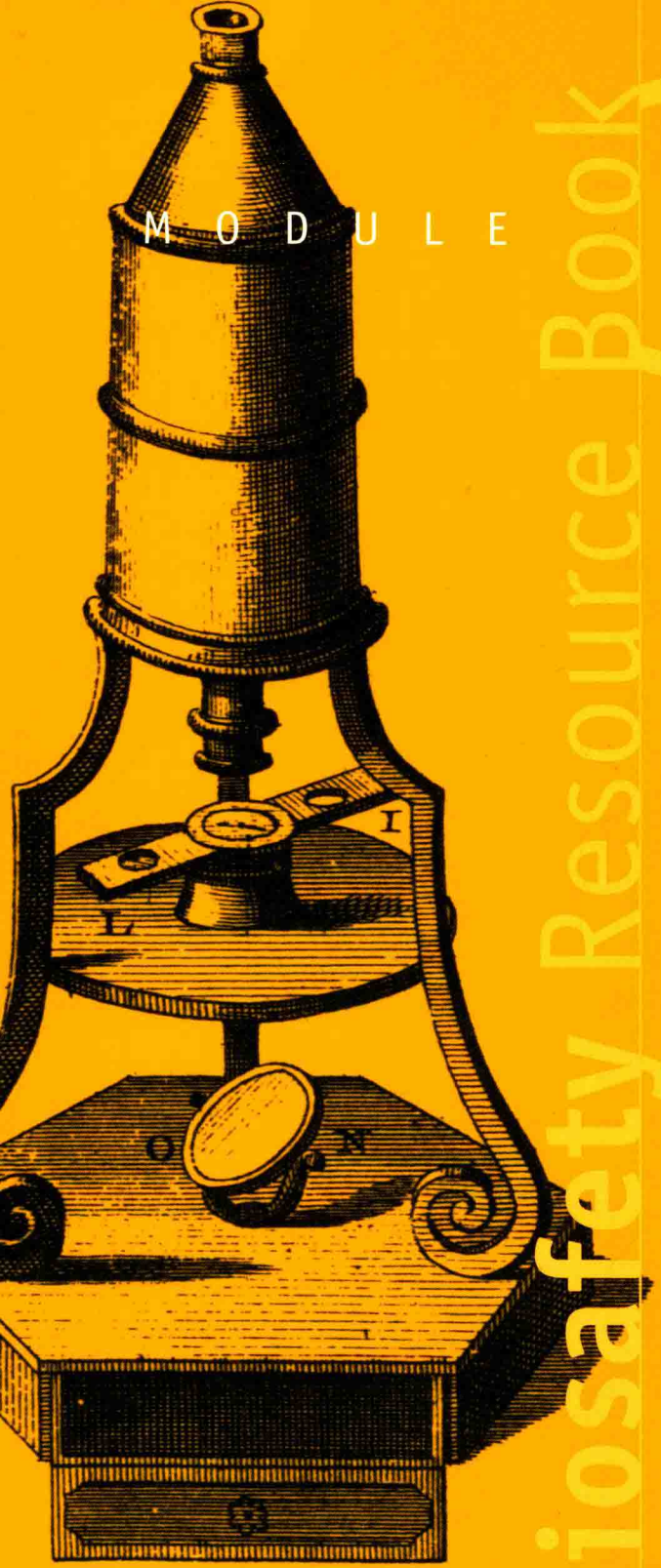

MODULE C

Biosafety Resource Book

RISK ANALYSIS

ISBN 978-92-5-106718-5

Biosafety Resource Book

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MODULE C

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LIST OF ABBREVIATIONS

ABS Access and benefit-sharing
AIA Advanced Informed Agreement
ASEAN Association of Southeast Asian Nations
BCH Biosafety Clearing-House
CBD Convention on Biological Diversity
Codex Codex Alimentarius
COP-MOP Conference of the Parties serving as the meeting of the Parties to the Protocol
CPB Cartagena Protocol on Biosafety
CPM Commission on Phytosanitary Measures
DNA Deoxyribonucleic acid
EC European Commission
EIA Environmental Impact Assessment
EU European Union
FAO Food and Agriculture Organization of the United Nations
FFP Food, or feed or for processing
GATT General Agreement on Tariffs and Trade
GDP Good Development Principles
GMO Genetically modified organism
IP Identity preservation
IPPC International Plant Protection Convention
ISPM International Standard for Phytosanitary Measures
ITPGRFA International Treaty on Plant Genetic Resources for Food and Agriculture
IUCN International Union for Conservation of Nature
LMO Living modified organism
NGO Non-governmental organization
OECD Organisation for Economic Co-operation and Development
OIE Office International des Epizooties
PGRFA Plant Genetic Resources for Food and Agriculture
PRA Pest Risk Analysis
SPM Sanitary and Phytosanitary Measures
SPS Sanitary and Phytosanitary Agreement
TBT Technical Barriers to Trade
TRIPS Agreement on Trade-related Aspects of Intellectual Property Rights
UN United Nations
UNECE United Nations Economic Commission for Europe
UNEP United Nations Environment Programme
UNIDO United Nations Industrial Development Organization
UPOV International Union for the Protection of New Varieties of Plants
USDA United States Department of Agriculture
WHO World Health Organization
WTO World Trade Organization

