GOVERNMENT OF PAKISTAN

HEALTH RESEARCH INSTITUTE — NATIONAL INSTITUTES OF HEALTH

NATIONAL BIOETHICS COMMITTEE (NBC-HRI)

REGULATORY FRAMEWORK

for the Registration of Institutional Ethical Review Boards (IERBs)

and Enforcement of Compliance

NATIONAL BIOETHICS COMMITTEE

Health Research Institute – NIH · Islamabad, Pakistan

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FOR THE REGISTRATION OF INSTITUTIONAL ETHICAL REVIEW BOARDS (IERBs) AND ENFORCEMENT OF COMPLIANCE

VERSION 1.2

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PREAMBLE:

This Regulatory Framework is issued under the powers conferred by the Health Research Institute – NIH Act, 2021. It is aligned with the Drug Regulatory Authority of Pakistan (DRAP) Act 2012, the Pakistan Medical and Dental Council (PM&DC) Code of Conduct, and international ethical standards for the protection of human research participants.

The National Bioethics Committee (NBC-HRI) is the sole statutory body mandated to oversee the ethical governance of human health research in Pakistan. Under the provisions of the NIH Act, the NBC-HRI serves as the central authority for the accreditation and standardization of all health-related ethics review bodies.

It is mandated that *"No institutional ethical review, approval, or oversight of health-related research—whether conducted in public or private sectors—may be undertaken by a committee that is not explicitly registered with the National Bioethics Committee (NBC-HRI)."*

Consequently, the operation of an unregistered Ethical Review Board undermines the national research integrity and exposes research participants to undue risk. Operating an IERB without registration, or failing to adhere to NBC-HRI standards is a violation of national standards.

PURPOSE: The purpose of this framework is to:

1. Mandate the registration of all IERBs reviewing human subject research with the NBC-HRI.
2. Establish standardized criteria for the composition, function, and operation of IERBs.
3. Define prohibited acts regarding the operation of unregistered or non-compliant IERBs.
4. Establish a penalty structure for institutions and individuals conducting research approved by unregistered boards.

SCOPE: This framework applies to all:

- Public and private research institutions, universities, and hospitals in Pakistan.
    - Universities and degree-awarding institutions (medical and non-medical).
    - Clinical Research Organizations (CROs).
    - Hospitals and healthcare facilities conducting research.
- Principal Investigators (PIs) relying on IERB approval.
- Sponsors and funding agencies utilizing unregistered ethics committees for trial oversight.

Definition of Violations (Offenses): A violation occurs when an institution or committee fails to adhere to the *Framework for Registration of IERBs*. Specific offenses include:

- **Operation of an Unregistered Board:** Conducting ethical reviews and issuing approval letters without a valid NBC-HRI Registration Certificate.
- **Non-Compliant Composition:** Operating an IERB that fails to meet the minimum quorum, lacks a lay member, or lacks independent external membership as defined by NBC guidelines
- **Failure to Renew:** Continuing to review and approve research proposals after the expiration of the three-year registration period without submitting a renewal application.
- **Falsification of Records:** Submitting fraudulent membership lists, CVs, or meeting minutes during the registration or annual reporting process.
- **Non-Compliant Composition:** Operating an IERB that fails to meet mandatory composition requirements (e.g., missing Lay Member, missing external member, or lack of gender diversity).
- **Failure to Report:** Neglecting to submit mandatory Annual Reports or failing to report Serious Adverse Events (SAEs) to the NBC-HRI.
- **Bypassing National Authority:** Accepting directives from foreign sponsors or international collaborators to bypass national registration requirements or ethical standards.
- **Conflict of Interest:** Approving research where IERB members had undisclosed conflicts of interest.

IMPLEMENTATION STANDARDS (MANDATORY REQUIREMENTS)

Institutions must ensure the following standards are met to achieve and maintain registration:

1. **Establishment and Independence**

- The IERB must be formally constituted by the Institutional Head.
- The IERB must operate independently of administrative or financial pressure to approve specific studies.

2. **Membership Requirements**

- **Minimum Size:** Five (5) members (total must be an odd number).
- **Lay Member:** At least one member who is not a medical practitioner or researcher (e.g., a lawyer, teacher, or community leader) and not affiliated with the institution.
- **External Member: At** least one member from outside the institution.
- **Gender Balance:** Representation of both genders is mandatory.

3. **Standard Operating Procedures (SOPs):** The IERB must maintain written SOPs for initial review, continuing review, reporting of adverse events, and conflict of interest management.

4. Training: All IERB members must undergo mandatory certified ethics training

CLASSIFICATION OF OFFENSES AND PENALTIES

This section governs non-compliance with NBC's Regulatory Framework for the Registration of Institutional Ethical Review Boards (IRBs), including non-compliance arising from the collection, storage, processing, transport, shipment, export, or international sharing of Human Biological Material (HBM) and of research data derived from human participants. It applies to every IRB/IERC registered or seeking registration with NBC, to the institutions that host them, and to any principal investigator, custodian, or courier acting under an NBC-approved protocol or Material Transfer Agreement (MTA).

