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**HANDOUT**

## **BT605**

Biosafety & Bioethics

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# BT605

## Biosafety & Bioethics

### HANDOUT

Biosafety and bioethics govern how biological research is conducted safely and responsibly. This handout covers biosafety levels and laboratory practices, risk assessment, biosecurity, national and international regulations, and the core principles of bioethics — including genetic engineering, GMOs, stem cells, cloning, and emerging biotechnologies.

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# MODULE 1: INTRODUCTION TO BIOSAFETY, BIOSECURITY, AND BIORISK

## Learning Objectives

- Define biosafety, biosecurity, biorisk, and biohazard
- Distinguish between biosafety and biosecurity
- Explain the biorisk management approach (AMP model)
- Identify sources of biological risk in the laboratory

## Key Definitions

**Biosafety** is the application of knowledge, techniques, and equipment to prevent unintentional exposure to pathogens and toxins or their accidental release into the environment — it protects people and the environment from the biological agent. **Biosecurity** refers to measures that prevent the loss, theft, misuse, diversion, or intentional release of pathogens and toxins — it protects the biological agent from people with malicious intent. A **biohazard** is any biological agent (or material containing one) that poses a threat to human, animal, or plant health or the environment. **Biorisk** is the combined risk of such adverse events, whether accidental or deliberate.

The modern framework is **biorisk management**: a systematic approach built on **Assessment, Mitigation, and Performance (AMP)** — assess the risks of the work, implement mitigation measures proportionate to the risk, and monitor performance to verify the measures work. This replaced the older purely prescriptive mindset with risk-based thinking promoted by WHO's Laboratory Biosafety Manual (4th edition) and ISO 35001.

## Why Biosafety Matters

Laboratory-acquired infections (LAIs) have been documented since the earliest days of microbiology — from brucellosis and tuberculosis among lab workers to more recent incidents. Beyond worker safety, accidental releases can seed community outbreaks, and the deliberate misuse of biology (bioterrorism, bioweapons programs) is a recognized international security concern addressed by the **Biological Weapons Convention (1972)**. Responsible science therefore requires both safe practice and security awareness — the dual foundation of this course.

## Categories of Biological Agents

Biological agents are classified by **risk group** (RG1-RG4) according to their pathogenicity, transmissibility, availability of treatment, and epidemic potential. RG1 agents (e.g., non-pathogenic *E. coli* K-12) pose minimal individual and community risk; RG4 agents (e.g., Ebola virus) cause severe, often untreatable disease with high transmission risk. Risk group classification is agent-based and informs — but does not dictate — the containment level required, because the actual risk also depends on the procedure (aerosol generation, quantities, worker immunity).

## Key Terms & Definitions

|                    |                                                                                                |
|--------------------|------------------------------------------------------------------------------------------------|
| <b>Biosafety</b>   | Preventing unintentional exposure to or accidental release of biological agents.               |
| <b>Biosecurity</b> | Preventing loss, theft, misuse, or intentional release of biological agents.                   |
| <b>Biorisk</b>     | The combined likelihood and consequence of accidental or deliberate adverse biological events. |
| <b>Risk group</b>  | Classification of pathogens (RG1-RG4) by hazard to individuals and the community.              |

#### Example: Biosafety vs. Biosecurity in Practice

Wearing gloves and working in a biosafety cabinet to avoid inhaling a pathogen is **biosafety**. Locking the pathogen freezer, maintaining an inventory log, and screening who may access it is **biosecurity**. Both failed in historical incidents: accidental exposures show biosafety gaps, while the 2001 anthrax letters in the USA showed biosecurity gaps.

### Module Summary

- Biosafety = protection from the agent; biosecurity = protection of the agent from misuse.
- Biorisk management follows the AMP model: Assess, Mitigate, Perform.
- Risk groups (RG1-RG4) classify agents by hazard; procedures determine actual risk.
- International concern over bioweapons is addressed by the Biological Weapons Convention.

#### Exam Pointers (Very Important)

- ★ Definitions: biosafety, biosecurity, biorisk, biohazard — and the difference between the first two.
- ★ What is the AMP model?
- ★ Describe risk groups RG1 to RG4 with one example each.

## MODULE 2: BIOSAFETY LEVELS AND LABORATORY DESIGN

### Learning Objectives

- Describe BSL-1 through BSL-4 facilities, practices, and equipment
- Match risk groups and procedures to appropriate containment
- Explain primary and secondary barriers
- List essential biosafety equipment and its correct use

### The Four Biosafety Levels

**BSL-1** is basic teaching/research space for RG1 agents: standard microbiological practices, open bench work, lab coats, handwashing, and decontamination of waste. **BSL-2** handles moderate-risk agents (e.g., *Staphylococcus aureus*, hepatitis B virus): adds restricted access, biosafety cabinets for aerosol-generating procedures, PPE including gloves and eye protection, an autoclave in the building, and biohazard signage.