occurrence. Thus the risk associated with a biological agent or organism is the probability of the occurrence of a particular adverse event at a specific time and the magnitude of the consequent damage caused, depending on various factors such as exposure to the hazard, the frequency of exposure and the severity of any consequent damage done. Many aspects of risk analysis are generic and can be applied to all classes of risk. Risk is a measure of the probability and severity of adverse effects.

It can be expressed as follows: **RISK = likelihood x consequence**

RISK
Likelihood of occurrence x consequence of an incident.

Biological risks can be classified into two broad categories: naturally occurring or human-caused:

» *Naturally occurring biological risks* include:
  (1) the emergence of antibiotic resistant bacterial infections (tuberculosis, pneumonia, flu epidemic);
  (2) naturally emerging pathogens attributed to deforestation (monkeypox, Ebola, Lassa fever);
  (3) spreading of a zoonosis, i.e. infected animal populations conveying the disease to humans via direct contact, vectors or water/foodstuffs;
  (4) toxins arising from certain molds and fungi (deoxynivalenol, aflatoxins, ochratoxin);
  (5) parasitic infection outbreaks in humans;
  (6) invasive alien species (plants, animals and micro-organisms).

» *Human-caused or related biological risks,* which can be further classified into:
  (1) deliberately induced risks such as the use of harmful biological agents through warfare or terrorism; and
  (2) biotechnological risks such as products of traditional cross-breeding and selection, mutation and modern biotechnology.

According to the hazard and the associated risk, hazard-based and risk-based measures can be taken:

WORKING DEFINITIONS FOR HAZARD-BASED AND RISK-BASED CONTROL MEASURES

Hazard based – A control measure that is based on quantified and verifiable information on the level of hazard control that is likely to be achieved but lacking quantitative knowledge of the level of protection that is likely to result.

Risk-based – A control measure that is based on quantitative and verifiable information on the level of protection that is likely to be achieved.

Adapted from: FAO, 2007.

1.2 CLASSIFICATION OF BIOLOGICAL AGENTS

The need to classify biological agents according to their risk arises from the high incidence of diseases contracted by people and because of the possible danger of spreading pathogenic agents in the environment. Furthermore, the growing field of biotechnology and the advances in genetic engineering require detailed analyses of the risks associated with genetically modified organisms. Those in contact with infectious biological agents, genetically modified material or any other potentially harmful biological agent must be made aware of the potential dangers that are associated with and the characteristics of the agents. Education in safe handling of such agents, using appropriate techniques, needs to be made available.

The personnel of research institutions, biomedical firms and veterinary quarantine services are among those that teach, research, produce and control biological materials or foods and feeds. Such materials can potentially represent sources of direct infection, by containing pathogenic micro-organisms. Moreover, the environment could become contaminated if an accidental escape of biological agents were to occur. Therefore, detailed knowledge about the classification of biological agents and material is required to assure appropriate handling and minimize potential risks.

1.3 BIOLOGICAL AGENTS AND RISK GROUPS

One way to **classify biological risks** is based on the risk posed by biological agents to human health and the environment upon accidental or intentional release. Biological agents are typically used in research or biomedical laboratories, and include the full range of micro-organisms: bacteria, viruses, fungi, protozoa and multicellular parasites. Laboratory acquired infections (LAI) have been documented since the beginning of the twentieth century. However, the advent of modern biotechnology raised awareness about the hazards of infectious micro-organisms and the risks they pose to laboratory workers who handle them, and to the community if they escape from the laboratory.

BIOLOGICAL RISK CLASSIFICATION
Based on the risk posed by biological agents to human health and the environment upon accidental or intentional release.

There are three ways that bring workers into contact with materials that may pose a biological risk. These are:

- ***Exposure*** *as a result of working with biological agents* – areas of work include microbiology laboratories, greenhouses and animal houses. Activities include isolation, identification and culture of micro-organisms or cells, including materials used for genetic modification and intentional contact with animals, plants and materials that originate from animals and plants as part of the experimental work.
- *Exposure which does not result from the work itself but is incidental to it, mainly because biological agents are present as contaminants* - areas and activities include farming, refuse collection, sewage treatment, handling human body fluids and excreta, and handling materials that may be contaminated by these materials, such as hypodermic needles or sewage treatment plants.
- *Exposure which is not a result of work* – unintentional contact with animals or animal and plant materials or people, in the workplace or elsewhere.

