

Towards an Efficient Governance
Framework for International Collaborative
Clinical Research:
A Dual Perspective of Private International
Law and Research Ethics

(Draft v0.3)

Wanhong Huang

huang-wanhong.com April 13, 2026

Abstract

The governance of international collaborative clinical research (ICR) stands at the intersection of at least three normative orders: domestic health law, international treaty regimes, and research ethics frameworks. Existing coordination mechanisms leave significant lacunae in jurisdiction, liability allocation, data sovereignty, and cross-cultural informed consent. This paper develops a governance framework grounded simultaneously in private international law methodology and contemporary research ethics theory. Drawing on an ontological decomposition of collaborative research relationships into six categories (entities, relations, attributes, events, processes, and states), and employing PIL as an *intermediate language* that routes each ontological element to its applicable domestic legal order, we diagnose the current normative landscape and propose targeted, operationalisable policy recommendations.

Keywords: private international law; research ethics; international clinical research; governance; multilateral framework; informed consent; data sovereignty; jurisdiction

Contents

I Overview: Research Definition, Objectives, and Ontological Foundations	5
1 Purpose, Scope, and Research Objectives	5
1.1 Background and Motivation	5
1.2 Scope	5
1.3 Research Objectives	6
2 Ontological Analysis	6
2.1 Motivation for an Explicit Ontology	6
2.2 The Epistemological Question	7
3 Research Questions	7
4 The $O \rightarrow E \rightarrow P$ Movement: Methodological Preamble	8
II Research Methods and Evaluation Framework	8
5 Research Design and Epistemological Commitments	8
5.1 Overall Research Design	8
5.2 Epistemological Commitments	9
6 The $O \rightarrow E \rightarrow P$ Framework as Analytical Instrument	10
6.1 The Three Moments	10
6.2 Formal Tabular Presentation of the Six Ontological Elements	11
7 Private International Law as Intermediate Language	22
7.1 The Intermediate-Language Thesis	22
7.2 Formal Characterisation of the Translation Operation	24
7.3 Limits of the Intermediate-Language Function	24
8 Comparative Legal Method	25

8.1	The Functional Approach	25
8.2	Tertium Comparationis	25
9	Cross-Cultural Ethics Analysis Method	25
9.1	The Problem of Incommensurability	25
9.2	Three-Step Analytical Procedure	26
10	Evidence Collection	26
10.1	Evidence Typology	26
10.2	Scope Limitations	28
11	State Inference Methodology	28
12	Evaluation Framework	29
12.1	Criterion 1: Efficiency (E)	29
12.2	Criterion 2: Operationality (Op)	30
12.3	Criterion 3: Controllability (C)	30
12.4	Criterion 4: Ethical Adequacy (Ea)	30
12.5	Summary: Evaluation Matrix	31
III	The Present Situation: Normative Landscape and Current Practice	32
13	International Collaborative Research Under Private International Law	32
13.1	Jurisdiction Over Disputes	32
13.2	Choice of Law for Research Contracts	33
13.3	Applicable Law for Non-Contractual Obligations	33
13.4	Recognition and Enforcement of Judgments	33
14	Domestic Law Frameworks for Clinical Research	34
14.1	Japan	34
14.2	China	34
14.3	European Union	34

14.4 United States	35
15 Multi-Regional Clinical Trial Practice	35
16 Cross-Cultural Research Ethics	35
16.1 The Principlist Framework and Its Limits	35
16.2 East Asian Relational Ethics	35
16.3 Ubuntu and African Communitarian Ethics	36
16.4 Islamic Bioethics	36
16.5 Towards Cross-Cultural Convergence	37
IV Analysis: Diagnosing the Governance Gap	37
17 Structured Gap Analysis by Ontological Category	38
18 Consolidated Gap Summary	48
V Policy Recommendations	49
19 Recommendations Addressing Efficiency Gaps	50
19.1 Tiered IRB/EC Mutual Recognition Framework [A]	50
19.2 Harmonised SAE Reporting Protocol [A/B]	50
20 Recommendations Addressing Operationality Gaps	51
20.1 Standard CTA Clauses with Mandatory-Rules Rider [B]	51
20.2 Culturally Adaptive Informed Consent Protocols [C]	51
21 Recommendations Addressing Controllability Gaps	52
21.1 Internationally Validated Federated Analysis Framework [A/B]	52
21.2 Standardised Cross-Border Audit Trail [B]	53
22 Recommendations Addressing Ethical Adequacy Gaps	53
22.1 Enforceable Post-Trial Access Obligations [A/B]	53
22.2 Community Benefit-Sharing Standards [C]	54