**BSL-3** is for agents causing serious disease via inhalation (e.g., *Mycobacterium tuberculosis*): all work in biosafety cabinets, controlled directional (negative-pressure) airflow, sealed windows and self-closing double doors, respiratory protection as needed, and effluent decontamination. **BSL-4** is maximum containment for dangerous RG4 pathogens: either a full-body positive-pressure suit with dedicated air supply, or Class III glove-box cabinets, in a physically isolated facility with dedicated ventilation, waste treatment, and airlocks with showers.

### Primary and Secondary Barriers

**Primary barriers** protect the worker directly: biological safety cabinets (BSCs), enclosed containers, and PPE (gloves, gowns, respirators, eye protection). **Secondary barriers** protect the environment and community: the facility design itself — directional airflow, airlocks, sealed surfaces, autoclaves, and effluent decontamination systems. Safe work requires both layers; PPE is the last line of defense, never the first.

### Biological Safety Cabinets

BSCs provide personnel, product, and (for Class II/III) environmental protection through HEPA-filtered laminar airflow. **Class I** protects personnel and environment but not the product (open front, inward airflow). **Class II** (types A2, B2) is the standard for BSL-2/3: HEPA-filtered downflow protects the work, inward airflow protects the worker. **Class III** is a gas-tight glove box for BSL-4. Cabinets must be certified annually, never used with the sash raised above the marked level, and never as chemical fume hoods for volatile toxics.

### Key Terms & Definitions

|                        |                                                                              |
|------------------------|------------------------------------------------------------------------------|
| <b>BSL-1 to BSL-4</b>  | Escalating containment levels matching increasing agent and procedural risk. |
| <b>Primary barrier</b> | Worker-level protection: BSCs, PPE, safe containers.                         |

|                          |                                                                                                    |
|--------------------------|----------------------------------------------------------------------------------------------------|
| <b>Secondary barrier</b> | Facility-level protection: airflow, airlocks, sealed construction, waste treatment.                |
| <b>HEPA filter</b>       | High-efficiency particulate air filter removing 99.97% of 0.3-micron particles; the heart of BSCs. |

### Example: Choosing Containment

Culturing non-pathogenic *E. coli* K-12 for a teaching lab: BSL-1, open bench. Diagnostic sputum culture for suspected tuberculosis (aerosol risk, RG3 agent): BSL-3 with all manipulations in a Class II BSC. Research on Ebola virus: BSL-4 with positive-pressure suits. The same agent may need different containment for different procedures.

## Module Summary

- BSL-1 to BSL-4 provide escalating containment for increasing risk.
- Primary barriers (BSC, PPE) protect workers; secondary barriers (facility design) protect the environment.
- Class II BSCs are standard for BSL-2/3; Class III glove boxes for BSL-4.
- PPE is the last, not the first, line of defense.

### Exam Pointers (Very Important)

- ★ List the defining features of each BSL (1-4).
- ★ Primary vs. secondary barriers with examples.
- ★ Classes of BSC and their protection profiles.
- ★ Match agents/procedures to the correct BSL.

## MODULE 3: RISK ASSESSMENT AND GOOD MICROBIOLOGICAL PRACTICE

### Learning Objectives

- Perform a structured biological risk assessment
- Apply the hierarchy of controls to laboratory risks
- Describe good microbiological practices and procedures (GMPP)
- Explain incident reporting and emergency response

### Conducting a Risk Assessment

Every procedure with biological agents begins with a **risk assessment**: (1) identify the hazards — the agent (risk group, infective dose, transmission route), the procedure (aerosol generation, sharps, quantities), and the people and environment at risk; (2) evaluate who might be harmed and how, considering existing controls; (3) decide on additional mitigation proportionate to the risk; (4) record the findings; (5) review periodically or when work changes. Risk assessment is the foundation of the WHO Laboratory Biosafety Manual 4th edition's risk-based approach.

### Hierarchy of Controls

Controls are applied in a strict hierarchy of effectiveness: **elimination/substitution** (use an attenuated strain or inactivated material instead of the virulent pathogen); **engineering controls** (BSCs, closed systems, safety centrifuge cups); **administrative controls** (training, SOPs, restricted access, supervision); and finally **PPE** (gloves, gowns, respirators). A common exam point: never rely on PPE when an engineering control could eliminate the exposure.

