowers and light bulbs of all 10 shelves.
3. Allow the ventilating system to work for five minutes; check the visual and audio warning systems.
4. Clean internal surfaces which are easily accessed with suitable disinfectants or other cleaning material you have at your disposal.
5. Once work is finished, clean and disinfect all inside surfaces and remove any material deposited on them.
6. Clean and disinfect internal accessible surfaces with suitable detergents or with whatever is available.
7. It is necessary to turn on the UV sterilization system (in case it has been installed) after the work has finished.
8. Allow the ventilating system to work for 5 minutes after the work has finished.
9. Blowers in the shelves must be turned off after the end of the work.

6.4.1.9. Transfer / Installation

Biological safety shelves must be disinfected before they can be transferred. To ensure that the filters are working properly, they must be tested after installation. Preliminary steps for this depend on the skill of your contractor. PM is responsible for arranging with the contractors to do this.

6.4.1.10. Methods of Cleaning Dangerous Biological Leaks

The following methods are employed for cleaning danger creating biological leaks from the inner part of biosafety cabinets.

- Laboratory uniforms must be worn.
- Gloves and goggles must be in perfect condition while cleaning.
- The cabinet may be permitted to continue the time of cleaning.
- Disinfectants must be used and be left for 20 minutes.
- Walls, work surfaces and any equipment in the machine must be cleaned with a disinfected tissue.
- Contaminated material must be disposed of using suitable techniques for dangerous wastes (such as autoclaves).
- Contaminated usable parts must be placed in dangerous biological packages and wrapped to be autoclaved; windows must be wrapped in newspaper before being cleaned and autoclaved.
- Protecting clothes worn while cleaning must be taken off and placed in a package to be autoclaved.

- Cabinets must be used 10 minutes after they have been cleaned and before work can continue or stop.

Sanctions

In I.R. of Iran, Scientists who, and institutions which fail to enforce the provisions or adhere to the intent of these Appendixes in this NBF may be penalized by the withdrawal of applicable or all government research grants. In addition, non-compliance on the part of private organizations awarded special incentives (e.g. funding from the government or tax incentives) for contributing to biotechnological research and development may result in the withdrawal of said incentives.

Scientists and institutions can be held accountable for all the evident consequences (accidents, medical emergencies and disturbances to the community or the environment) of their failure or neglect to comply with the terms and principles of national biosafety guidelines.

The National Biosafety Committee shall update and inform the Director of DOE on all issues pertaining to the violations of these Guidelines. The director reserves the authority to issue public statements on any such issues of infraction, deliberate or otherwise.

Appendixes 7 and 8 are related to the second stage of risk assessment applied field research

Appendix 7
Guidelines for Field Experiments

The present guidelines cover all research work involved in the field test/trial of genetically manipulated plants and microorganisms. As a standard practice, genetically manipulated organisms from laboratory work must be field tested before planned commercial application or planned release into the environment. Such genetic manipulation field work is meant to address the following, underlying objectives:

- To confirm the observations made during laboratory work, and the results from tests conducted at the laboratory level;
- To gather accurate information/data on the stability, transmission/heredity and expression of transgenes under field conditions;
- To Assess the viability (e.g. survival, propagation, competitive ability) of genetically manipulated organisms under field conditions;
- To Assess the adaptive or evolutionary potential of genetically manipulated organisms under changing environmental conditions.

For the purposes of these guidelines, regulated material shall likewise refer to all genetically manipulated material (DNA and RNA preparations, viroids, viruses, cells and organisms, modified or constructed through genetic engineering), derivatives thereof and the wastes or by-products of genetic engineering practices (containing viable organisms or otherwise).

7.1. Categories of Plants and Microorganisms for Field Work - Genetically Modified Plants

Field work with genetically modified plants must first take into consideration the nature or character of the biological system, as follows.

7.1.1 Experimental plants with a history of safe use in field work

For experimental plants, considered to have a history of safe use in field work, let work proceed in accord with the basic standards appropriate to the particular plant.

A. Modified plants that result from conventional breeding practices (e.g. selective breeding, mutagenesis, protoplast fusion or embryo rescue);
B. Genetically modified plants, having inherent characteristics typical of modified plants from conventional breeding practices;
C. Plants, with genetic inserts that are known to be harmless and inoffensive to the environment.

7.1.2. Experimental plants which do not meet the conditions of 7.1.1

For experimental plants which do not meet the conditions of 7.1.1, let work proceed under the appropriate containment level and criteria. Said measures of containment must be effective, if any one of the following conditions is met, or is to be adopted:

A. There is no cross-hybridization;
B. There are arrangements to contain the dispersal of plants and plant materials;
C. Introduced gene expression is stable, and does not fluctuate with changing environmental conditions.

7.1.3. Plants which do not have a history of safe use in field work under the conditions of 7.1.2

In the notable case of plants which do not have a history of safe use in field work under the conditions of 7.1.2, let work proceed with a preliminary risk assessment to determine the full range of possible environmental effects:

A. Effects on the ecology, at the trial site
    - Heightened resistance to diseases and pests
    - Propensity for weediness
    - Harm to other target and non-target organisms
B. Effects on the ecology, in the open environment
    - Potential for cross-hybridization
    - Promotion of, and stimulus for the growth and development of weeds
    - Invasion of feral populations, beyond the trial site
C. Effects on other elements of the surroundings.

7.2. Microorganisms lacking above conditions

These are laboratory microorganisms which lack the above conditions. Work with such organisms is carried out according to suitable levels of containment (appendices 2B-C-D) and according to rules and regulations of physical containment (appendices 2A-E). In order to determine the degree of containment one or more of the following conditions must apply.

1. Suitable biological containment is present in conditions when:
    - Microorganisms do not generate new reproduction before field tests.
    - Changes carried out are to restrict the living organisms and to contain them in target areas.
2. Inserted genes and their structures may have undergone change or transfer to other organisms only in restricted areas.
3. There should exist certain physical arrangements in order to prevent the distribution of microorganisms in target areas and laboratory places.

7.2.1. Microorganisms lacking history

In cases where microorganisms under experiment lack history, work starts with a preliminary risk assessment in order to determine possible environmental effects. These microorganisms are known as difficult or problematic microorganisms, which are engineered for the following cases:

- Production of nutritional matter for plant species which disintegrate as a result of over-production of that plant tissue;
- Results in the destruction of the residue toxin which might cause secondary shock;
- Biological control of plant pesticides which might control target species and result in the production of toxin or pathogenic metabolites, and the spread of disease among the wild population in the place of experiment.

7.3. Genetically modified animals

Researchers working in this field must register complete documentation of the rDNA and send them to the secretariat of IBC for approval and start their experiments only after approval. Levels of animal biosafety are explained in details in appendix 6. In addition, the Department of Environmental must also confirm documents approved by the IBC.

Breeding of genetically modified animals must be done according to the following:

- Breeding and keeping of genetically modified animals should be done in containers distinguishable from those containers for non-engineered animals. Also, genetically modified animals should be kept separately.
- Unusable parts related to genetically modified animals (including dead bodies) should be incinerated and destroyed after sterilization.
- In transferring genetically modified animals outside the work environment, speical containers, which are strong enough to prevent the animals from escaping, must be used. Moreover, specification of containers and safe transfer of animals must conform to appropriate international safety standards.
- The sentence ***"Carry with Care"*** must be printed clearly on all containers carrying genetically modified animals.
- All equipment used in such experiments must be maintained, serviced and frequently tested.
- The special sign for genetically modified animals must be used in all sites of work with them.
- Work places must be kept clean.
- Work clothes must only be worn in work places.

- When transferring genetically modified animals the person responsible for receiving them must pay attention to receiving all the information related to them.