Conclusion	54
A Glossary of Key Terms	57
B Summary of Domestic Regulatory Frameworks	58
C Model Contract Clause: Liability and Mandatory-Rules Rider	58

Part I

Overview: Research Definition, Objectives, and Ontological Foundations

1. Purpose, Scope, and Research Objectives

1.1. Background and Motivation

International collaborative clinical research has expanded dramatically over the past two decades. Multi-site trials spanning multiple legal jurisdictions have become standard practice in pharmaceutical development, epidemiology, and translational medicine. Yet the governance infrastructure that was adequate for bilateral agreements among states sharing similar legal traditions has not kept pace with a research landscape that now routinely involves sponsors, contract research organisations, investigator sites, data custodians, and participants distributed across five or more distinct legal systems.

The inadequacy raises substantive questions of justice: under which legal order are participants' rights protected when harm occurs? Which law governs the validity of an informed-consent procedure conducted in a language that is neither the sponsor's nor the participant's mother tongue? Who owns genomic data generated by a site in one country, processed by an algorithm developed in a second, and stored on servers in a third? These questions are not answered, and in many cases not even posed, by current regulatory frameworks.

This paper addresses the governance deficit by constructing a framework that is simultaneously (i) legally rigorous, rooted in private international law methodology; (ii) ethically defensible, grounded in cross-culturally validated research ethics principles; and (iii) operationally tractable, yielding actionable recommendations rather than normative ideals.

1.2. Scope

The paper focuses on *collaborative* clinical research, defined as research in which at least two legally distinct institutions located in at least two sovereign jurisdictions jointly plan, conduct, analyse, and disseminate findings from a study involving

human participants. “Clinical research” is taken broadly to include interventional trials, observational cohort studies, biobanking projects, and genomic research, but excludes purely epidemiological surveillance conducted by public health authorities exercising sovereign powers.

Illustrative examples are drawn primarily from East Asian regulatory contexts (Japan, China) and their interactions with European and North American research systems, reflecting the author’s empirical background.

1.3. Research Objectives

1. **Descriptive objective.** To map the current normative landscape of international collaborative clinical research governance, identifying existing legal instruments, institutional practices, and ethical standards, and their limitations.
2. **Analytical objective.** To diagnose the gap between the current landscape and the normative ideals of efficiency, operationality, controllability, and ethical adequacy, using the ontological framework of §2.
3. **Prescriptive objective.** To derive targeted, jurisdiction-sensitive policy recommendations aimed at closing identified gaps, addressable to distinct stakeholder categories.

2. Ontological Analysis

2.1. Motivation for an Explicit Ontology

Governance frameworks are only as coherent as the conceptual vocabulary they employ. An explicit ontology provides the conceptual foundation on which both legal analysis and ethical argument can be built. Following the general ontology widely adopted in social-science methodology [15], we distinguish six fundamental ontological categories:

1. **Entities:** the independently existing objects of inquiry, including persons, institutions, documents, biological specimens, and datasets.
2. **Relations:** durable, structured connections between entities, including contractual bonds, regulatory mandates, and sponsorship arrangements.
3. **Attributes:** properties inhering in entities or relations, including nationality, competence, vulnerability, and scientific merit.

4. **Events:** spatiotemporally bounded occurrences such as the signing of a contract, the occurrence of an adverse reaction, and cross-border data transfer.
5. **Processes:** temporally extended sequences of causally connected events, including the informed-consent procedure and the ethical review process.
6. **States:** stable configurations that obtain over a period, such as a participant's enrolled status or a study's regulatory approval state.

2.2. The Epistemological Question

Once the ontological categories are fixed, the epistemological question concerns how we come to know instances of each category in the specific context of ICR. The relevant epistemology is not purely empirical: legal facts are institutional facts whose existence is constituted by normative recognition [15]. A participant is enrolled not merely by having ingested a study drug but by being in a state recognised as enrolled by the applicable regulatory and ethical framework.

3. Research Questions

The central research question is:

How, within a multilateral legal and cultural framework, can the six ontological elements of ICR be understood (epistemological dimension) and organised into an operationalisable, efficient, and evaluable governance framework (practical dimension)?