EXPOSURE
The contact to biological agents that may represent a danger to human health or the environment.

The World Health Organization (WHO, 2004) has recommended an agent **risk group** classification for laboratories, aimed at defining the appropriate containment levels

RISK GROUPS
Four risk groups for biological agents were defined, based on factors such as pathogenicity, mode of transmission, availability of preventive measures and treatment.

required to protect people working with biological agents and ensuring they do not get infected, based on risk criteria/factors described below:

» *Pathogenicity of the agent or its product* - inherent risks of a pathogen are based on factors such as the severity of the disease it causes, its virulence and infectivity. Diseases caused by products of a biological agent include toxicity, allergenicity, and modulation of physiological activity.

» *Mode of transmission and host range of the agent* – these are influenced by existing levels of immunity, density and movement of the host population, presence of appropriate vectors and standards of environmental hygiene.

» *Availability of effective preventive measures* - these may include: prophylaxis by vaccination or antisera; sanitary measures, e.g. food and water hygiene; the control of animal pathogen reservoirs or arthropod vectors; the movement of people or animals; and controlling the importation of infected animals or animal products.

» *Availability of effective treatment* - includes passive immunization and post-exposure vaccination, antibiotics, and chemotherapeutic agents, taking into consideration the possibility of emergence of resistant strains.

Other considerations that may be taken into account in classifying biological agents include:

» *Origin/source* – indigenous (native, local) or exotic (foreign, alien) origin; exotic agents pose higher risks to human health because they may cause more severe infections with no available treatment.

» *Ability of the organism to survive* – dormancy or resting period during unfavourable conditions.

» *Number/concentration of pathogens* – the higher the number and concentration of a pathogen, the greater the likelihood of infection.

» *Nature and route of transmission* – inhalation (dust, aerosol), ingestion (food, drink, saliva), direct contact (cuts, bites, injection).

The *National Institute of Health, USA (*NIH, 2002*)* established a **classification of genetically modified agents** into a particular risk group using the same criteria indicated above. Many countries have adopted the WHO and NIH risk group classifications and criteria.

GMO CLASSIFICATION
Classicication of GMOs into four risk groups, according to the potential danger they represent.

The four resulting WHO and NIH risk groups are presented below in Table 1.2:

Table 1.2 | **Risk group classification of biological agents**

RISK GROUP Classification	NIH Guidelines For Research Involving Recombinant DNA Molecules, 2002	World Health Organization Laboratory Biosafety Manual 3rd Edition 2004
Risk Group I	Agents that are not associated with disease in healthy adult humans	A micro-organism that is unlikely to cause human disease or animal disease. (No or low individual and community risk.)
Risk Group II	Agents that are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are often available	A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to laboratory workers, the community, livestock, or the environment. Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread is limited. (Moderate individual risk; low community risk.)
Risk Group III	Agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions may be available.	A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another. Effective treatment and preventive measures are available. (High individual risk; low community risk.)
Risk Group IV	Agents that are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are not usually available.	A pathogen that usually causes serious human or animal disease and that can be readily transmitted from one individual to another, directly or indirectly. Effective treatment and preventive measures are not usually available. (High individual and community risk.)

Adapted from: BMBL, 2007.

Using the above criteria of classification, hazard groups can be summarized in the following scheme (Table 1.3):

Table 1.3 | **Hazard group classification**

Hazard Group	Pathogenicity for humans	Hazard to workers	Spread to the community	Effective prophylaxis or treatment
1	Unlikely to cause human disease	Low	Unlikely	Available
2	Can cause human disease	Intermediate	Unlikely	Usually available
3	Can cause severe human disease	Likely/ possibly serious	May spread	Usually available
4	Causes severe human disease	Serious	Likely	Unavailable

The four-risk group classification of biological agents is widely recognized but disagreements exist in allocating agents to a particular risk group. WHO recommends each country draw up its own classification by risk group of the agents encountered in that country based on the above-mentioned criteria and considerations.

1.3.1 Classification of biological agents that affect animals

BIOLOGICAL AGENTS AFFECTING ANIMALS/ PLANTS
As for human pathogens and potentially dangerous biological agents, risk groups for classification of animal/plant pathogens have been defined.

The classification of the WHO is used in the initial stages of establishing laboratory biosafety procedures, but is not strictly applicable to animals. Instead, a working group within the International Veterinary Biosafety Working Group recommended that biological agents that affect animals be classified into four risk groups:

» Low risk animal pathogens: Agents that cause diseases of minor importance for animal health and for which transmission is poor.

- Moderate risk animal pathogens: Agents that cause diseases with a moderate risk of transmission with a certain level of morbidity, but seldom cause mortality.
- High risk animal pathogens: Agents that cause serious, easily transmissible diseases with a high level of morbidity and occasional mortality.
- Very high risk animal pathogens: There is a dual definition for this group. It includes pathogenic agents that cause serious diseases and which can be highly transmissible within the animal population. It also includes micro-organisms that cause serious diseases, are highly transmissible and are associated with high morbidity and mortality.