7.4. Proposal draft to obtain permits for research in field trials

1. Title of the project
2. Name of the organisation
3. Name and full address of project manager
4. Place of release (Release is going to happen in which province?)
5. What is the time of release?
6. On what date do you expect release to end?
7. What is the level of release? (i.e., the number of animals and plants involved in the project)
8. What is your prediction for next release so far as time and level are concerned?
9. What are the main objectives of this release?
10. Date and the signature of the project manager

Appendix 8
Regulations and restrictions for field experiments

8.1 Field Tests of Genetically Modified Microorganisms

8.1.1 Experimental Microorganisms with a History of Prior Work

Field testing experimental microorganisms with a history of prior field work, still requires for submission to the IBC, a project notification or proposal form. The IBC shall evaluate the proposed ambient working conditions through to the accredited containment resources, in determining the sufficiency of biosafety provisions. Measures for the control and containment of field work should observe relevant, past regulations and must address the particular microorganism(s) under study. Only after receiving IBC endorsement may work begin. The IBC must forward all proposals and the committees, assessments thereof, to the NBC for records and information.

8.1.2 Experimental Microorganisms with No History of Prior Field Work

Field testing experimental microorganisms with no history of prior field work should proceed under the advice, counsel and direction of the IBC and NBC. In both cases, committee recommendations and the command of work, shall be grounded on the biosafety concerns that may be gathered from the written proposals submitted. The project supervisor is prohibited from initiating work before consent is granted directly by the NBC.

Considering the risks involved with 'raw' or untested experimental microorganisms, measures for the control and containment of field work at this level must set aside provisions for the following, assorted interests:

A. The medium for testing experimental microorganisms (e.g. soil, water, or air) is regulated and contained, at levels directed by the NBC.
B. The boundaries of testing areas need to be clearly demarcated, and posted with "No Entry" signs. Use of testing areas is strictly regulated.
C. The dispersal of experimental microorganisms is monitored closely with a reliable and effective technique, approved by the NBC.
D. Arrangements are made to destroy/inactivate experimental microorganisms, at the conclusion of work.
E. Other interests, which the NBC or IBC deems suitable.

8.2 Field Tests of Genetically Modified Plants

8*.2.1 Experimental Plants with a History of Prior Field Work*

Field testing experimental plants with a history of prior field work, still requires for submission to the Institutional Biosafety Committee (IBC), a project notification or proposal form. The IBC shall

evaluate the proposed ambient working conditions through to the accredited containment resources, in determining the sufficiency of biosafety provisions. Measures for the control and containment of field work should observe relevant past regulations and address the particular plant(s) under study.

Only after receiving IBC endorsement may work begin. The IBC must forward all proposals and the committees, assessments thereof, to the National Biosafety Committee (NBC) for records and information.

8.2.2. Experimental Plants with No History of Prior Field Work

Field testing experimental plants with no history of prior field work should proceed under the advice, counsel and direction of the IBC and NBC. In both cases, committee recommendations and the command of work, shall be grounded on the biosafety concerns that may be gathered from the written proposals submitted. The project supervisor is prohibited from initiating work before consent is granted directly by the NBC.

Considering the risks involved with 'raw' or untested experimental plants, measures for the control and containment of field work at this level must set aside provisions for the following, assorted interests:

A. Contained tests may be conducted in conservatories or plant glasshouses, on site. The scale and period of contained cultivation is appropriate to both the nature of the investigation, and the nature of the particular plant.
B. The site chosen is befitting of (or made to suit) the particular plant under study. Test plots are fenced in and isolated from feral populations. "No Entry" signs are put up at regular intervals around the perimeter.
C. Arrangements are made collect, burn and destroy experimental plants and plant materials at the conclusion of work.
D. The cultivation of plants is surveyed and directed by the IBC, at regular intervals, as appropriate to the growth or developmental patterns of the particular plant.

8.3. Genetically Modified Animals

Experiments on genetically modified animals which have a history will start after obtaining permission from IBC. IBC must send all related proposals to NBC for final approval Experiments on genetically modified animals which have no history are done under the supervision and consultation of IBC. The official responsible for the project must avoid starting work before a permit is obtained from NBC.

Bearing in mind the dangers that exist in experiments with genetically modified animals, all conditions of experiment control and containment must be observed.

Appendix 8-Section A
Instruction for the preparation of project proposal for permission to undertake Field Trial Work

The project proposal for permission to undertake Field Trial Work (along with all attachments and supplements) will serve as the principal source of reference for the IBC in the consideration and approbation of field work regulated under these Guidelines .On the basis of information provided in and of risks/concerns that may be inferred from these proposals ,the IBC shall classify field work and determine additional biosafety measures to be adopted/implemented as necessary, including site relocation and procedural amendments.
Proposals may also be reviewed by the MBC and the NBC, and whatever details provided will constitute the framework for assessment and recommendations.

Recognising that assessments depend on the written proposals, researchers should be through yet concise, and clear as to their intentions ,so that the committees may readily and fully understand the nature of proposed work. All important details should be included.

Prominent intents should be stressed. All data and relevant scientific literature must support your statements. Full disclosure of data or published literature, that allude to potential adverse effects of genetically modified organisms or products thereof to be released, must be made in the project proposal/application .It is critically important that all relevant core questions on pages 67 to 70 are seriously considered and included in the proposal /application under appropriate “headings” or as an attachment .References should be fully documented ,and attached to the proposal/application .In making as assessment ,the IBC shall consider together with other relevant matters .whether data obtained in the laboratory or under contained conditions provide sufficient basis to allow release of the LMO and/or products thereof . The IBC shall consult and discuss with the proponent, make suggestions for revision of the proposal or require further experimental work under contained conditions as it deems necessary The project manager must submit three typed, completed project proposals to the supervising IBC (which shall forward two copies to the MBC/NBC for formation/processing)and retain one copy for records and reference. For work supported by two or more institution, all IBCs must be notified. Cover sheet of the project must be singed and dated by the project supervisor before submission to the IBC. For field work employing multiple project supervisors, the name and professional address of the supervisor preparing and submitting the proposal should be indicated , and the said individual shall sign and date the proposal before submission to the IBC.

8.A.1. Important directive

Researchers must procure a copy of the corresponding project proposal for assessment of Laboratory Genetic Manipulation Work, which precedes the initial genetic engineering of this biological system to be field tested. Attach this form to the back page of the project proposal for Assessment of Genetic Manipulation Field Work before submission to the responsible IBC.
Some information in this proposal is critical to IBC assessment.

8.A.2. Approval of proposals and commencement of work

Work assessed as low to medium risk may commence after a proposal has been assessed and approved by the IBC. Work must be conducted as recommended by the IBC. Work assessed as high risk by the IBC must not commence without the specific approval of the MBC or NBC as the case may be.

8.A.3. CONDUCT OF WORK

The Principal Investigator must ensure that the recommendations of the IBC, MBC and NBC are complied with, and that physical containment requirement and procedures are met during the course of the work.

Appendix 8 - Section B

Format of project proposal for permission to undertake field trials

SECTION B1 - INTRODUCTION

- **Project Title**
  - Rationale of studies

- **Project Objectives**
  - Overall Objective
  - Specific Objectives
    i)
    ii)
    iii)

  - Objectives during 1st Year

    0 12 24 36
    Mounths

  - Time Schedule
    Objective -1
    Objective -2
    Objective –3

- **Intended Date of Commencement : ……..**

- **Expected Date of Completion ……...**

- **Proposed Risk Category**

[ ] Category 1 [ ] Category 2 [ ] Category 3

- **Anticipated Future Release and/or End use.**

SECTION B2 - MATERIALS AND METHODS

- **Site of Field Work**

  - Location of trial and how plots are to be arranged on site .
  - Details of the physical environment and ecology .
  - Facilities available on site .
  - Reasons for the choice of location .

- **Scale of Field Work**
  - Approximate number of organisms involved and the size of test plots .

- **Methodology and Protocol**

- Descriptions of the main experimental procedures.
- Indicate the developmental stages involved ,and identify the control ,test and challenge goups .