Violations are classified by the risk they pose to research participants, to biosafety and biosecurity, to the integrity of the national research ecosystem, and to Pakistan's interests in its genetic and biological resources, and are graded across three severity tiers Category A (minor), Category B (major), and Category C (severe) each carrying a distinct penalty scale.

DEFINITIONS:

Human Biological Material (HBM): any material of human origin obtained for research, including blood, serum, plasma, tissue, cells, nucleic acids (DNA/RNA), and their derivatives, together with any data generated from their analysis.

Material Transfer Agreement (MTA): the NBC-countersigned agreement governing transfer of HBM between an exporting institute in Pakistan and a receiving institute, setting out permitted use, benefit-sharing, and re-transfer restrictions.

De-identified / Anonymized Data: research data from which direct and indirect identifiers have been removed or altered such that the data subject cannot reasonably be re-identified by the recipient.

Sensitive Personal / Health Data: data revealing an individual's health status, genetic information, or biometric data capable of uniquely identifying a natural person.

Infectious Substance – Category A / Category B (transport classification): the UN/IATA/WHO classification used for shipping: Category A (UN 2814, infectious to humans; UN 2900, infectious to

animals only) covers substances capable of causing permanent disability or life-threatening or fatal disease; Category B (UN 3373) covers substances not meeting Category A criteria. This transport-safety classification is distinct from and must not be confused with the offense-severity tiers "Category A / B / C" used elsewhere in this section.

Data Sharing Agreement (DSA): a written agreement, approved by NBC, governing the cross-border transfer, storage, and use of research data derived from human subjects.

Benefit-Sharing: the fair and equitable sharing of monetary and non-monetary benefits arising from the utilization of Pakistan's genetic resources, consistent with the Nagoya Protocol.

Chain of Custody: the documented, unbroken record of the collection, handling, storage, and transfer of HBM from collection to final disposition (use, return, or destruction).

Biosafety / Biosecurity Incident: any unplanned event involving HBM in transit or storage that results in, or creates a material risk of, exposure, spillage, loss, theft, or unauthorized access.

Competent Authority: NBC-HRI and, as applicable to the specific approval sought, the Drug Regulatory Authority of Pakistan (DRAP), Pakistan Customs, and the Strategic Export Control Division (SECDIV).

Classification of Offenses and Penalties:

The NBC-HRI holds enforcement authority through an Inquiry Committee that investigates alleged violations and recommends penalties. The accused institution or IRB Chairperson shall be given an opportunity to respond to the allegations before any penalty takes effect.

Category A Minor Violations (Administrative Non-Compliance):

Corrective, low-severity response. No suspension of registration; intended to secure prompt correction and closer monitoring.

Offenses:

(a) Filing the IRB's annual report up to 30 days after the deadline.

(b) Unintentional administrative errors in the documentation of meeting records (e.g., a missing signature or date, corrected on request).

(c) A brief lapse in quorum during a meeting, provided no study approvals were issued while quorum was not met.

(d) Submitting the signed copy of a Material Transfer Agreement (MTA) to NBC more than 14 working days after an otherwise properly authorized HBM shipment has left Pakistan, where the shipment itself was fully authorized in advance.

(e) Incomplete or delayed entries in the shipment or chain-of-custody log for an authorized HBM transfer, where the underlying shipment was authorized and no material left the country improperly.

(f) A courier, packaging, or labeling error on an otherwise correctly classified and approved shipment (e.g., a typographical error in the shipper's name or address) that does not affect the UN/IATA safety classification of the substance and does not create a biosafety risk.

(g) Failure to notify NBC, within the required timeframe, of a routine change to an already-approved international courier or logistics provider for a low-risk (Category B, UN 3373) shipment.

(h) Failure to renew, within the grace period, a lapsed individual biosafety/shipment-handling training certificate for staff who pack or dispatch HBM, where no shipment was made during the lapse.

Penalties:

1. Written Warning: a Notice to Show Cause (NTC) issued to the IRB Chairperson and Institutional Head.

2. Mandatory Remediation: submission of the corrected documentation including, where the violation concerns HBM, the outstanding MTA copy or shipment/chain-of-custody log within 14 working days.

3. Enhanced Monitoring: increased scrutiny of the IRB's next quarterly report and, where the violation concerned HBM or data transfer, of its next shipment or international data-transfer request.

Category B Major Violations (Regulatory Breaches):

Suspension of registration, financial penalty, and nullification of affected approvals. Applies to regulatory breaches that are procedural or negligent rather than deliberately concealed.