### GMPP and Emergency Response

**Good microbiological practices and procedures** include: no eating, drinking, or mouth pipetting in the lab; handwashing on exit; minimizing aerosols and splashes; safe sharps handling (never recap needles — use sharps containers); decontaminating work surfaces daily and after spills; and autoclaving or chemically disinfecting all infectious waste. Every lab needs a **spill response plan**, eyewash/safety shower access, first-aid provisions, and a clear **incident reporting** system — near-misses are reported and investigated just like accidents, because they reveal systemic weaknesses.

### Key Terms & Definitions

|                              |                                                                                        |
|------------------------------|----------------------------------------------------------------------------------------|
| <b>Risk assessment</b>       | Systematic identification and evaluation of biological risks before work begins.       |
| <b>Hierarchy of controls</b> | Elimination > substitution > engineering > administrative > PPE.                       |
| <b>GMPP</b>                  | Good microbiological practices and procedures; the behavioral foundation of biosafety. |

|                  |                                                                                    |
|------------------|------------------------------------------------------------------------------------|
| <b>Near-miss</b> | An incident that could have caused harm but did not; a free lesson for prevention. |
|------------------|------------------------------------------------------------------------------------|

## Module Summary

- Risk assessment: identify hazards, evaluate who is harmed, add proportionate controls, record, review.
- Hierarchy of controls ranks elimination highest and PPE lowest.
- GMPP covers behavior: no food/drink, hand hygiene, sharps safety, surface and waste decontamination.
- Report incidents and near-misses; every lab needs a spill and emergency plan.

### Exam Pointers (Very Important)

- ★ Steps of a biological risk assessment in order.
- ★ The hierarchy of controls with one lab example per level.
- ★ List six GMPP rules. What is done with a sharps injury?

## MODULE 4: DECONTAMINATION, STERILIZATION, AND WASTE MANAGEMENT

### Learning Objectives

- Distinguish cleaning, disinfection, and sterilization
- Compare autoclaving, chemical, and radiation methods
- Classify laboratory waste and its treatment routes
- Select appropriate disinfectants for common agents

### Levels of Microbial Control

**Cleaning** removes dirt and organic matter but does not reliably kill microbes — it is the essential first step because organic load inactivates many disinfectants. **Disinfection** kills most vegetative pathogens but not necessarily bacterial spores. **Sterilization** destroys all microbial life including spores. **Antisepsis** is disinfection applied to living tissue (e.g., skin). Choosing correctly matters: a bench spill of bacteria needs disinfection; culture media and infectious waste need sterilization.

### Sterilization and Disinfection Methods

**Moist heat (autoclaving)** — 121°C at 15 psi for 15-20 minutes — is the gold standard for sterilizing media, instruments, and infectious waste; efficacy is verified with chemical indicators and biological indicators (*Geobacillus stearothermophilus* spores). **Dry heat** (160-170°C for 2+ hours) suits glassware and oils. **Chemical disinfectants** include chlorine compounds (sodium hypochlorite — broad, cheap, corrosive, inactivated by organic matter), alcohols (70% ethanol/isopropanol — rapid, for skin and surfaces, not sporicidal), aldehydes (glutaraldehyde — high-level disinfection/sterilant, toxic vapors), and hydrogen peroxide vapor for room decontamination. **Filtration** (0.22 µm) sterilizes heat-sensitive liquids; **UV and ionizing radiation** are used for surfaces, air, and single-use plastics respectively.

### Biological Waste Management

Laboratory waste is **segregated at source**: infectious waste (cultures, contaminated plastics) in autoclavable biohazard bags; sharps in puncture-proof containers; chemical and radioactive wastes in their own streams — never mixed. Infectious waste is treated by **autoclaving or incineration** before leaving the facility, with validation of the process. Liquid infectious waste may be chemically disinfected with a validated concentration and contact time. Records of waste treatment are part of biorisk documentation, and national regulations govern transport of infectious substances (UN3373 Category B, UN2814 Category A packaging with triple containment).

### Key Terms & Definitions

|                      |                                                                                        |
|----------------------|----------------------------------------------------------------------------------------|
| <b>Sterilization</b> | Destruction of all microbial life including spores.                                    |
| <b>Autoclave</b>     | Moist-heat sterilizer: 121°C, 15 psi, 15-20 min; validated with biological indicators. |

|                              |                                                                                                |
|------------------------------|------------------------------------------------------------------------------------------------|
| <b>Segregation at source</b> | Separating waste streams (infectious, sharps, chemical) where they are generated.              |
| <b>UN3373 / UN2814</b>       | UN numbers for shipping Category B biological substances and Category A infectious substances. |

#### **Example: Spill Response**

A culture tube of Salmonella breaks on the bench. Response: alert others, don PPE (gloves, gown, eye protection), cover the spill with absorbent material, apply freshly prepared 1% sodium hypochlorite from the outside inward, allow 20-30 minutes contact time, collect sharps with forceps into a sharps container, wipe up, disinfect again, autoclave all waste, wash hands, and file an incident report.