❑ **Precautions and Safeguards (please describe in full)**
- Measures for containment of test plots and experimental organisms.
- Arrangements for the disposal of experimental organisms ,and for the clean up of organic residues ,at the completion of work .
- Contingency plans

❑ **Results from Laboratory Tests of Biological System**

A. Characterization of Genetic Modification
- Stability of Introduced Genetic Traits
- Heredity of genetic Inserts
- Level of expression and regulation of transgenes
- Traces of recombinant vectors in the final construct (where applicable)

B. Effects of Genetic Modification
- Changes in Phenotype and Novel Physiological Traits

C. Evolutionary Potential
- Competitive or Selective Advantage ,conferred by genetic modification.
- Potential for Mutation and/or Adaption of field conditions

D. Noxious or Harmful Characteristics
- Nature of Harmful Agent
- Known and/or likely Modes of Transmission

E. Ecological Context(Auto Ecology)
- Viability in Open Environments
- Known predators and parasites
- Natural Crossing Possibilities to Related Species
- Propensity for Transfer of Genetic Inserts

❑ **History of Prior Field Work (with the experimental organisms(s) or with related biological systems)**

❑ **Assessed Course of Work**
- Anticipated direct, and indirect ecological effects
- Possible secondary genetic effects

SECTION B3 - PERSONNEL INVOLVED WITH RESEARCH WORK PROPOSED

❑ **Details of Personnel**
- Name ,Qualification and Experience .
- Responsibilities and Duties .
- Medical History .

SECTION B4 - "CORE QUESTIONS" FOR CONSIDERATION IN THE PROPOSAL IN THE PROPOSAL FOR GENERAL RELEASE

- **Species to be used**

A. What is the species of organism to be used/released? Where relevant give information on the strain, cultivar etc.

B. Is the parent organism or the LMO capable of causing disease or other ill-health in humans, plants or animals? If so, what are the possible effects?
   i) What is the origin of the inserted DNA?
   ii) Does the inserted DNA come from an organism that causes disease or other ill-health in humans, plants or animals? If so,what are the possible effects ?

- **Aim**

A. What is the intended use of the LMO ?

B. What is the nature of the general release ?

C. What is the nature of the activities that have the potential to lead to an unintended release ?

- **Location**

A. Location of the activities that have the potential to lead to and unintended release. For example for genetically manipulated seeds to be imported for processing, the type of container, the location of entry the seed into I.R of Iran, the transport routes, and the location of the processing facility .

B. i) Relevant features of the physical environment in the area Of the activities, particularly those which may minimize or exacerbate undesirable effects.
   ii) Proximity of the site of activities to population centres fields of agricultural activity, or the habitat of biota that might affect ,or affected by the proposed release ?

- **Habitat and ecology**

A. i) What is the natural habitat of the parent organism and Its range ?
   ii) Where was the parent organism normally isolated ?
   iii) What is the distribution of the parent organism in west Asia ?
   iv) Is the parent organism already present at or near the site of the activity ?If so, provide available date on populations.
   v) Is the parent organism exotic to the west Asia ?

B. Are there known predators or parasites of the organism in West Asia ? If so, describe.

C. Could release of the LMO prejudice any beneficial function of the parent organism in the environment ?

- **Genetics of the LMO**

A. What genetic modification has been made ? (a detailed description of the steps undertaken in its construction).

B. Does the LMO have a potentially unstable genotype ?

C. i) To what extent is the genetic modification characterised ?
   ii) What is the location of the inserted DNA in the final ,and how many copies are present?

iii) What markers or sequences will enable the LMO to be identified in the laboratory and under field conditions.

D. i) What type of vector was used in the transfer? A description of the vector, showing the position the inserted DNA and any other control sequences or markers in the vector, will be helpful to the reviewers .
ii) Can the vector transfer to other hosts? If so, provide information on its host range .
iii) Is the recombinant vector present in the final construct ? If not, how was it removed ?

E. If no vector was involved:
i) How was the DNA introduced ?
ii) How many copies of the gene were inserted ?

F. i) How does the modification change the phenotype of the organisms to be used ? Present date to demonstrate the effect of the modification ,including level of expression and regulation of the genetic insert .
ii) What secondary genetic effects may be anticipated ?

G. i) What intrinsic genetic feature, if any ,of the LMO regulate its survival in an unmanaged environment ?How stable are these features ?
ii) What genetic changes ,if any, have been inclused in the LMO to limit or eliminate its capacity to reproduce or transfer its genes to orther organisms ?

- **Stability, survival and transfer**

A. On the basis of contained experiments ,provide date on :
i) The survival times of the LMO in habitats relevant to the activity;
ii) The growth rate (or generation time) or the parent organism and LMO in the range of environmental conditions characteristic for the place and date of the activity ;
iii) The frequency of reversion or less of the genetic change .

B. Is the LMO likely to be able to establish in the open environment outside the sites to be used for the proposed activities ?

C. i) What is the capability of the LMO to disperse into the open environment?
What are the dispersal mechanisms
ii) Can the parent organism form long-term survial structures such as seeds or spores ?

D. Is there any evidence that the inserted genetic trait can be transferred to other organisms found in the area and surrounding environment :If so,
i) To what organisms and at what frequencies ?List the species that have been tested for transfer and explain the rationale for this choices .
ii) What transfer mechanisms are involved ?
iii) What techniques have been used to demonstrate transfer ?
iv) What are the possible adverse effects of the transfer ?

E. Does the modified trait confer a selective advantage on the LMO under certain conditions ? If so, what are these conditions ? Provide data on growth rates with an without selection pressure.

F. Would you expect the LMO to show any competitive advantages over its unmodified parent in mixed populations under the conditions in the area to be used for the proposed activities ? if so, what are the advantages ?

- **Experimental procedures, monitoring and contingency plans**

A. i) Detailed overall protocol for the activities that have potential to lead to an unintended release include procedures for transporting the LMO and according for transported organisms, if relevant.
ii) How many organisms will be involved in these activities ?
iii) What will be the frequency of these activities (in terms of site years = number of sites X number of years of testing)?
iv) Will the activities be ongoing or for a limited period ?

B. Details of any structures or procedures that will be in place to minimise the likelihood of establishment of the LMO in the environment.

C. If release of the LMO into the environment occurs .what might be the consequences (e.g. weediness of plants, problems related to feral animals, secondary ecological effects ,toxicity of the LMO or its products to animals or humans)?

D. What contingency measures ,if any will be adopted to rectify any unintended consequence if a hazard becomes evident during the course of the release ?

E. Details of site supervision procedures and any safety procedures undertaken by staff:

- **Other assessments**

A. Has a similar proposal for the construction of the LMO been assessed in any country in West Asia, South West Asia, South Asia, Europe or American continent? If so, please provide details, a copy of the proposal together with assessment report .

B. i) Have releases of the LMO been made before either in or outside of I.R. of Iran? If so, what were the beneficial or adverse consequences ? Provide or reports of previous assessments .
ii) Has any other neighbouring countries refused an application for the release or use of this organism ?
iii) What factors might suggest greater or less risk with the proposed activity in I.R of Iran. Please provide references or reports of assessments.

C. For an important LMO ,indicate the date of importation or intended importation ,documentation of clearance of assessment from the National Regulatory Body of the country of export .

D. Is there any reason to think that the LMO ,if released, could constitute a hazard, not discussed elsewhere in the proposal ,a) in the area designated ,or b) elsewhere in I.R. Iran?

E. If the organisms are to be consumed as food ,please attend to the following additional points:
i) Is the parent organism or the donor organism already used in food production or eaten as food ? If so, a) at what level of daily/weekly intake , and b) is any processing needed or commonly used before consumption?
ii) Does the LMO produce metabolites which may have adverse effects on the consumer (humans or animals)? If so elaborate .Provide available date on toxicology allergenicity and other possible adverse effects .Can any product of the LMO concentrate in the food chain to levels which may become toxic ? If so, elaborate.
iii) Will the nutritional quality of the food be changed by genetic modification ? If so, how?
iv) Will the LMO be processed during the production of the food " If so, elaborate .
v) Will the LMO be the major component of the food, or it in small numbers in the final product (e.g. yeast cells in bread making)?

F. Any other information that could assist assessment of the proposal .

SECTION B5 - ADDITIONAL POINTS IF YOUR PROPOSAL IS FOR RELEASE OF MICROORGANISMS

- **Aim**

A. i) What is the intended eventual use of the LMO ?
ii) What is the aim of the trail?

- **Location**

A. Describe the size of the release and where relevant the area of land to be used and its location .Provide location and site maps where relevant .

