In the name of Allah ,The Beneficent, The Merciful

An Introduction to

Biosafety issues & Risk Assessment of GMOs

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What is a Risk?

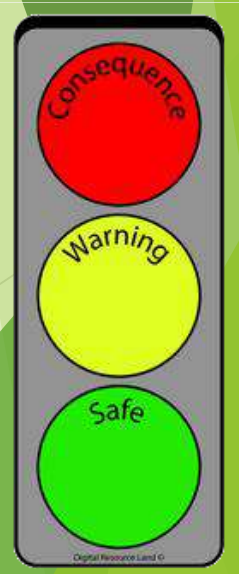
- Colloquial:
  - Danger, Venture, or even, Opportunity!
  - Possibility of bad happenings!
- Technical:
  - Hazard, Probability, Consequence
- Insurance:
  - Chance, Uncertainty

Risk: Scientific Definition

- The potential for realizing
  - unwanted
  - adverse consequences to
- Human life, human values
- Health, well being
- Property, wealth
- Environment
  - under specific condition.

Risk is:

- A combination of two factors:
  - The probability that an adverse event (hazard) will occur
  - The consequence of that adverse effect.
- Risk=Likelihood X Consequence
- A measure of probability and severity of adverse effects



Risk Analysis

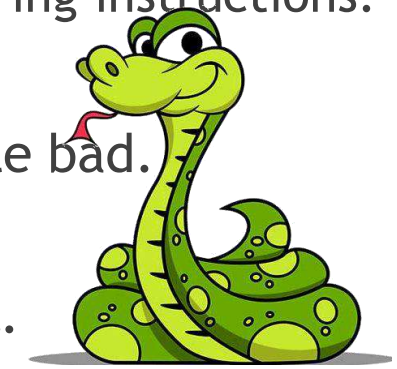
- The understanding of risk,
- The methods of
  - **Assessment**
  - **Management**,
- The descriptions of risk,
- The definitions of risk,
- Differ in different practice areas: business, economics, environment, finance, information technology, health, insurance, safety, security, GMOs, etc.

Types of Lab Hazards

- Biological (Biohazards):
  - Things that cause diseases: germs, living tissues, medical wastes, …
- Physical:
  - Things that get in your way: moving things, sharps things, …
- Chemical:
  - Toxic, corrosive, and flammable substances: acids, bases, reactives, …
- Radiation:
  - Nuclear including: gamma, beta, alpha, and even bright light.

Types of Lab Hazards

- Noise (Acoustic):
  - Cause hearing damage, prevent from hearing instructions.
- Animal:
  - They bite, scratch, smell and often taste bad.

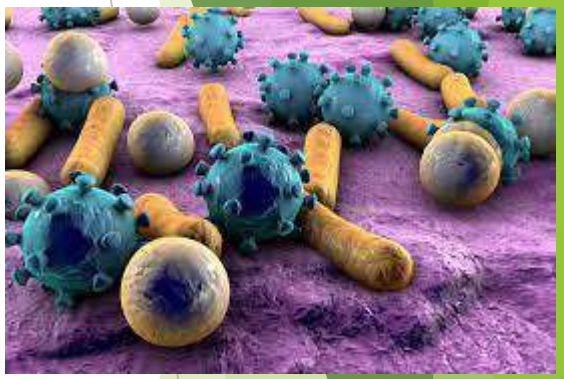


- Psychological:
  - Emothonal stress, workplace bullying, …

- Social and Economical:
  - Socio-economic risk arises from uncertainty about economic outcomes, eg. exchange rates, government regulation, or political stability that will affect an investment or a company's prospects
- Electrical:
  - High voltage apparatus, machinery with moving parts, …

Biological Hazards

- Biological health hazards include medical waste, toxins, and samples of microorganisms such as bacteria, viruses, parasites and moulds or fungi.
- They can pose a threat to human or animal health when they are inhaled, eaten or come in contact with skin.
- The risk can be:
  - **Direct** through infection
  - **Indirect** through damage to environment
- Infectious agents can replicate and give rise to largr numbers of organisms when small numbers are released from controlled situation.



Main Categories of Biological Risks

Two board categories of Biological Risks:

- 1. Risk to those who work the biological sciences including Biotechnology:
  - **Potential exposure of employees to biological agents in the workplace**

- 2. Risk to the environment and public health:
  - **Deleterious effects that may be experienced upon accidental or intentional release of harmful organisms into the environment.**

Hazard Group Classification

Basic for categorization of pathogens:

- Is the organism pathogenic for humans?
- Is it hazardous for laboratory workers?
- Is it transmissible to the community?
- Is effective treatment or prophylaxis available?

Risk Group Classification of Biological Agents

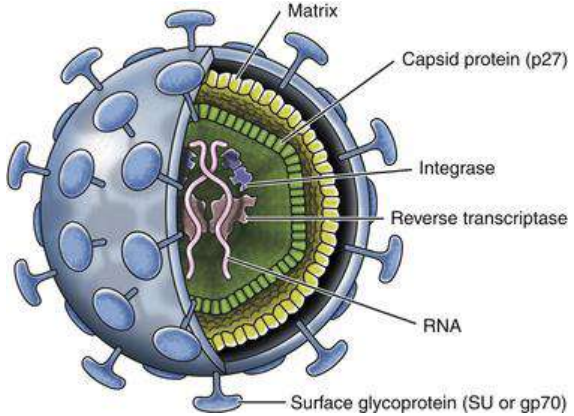
Risk Group	Potential to Cause Disease to Humans	Hazard Degree to Workers	Spread to the Community	Effective Treatment or Preventive Measures
1	Unlikely	Low	Unlikely	Available
2	Likely but minimal potential to become serious hazards	Intermediate	Unlikely	Commonly available
3	Likely to cause serious diseases but treatment or measures may be present	Possibly serious	Possible	Commonly available
4	Likely to cause serious diseases but treatment or measures may not be present	Serious	Likely	Unavailable

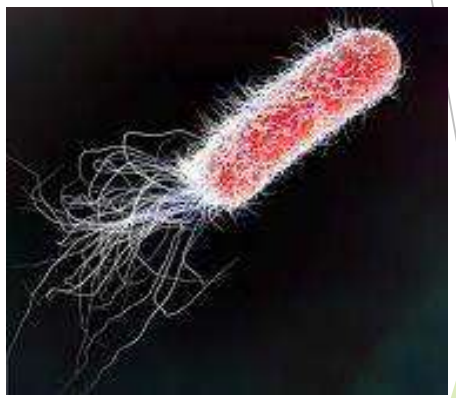
Risk Group I:

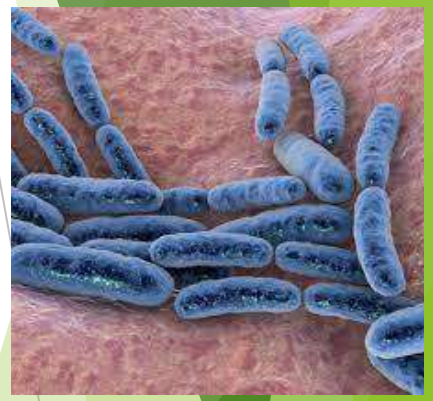
Description: Low individual risk, Low community Risk

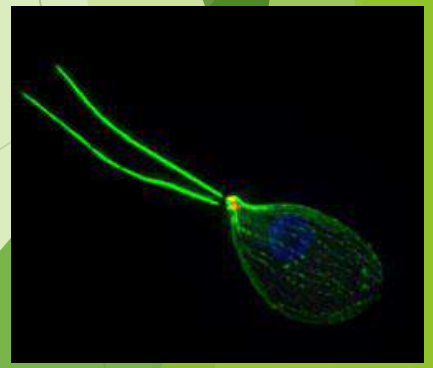
Explanation: An organism or microorganism that is unlikely to cause human disease or animal disease of veterinary importance.