1.3.2 Classification of biological agents that affect plants

In the case of plants, the classification enables the definition of the risks for the environment resulting from handling of biological agents, facilitating therefore the development of criteria for biosafety procedures in plant facilities. Because some of these agents can affect human health they are included in the classification.

The European Federation of Biotechnology (EFB) developed the first system of classification in 1985, which was then revised in 1992 by the working group on biosafety of the same federation, and they proposed a new system for classification of micro-organisms causing plant diseases (Kuenzi *et al.*, 1987).

The factors affecting development of a disease include:

- inoculum density;
- resistance of the pathogen to environmental conditions (humidity, temperature, cultural practices and chemical application);
- means of dissemination: water, air, soil or vectors;

» presence of susceptible hosts;
» spatial relationship between susceptible hosts and pathogens;
» virulence of the pathogen.

The classification proposed by the working group was:

» Class 1. Micro-organisms that can cause diseases in plants of minor importance. They generally include indigenous species and do not require special biosafety measures to be worked with, except good laboratory practices (GLP).
» Class 2. Micro-organisms that cause important disease outbreaks in crops, ornamental plants and forests. Work with such pathogens is subject to national regulations.
» Class 3. Micro-organisms included on quarantine lists. Importation and handling of these is generally prohibited. Work with them generally requires authorization from national bodies.

For genetically modified organisms (GMOs), the four-risk group classification is employed depending on the risk associated with the selected donor, the recipient, the host-vector relationship and the resultant GMO.

CHAPTER 2

THE RISK ANALYSIS PROCESS: BASIC CONCEPTS

Risk analysis can be broadly defined as an integrated process consisting of three major components: risk assessment, risk management and risk communication. The individual components are distinct, but are linked to achieve a well-functioning risk analysis process that forms the basis for decision-making on any operation or dealing of GMOs (Australian Government, 2005).

RISK ANALYSIS
An integrated process to analyse risk and form the basis for further decision-making.

In the case of biosafety, risk analysis involves a scientific process to estimate the risks to human life and health, as well as the impact on the environment, associated with the use of a particular GMO or its products. The prevention, reduction or elimination of these risks requires methods of risk management that are normally implemented as actions conforming to particular regulations. Risk assessment and risk management have to be implemented along with risk communication, which involves all interested parties and allows for an iterative process of risk analyses.

Risk assessment is important in the process of risk analysis given that if a particular risk is not identified, the steps taken to reduce it cannot be formulated in the risk management process. Risk assessment relies on a solid scientific base. Each case has to be dealt with individually and a separate evaluation has to be undertaken for each phase of obtaining, researching, testing, producing and releasing into

RISK ASSESSMENT
A rigorous science-driven process used to identify a hazard and obtain qualitative or quantitative estimates of the levels of risk posed by a hazard.

the environment of GMOs on a large or small scale. The complexity of the risk analysis process applied to a large variety of genes and gene combinations is very high, since this can result in a vast range of effects and interactions. In this sense, evaluation of possible impacts over the long term presents many difficulties. Moreover, the results of risk assessments from small-scale tests cannot be extrapolated to the large scale.

2.1 COMPONENTS OF RISK ANALYSIS

Risk assessment is the first and the *scientific component* of risk analysis. It is a rigorous science-driven process used to identify a hazard and obtain qualitative or quantitative estimates of the levels of risk posed by a hazard, including possible adverse effects on human health and the environment. It typically consists of four steps: (1) hazard analysis (identification and characterization), (2) likelihood estimation, (3) consequence evaluation; and (4) risk estimation. A more detailed discussion of risk assessment is presented in Chapter 3.

RISK MANAGEMENT
Is concerned with evaluating whether the risks identified by the risk assessment process are acceptable and manageable, then selecting and implementing the control measures as appropriate to ensure that risks are minimized or controlled.

Risk management is the second and *decision-making component* of the process of risk analysis. It is primarily supported by risk assessment but is also supported by other risk considerations. Risk management is concerned with evaluating whether the risks identified by the risk assessment process are acceptable and manageable, then selecting and implementing the control measures as appropriate to ensure that risks are minimized or controlled. A more detailed discussion on the methodology of risk management and other considerations is presented in Chapter 4.

RISK COMMUNICATION
The process of exchange of information and opinions concerning risk and risk-related factors among various stakeholders concerned with risk.

Risk communication is recognized as the third component that underpins the risk assessment and risk management processes. It is the process of exchange of information and opinions concerning risk and risk-related factors among various stakeholders concerned with risk (Codex Alimentarius Commission, 2003). It strengthens the overall process of risk analysis by helping to define the issues and