B. i) What are the reasons for the choice of location ?
ii) Describe in detail the relevant features of physical environment . Particularly those which may minimize or exacerbate undesirable effects .
iii) How close is the site to population centres .FIELDS of agricultural activity ,or the habitat of biota that might affect ,or be affected by the release ?

- **Experimental procedures, monitoring and contingency planning**

A. i) Describe in detail the overall experimental protocol for the release, including the protocol for control, test and challenge organisms, if appropriate .
ii) How many organisms are to be released ?
iii) How many releases of the LMO are proposed ?

B. i) What are the arrangements for producing the LMO quantity ,transporting it to the site and accounting for the transported organisms ?
ii) How will the LMO be released ?

C. i) What methods are to used to test for batch to batch consistency if large scale production is required to produce LMOs for release ?
ii) What specific have been taken or will be taken in the production process to ensure the quality/purity of the LMO to be released ?

D. i) How will the survival of the LMO be monitored ? Provide a description of techniques for monitoring the presence of LMOs or transferred genetic material beyond the primary site, including specificity sensitivity and reliability of detection methods .
ii) If the release is likely to affect the characteristics or abundance of other species ,how will this be monitored ?
iii) How will transfer of the introduced gene to other species be monitored ?

E. i) What potential hazards or deleterious effects can postulated.
ii) Measures that will adopted to reduce dissemination of the LMO.
iii) If transfer of the inserted genetic trait to other organisms could result in adverse consequences. What methods will be used to minimize these effects ?

F. i) Will the LMO remain in the environment after the release? If so a) for what period of time , and b)what might be the consequences ?
ii) Will measures be taken to reduce populations or dispose of the LMO once the release is completed ?If so ,provide details .
iii) What monitoring is to be undertaken after the release is completed ?
iv) Provide details of the procedures to be used for collection, storage and transport of seeds collection from the LMO ,if appropriate.

G. What contingency measures will be adopted to remove the LMOs if a hazard become evident during the course of the release ?
   i) What will be the site supervision procedures and any safety procedures undertaken by staff? What is the distance of the site from the location of the IBC.
   ii) What measure have been adopted to train the staff responsible for conducting the release

Section B6 - Additional points if your proposal is for the release of plants

A. Has the parent plant an extended history of cultivation and of safe use ? If not ,explain .

B. What , if any ,unintended pleiotropic effects ,including undesirable effects on agronomic characteristics of the plant ,may result from the expression of the transgene in the LMO (e.g. reduced fertility , increased prevalence ,production lossess ,grain shedding)? Indicate the likelihood of these events .

C. i) Describe the mechanism of pollen spread (by insect vectors or by other means) in the plant .
   ii) Provide available date on pollen viability for the plant.
   iii) Indicate potential pollinators and their range and distribution in I.R Iran.

D. i) Are any members of the genus of unmodified parent known to be weeds in any environment ?If so, specify ?
   ii) Are there literature reports on cross-pollination between the species to which the LMO belongs and wild relatives known to be weeds ? If so, please list .

E. i) Provide quantitative date on successful cross-pollination between the plant and its wild relatives .
   ii) If you know that sexually compatible plants live near the site of the release ,give details and quantify the chances for cross-pollination .
   iii) If cross-pollination occurred ,would the resulting plants survive/compete well ? If not, why not?

F. If there is any possibility that the imported characteristic could be in integrated into other species :
   i) Would it have the potential to effect the distribution and abundance of the other species? If so ,specify ,Date on the factors which normal control populations of these other species in the natural environment (e.g. pathogens , herbivory ,physiological stress) may be relevant;
   ii) Could it have any other adverse consequence ?
   iii) Has any attempt been made to minimise the risk (e.g. by imparting male sterility or other means of reproductive isolation)? If not, why not?

G. i) Will the plants in this release set seeds? If not, is this planned for later releases ?
   ii) If plants are allowed to set seed, does the mature seed normally remain contained within an year, capsule, pod etc. so that practically all of the seed can readily by harvested, or is the seed shed soon after it matures ?
   iii) Can the seed be dispersed by natural mechanisms ? If so, describe.
   iv) Are the seeds capable of being dormant for a long time? If so, how long?

H. Can the plant be dispersed by vegetative propagation? If so, describe the possible mechanisms.

I. How might the plan's competitive advantage (fitness) be changed (i) in the agricultural setting; (ii) in the natural environment ? Explain.

J. Does the novel characteristic change the capacity of the plant to add substances to or subtract substances from the soil (e.g. nitrogen, toxic compounds)? If so, describe the change .

K. i) Is there any likelihood that the introduced gene could cause an increase in toxicity of the plant for animals and humans ?If so, provide available date .
ii) Could any products of the plant concentrate in the natural or human food chain to levels which become toxic ? If so ,explain .
iii) Is the biodegradability of the plant changes ?If so ,how ?

L. What secondary ecological effects might result from release of the LMO (e.g. effect on endangered native species, resistance of insect populations to an insecticide, reduction or increases in numbers of prey or parasites)?

M. If the construct involves resistance to a chemical agent (other than selective agents ,such as antibiotics ,used in strain construction) :
i) Provide data on the degradability ,selectivity and toxicity of the chemical concerned :
ii) What is the agronomic significance of the chemical ?
iii) What is the biological activity of the chemical ?
iv) How is the chemical applied and used ?

N. If the construct involves resistance to herbicide ,explain or describe :
i) The farming system into which the crop is to be integrated and the effect the release will have on this system ;
ii) What impact the release will have on use of the herbicide to which the LMO has been made resistant (provide forecasts on areas to be sprayed and volumes to be applied).
iii) What impact the release will have on total use of other herebicides and insecticides ;
iv) What impact the release will have on weed control .
v) How the release will affect programs designed to involve environmentally friendly chemicals or practices ;
vi) The development and operation of future Integrate Peat Management (IPM) strategies for farming system in which the LMO is used .In particular, describe how the strategies would minimise or avoids (a) the potential for the LMO itself to become an environmental weed ; (b) the potential emergence of herbicide-resistant weeds; and (c) the persistence of the transgene or LMO in the farming system such that herbicide-resistant volunteer plants appear within subsequent crops of a rotational system .

Section B7 - Additional points if your proposal deals with <u>microorganisms living in or on animals</u>

A. What is the animal host species ?

B. Has the parent organism an extended history of use in agriculture ?If so ,please elaborate .

C. i) What new capacity will the LMO provide for the host species ? (e.g. ability to degrade plant pasture toxis)?
ii) What secondary effects can be postulated from conferring that capacity on the host?

D. Will the competive advantage or ecological fitness of the host be altered ?Provide data to support your answer .

E. Is there evidence that the LMO might be capable of establishing in or on other animals, including feral animals ? If so, what are these animals and what are the effects?

F. What other effects (including secondary effects) are likely on other plants or animals in the agricultural and natural environments ?

G. What secondary effects can be postulated from the introduction of the LMO into or onto the host ? (For example , is there a possibility of the genetic insert being transferred to other organisms in the host or to host cells ?

H. Will the LMO be excreted or otherwise leave animal? If so, for how long does it survive outside the animal ?
   i) What is survival and dispersal of the LMO in natural waters and soil ?
   ii) What could be the effects of the LMO on water quality ?
   iii) Does the LMO produce sports ?
   iv) Is the LMO resistant to desiccation ?

I. What sterilising and anti-microbial agents are active against the LMO? Is the LMO susceptible to UV and ionizing radiation ?

Section B8 - Additional points if your proposal deals with <u>microorganisms as live vaccines</u>

A. i) What disease is to be controlled by the use of this vaccine ?
   ii) On what host species is the vaccine to be used ?
   iii) What is the host range of the parent organism from which the vaccine was constructed?

B. If the vaccine is intended for humans ,what are the proposed target groups for the vaccine? Specify age range ,risk factor groups and geographic area (District/Province),If applicable .