- Bacteria:
  - *Escherishia coli* K12, genetically crippled
  - *Lactobacillus* spp.
- Viruses:
  - Feline leukemia virus (FelV)
- Fungi:
  - *Aspergillus* spp.
- Parasites:
  - *Naegleria gruberi* Protozoa (free-living amoebae)







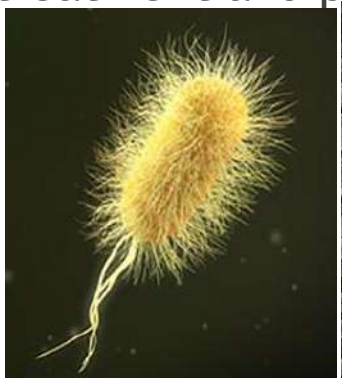


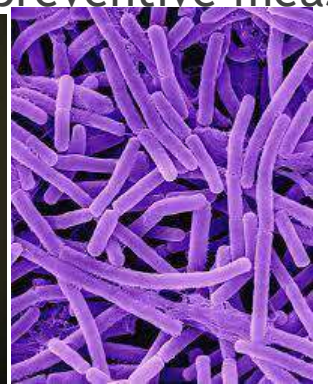
Risk Group II:

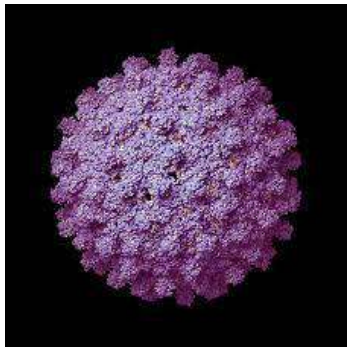
Description: Moderate individual, Limitted community Risk

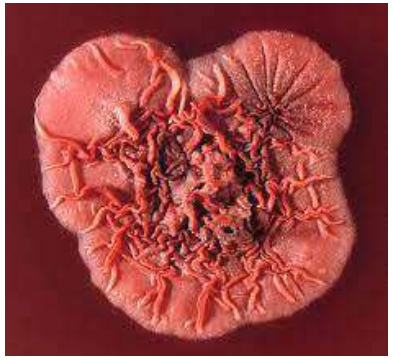
Explanation: Can cause human or animal disease but is unlikely to be a serious hazard to lab workers, the community or environment. Effective treatment and preventive measures available. Limited risk of spreading.

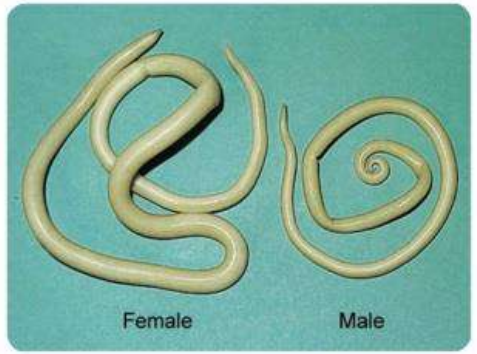
- Bacteria:
  - *Escherishia coli*, pathogenic strains
  - *Bacillus anthracis*
- Viruses:
  - Hepatitis A, B, C and D
  - Cowpox virus
- Fungi:
  - *Penicillium marneffei*
- Parasites:
  - *Ascaris lumbricoides*









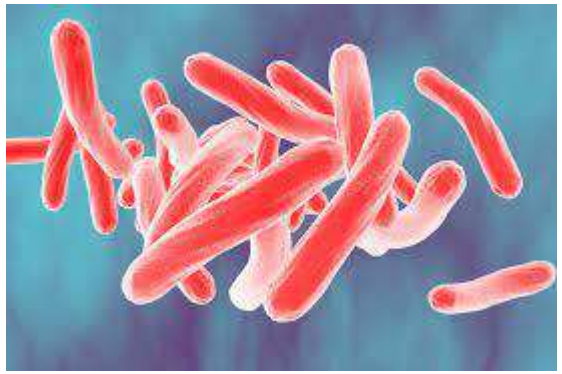


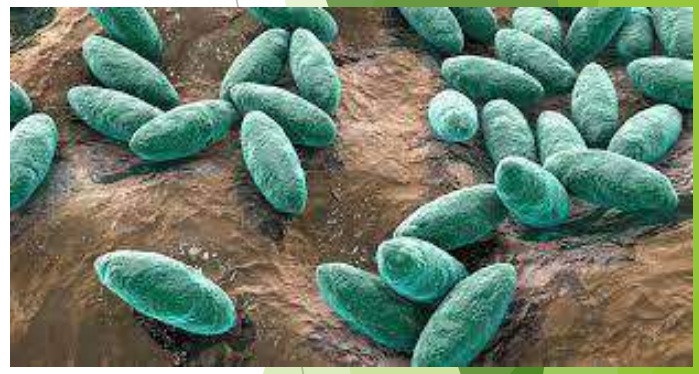
Risk Group III:

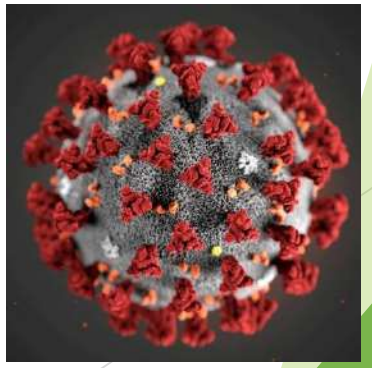
Description: High individual risk, Low community Risk

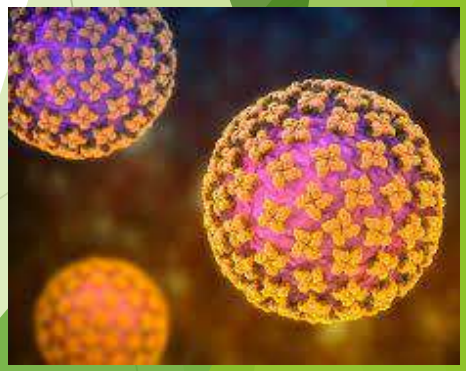
Explanation: Usually produces serious human disease but does not ordinarily spread from one infected individual to another.