### **Module Summary**

- Cleaning < disinfection < sterilization; match the method to the target.
- Autoclaving is the gold standard for sterilization; validate with spore indicators.
- Choose disinfectants by spectrum, contact time, and compatibility; chlorine is broad but inactivated by organic matter.
- Segregate waste at source; treat infectious waste by autoclave/incineration; ship under UN regulations.

#### **Exam Pointers (Very Important)**

- ★ Distinguish cleaning, disinfection, sterilization, antisepsis.
- ★ Autoclave parameters and how efficacy is verified.
- ★ Name three disinfectant classes with one advantage and one limitation each.
- ★ Waste segregation categories and treatment routes.

## MODULE 5: NATIONAL AND INTERNATIONAL BIOSAFETY FRAMEWORKS

### Learning Objectives

- Outline Pakistan's biosafety regulatory framework
- Describe WHO, CBD/Cartagena, and BTWC roles
- Explain institutional biosafety committees and their functions
- Describe biosecurity measures: inventory, access control, personnel reliability

### Pakistan's Framework

In Pakistan, biosafety oversight for modern biotechnology is anchored in the **Pakistan Biosafety Rules (2005)** issued under the Pakistan Environmental Protection Act (1997), with the **National Biosafety Committee (NBC)** as the apex decision-making body and **Institutional Biosafety Committees (IBCs)** at research institutions reviewing local projects. The **Pakistan Environmental Protection Agency (Pak-EPA)** and provincial EPAs handle environmental aspects, while work with particularly dangerous pathogens falls under health-security coordination. Researchers must obtain NBC approval for contained use, field trials, and commercial release of GMOs through a tiered, case-by-case assessment.

### International Instruments

The **WHO Laboratory Biosafety Manual** (4th ed., 2020) is the global reference for safe laboratory practice. The **Cartagena Protocol on Biosafety** (under the Convention on Biological Diversity) governs transboundary movement of living modified organisms (LMOs), requiring advance informed agreement. The **Biological and Toxin Weapons Convention (BTWC, 1972)** prohibits development and stockpiling of bioweapons. **ISO 35001** provides a management-system standard for biorisk. Together these create overlapping obligations: protect workers, protect the environment, and prevent misuse.

### Institutional Biosafety Committees and Biosecurity Practice

An **IBC** reviews proposed work with pathogens, GMOs, and toxins; verifies risk assessments and containment; inspects facilities; and advises on training and incidents. Effective **biosecurity** combines: a live **inventory** of pathogen stocks (what exists, where, how much); **access control** (locks, card readers, two-person rules for high-risk agents); **personnel reliability** (training, background awareness, a culture where concerns can be raised); **material transfer** documentation; and cybersecurity for sensitive data. The goal is to make theft or diversion difficult to attempt and easy to detect.

### Key Terms & Definitions

|                           |                                                                                     |
|---------------------------|-------------------------------------------------------------------------------------|
| <b>NBC</b>                | National Biosafety Committee of Pakistan; apex body under the Biosafety Rules 2005. |
| <b>IBC</b>                | Institutional Biosafety Committee; local review of pathogen/GMO work.               |
| <b>Cartagena Protocol</b> | International agreement on safe transboundary movement of LMOs.                     |

**Module Summary**

- Pakistan: Biosafety Rules 2005, National Biosafety Committee, Institutional Biosafety Committees.
- International: WHO Biosafety Manual, Cartagena Protocol (LMOs), BTWC (bioweapons ban), ISO 35001.
- IBCs review and approve local high-risk biological work.
- Biosecurity rests on inventory control, access control, personnel reliability, and transfer documentation.

**Exam Pointers (Very Important)**

- ★ Pakistan's biosafety regulatory hierarchy.
- ★ Purpose of the Cartagena Protocol and the BTWC.
- ★ Functions of an Institutional Biosafety Committee.
- ★ Five elements of an effective biosecurity program.