C. i) Provide data regarding level and duration of immunity produced in the host species after vaccination with the LMO.
   ii) Over what period can the vaccine organism be detected in the vaccinated animals or their excretions ?Provide supporting data

D. Can the vaccine organism spread from vaccinated to non- vaccinated animals or to other species (including humans) ? If so, what is the mechanism and frequency? Provide data,if available .

E. Is there any evidence to indicate whether the susceptibility of the host to the vaccine organism could be affected by the current state of the host (e.g. immunosuppression or superimposition of other disease) or by other treatments (e.g. drugs) ?If so, elaborate .

F. Does the genetic material of the vaccine organism have the potential to become incorporated in whole or in part into the genome of any cells of the vaccinated host ?

G. If this is a viral vaccine ,can the nucleic acide of the virus in the vaccine be rescued or be restored to wild type , by recombination or complementation with intracellular viruses ?

H. i) If the proposal is for permission for field trials, is it proposed to dispose off waste which contains vaccine organisms? If so, describe the arrangements .
   ii) What is the fate of the vaccinated animals at the conclusion of the trail?

I. Will the vaccinated humans or animals carry live vaccine organisms at the end of the trail ? If so:

i) Will they be likely to disseminate the live vaccine organisms to their family contacts or to the general population ?
ii) What measures, if any, will be taken to minimise this possibility ?
iii) Will the organisms be able to cross the placenta ?

J. Is the use of this vaccine organism likely to preclude its use for vaccination against other diseases subsequently? Will its usefulness for other vaccinations be affected ?

K. Is the vaccine likely to have any deleterious effects on pregnant humans or animals ?If so, specify ,For humans provide data from animal models .

L. Is the vaccine teratogenic (i.e. causing development defects) for the foetus at any stage of gestation ? If so, elaborate .

M. Does the LMO produce spores ?

N. Is the LMO resistant to desiccation?

O. What sterilising and anti-microbial agents are active against the GMO ? Is the GMO susceptible to UV and ionizing radiation ?

SECTION B9 - ADDITIONAL POINTS IF YOUR PROPOSAL DEALS WITH MICROORGANISMS NOT FALLING UNDER APPENDIX2 B-G SECTIONS

(Which are associated with plants and microorganisms which might be applied to modify the physical or chemical environment (e.g. microorganisms to modify soil properties).

A. For microorganisms associated with plants ;
i) What is the partner species of plant ?Describe the specificity of the interaction and indicate the range of plant species with which the LMO can interact .
ii) Has the parent organism an extended history of use in agriculture ? If so, please elaborate .
iii) What is the effect of the LMO on the plant species and how will this be monitored ?
iv) What other secondary effects might the LMO have on the plant ?
v) Does the modification cause any change to the range of host plant species available to the organism ?
vi) What effect of the LMO, if any, is anticipated on the distribution and abundance of the host plant species and other species with which the organism can interact.

B. If the plant species are food crops will, it effect the suitability of the resultant produce for human or animal consumption ? If so, explain.

C. What are the effects expected on soil chemistry (e.g. PH, mineral leaching, chelation , nutrient level)?

D. What is the survival and dispersal of the LMO in natural waters and soil ?

E. What could be the effects of the LMO on water quality ?

F. Does the LMO produce spores ?

G. What effects might the LMO have on soil organisms which are known to be beneficial to plants (e.g. Rhizobium, Azospirillum, Frankia and Mycorrhizal funji) and are likely to be in the test area ?

H. What is known about interactions between the LMO closely related microorganisms in the partner plant (if applicable) or the environment of the release site ?

I. For LMOs associated with plants , what effect might the LMO have on insects ,birds and animals (including humans) which may eat the plant ?

J. Does the LMO exchange genetic material with known plant pathogens ?If so, elaborate .

K. Is the LMO resistant to desiccation ?

L. What sterilising and anti-microbial agents are active against the LMO ? Is the LMO susceptible to UV and ionizing radiation ?

SECTION B10 - ADDITIONAL POINTS IF YOUR PROPOSAL DEALS WITH ORGANISMS FOR BIOREMEDIATION

A. i) What is the target substrate for bioremediation ?
ii) What effect does the parent organism have on the target substrate ?
iii) What effect does the LMO have on the target substrate ?

B. What other substances can be metabolised by the LMO which cannot be metabolised by the parent organism ?

C. Will the LMO be self-sufficient if added to the contaminated site or will additional measures be required (e.g. provision of supplementary nutrients and growth factors or other environment modifications)?

D. Does the LMO produce metabolites which may have deleterious effects directly on other organisms or indirectly concentration in the food chain ? If so, specify .

E. What effects might the LMO have on water , air or soil quality ?

F. What effects might the LMO have on organisms which ingest it ?

G. Will the LMO be dispersed from the site of application? If so ,describe the mechanisms involved and the consequences .

SECTION B11 - ADDITIONAL POINTS IF YOUR PROPOSAL DEALS WITH ORGANISMS FOR BIOLOGICAL CONTROL

A. i) What is species targeted for biological control ?
ii) What direct effects does the parent organism have on the target species ?
iii) What direct effects does the LMO have on the target species ?

B. i) What is the host range of the LMO ?If the host range of the LMO is likely to be different from that of the parent organism ,explain why .
ii) What non-target organisms have been tested for susceptibility to the LMO ?
iii) What is the rationale for the choices tested ?

C. How is the LMO transferred from one target individual to another and what factors affect this transferability ?

D. What secondary effects can be envisaged on predators, prey or parasites of the target species?

E. i) Explain the consequence of the removal or reduction of target species on the management of agriculturally significant plants or farm animals.
ii) Predict any change in the ecosystem resulting from a reduction in the population of the target organism.

F. Does the LMO produce metabolites which may have deleterious effects directly on other organisms or indirectly through concentration in the food chain ? If so elaborate.

G. If the modified genetic traits can be transmitted to other organisms which are likely to be in the environment are these organisms likely to affect non-target species ?

SECTION B12 - ADDITIONAL POINTS IF YOUR PROPOSAL DEALS WITH ORGANISMS TO BE CONSUMED AS FOOD

- **If the product is enzyme**

A. Is the parent organism or the donor organism already used in food production or eaten as food ? If so, (i) at what level of daily/weekly intake, and (ii) is any processing needed or commonly used before consumption ?

B. i) Does the LMO produce metabolites which may have adverse effects on humans or animals ? If so, elaborate. Provide available data on toxicology, allergenicity and other possible adverse effects.
ii) Can any products of the LMO concentrate in the food chain to levels which may become toxic ? If so, elaborate.

C. Will the nutritional quality of the food be changed by the genetic modification ? If so, how ?

D. D….Is the LMO to be processed during the production of the food ? If so, elaborate.

E. Is the LMO the major component of the food as eaten, or is it in small numbers in the final product ?

- **If the product is fish and aquatic organisms such as crustaceans**

A. i) Could the LMO produce any 'new' metabolites or toxins likely to have deleterious effects on parasites or predators ? If so, elaborate.
ii) What other unintended effects may result from the release ? Your answer should include consideration of the lMO on the community ecology at the release site.
iii) Are any of the likely gains directly linked to losses in other characteristics of the organisms ?

B. i) Will the LMO in this release be allowed to breed ? If not , is breeding planned for later releases or commercial use ?
ii) Are the arrangements for handling any offspring the same as those for the experimental organisms ? If not, please specify the arrangements.

C. Can the changed or added genetic material be transmitted by means other than by reproduction normal for the species or to any other species ? If so, specify, an elaborated its effects.

D. Do natural populations of the parental organism exist in I.R. of Iran (including in rivers, lakes, dams or coastal waters) ? If so, do the natural populations cause problems with other organisms ? Specify the organisms and the problems .

E. If no natural populations of the organisms to be modified exist in I.R. of Iran ,could the modified characteristics enhance the ability of the species to establish populations in aquatic habitats ?

F. Has any experimental work been done on phenotypic expression of the novel genetic materials in naturally occurring organisms (e.g. cross-breeding of LMOs with wild or domesticated animals) ? If so ,what were the results ?

G. What is the likelihood of the novel genetic material entering the gene pool of natural populations ?

H. Could the entry of the novel genetic material into gene pool of a natural organism have any effect on the distribution and abundance of the organism or on associated fisheries ,the environment or public health ? If so ,please explain .