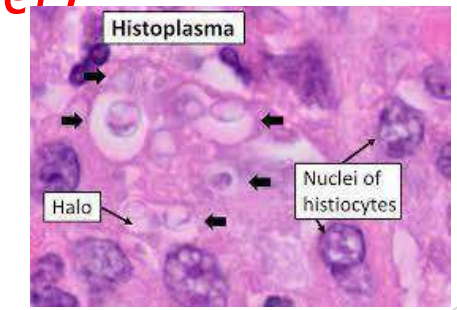
- Bacteria:
  - *Mycobacterium tuberculosis*
  - *Brucella spp.*
- Viruses:
  - *Human Immunodeficiency Virus (HIV)*
  - *Hantaan (Korean haemorrhagic fever)*
- Fungi:
  - *Histoplasma capsulatum*









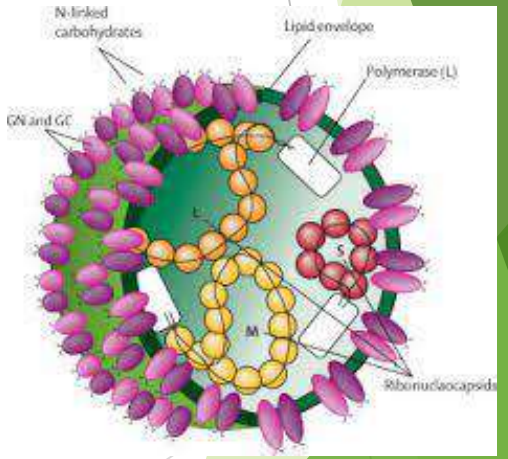


Risk Group IV:

Description: High individual risk, High community Risk

Explanation: Usually produces serious human disease and may be readily transmitted from one infected individual to another, directly or indirectly.

- Viruses:
  - *Ebola* Virus *(FelV)*
  - Congo-Crimean haemorrhagic fever



Some Rules for Classifying

- Biological agents in Hazard Groups 2, 3 and 4 are referred to as pathogens.
- If not on the list seek evidence of pathogenicity:
  - Not automatically in group 1.
- All viruses isolated from humans assigned to not less than group 2.
- If there is any uncertainty, then the higher of the two possible groups should be chosen.

Safety

- Safety is the state of being "safe", the condition of being protected from harm or other danger.
- Safety can also refer to the control of recognized hazards in order to achieve an acceptable level of risk.
- Safety is and exercise in recognizing what the risks are, and then introducing
  - Procedures
  - Practices
  - Equipment, and
  - Facilities
- To control the identified risks or reduce them to acceptable levels.

Biosafety

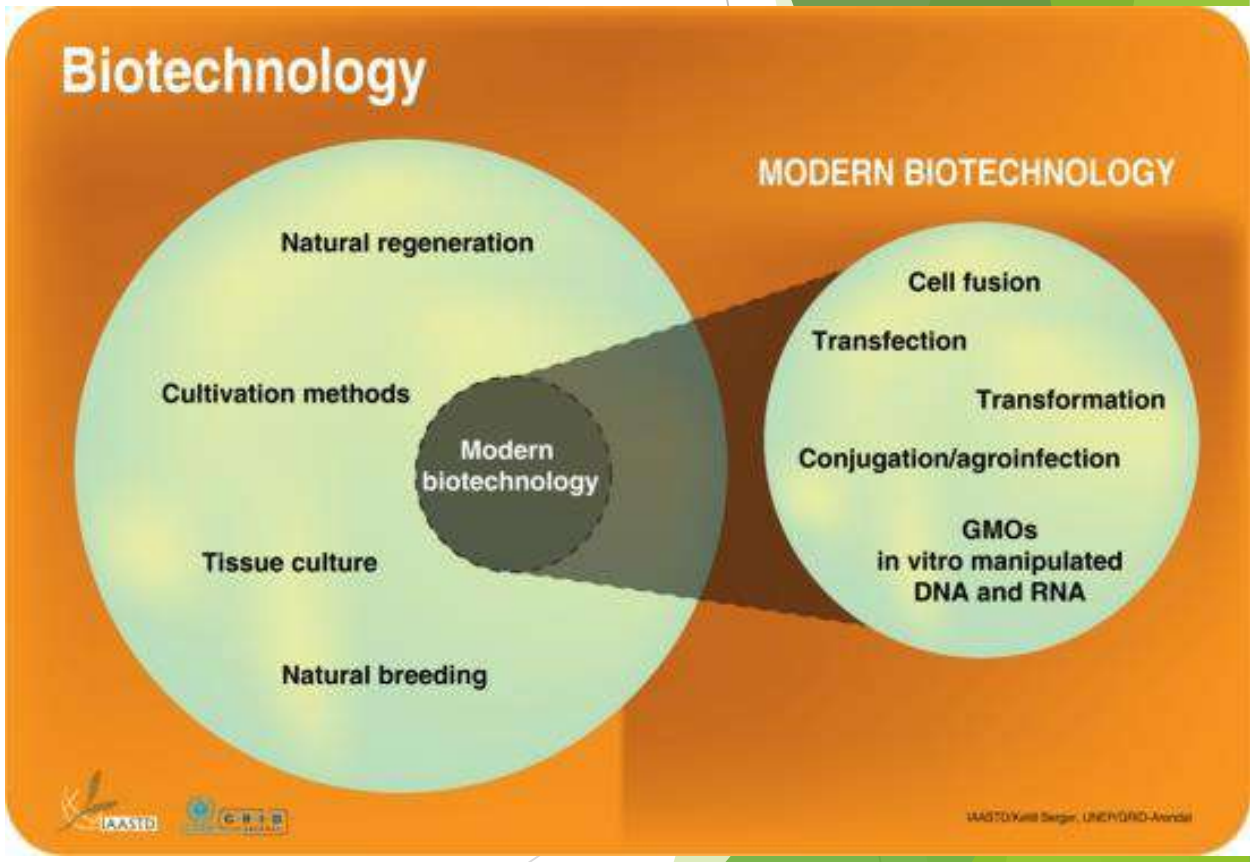
- Biosafety is a strategic and integrated approach to **analysing and managing relevant risks to human, animal and plant life and health and associated risks for the environment.**
- Biosafety is the safe working practices associated with handling of biological materials, particularly infectious agents.
- It is based on recognition of the critical linkages between sectors and the potential for hazards to move within and between sectors, with system-wide consequences.
- It addresses containment principles, technologies and practices that are implemented to prevent the unintentional exposure to potentially hazardous biological agent including pathogens and toxins, or their accidental release.