## MODULE 6: INTRODUCTION TO BIOETHICS — PRINCIPLES AND FRAMEWORKS

### Learning Objectives

- Define bioethics and its scope
- Apply the four principles: autonomy, beneficence, non-maleficence, justice
- Distinguish ethics, morals, and law
- Explain informed consent and its elements

### What is Bioethics?

**Bioethics** is the systematic study of the ethical questions raised by biology, medicine, and biotechnology — what we *can* do versus what we *should* do. It draws on philosophy, law, medicine, and the life sciences. **Morals** are personal or cultural beliefs about right and wrong; **ethics** is the systematic, reasoned reflection on those beliefs; **law** is the enforceable minimum standard set by society. An action can be legal but unethical (e.g., exploiting a legal loophole in clinical trials), or ethical but illegal in some jurisdictions.

### The Four Principles (Beauchamp and Childress)

The dominant framework in biomedical ethics is **principlism**: (1) **Autonomy** — respect for persons and their right to make informed decisions about themselves; (2) **Beneficence** — act to promote the well-being of others; (3) **Non-maleficence** — 'first, do no harm' (primum non nocere); (4) **Justice** — fair distribution of benefits, risks, and resources. Principles can conflict — e.g., a patient's autonomy (refusing treatment) versus beneficence (the doctor's desire to treat) — and real ethical reasoning weighs and balances them in context rather than applying them mechanically.

### Informed Consent

**Informed consent** operationalizes autonomy in research and medicine. Valid consent requires: **disclosure** (purpose, procedures, risks, benefits, alternatives), **comprehension** (information the participant can actually understand), **voluntariness** (no coercion or undue inducement), and **competence** (capacity to decide). Special protections apply to vulnerable populations — children, prisoners, the mentally incapacitated, and economically disadvantaged groups. Research ethics committees (IRBs/ethics boards) review protocols to ensure these standards, following codes from Nuremberg (1947) through Helsinki to the Belmont Report.

### Key Terms & Definitions

|                    |                                                                             |
|--------------------|-----------------------------------------------------------------------------|
| <b>Bioethics</b>   | Systematic study of ethical issues in biology, medicine, and biotechnology. |
| <b>Principlism</b> | Beauchamp and Childress's four-principle framework for biomedical ethics.   |

|                               |                                                                                      |
|-------------------------------|--------------------------------------------------------------------------------------|
| <b>Informed consent</b>       | Voluntary, competent, comprehending agreement based on adequate disclosure.          |
| <b>Vulnerable populations</b> | Groups needing extra protection in research: children, prisoners, the incapacitated. |

### Example: Principles in Conflict

A tuberculosis patient refuses isolation, exercising autonomy — but risks infecting others, engaging public-health duties of non-maleficence and justice. Most ethical and legal frameworks resolve this by limiting autonomy when it foreseeably harms others: mandatory treatment/isolation for infectious TB is widely accepted. Bioethics is the disciplined weighing of such competing principles.

## Module Summary

- Bioethics asks what we should do with biological knowledge and power.
- Four principles: autonomy, beneficence, non-maleficence, justice — balanced, not mechanical.
- Valid informed consent needs disclosure, comprehension, voluntariness, competence.
- Research ethics evolved from Nuremberg to Helsinki to the Belmont Report; IRBs enforce it.

### Exam Pointers (Very Important)

- ★ Define bioethics; distinguish ethics, morals, and law.
- ★ State and explain the four principles with one example each.
- ★ Elements of valid informed consent.
- ★ Give an example of two principles in conflict and how it is resolved.

## MODULE 7: BIOETHICS OF GENETIC ENGINEERING AND GMOS

### Learning Objectives

- Describe ethical issues in genetic engineering of microbes, plants, and animals
- Evaluate arguments for and against GM crops
- Explain gene flow, superweeds, and ecological risk concerns
- Discuss labeling, choice, and socioeconomic justice issues

### Genetic Engineering: The Ethical Landscape

**Genetic engineering** — deliberately altering an organism's DNA with recombinant DNA technology — raises distinct ethical questions at each level. **Microbial** engineering is largely accepted under containment but raises dual-use concerns (engineering pathogens). **Plant** engineering (GM crops) is the most publicly contested. **Animal** engineering raises welfare concerns (suffering in engineered animals) and the 'playing God' objection — the idea that some interventions violate a natural or sacred order, an objection ethicists evaluate by asking what moral work 'naturalness' actually does.

### GM Crops: Arguments and Evidence

Proponents cite **beneficence**: insect-resistant Bt crops reduce pesticide use; biofortified crops (e.g., Golden Rice with provitamin A) address malnutrition; herbicide tolerance can enable conservation tillage. Critics raise **non-maleficence** concerns: allergenicity and unintended effects (assessed case-by-case by regulators), **gene flow** to wild relatives creating **superweeds**, harm to non-target organisms, and evolution of resistant pests — all requiring resistance-management strategies. Justice concerns include corporate control of seed markets, terminator technologies, and whether benefits reach smallholder farmers.