I. What mechanisms will be used to prevent dispersal of the LMO into other ecosystems ?

- **If the product is Invertebrates**

A. i) What effects might the LMO have on the food chain ?
ii) Could the LMO produce any 'new" metabolites or toxins likely to have deleterious effects on parasites or predators ? If so, elaborate.
ii) What other unintended effects may result from the release ? Your answer should include consideration of the LMO on the community ecology at the release site.

B. i) Will the lMO in this release be allowed to breed ? If not, is it intended to use fertile organisms in later releases ?

C. Do population of the parental organisms exist in the I, R, of Iran? If so, do these populations cause agricultural ,environmental or public health problems or benefits ?

D. i) Can the changed or added genetic material be transmitted by means other than by reproduction normal for the species or to any other species ? If so, specify, an elaborated its effects .
ii) What is the likelihood of the novel genetic material entering the gene pool of natural populations?
iii) Can the changed or added genetic material be transmitted to any other species ? If so, specify the mechanism of transfer and it's the species .

E. Has any experimental work been done on phenotypic expression of the novel genetic material in other genetic backgrounds (e.g. cross-breeding of modified strains with wild animals) ? If so, what were the results ?

F. Could the entry of the novel genetic material into gene pool of a natural populations of organism have any effect on the distribution and abundance of the natural populations ?What would be the effect of this change ?

G. What mechanisms will be used to prevent dispersal of the GMO into other ecosystems ?

SECTION B13 - REPORT ON FIELD TRIAL

When the field trials have been completed, a report must be prepared in four copies. One will be filed in project records, another one will be submitted to the relevant IBC, the two remaining copies will be sent to the relevant MBC and to the NBC for record.

COVER SHEET

PROPOSAL FOR PERMISSION TO CONDUCT FIELD TRIALS

1	**Reference numbers: (IBC numbers for proposals, previously submitted from which this deliberate release proposal has developed)**		
2	**Project title:**		
3	**Name of organisation:**		
4	**Supervising IBC:**		
5	**Project manager:**		
Name		Position	
Address			
Telephone	Fax		Email
6	**Location of release:**		
7	**In which district/province the release will take place?**		
8	**When is the release to occur?**		
9	**When is the release expected to end?**		
10	**Scale of release (number of animals involved, size of plot etc.):**		
11	**What is the size, scale and timing of anticipated future releases?**		
12	**Main objectives to be achieved from the release:**		
13	**Signature of principal investigator submitting this proposal.**		
			Date:

IBC ASSESSMENT OF PROPOSAL FOR FIELD TRIAL

1	**Reference numbers: (IBC numbers for proposals, previously submitted from which this deliberate release proposal has developed)**
2	**Project title:**
3	**Name of organisation:**
4	**Supervising IBC:**
5	**Project manager:**

Name	Position
Address	

Telephone	Fax	Email

6	**Location of release:**
7	**In which district/province the release take place?**
8	**When is the release to occur?**
9	**When is the release expected to end?**
10	**Scale of release (number of animals involved, size of plot etc.):**

11	What is the size, scale and timing of anticipated future releases?
12	IBC assessment: (Give an evaluation of the project including a comment on the project manager's capability to mange the work, the adequacy of the project design, site selection and contingency plans.)

SECTION B - IBC RECOMMENDATION

13	The project has been reviewed by the IBC as assessed above and the Committee does not endorse [ ] the work as proposed; endorses [ ] the work with the following provisions.
	Provide additional information/documents on Follow condition/amendments in your research as follows
14	The following special provisions must also be adopted

SECTION C - IBC REQUESTS MBC

15	The Project Proposal has been reviewed by the IBC and as assessed above, the Committee requires and requests MBC for specific advice/action regarding the following
i)	
ii)	
iii)	
iv)	
16	Signature of IBC Chairperson
	Date / /

SECTION D - MBC REQUESTS NBC

15	The Project Proposal has been reviewed by the IBC and the MBC as assessed above, the Committees require and request specific advice/action regarding the following
i)	
ii)	
iii)	
iv)	
16	Signature of MBC Chairperson
	Date

/ /

SECTION E

15	The NBC has reviewed the IBC/MBC assessment/request for advice and approved the following actions:
i)	
ii)	
iii)	
iv)	
16	Signature of NBC Secretary
	Date / /

Appendix 9
Transfer and transboundary movements of LMOs
(export, import and labelling)

Individuals who wish to import viable microorganisms, plants or animals, genetically modified or constructed, must proceed in accordance with the relevant guidelines presented here and are strongly encouraged to consult with the IBC regarding the specifics of their intent. Import of live or whole organisms of another nature is regulated directly by the various orders and enactments presented under this appendix . On the other hand, international postage or export of regulated material must strictly comply with the revised provisions and requirements of The Non-Infectious and The Infectious Perishable Biological Substances Services as agreed to by the International Postal Union (IPU).

9.1. Transport of LMOs

In order to decrease probable risks and damages involved in the uncontrolled transfer of LMOs and their products, it has been decided that the transfer of such material from one laboratory to another or from a laboratory to field trials inside the country and their export and import for commercial or research purposes be under control.

For the purposes of serious prevention, until there is undisputable proof that the LMO constitutes no risk for the environment, biodiversity, human and animal health, no permit must be issued. This is a serious and important requirement. Danger is normally defined as “the extent and intensity of estimated danger to the probability of the occurrence of danger”. Decisions should be made based on the principle of prevention and according to available data. In other words, if there is evidence of damage even in the absence of scientific reasons, there is no reason why applications cannot be rejected or approved conditionally.

In general, in transporting LMOs the following data are needed:

A. The receiving environment, including information about location, geographical region, climate and ecological features, information on biodiversity and the main source and origin of the receiving environment, possibly potential, such:
   - ✓ Whether the LMO is forbidden in the importing or exporting country, and the reasons for it being banned;
   - ✓ Result, purpose and any information regarding the transported LMO by the importer to other countries;
   - ✓ Confirming the validity of the above mentioned information.

B. The exporting party must guarantee that there are legal provisions for the validity of the information offered by the exporter.

9.2. Bilateral, regional and multilateral agreements and arrangements for the transport of LMOs

Parties of agreement can achieve bilateral, multilateral or regional arrangements and agreements considering internal and international transport of LMOs which are compatible with the objectives of their country's directive, and based on the condition that such arrangements and agreements are of a lower level of protection of human and animal health, biodiversity and the environment. The parties will inform each other of lateral, multilateral or regional agreements through the biosafety clearing house. Each party may stipulate that their internal regulations will be exercised for certain importations, and they must announce such decisions through the biosafety clearing house.

9.3. Informing

9.3.1. Sending notice before transportation

Before internal and international transport of LMOs (including plants, animals and microorganisms), the exporting party must give notice of its intentions to the importer or the internal receiver and through the national center to the national competent authority in the country.

The exporter or the internal producer must make sure that the said notice has been submitted to the national authority in writing.

The notice must contain the following information:

A. Name, address and contact details of the exporter or the internal producer;
B. Name, address and the contact details of the importer and the internal receiver;
C. Name and identity of the LMO, and also internal classification and, if information is available, the biosafety level of the LMO in the exporting or producing country;
D. Specific date or dates of internal and international transportations if information is available;
E. Classification, generic name;
F. Location of collection or acquisition;
G. Features of the receiving organism in relation to parent organisms related to biosafety;
H. The main center of production or genetic diversity centers if from receiving organism or parent organism and a description of the habitat of the organism due to which the creature can resist and reproduce;
I. Classification, generic name, location of collection or acquisition and features of the donor organism as related to biosafety;

J. Description of the nucleic acid or the modification and adjustment created, the applied biotechnology and the features created in the LMO;
K. Purposeful use of the LMO or its resulting products, i.e. material under the process resulting from the source of the LMO, including new discoverable combinations of reproducible genetic matter which has been obtained as a result of the application of advanced biotechnology;
L. Amount or volume of the LMO to be transported;
M. A report of prior and existing risk assessments according to this directive.