Biosafety vs. Biosecurity

- **Biosafety** provides policies and practices to prevent the unintentional or accidental release of specific biological agents and toxins.
- Biosafety measures aimed at regulating and ensuring the safe use of biological agents and procedures including genetic engineering.
- **Biosecurity** provides policies and practices to prevent the intentional or negligent release of biological materials or the acquisition of knowledge, tools, or techniques that could be used to cause harm.
- Biosecurity measures aimed at countering terrorist attacks involving biological agents or toxins.

Modern Biotechnology

- Biosafety in biotechnology aimed to ensure the Safe Use of **Modern Biotechnologies**.
- **Modern Biotechnology**: biotechnological techniques for the manipulation of genetic material and the fusion of cells beyond normal breeding barriers.
- Under international environmental law and policy:
  - biosafety refers to the need to protect the environment and human health from the possible adverse effects of genetically modified organisms (GMOs) and products resulting from modern biotechnology.



Goals for Biosafety Procedures

- Anticipate daterminal effects that might follow the release of a GMO during experimentation or commercialization.
- Design monitoring systems for the early detection of adverse outcomes.
- Plant intervention strategies to avert and, if necessary, remediate adverse environmental or health effects.
- Define regulatory authority to prevent the development and/or importation of potentially dangerous GMOs (eg. Recombinant pathogens).
- Encourage continued development of increasingly effective biosafety principles and procedures.
- Provide public information about biosafety, and urging that such information become part of school curricula and teacher education.

Safety Classification

Code	Name	Safety Category Definition Criterion
I	Safe	The system state resides mainly inside the 'green' zone. As a maximum, the system state may stay, for a short time in close proximity to the operational constraints, i.e. inside the 'yellow' zone, but must leave it by the end of the situation
II-a	Conditionally Safe – a	As a maximum, the system state may stay temporarily, or for a medium time, in close proximity to the operational constraints, i.e. inside the 'yellow' zone
II-b	Conditionally Safe – b	As a maximum, the system state may stay for a long time in close proximity to the operational constraints, i.e. inside the 'yellow' zone
III	Potentially Unsafe	As a maximum, the system state may violate operational constraints, i.e. enter the 'red' zone, for a short or between short and medium time, but must leave it by the end of the situation
IV	Dangerous (Prohibited)	As a maximum, the system state may stay beyond the operational

Genetically modified organisms

- A GMO is a plant, animal or microbe in which one or more changes have been made to the genome, typically using high-tech genetic engineering, in an attempt to alter the characteristics of an organism.
- A genetically modified organism contains DNA that has been altered using genetic engineering.
- Genetically modified animals are mainly used for research purposes of contained use, while genetically modified plants and microorganisms are common in today's food supply.
- Fortunately, genome-edited organisms have been excluded from this definition.

Potential Risks of GMOs and Their products

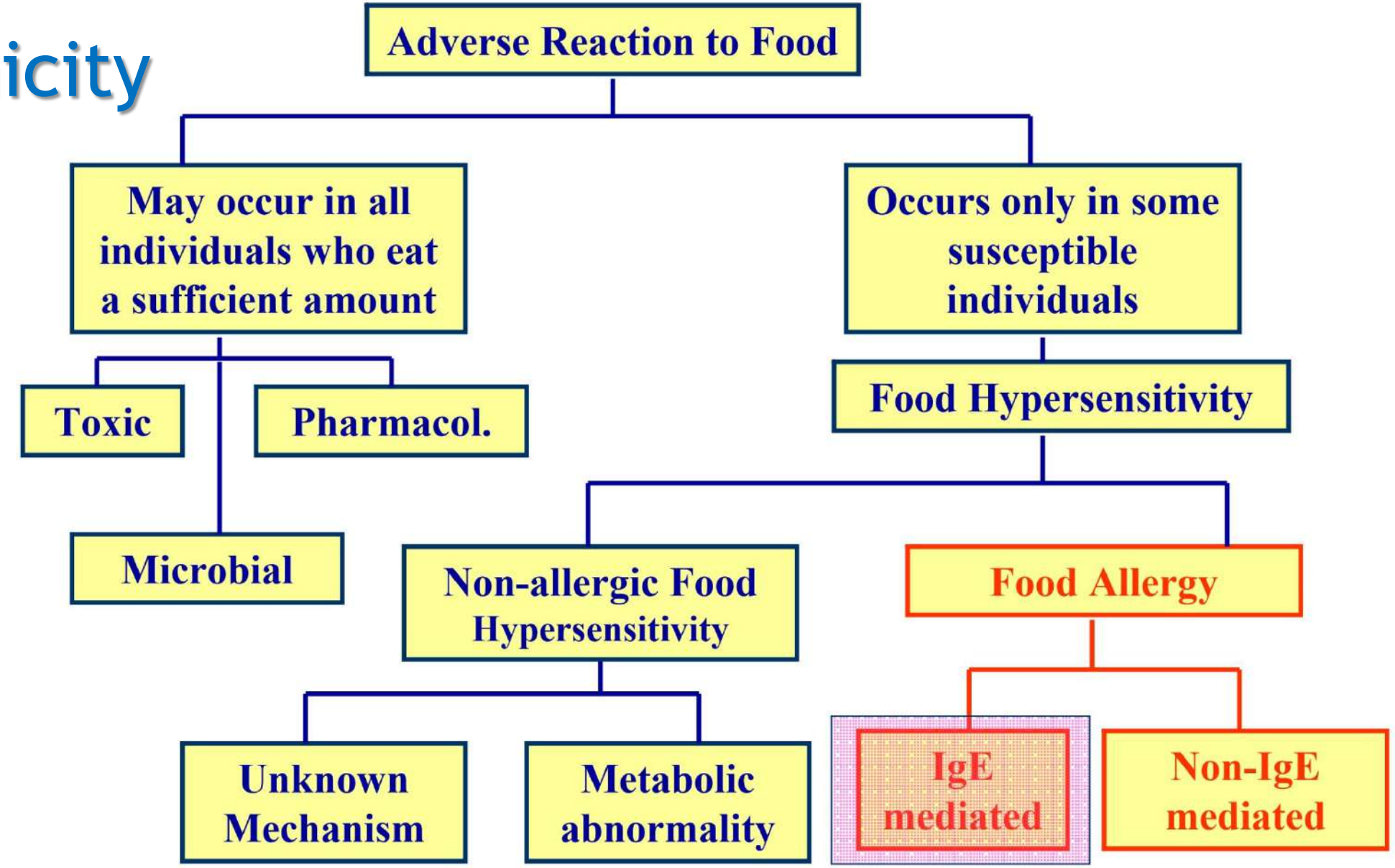
1. Human Health Risks

- Toxicity
- Allergenicity (new allergenities)
- Horizontal gene transfer and antibiotic resistance
- Changes in nutrient levels

Note:

- **There is no evidence so far that GM-crop or their products to create any toxicity.**
- **It is most likely to prove that horizontal gene transfer into microorganisms living in digestion system of humans (or even livestocks) did not occure so far.**

Allergenicity



Prediction of Allergenic Potential

Most known food allergens have certain properties in common:

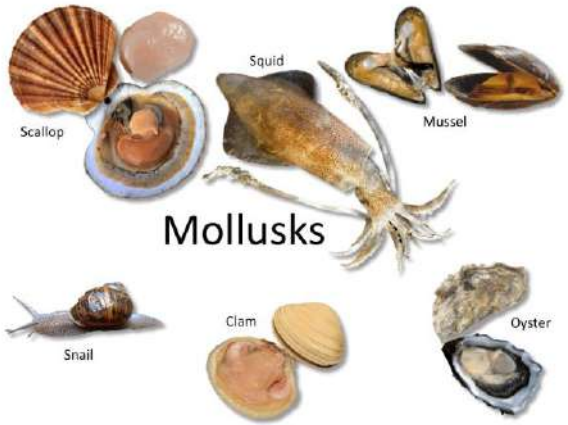
- Resistance to digestion
- Resistance to processing
- Molecular weight 10-70 kDa
- Prevalence in the food greater than 1 percent
- Aminoacid sequence homology with known allergens.