Ethically, the debate is not only about safety data but about **autonomy and choice** (labeling of GM foods so consumers can decide), **precaution** under uncertainty, and who bears risks versus who captures benefits.

### Regulation and the Precautionary Approach

Regulatory philosophies differ: the **US** system is largely product-based (is the food safe?), while the **EU** is process-based with strong precautionary regulation and mandatory labeling. The **precautionary principle** holds that lack of full scientific certainty should not postpone measures against plausible serious harm — but critics warn it can block beneficial innovation. Pakistan's NBC evaluates GMOs case-by-case, requiring contained trials and environmental risk assessment before any release.

### Key Terms & Definitions

|                  |                                                                            |
|------------------|----------------------------------------------------------------------------|
| <b>GMO/LMO</b>   | Genetically/living modified organism carrying deliberately introduced DNA. |
| <b>Gene flow</b> | Movement of transgenes to wild relatives via cross-pollination.            |

|                                |                                                                       |
|--------------------------------|-----------------------------------------------------------------------|
| <b>Superweed</b>               | Weed acquiring herbicide resistance via gene flow or selection.       |
| <b>Precautionary principle</b> | Acting against plausible serious harm despite scientific uncertainty. |

### Example: Golden Rice

Golden Rice is engineered to produce beta-carotene (provitamin A) in the grain to combat vitamin A deficiency, which blinds hundreds of thousands of children yearly. Supporters frame it as a moral imperative (beneficence); opponents question its efficacy versus supplementation programs, corporate patent arrangements, and cultural acceptance — illustrating that GMO ethics blends safety science with justice and autonomy concerns.

## Module Summary

- Genetic engineering ethics differ for microbes, plants, and animals.
- GM crop debate: benefits (yield, nutrition, fewer pesticides) vs. risks (gene flow, resistance, corporate control).
- Labeling protects consumer autonomy; precaution balances innovation against uncertain harm.
- Regulation varies: product-based (US) vs. process/precautionary (EU); Pakistan uses case-by-case NBC review.

### Exam Pointers (Very Important)

- ★ Ethical issues specific to engineered microbes, plants, and animals.
- ★ For/against GM crops: give two arguments each side.
- ★ What is gene flow and why does it matter ethically?
- ★ Explain the precautionary principle and its criticism.

## MODULE 8: HUMAN GENETICS, STEM CELLS, AND CLONING

### Learning Objectives

- Discuss ethics of genetic testing, screening, and counseling
- Compare embryonic, adult, and iPS stem cells ethically
- Distinguish reproductive from therapeutic cloning
- Explain germline vs. somatic gene therapy ethics

### Genetic Testing and Screening

**Genetic testing** reveals predispositions (e.g., BRCA1/2 for breast cancer, Huntington's disease) before symptoms. Ethical tensions: the **right to know vs. the right not to know** (Huntington's has no cure — should at-risk people be tested?); **privacy and discrimination** (use of genetic data by insurers or employers — addressed by laws like the US GINA); **psychological harm**; and duties to **family members** who share the genes. **Genetic counseling** must be non-directive, supporting autonomous decisions. Population **screening** (e.g., newborn screening) is justified when early detection enables effective intervention — beneficence outweighs the small autonomy cost.

### Stem Cells

**Embryonic stem cells** (from blastocysts) are pluripotent but their derivation destroys an embryo — the central moral-status-of-the-embryo debate. **Adult stem cells** avoid this but are multipotent and harder to expand. **Induced pluripotent stem cells (iPSCs)**, reprogrammed from adult cells (Yamanaka, Nobel 2012), largely bypass the embryo controversy while raising new issues: tumorigenicity, consent for cell donors, and the theoretical possibility of creating gametes. Ethical oversight requires donor consent, limits on embryo culture (the **14-day rule**), and prohibition of reproductive use of engineered embryos in most jurisdictions.

### Cloning and Gene Therapy

**Reproductive cloning** (creating a human copy, as with Dolly the sheep via SCNT) is widely condemned and legally banned in most countries: safety risks, identity and dignity concerns, and instrumentalization of the child. **Therapeutic cloning** (SCNT to make patient-matched embryonic stem cells) is debated but less universally rejected. **Somatic gene therapy** (treating the patient only) is increasingly accepted with proper trials; **germline editing** (heritable changes, e.g., the 2018 CRISPR-babies case) is widely condemned as premature and unethical because changes pass to future generations who cannot consent — most frameworks demand broad societal consensus before any heritable editing.