9.3.2. Announcement of receipt

The importer or the internal receiver must acknowledge in writing receipt of the above notice and information related documentation within 90 days to the exporting party and the national center.

Acknowledgement of receipt on the part of the importer or receiver must include the following:

A. Date of receiving informing documentation notice – warning) in writing;
B. Whether the documentation regarding the transport of the LMO is complete;
C. Decision making process which must be followed according to this directive.

Failure to announce the receipt of the information documentation on the part of the importer or internal receiver will not indicate approval of transportation.

9.3.3. Decision making processes

9.3.3.1. Internal or international transportation to use LMOs

The decision making process regarding the transportation of LMOs will be based on the following:

1. Measure are taken based on risk assessment or according to the procedures stipulated by the national competent authority, and must be according to the risk assessment found in this directive.
2. The importer or the internal receiver will advise the informing party, within 90 days and in writing, how internal transportation can be done: a) only after the importing party has agreed in writing and b) after 90 days without following written permission.
3. Within 270 days after receiving written informing documentation, the importing party will submit, in writing, to the informing party and the national biosafety committee, the decision regarding the issue in paragraph A: a) approval and confirmation of transportation, with or without conditions, including how the said decision will be applied to following transportations of the same LMO; b) rejection of transportation; c) request for additional related information according to the internal rules and regulations or informing documents. The period of time during which the importing party has to wait for additional information will

not be included. d) Notice will be given that the above time has been extended to a particular date.

4. Except for cases when approval is given unconditionally, any decision under paragraph 3 above must be announced accompanied by reasons why the decision has been made. In case the importing party or the internal receiver does not announce any decision within 270 days from the date of being informed, an approval of transportation will be assumed. Lack of adequate knowledge or information about potential harmful effects of the LMO regarding the protection of natural resources and sustainable use of genetic diversity, and also risks to human health, in order to reduce probable potential risks as mentioned in paragraph 3, will not stop the importing party from not making a decision.

9.3.3.2. Internal or international transfer for direct use as food, feed or for processing

1. The party which makes the final decision for the internal use or the processing of the LMO, if desiring internal or international transportation for direct use as food, feed or processing, must within 15 days of decision making inform the parties involved in the agreement through the biosafety Clearing House. This information must include a minimum of the information stipulated above. The involved party will submit a written copy of the related information to the national center of those parties who previously informed the secretariat that they lack a Biosafety Clearing House. These contents will not be used to make decisions for field trials.
2. The deciding party of the agreement must make sure that the information presented by the applicant is legally valid.
3. Any of the parties can ask national competent authority for additional information such as:
   A. Name and contact details of the applicant for decisions for domestic use;
   B. Name and contact details of the national competent authority responsible for decision making.
4. The importing or exporting party can make decisions regarding the LMOs for direct use as food, feed or processing only if it is compatible with the objectives of Iran's existing laws.
5. If transportation is international, each party must make their internal rules and regulations and their current guidelines available to the biosafety clearing house for the importation of LMOs to be used directly as food, feed or for processing.
6. Lack of knowledge or information regarding the potential harmful effects of LMOs to be used directly as food, feed or for processing on the protection of natural resources and sustainable use of biodiversity, as well as risks to human health, to minimize potentially harmful effects, will not stop the importing party from making a decision.
7. The importing party of the agreement has the right to change a decision according to new scientific information regarding potentially harmful effects related to the protection of natural

resources and sustainable use of biodiversity and also risks to human health, and revise a decision regarding intentional internal and international transport. In such cases, the said party will give notice to the notifier within 30 days that previously the decision has been based on such a decision and will also inform the biosafety clearing house and will present reasons for the decision.

8. The exporting party could also ask the importer to revise a decision according to the results of risk assessment.

9.3.4. Confidential Information

1. The party of import shall consult the notifier to see whether the information received is confidential or not. Before broadcasting any information received, the informing party must be informed of the decision made and of its reasons, and be given opportunity to negotiate and internally review this decision.
2. As part of the Advanced Informed Agreement, the importing party will give permission for the identification of the information presented according to this directive or the necessary information to the NBC and national competent authority, which has been done confidentially. Relevant details involved in such cases will be offered on demand.
3. Both parties must protect the confidential information that they have received based on this directive. Both parties must guarantee that the manner of protecting confidential information is such that it is not less serious than protecting confidential information regarding local LMOs.
4. The importing party must not use such information for commercial purposes, unless when the informing party has given a written permission.
5. If the informing party changes its mind and decides not to give information, the importing party will respect the confidentiality of the industrial and commercial information, including research and production information and also information the confidentiality of which is not accepted by the informing party.
6. Without damaging the contents of paragraph 5 above, the following information will not be considered confidential:
   A. Name and address of the informing party;
   B. A general description of the LMO;
   C. A summary of the assessment of harmful effects on the protection of natural resources and the sustainable use of biodiversity while considering the risks of illegal international transportations.

9.4. Safety precautions regarding the transportation of living modified organisms

Those researchers who distribute LMOs among institutes and internal or foreign scientists must inform the receiver of the requirements and regulations of their biological and biochemical containment, safety precautions and any specific instruction regarding work with the received material.

In addition, researchers must announce the details of the origin of the LMOs to the receivers so that they can be used as reference. In cases where there is no local prior relation or background of genetic engineering and biotechnology, the distributor must accept an additional responsibility to guarantee that the receiver has been informed of the national regulations for work in this field.

Receipt or distribution of any kind of LMO must be reported to the chairperson of the related organization for legal measures.

9.4.1. Transportation of LMOs between and inside institutes

Special care must be taken while transporting LMOs inside a department or from one to another. LMOs (transgenic plants and animals and their products such as saplings, shoots, seeds, pits and plant tissues) must be carefully sealed in double layered containers and then transported. Each package must have an inside layer to protect organism(s) or cultured treatments and a second surrounding wall to be disinfected easily. These packages must have labels so that they can be put inside the strong outside layer and then display clearly the details and address to make inspection easy, expedite the delivery, and provide emergency contact details of the owners of the goods if necessary. Transportation of residues or side products of genetic engineering processes require similar packaging and transportation conditions.

9.4.2. Transporting LMOs

Obligatory limitations in the transportation of LMOs give permission of transport only to those agreements which clearly stipulate that no transgenic organism which has been recognized as dangerous for the environment or the society will be transported while the packages or parcels are being inspected. Those types which have been classified as “benign” for humans or the environment can be transported in packages and parcels following basic standards. Microorganisms, pathogens and infectious or traumatizing factors can be transported only if the type of transport guarantees suitable disinfecting conditions.

9.4.3. Transporting genetically modified plants and animals

Transportation of living genetically modified plants and animals must be done by an individual who has had adequate experience and knowledge in work with living genetically modified species and plans to control the population of these species so that there will be no trouble in emergencies.

Selected extreme containments must be designed and applied at the highest possible level to minimize the potential for the escape of these species during an emergency and to prevent free reproduction of transgenic species and their stabilization in the environment. Suitable agreements must be prepared to determine and execute the transportation of each plant, animal or parcel.

For the transport of living genetically modified plants it is recommended that complete plants be placed inside mesh nets and that theirs flowers be separated before transportation. Plants containing seeds must not be transported.

Importing living or complete organisms from other environments must be done under direct control of state rules and regulations. On the other hand, international transportation or exportation of living living modified organisms must be with the observation of all conditions and requirements of "perishable infectious or non-infectious biological matter" according to the "international mail agreement."

Import and export of pathogens must be subjected to quarantines. Import of living genetically modified plants must be under Plant Quarantine Act under any circumstances.