In general, homology (and finally, allergenicity) of the transgene (including its genetic elements) and also its products (mRNAs, poly peptides, …) should be aligned with the known allergens information deposited in nucleic acid and protein data banks.

The Most Food Allergens

The eight most common food allergens cause more than 90 percent of all food allergic reactions:

- Milk
- Shellfish (*crustacea* and mollusks)
- Eggs
- Wheat
- Fish
- Peanuts
- Soy
- Tree nuts (e.g. Walnuts)



A Conclusion on Allergenicity

- After several years of testing dozens of proposed transgenic crops, only two potential problems have been uncovered.
  - **Pioneer soybean**
  - **Aventis StarLink corn**
- The extensive studies carried out on these cases showed that both crops had no more allergenicity rather than their non-transgenic counterparts.

Note:
There is no evidence so far that genetically engineered foods are more likely to cause allergenic reaction than are conventional foods.

Changes in nutrient levels

- Nutritional assessments of genetically modified crops are a critical component of the regulatory safety process.
- Carbohydrates, fat, ash, calory, total protein, and moisture of edible parts, leaves, and seeds are usually subjecting to the assessment.
- In some cases (if necessary), amino acid profile, fatty acid profiles, vitamins and minerals, and also other metabolites and components may also considered for the analysis.
- Nutritional components of a GM-crop should be similar to its conventional counterpart.
- Targeting a single nutrient may lead to unintended alterations in levels of other constituents, and specialized analytical methodologies may be required to assess changes in overall nutrient profile.

Industry Studies: Nutritional components commonly tested are similar in GM- and Conventional foods

GM-Cotton, MON15985 Seeds nutrition analysis

Table 3: Compositional endpoints in cotton seeds harvested from field trials with cotton MON 15985 and its conventional counterpart (DP50 in 1999 and Giza-90 in 2007) for which a statistically significant difference was observed in the across-site analysis

Parameter	Conventional counterpart	MON 15985	Commercial non-GM varieties (range min.–max. values)
Field trials in 1999			
14:0 Myristic acid (% total FA)	0.99 ± 0.06	1.12 ± 0.06	0.55–1.28
16:0 Palmitic acid (% total FA)	25.08 ± 0.33	24.84 ± 0.33	21.23–26.45
18:0 Stearic acid (% total FA)	2.19 ± 0.053	2.49 ± 0.05	1.99–2.48
18:2 Linoleic acid (% total FA)	53.39 ± 0.73	53.08 ± 0.73	49.90–56.88
20:0 Arachidic acid (% total FA)	0.28 ± 0.01	0.29 ± 0.01	0.25–0.33
Dihydrosterculic acid C19 (% total FA)	0.15 ± 0.01	0.17 ± 0.01	0.13–0.24
Calcium (% DW)	0.13 ± 0.01	0.13 ± 0.01	0.10–0.16
Copper (mg/kg DW)	7.07 ± 0.91	6.70 ± 0.91	3.54–11.14
Iron (mg/kg DW)	49.96 ± 1.63	46.58 ± 1.64	40.58–56.54
Phosphorus (% DW)	0.69 ± 0.02	0.65 ± 0.02	0.60–0.84
Potassium (% DW)	1.09 ± 0.02	1.06 ± 0.02	0.98–1.14
Free gossypol (% DW)	0.87 ± 0.04	0.82 ± 0.04	0.53–1.20
Total gossypol (% DW)	0.99 ± 0.05	0.92 ± 0.05	0.57–1.42
Field trials in 2007			
14:0 Myristic acid (% total FA)	0.70 ± 0.03	0.79 ± 0.03	0.49–0.78
16:0 Palmitic acid (% total FA)	23.22 ± 0.57	22.35 ± 0.56	20.45–24.35
16:1 Palmitoleic acid (% total FA)	0.77 ± 0.02	0.82 ± 0.02	0.60–0.81
α-Tocopherol (mg/kg DW)	63.72 ± 11.24	77.71 ± 11.07	29.64–99.98

Values are expressed on a dry weight basis. The mean values with standard errors are given.
DW, dry weight; FA, fatty acids.

Potential Risks of GMOs and Their products (continued)