Offenses:

(a) Reviewing or approving studies under an expired IRB registration.

(b) Operating without the mandatory lay (non-scientific, community) member on the review committee.

(c) Approving research without a properly constituted quorum.

(d) Exporting or shipping HBM internationally without a valid, NBC-countersigned Material Transfer Agreement (MTA) in place prior to shipment.

(e) Sharing individual-level or identifiable health, genomic, or other research data internationally including via cloud storage, external servers, collaborating laboratories, or third-party repositories without an NBC-approved Data Sharing Agreement, or without applying the de-identification/anonymization required by the approved protocol.

(f) Using HBM, or data derived from it, for a purpose or with a recipient materially outside the scope of the approved MTA or protocol (e.g., an undisclosed secondary research use, or sharing with a collaborator not named in the agreement) without prior written consent from the exporting institute and NBC.

(g) Failing to acknowledge Pakistan as the country of origin of the HBM or data in resulting publications, as required under the MTA.

(h) Misclassifying the UN/IATA transport category of an infectious substance for shipment (e.g., packaging or documenting a substance under Category B, UN 3373, requirements when it in fact meets Category A, UN 2814/2900, criteria), where the error is discovered before it results in exposure, spillage, or a public-health incident.

(i) Shipping HBM internationally without the DRAP export authorization in case of clinical trials, customs clearance SECDIV clearance in case of pathogens only as per the list, or other required national permit, where the shipment itself was disclosed to and known by NBC (i.e., a procedural failure rather than a concealed or undeclared export).

(j) Retaining HBM, or the data derived from it, beyond the period authorized in the MTA or approved protocol, without having obtained an approved extension.

(k) Proceeding with international transfer or sharing of a participant's sample or data without the specific informed consent required for that transfer, where the participant's original consent did not extend to international sharing.

(l) Sub-contracting sample analysis or data processing to a third-party laboratory, biobank, or cloud service provider located outside Pakistan without prior NBC notification and approval.

(m) Failing to report a biosafety or biosecurity incident in transit or storage (breakage, leakage, loss, or theft of HBM) to NBC within the required timeframe, where the incident did not result in harm to any person.

Penalties:

1. **Suspension of Registration:** immediate suspension of the IRB's authority to review new protocols including new HBM export or international data-sharing requests for a period of 6 months.

2. **Institutional Fine:** up to PKR 500,000, or as defined by the IRB Oversight committee of NBC in HRI-NIH, after receiving the recommendation of the Inquiry Committee.

3. **Recall and Accounting:** where feasible, the institution must recall, return, or arrange verified destruction of samples or data transferred in breach of this section, and must furnish NBC a full written accounting of what was transferred, to whom, and when.

4. **Nullification of Approvals:** all study approvals, and any HBM export or data-sharing authorizations, granted during the non-compliance period are declared void; affected studies and transfers must halt pending review.

Category C Severe Violations:

Criminal referral, permanent blacklisting, and license revocation. Applies to willful, concealed, fraudulent, or repeated violations, and to any violation causing serious harm.

Offenses:

(a) Willful operation of a fake or "ghost" IRB that issues approvals without conducting genuine ethical review.

(b) Forging NBC registration certificates or falsifying an IRB's registration status.

(c) Repeated failure to report Serious Adverse Events (SAEs), where this results in harm to research participants.

(d) An IRB knowingly approving fraudulent research.

(e) Undeclared or clandestine export of HBM that bypasses NBC, DRAP, and customs controls entirely, including any transfer effected without the knowledge or authorization of the exporting institute ("biopiracy").

(f) Commercializing, patenting, or transferring HBM or data derived from it to a third party for commercial gain without the benefit-sharing consent required under the Nagoya Protocol on Access to Genetic Resources and Benefit-Sharing (Pakistan acceded 21 February 2016) and applicable national law.

(g) Sharing identifiable health or genomic data internationally in a manner that results in a serious breach of participant confidentiality, enables re-identification of participants, or violates the end-use

certification (including obligations under the Export Control Act, 2004) accompanying the material or data.

(h) Deliberately mis-declaring or mis-packaging a Category A infectious substance (UN 2814/2900) as Category B (UN 3373) or as a non-biological good, to evade biosafety/biosecurity controls, where this results in, or creates a serious risk of, exposure, spillage, or a public-health incident.

(i) Transferring HBM or associated data in a manner that facilitates a dual-use or weapons-related application, or that is directed to a sanctioned or export-restricted entity or jurisdiction, in breach of end-use certification obligations.

(j) Repeated or willful breach of an MTA's re-export or re-transfer prohibition after the institution has already received a Category B penalty for a related violation.

(k) Deliberate falsification of chain-of-custody, shipment, or MTA records to conceal an unauthorized transfer of HBM or data.

(l) Retaliation against, or coercion of, any individual who in good faith reports or deals the inquiry of a suspected violation under this section (see Section 4).