9.4.4. Application form for the transportation of living living modified organisms and related products

When a living living modified organism and its related products have been tested in filed trials and there is enough data, it is possible to fill in a request to place the said living living modified organism and related products under particular regulations. Request / proposal must include details about data from field trials and related biological and molecular data so that the individual reading the request is assured that using that matter involves no harmful effect. This request may include opinions / decisions regarding similar products or data obtained from other sources. This information will include advantages and dangers in using the particular matter. It is better if application for commercializing organisms and their products is lodged with the following forms:

APPLICATION FOR PERMISSION FOR THE MOVEMENT OF REGULATED MATERIALS

1. Name and full professional address of Applicant:	2. Permission Requested	3. This Request is
Tel: Fax: Email	Limited in–country Movement [ ] Limited - Importation [ ]	New [ ] Renewal [ ] Supplemental [ ]
	5. Permission Requested ("X" one)	
	Mail [ ] Baggage or hand-carried [ ] Common-*carrier* [ ] By Whom _____	

6. Give the following, if applicable (if more space is needed attach additional sheet)

	Scientific Name	Common Name	Trade Name	Other Designation
i) Donor organism				
ii} Recipient organism				
iii) Vector Agent				
iv) Regulated organism or product				

7. Quantity of regulated article to be introduced and proposed schedule and number of introductions.	8. Date (or inclusive dates of period) of importation or in country movement .
9. Country or point of origin of the regulated article.	**10. Port of arrival/destination movement or specific location.**

11. Any biological material (e.g. culture medium or host material) accompanying the regulated article during movement.

12. State why you believe the organism or product does not come within the definition of a regulated article .

13. Certificate : I hereby certify that the informaition in the application and all attachments is complete and accurate to the best of my knowledge and belief

14. Signature of Applicant	15. Printed name and title	16. Date

APPLICATION FOR PERMISSION TO
IMPORT OR TRANSPORT ORGANISMS OR VECTORS

1. Mode of transportation (Please circle) .	**2. Port of Entry**
AIR SEA LAND ANY	
3. IMPORTER: (Name, complete address, telephone, and fax number).	**4. SHIPPER: (Name and address of foreign producer)**
Tel: **Fax:** **Email:**	**Tel:** **Fax:** **Email:**
5. DESCRIPTION (material, country of origin, animal source recombinant system & genetic inserts conditions of imported preparation, antibody immunogens etc.)	
6. Quantity and frequency of imports (estimate)	
7. Proposed use of material, expected completion date, and final disposition (method)	
8. Description of applicants facilities and equipment for handling	
9. Qualifications of technical personnel working with this material (if applicable)	
10. Treatment of material prior to importation (processing/purification methods, treatments, disease safeguard, etc.)	
11. Work objectives, proposed plan of work, and additional pertinent information (animal model, use of derivatives, etc.)	
12. Pertinent Published Paper/Abstract regarding material to be imported – attach copy. if available	
13. Certificate: I hereby certify that this material will be used in accordance with all restrictions and precautions as may be specified in the permit.	
14. Signature of Applicant	**15. Printed name and title**	**16. Date**

APPLICATION FOR PERMISSION TO
IMPORT OR TRANSPORT PLANT OR PLANT PRODUCTS

1. PLANTS OR PLANT PRODUCTS TO BE IMPORTED		
COUNTRY OF ORIGIN **Make separate entry for each Country.**	**QUANTTTY AND NAME OF PLANTS OR PLANT PRODUCTS** **Scientific (Botanical) or English names must be included. List whether seeds, bulbs, plants, cuttings, cut flowers, fruits, etc. Indicate whether for planting, consumption or other purpose.**	**PORT OR PORTS OF ARRIVAL** **OF THE I. R. OF IRAN**

Use additional pages if more space is needed (continued on next page)

2. MEANS OF IMPORTATION			
Air Mail or Parcel post [ ] **Car [ ]**		**Air Freight [ ]**	
Surface Mail or Parcel Post [ ] **[ ]**		**Truck, Rail, or ship [ ]**	**Bagage**
3. Approximate Date Of Departure For I.R. Iran	**Arrival date**	**4. Are Other Importation Contemplated Within The Next Two Years**	
ANSWER 5, 6, 7, AND 8 ONLY IF IMPORTED MATERIAL WILL BE RESHIPPED TO ANOTHER COUNTRY			
5. Reshipment will be by:	**AIR [ ]** **[ ]**	**WATER**	
6. Port of exit from I.R.Iran		**7. Country of final destination**	
8. NAME AND ADDRESS OF APPLICANT			
9. Signature of Applicant	**Telephone**	**Fax**	**Email**

(Continued on next page)

	ENCLOSURES	ENCLOSED (''X'')	IF PREVIOUSLY SUBMITTED LIST DATE & PERMIT NO.
a	Names, addresses, and telephone number of the persons who developed/or supplied the regulated article.		
b	A description of the anticipated or actual expression of the altered genetic material in the regulated article and how that expression differs from the expression in the parental organism (e.g. morphological or structural characteristics, physiological activities and process, number of copies of inserted genetic material, the physical state of this material inside the recipient organism (integrated or extrachromosomal), products and secretions, growth characteristics).		
c	A detailed description of the molecular biology of the LMO (e.g. donor-recipient-vector) which is or will be used to produce the regulated article.		
d	Country and locality where the donor organism, recipient organism and vector or vector agent were collected, developed and produced.		
e	A detailed description of the purpose of the introduction of the regulated article including a detailed description of the proposed experimental and or production design.		
f	A detailed description of the processes, procedures, and safeguards which have been used or will be used in the country of origin and in I.R. of Iran to prevent contamination, release, and dissemination in the production of the donor organism; recipient organism; vector or vector agent; constituents of each regulated article which is a product; and regulated article.		
g	A detailed description of the intended destination (including final and all intermediate destinations), uses, and/or distribution of the regulated articles (e.g. greenhouses, laboratory, or growth chamber location, field trial location, pilot project location, production, propagation, and manufacture location, proposed sale and distribution location).		
h	A detailed description of the procedures. Processes. and safeguards which will be used to prevent escape and dissemination of the regulated article at each of the intended destinations.		
i	A detailed description of the proposed method of final disposition of the regulated article.		

9.5. Liability and Redress

- Where liability under this section is incurred by a body corporate any director manager secretary or similar officer of the body corporate shall be similarly liable unless he/she can show that he/she did everything in his/her power to prevent the import, deliberate release, placing on the market or contained use which caused the damage in question.

- Where proceedings are brought against more than one person it shall not be a requirement for the person bringing the proceedings to identify the person who caused the damage in question provided that he/she can prove that one or more of the persons so proceeded against could have caused the damage.

- Liability shall also extend to harm or damage caused directly or indirectly by the LMO(s) or products there of to the economy social or cultural practices livelihoods indigenous knowledge systems, or indigenous technologies. Such harm includes the following: disruption or damage to production systems, agricultural systems, reduction in yields, and damage to the economy of an area or community.

- An applicant shall indemnify:
  (i) any other person who deliberately releases or markets LMO(s) or products thereof; and
  (ii) any person who manufactures, processes or markets food, food ingredients or animal feed containing or derived from LMO(s)

against any civil liability where the LMO(s) or products thereof in question was first imported, deliberately released, used in contained conditions, or placed on the market by the applicant.

- An applicant shall indemnify against any civil liability any person who fails to label seeds, food, a food ingredient or animal feed containing or derived from GMO(s), but where the applicant can show that he took all reasonable steps to prevent such failure the indemnity shall not apply.

- The right to bring any action to redress the harm caused by the GMO(s) or products thereof shall lapse only after a reasonable period from the date on which the affected person or community could reasonably be expected to have learned of the harm, taking due account of:
  (a) the time the harm may take to manifest; and
  (b) the time that it may reasonably take to co-relate the harm with the GMO(s) or products thereof, having regard to the situation or circumstance of the person or community affected.

- Any person or group of persons may be entitled to bring a claim and seek relief in respect of the breach or threatened breach of any provision of this Act, including any provision relating to damage to the environment and biological diversity:
  (i) in that person's or group of person's interest;

(ii) in the interest of, or on behalf of, a person who is, for practical reasons, unable to institute such proceedings;

(iii) in the interest of, or on behalf of, a group or class of persons whose interests are affected;

(iv) in the public interest; and

(v) in the interest of protecting the environment or biological diversity.

No costs shall be awarded against any of the above persons who fail in any action as aforesaid if the action was instituted reasonably out of concern for the public interest or in the interest of protecting the environment or biological diversity.

- It shall not be a defence to any claim for compensation or damage that the activity had been consented to by the competent authority.

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