### Key Terms & Definitions

#### Genetic counseling

Non-directive support helping individuals understand and decide on genetic information.

|                         |                                                                                       |
|-------------------------|---------------------------------------------------------------------------------------|
| <b>iPSCs</b>            | Induced pluripotent stem cells; reprogrammed adult cells avoiding embryo destruction. |
| <b>SCNT</b>             | Somatic cell nuclear transfer; the cloning technique behind Dolly.                    |
| <b>Germline editing</b> | Heritable genome changes; subject to near-universal moratorium demands.               |

#### **Example: The CRISPR-Babies Case (2018)**

He Jiankui announced twin girls whose embryos he had edited with CRISPR to disable CCR5 (HIV resistance). The global scientific community condemned it: the edit was medically unnecessary (HIV is preventable/treatable), off-target risks were unquantified, consent was flawed, and germline changes affect descendants. He was imprisoned in China. The case is now the textbook example of unethical germline editing.

### **Module Summary**

- Genetic testing ethics: autonomy (right not to know), privacy/discrimination, family implications; counseling must be non-directive.
- Stem cell ethics center on the embryo's moral status; iPSCs bypass much of the controversy.
- Reproductive cloning is widely banned; therapeutic cloning is debated.
- Somatic gene therapy is cautiously accepted; heritable germline editing faces a global moratorium consensus.

#### **Exam Pointers (Very Important)**

- ★ Ethical issues in predictive genetic testing (four points).
- ★ Compare embryonic, adult, and induced pluripotent stem cells ethically.
- ★ Reproductive vs. therapeutic cloning: definitions and ethical status.
- ★ Why is germline editing treated differently from somatic therapy?

## MODULE 9: EMERGING BIOTECHNOLOGIES AND DUAL-USE DILEMMAS

### Learning Objectives

- Define dual-use research of concern (DURC)
- Discuss synthetic biology and gain-of-function ethics
- Explain publication and oversight dilemmas
- Describe responsible conduct: codes, oaths, and education

### Dual-Use Research of Concern

**Dual-use research of concern (DURC)** is life-sciences research that could be directly misapplied to cause harm — the same experiment that reveals how a virus becomes transmissible (valuable for pandemic preparedness) also teaches how to make it more dangerous. Classic cases: the 2001 mousepox/IL-4 experiment (accidentally showing how to defeat immunity), synthesis of poliovirus from scratch (2002), reconstruction of the 1918 influenza virus (2005), and H5N1 **gain-of-function** transmission studies (2011-12), which triggered a global debate and a US funding pause. Oversight frameworks (e.g., the US DURC policies, WHO guidance) require institutional and sometimes national review of such work.

### Synthetic Biology and De-extinction

**Synthetic biology** engineers biological systems from standardized parts and can now synthesize entire viral genomes from sequence data ordered online — collapsing the barrier between information and pathogen. Ethical questions: should DNA synthesis be **screened** for dangerous sequences (the International Gene Synthesis Consortium does this voluntarily)? Who governs 'garage' biology and DIY bio? **De-extinction** (e.g., mammoth revival) raises welfare questions for resurrected animals and ecological questions about reintroduction. **Gene drives** that force engineered traits through wild populations (e.g., malaria-resistant mosquitoes) could eradicate disease — or irreversibly alter ecosystems without the consent of affected communities.

### Responsibility of Scientists

Scientists bear special responsibility because they create the capabilities others might misuse. Responses include: **codes of conduct** (e.g., the Hague Ethical Guidelines for chemists, adapted calls for a biologists' Hippocratic oath); **ethics education** integrated into life-science training; **responsible publication** norms — weighing open science against information hazards (the H5N1 papers were eventually published in full after review); and **whistleblower protections** so concerns about dangerous work can be raised safely. The core ethical stance: maximize the benefits of biology while minimizing foreseeable harm — the **dual responsibility** of every life scientist.

### Key Terms & Definitions

#### DURC

Dual-use research of concern; research with foreseeable misuse potential.

|                           |                                                                                 |
|---------------------------|---------------------------------------------------------------------------------|
| <b>Gain-of-function</b>   | Experiments enhancing pathogen transmissibility, virulence, or immune evasion.  |
| <b>Gene drive</b>         | Engineered inheritance bias spreading a trait rapidly through wild populations. |
| <b>Information hazard</b> | True information whose broad spread foreseeably causes net harm.                |

#### **Example: The H5N1 Transmission Studies**

In 2011-12, two groups engineered H5N1 avian influenza to transmit between ferrets (a human-transmission model). Proponents argued the work identified pandemic-risk mutations for surveillance; critics argued it created a potential pandemic pathogen and published a blueprint. The NSABB recommended redaction; after review, papers were published in full. The episode reshaped DURC oversight worldwide.