2. Environmental impact

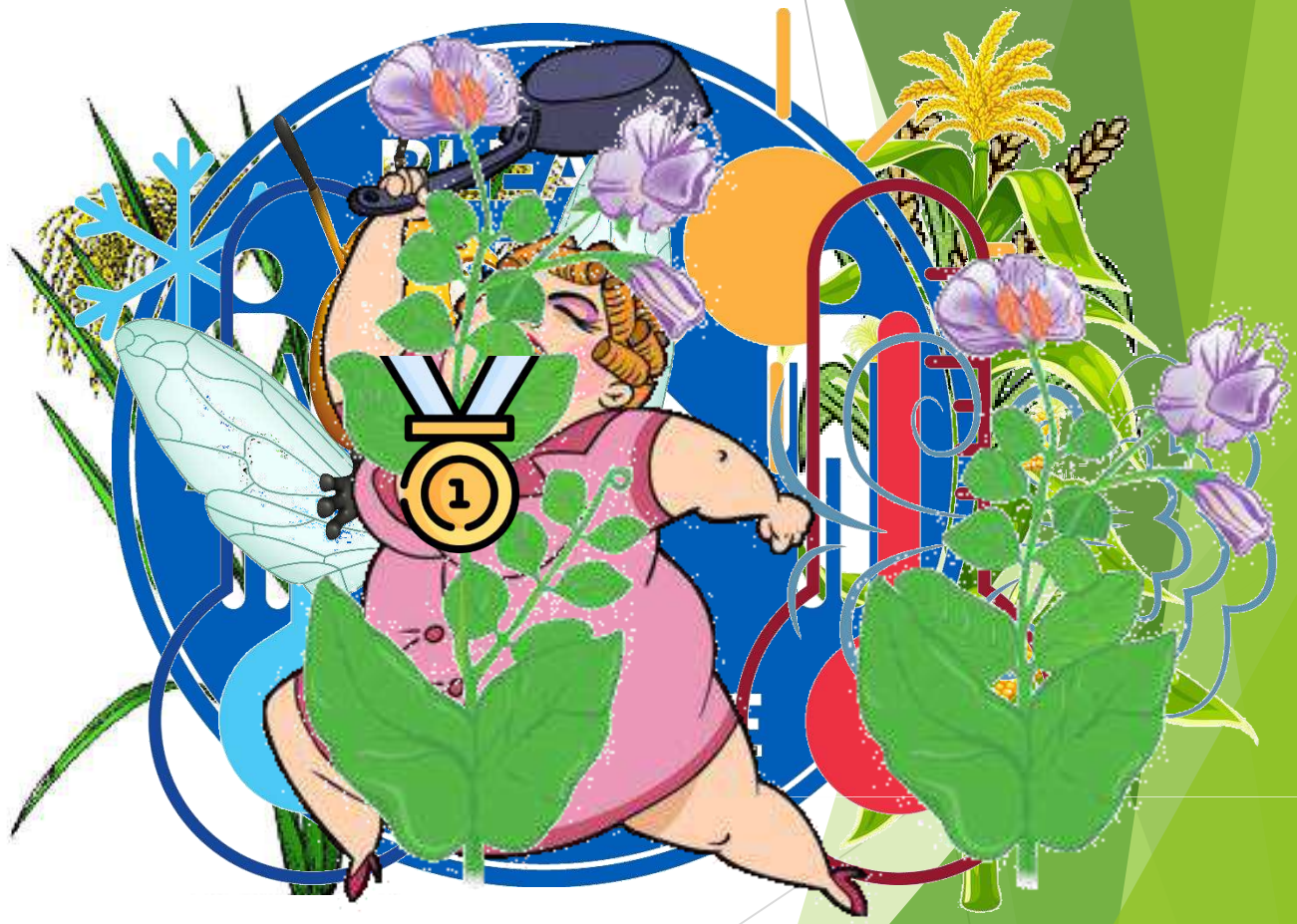
- Gene transfer to wild relatives (Gene Flow)
- Evolution of pests resistance to GM-crop
- Effect on non-target organisms
- Impact on food chain
- Weediness
- Effect on pesticide use

Gene flow or Gene Transfer to Wild Relatives

- Gene flow is the process by which certain alleles (genes) move from one population to another geographically separated population.
- In plant pathology, gene flow is very important because it deals with the movement of virulent mutant alleles among different field populations.
- In biosafety, gene flow is defined as a change in the genes of a particular group of plants due to the movement of pollen, seed, or live plants carrying modified DNA sequences (transgenes).
- Examples of the risks mentioned in the context of gene flow from GM plants are:
  - i) creation of new weeds resulting from an escape by the crop itself;
  - ii) creation of superweeds by hybridization of a (wild/weedy) species with the transgenic crop;
  - iii) genetic erosion (loss of original diversity of wild relatives).

How Much Gene Flow is Possible for GMOs?

- Gene Flow barriers:
  - Self or cross pollinating nature of a GMO
  - Recipient wild relatives
  - Distance between donor and recipient plar
  - Temperature
  - Wind or insects
  - Capability of stigma for acceptance of poll
  - Selective advantage of the transgene in th
- There is an important difference pollination.

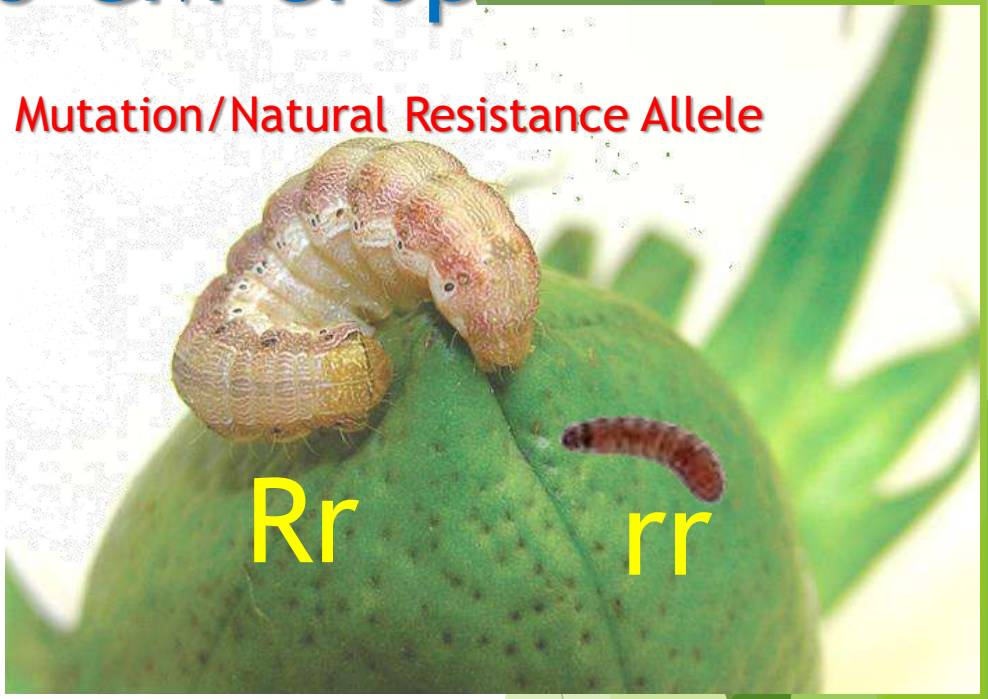


Note:

Most studies have shown that the gene flow is not a likely routine process, and EFSA confirmed that there has not reported a real superweed so far.

Evolution of Pest resistance to GM-Crop

- Evolution of pests resistance is a natural process that occures in any agricultural systems (including cultivation of Bt-crops) in which a pesticide is used.
- On average, the first observation of resistance to unique GM traits occurs after six years, but in many cases pests have remained susceptible for more than 10 years.
- Crop rotation, employment of different *cry* genes in GM-crops, and cultivation of non-GM seeds as a small percentage of total seed in a GM-crop farm can be used to postpone the evolution of the pest (Risk Management).



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Effect of a Bt Crop on Non-Target Organisms

- It is proven that Bt toxins and related *cry* genes have specific effects to their target organisms (eg. Lepidoptran, Coleopteran, and Dipteran insects).
- Non-target organisms do not affect by a cry gene of interest.
- Monarch Butterfly story in North America is a typical example.
- Monarch caterpillars are feeding on milkweed leaves that may surrounded by Bt-corn pollen that may affect them.
- A consortium of federal, university and industry scientists led by USDA's ARS conducted two years research.
- The research group finally concluded that Bt-corn pollen grains are not a likely threat to monarch butterflies.