Penalties:

1. Criminal Prosecution: referral to the Federal Investigation Agency (FIA) and relevant courts for prosecution under applicable fraud statutes and, where applicable, the Customs Act, 1969, and the Export Control Act, 2004.

2. Permanent Blacklisting: the institution and IRB Chairperson are barred from receiving government grants, NBC approvals, or participating in national health research, and for HBM or data offenses from any further authorization to export biological material or share research data internationally.

3. License Revocation: NBC recommends to PM&DC/HEC/DRAP that the licenses or registrations of the institution or principal investigators be cancelled.

4. Referral to Competent Authorities: for undeclared export, benefit-sharing violations, or confidentiality/dual-use breaches, NBC additionally refers the matter to the Ministry of National Health Services, Regulations & Coordination and, where dual-use or biosecurity concerns arise, to the Strategic Export Control Division (SECDIV).

5. Mandatory Compliance Audit: at its own cost, the institution must undergo independent third-party compliance audits for a period of 2 years following any reinstatement of its registration.

6. Fines/Other Penalties: to be determined based on the Inquiry Committee's recommendation.

Self-Reporting and Whistleblower Provision:

Consistent with international good-practice standards for research-integrity enforcement, an institution or IRB that proactively discovers and discloses a violation to NBC before an Inquiry Committee investigation is initiated may, at the Inquiry Committee's discretion, be treated one severity tier lower than the violation would otherwise warrant except where the violation resulted in actual harm to a research participant, in which case no reduction applies.

Any individual who, in good faith, reports a suspected violation under this section whether by a colleague, an IRB, or an institution shall be protected from retaliation, demotion, or adverse action by their institution on account of that report. Retaliation is itself a Category C offense under Section **3.**

Investigation, Due Process, and Appeals:

All alleged violations are investigated by an NBC Inquiry Committee, which recommends the applicable penalty to NBC-HRI. The accused institution or IRB Chairperson shall be given a reasonable opportunity to respond to the allegations, including access to the evidence relied upon, before any penalty takes effect.

A two-tier appeal process is available: a first appeal to the NBC Chairperson at HRI-NIH, within 15 working days of the decision, and a second appeal to the Chief Executive Officer NIH within 15 working days of the Executive Director's decision, with final resolution within 8 weeks.

Effective Date and Periodic Review:

This section takes effect on the date of NBC's approval and publication, and applies to violations occurring on or after that date. NBC shall review this section at least every 3 years, or sooner if warranted by changes to the international instruments referenced in the Appendix, to keep it consistent with current international standards for HBM transport, sample shipment, and cross-border data sharing.

Appendix: International Standards and Regulatory Instruments Referenced:

This section was drafted to align with, and is intended to be read alongside, the following international and domestic instruments. Where a domestic instrument is still pending enactment, this framework adopts the relevant principle as a matter of NBC policy pending, or alongside, formal domestic legislation.

1. **WHO Guidance on Regulations for the Transport of Infectious Substances 2025–2026:** applicable from 1 October 2025 classification and packaging of Category A (UN 2814/UN 2900) and Category B (UN 3373) infectious substances.
2. **IATA Dangerous Goods Regulations:** carrier-level shipping, packaging (e.g., P620/P650), labeling, and documentation requirements for biological substances.
3. **Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization:** Pakistan acceded 21 February 2016 prior informed consent (PIC) and mutually agreed terms (MAT) for utilization of genetic resources.
4. **GA4GH Framework for Responsible Sharing of Genomic and Health-Related Data:** international consensus principles (Global Alliance for Genomics and Health) for responsible cross-border genomic and health data sharing.
5. **ISO 20387:2018, Biotechnology Biobanking General Requirements for Biobanking:** quality, traceability, and chain-of-custody requirements for biological repositories.
6. **International Health Regulations (IHR, 2005), World Health Organization:** reporting obligations for events of international public health concern.
7. **Declaration of Helsinki (WMA) and CIOMS International Ethical Guidelines for Health-Related Research Involving Humans:** informed consent standards for international use and transfer of human samples and data.
8. **Export Control Act, 2004 (referred to in NBC's own documents as "SECA-2004"), administered by the Strategic Export Control Division (SECDIV):** controls on dual-use biological items and end-use certification.
9. **Customs Act, 1969, and DRAP's Guidelines for Import and Export of Therapeutic Goods:** national export/import permit requirements applicable to biological material.
10. **Prevention of Electronic Crimes Act (PECA), 2016, and Pakistan's Personal Data Protection Bill (pending enactment as of 2026):** current and forthcoming domestic legal basis for cross-border data-transfer regulation.
11. **NBC's own Material Transfer Agreement (MTA) Template and Guidelines for Collection, Usage, Storage, and Export of Human Biological Material:** the existing NBC instruments this section is designed to enforce.