### **Module Summary**

- DURC: the same research can protect against pandemics or enable bioweapons.
- Landmark cases: mousepox IL-4, synthetic polio, 1918 flu reconstruction, H5N1 GOF.
- Synthetic biology, gene drives, and de-extinction raise governance and ecological ethics questions.
- Scientists' dual responsibility: codes of conduct, ethics education, responsible publication, whistleblowing.

#### **Exam Pointers (Very Important)**

- ★ Define DURC and give two historical examples.
- ★ Arguments for and against gain-of-function research.
- ★ What is a gene drive and why is it ethically controversial?
- ★ List four ways scientists discharge their dual responsibility.

## MODULE 10: BIOETHICS IN RESEARCH, ENVIRONMENT, AND SOCIETY

### Learning Objectives

- Apply the 3Rs to animal research ethics
- Discuss bioprospecting, benefit-sharing, and biopiracy
- Explain environmental ethics of biotechnology
- Describe public engagement and the role of bioethics committees

### Animal Research Ethics: The 3Rs

Animal experimentation is justified by most ethical frameworks only when necessary and humane, governed by the **3Rs**: **Replacement** (use non-animal methods — cell cultures, computer models — where possible), **Reduction** (use the minimum number of animals for valid statistics), and **Refinement** (minimize pain, suffering, and distress — anesthesia, humane endpoints, enriched housing). Institutional animal ethics committees review protocols; the 'necessary suffering' must be proportionate to the expected knowledge benefit. Growing capabilities in organoids and organs-on-chips are expanding replacement options.

### Bioprospecting and Justice

**Bioprospecting** — searching biodiversity (often in developing countries) for useful genes and compounds — raises justice questions: the **Nagoya Protocol** (under the CBD) requires prior informed consent of provider countries and **fair benefit-sharing** from commercialization. **Biopiracy** is the pejorative term for taking genetic resources or traditional knowledge without consent or compensation (classic cases: neem, basmati, turmeric patents — several revoked after challenges). For Pakistan, with rich biodiversity and traditional medicinal knowledge, these frameworks directly affect national interests.

### Environment, Public Engagement, and Committees

Environmental release of engineered organisms demands **ecological risk assessment**: invasiveness, effects on non-target species, and reversibility — an ethical duty to future generations and to ecosystems themselves (different ethical theories weigh nature's intrinsic value differently). Because biotechnology affects everyone, **public engagement** — honest communication, not one-way persuasion — is an ethical obligation, and mistrust often reflects legitimate concerns about power and transparency rather than ignorance. **Bioethics committees** at institutional and national levels (e.g., Pakistan's National Bioethics Committee) provide ongoing deliberation, guidelines, and review — ethics is a practice, not a one-time approval.

### Key Terms & Definitions

|                        |                                                                             |
|------------------------|-----------------------------------------------------------------------------|
| <b>3Rs</b>             | Replacement, Reduction, Refinement in animal research.                      |
| <b>Nagoya Protocol</b> | International agreement on access to genetic resources and benefit-sharing. |

|                                   |                                                                              |
|-----------------------------------|------------------------------------------------------------------------------|
| <b>Biopiracy</b>                  | Uncompensated commercial use of genetic resources or traditional knowledge.  |
| <b>Ecological risk assessment</b> | Evaluating environmental consequences before releasing engineered organisms. |

#### **Example: The Turmeric Patent**

In 1995 a US patent was granted on turmeric's wound-healing use — knowledge documented in ancient Indian texts. India's CSIR challenged it with prior-art evidence and the patent was revoked in 1997. The case became emblematic of biopiracy and helped drive traditional-knowledge databases and the Nagoya Protocol's benefit-sharing regime.

### **Module Summary**

- Animal research follows the 3Rs: replace, reduce, refine; ethics committees review protocols.
- Nagoya Protocol mandates consent and benefit-sharing for genetic resources; biopiracy is its violation.
- Environmental release requires ecological risk assessment and intergenerational responsibility.
- Public engagement and standing bioethics committees keep ethics a living practice.

#### **Exam Pointers (Very Important)**

- ★ State the 3Rs with one example each.
- ★ What is the Nagoya Protocol? Define biopiracy with an example.
- ★ Ethical considerations in environmental release of GMOs.
- ★ Why is public engagement an ethical obligation, not just PR?