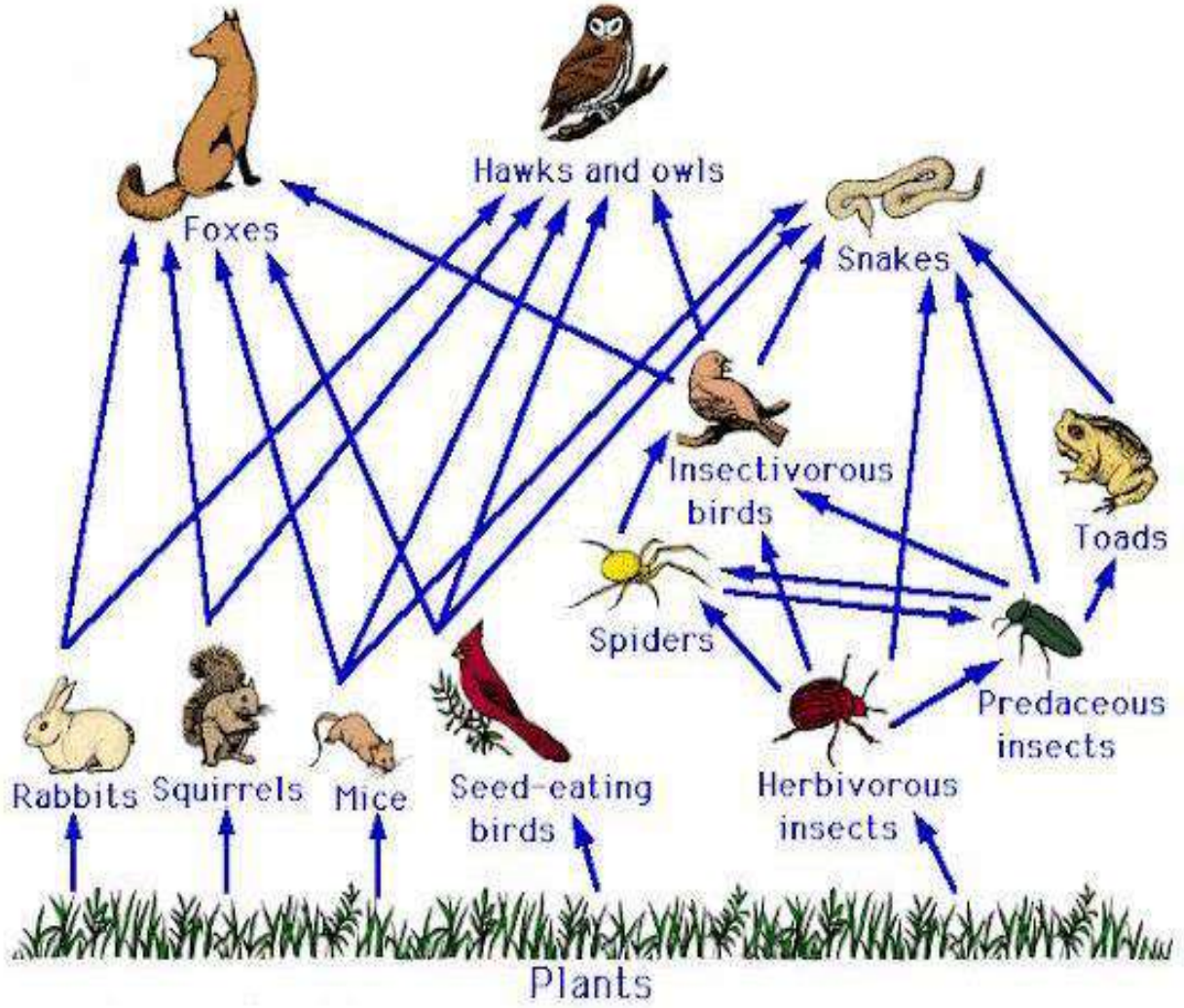
Impact on Food Chain

Bt Corn

Secondary Consumer

Primary Consumer

Simple Food Chain



Potential Risks of GMOs and Their products

3. Socio-Economic impact

- Effects of changing cropping patterns
- Increased use of monoculture (uniformity leads to vulnerability)
- The loss of in-Situ agricultural biodiversity
- Loss of farmers access to plant material
- Impact of “Terminator” technologies
- Farmers dependency on GM-Seeds companies
- Impacts on Food Security

Risk Analysis of a GM-Crop

Salient steps involved in the journey of a GM-Crop from lab to the Farmer's Field

Transgenic Plant Confirmed i

Greenhouse Tests

Limited Field Tests

Ecological and Biosafety Anal

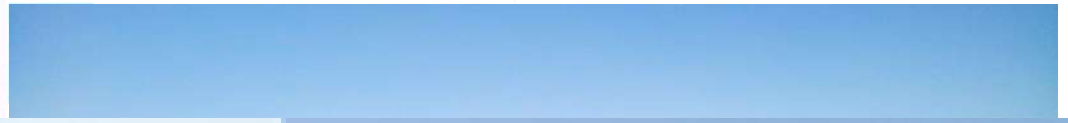
Regulatory Permit for Large-S

Proprietary Arrangements

Commercial Deployment

Continued Monitoring of Effic

معاونین محترم وزیر
روسای محترم سازمان‌ها، مؤسسات و شرکت‌های تابعه
روسای محترم سازمان جهاد کشاورزی استان‌ها



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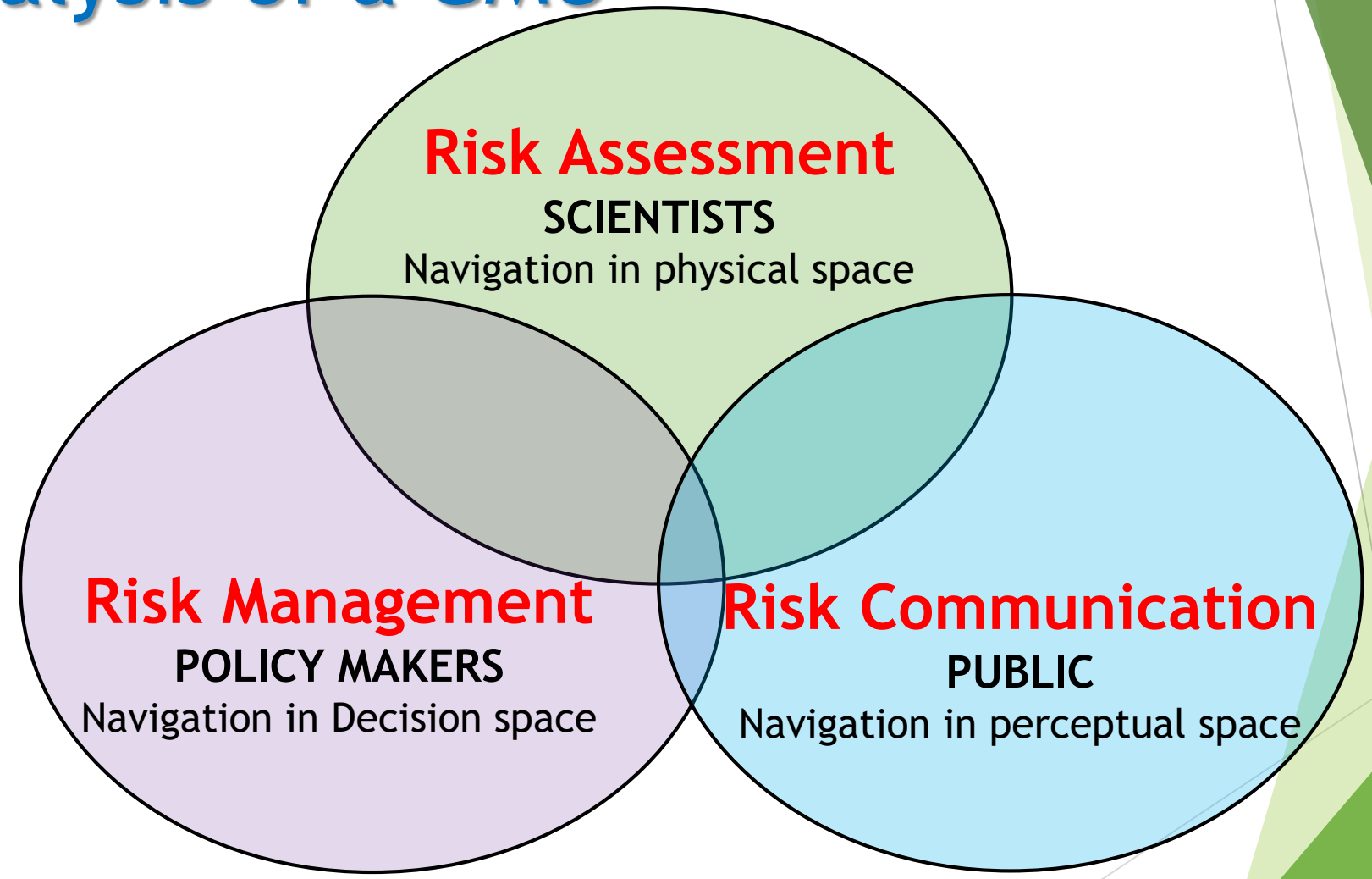
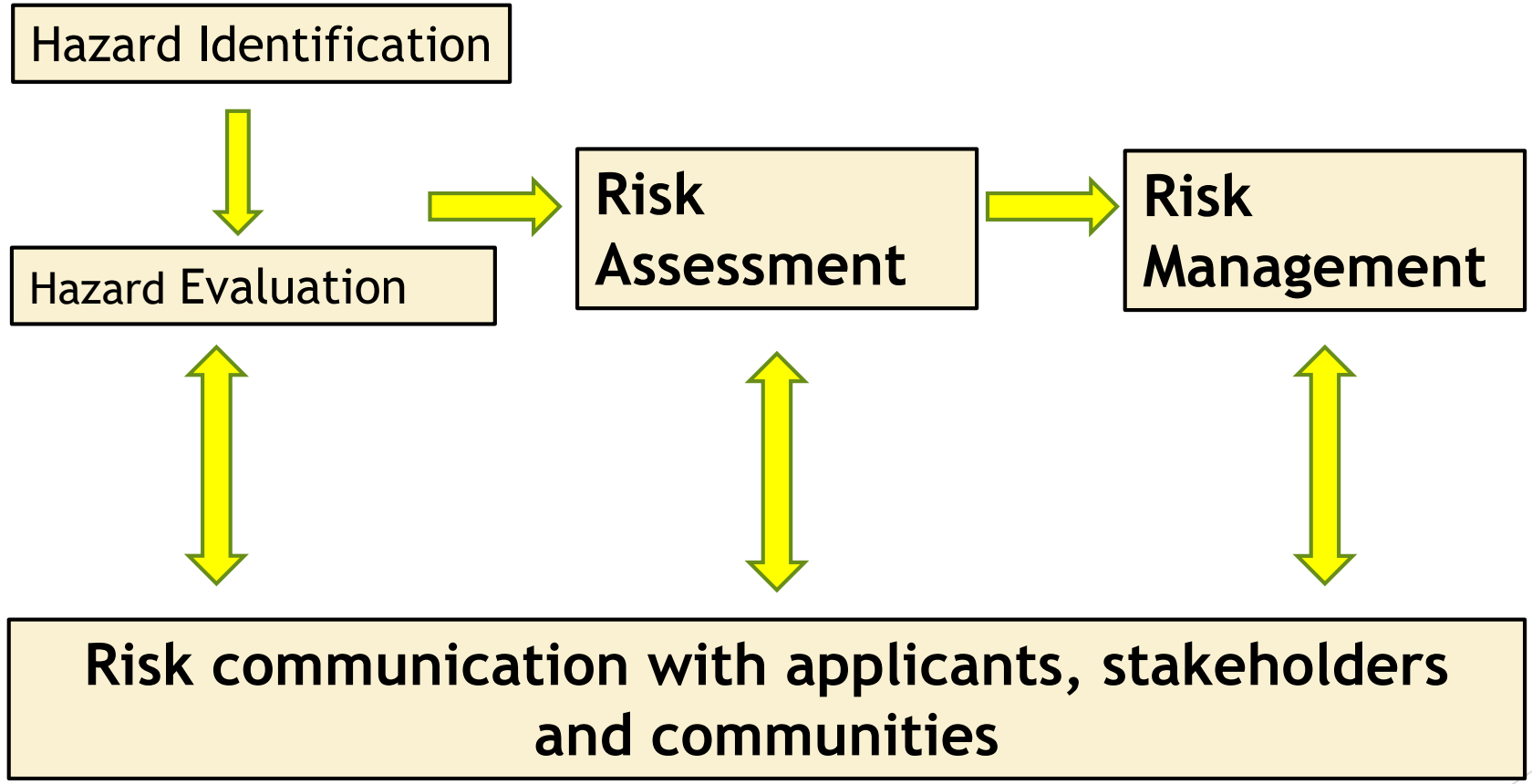
Risk Analysis of a GMO



The Basic Risk Analysis Framework



Risk Assessment

- Inherently the most critical component of biosafety implementation.
- A means for dealing with uncertainties and incomplete data in order that decisions may be in full considerations of potential consequences.
- Risk assessment is influenced by:
  - Policy choices
  - Individual experiences
  - Public reaction

Essentials of Biotechnology Risk Assessment

- Identify potential adverse effects on human health and/or environment.
- Estimate the likelihood of these adverse effects being realized.
- Evaluate the consequences should the identified effects be realized (the risks).
- Consider appropriate risk-management strategies.
- Estimate the overall potential environment impact, including a consideration of potential impacts that may be beneficial to human health or the environment.

Other Important Topics on Risk Assessment

- Methods of Risk Assessment
- Matrix of Analysis
- Table of Decision
- Substantial Equivalence
- Risk assessment based Risk Management
- …


Thank You