Subsidiary questions:

- SQ1.** What legal instruments and regulatory regimes currently govern the six ontological categories in cross-border clinical research, and where do they conflict or remain silent?
- SQ2.** How do dominant research ethics frameworks differ in their treatment of the six categories, and where are these differences governance-relevant?
- SQ3.** What is the measurable gap between current governance practice and the normative ideals of efficiency, operationality, controllability, and ethical adequacy?
- SQ4.** What targeted policy interventions would most effectively close the identified gaps?

4. The $O \rightarrow E \rightarrow P$ Movement: Methodological Preamble

A governance framework that rests on ontology alone is structurally incomplete. Knowing *what* entities, relations, events, processes, and states exist is only the first moment of analysis. The second moment asks how each element is *constituted* and *recognised* within the distinct normative orders governing international research: private international law, comparative domestic regulatory law, and cross-cultural research ethics. The third moment asks what *canonical practical activities* in clinical research realise these ontological elements under the epistemological conditions identified at the second moment. The governance gap arises precisely when the same ontological element is constituted differently across normative orders, or when the praxeological activity that realises an element in one legal or cultural context cannot be transposed into another. The full $O \rightarrow E \rightarrow P$ mapping for each of the six categories is presented formally in Part II, Tables 1–3.

Part II

Research Methods and Evaluation Framework

This part presents the methodological architecture of the paper. It serves two complementary functions. First, it specifies the analytical operations that are performed on the evidence assembled in Part III in order to produce the governance gap diagnosis of Part IV. Second, it defines the evaluative criteria against which the current landscape is measured. The methods are placed here—between the problem definition of Part I and the evidentiary record of Part III—because they constitute the interpretive framework within which evidence is both collected and assessed. A method that is declared after the evidence it governs cannot constrain the selection of that evidence.

5. Research Design and Epistemological Commitments

5.1. Overall Research Design

The paper adopts a *normative-analytical* research design that integrates three distinct methodological orientations, each governing a different part of the paper:

1. **Descriptive-documentary method** (Part [III](#)): systematic reconstruction of the current normative landscape from primary legal, regulatory, and ethical sources. The goal at this stage is comprehensiveness and fidelity: to represent what the relevant normative orders actually require, not what they ideally should require.
2. **Analytical-comparative method** (Part [IV](#)): structured comparison of the current landscape against the target normative framework defined in §[12](#) below, producing a diagnosis of governance gaps classified by ontological category and severity.
3. **Prescriptive-design method** (Part [V](#)): derivation of targeted, feasibility-constrained policy recommendations from the gap diagnosis, addressed to distinct categories of stakeholder.

5.2. Epistemological Commitments

The paper adopts two complementary epistemological orientations.

Evidentialism. All claims about the current state of governance are grounded in publicly verifiable evidence: treaty texts, domestic legislation, regulatory guidance documents, institutional practice records, and peer-reviewed empirical studies. No claim about the current landscape is advanced on the basis of assumption or anecdotal illustration alone. Part [III](#) functions as the evidentiary record; Part [IV](#) performs the inferential step. These two moments are methodologically separated to maintain the discipline of evidence-based reasoning: the gap diagnosis emerges from the evidence, not prior to it.

Methodological Traditionalism. Legal and ethical texts are interpreted within the tradition of doctrinal development from which they emerge. A treaty provision, a statutory clause, or a research ethics principle cannot be understood in isolation from the interpretive history and conceptual vocabulary of the system to which it belongs. Comparative analysis presupposes, and respects, the internal coherence of each tradition before mapping across traditions.

These two orientations are not in tension. Evidentialism provides the discipline of grounding; traditionalism provides the depth of interpretation. Together they generate claims that are empirically constrained and conceptually precise.

6. The $O \rightarrow E \rightarrow P$ Framework as Analytical Instrument

6.1. The Three Moments

The ontology–epistemology–praxeology framework introduced descriptively in §4 functions in this paper not merely as a descriptive taxonomy but as an *analytical instrument*: a procedure for identifying, locating, and diagnosing governance gaps with precision.

Moment O — Ontology. At this moment we ask: *what is this?* For each of the six categories—entity, relation, attribute, event, process, state—we establish a characterisation that is cross-jurisdictionally stable, prior to any question of how the element is constituted in a particular legal or ethical system. This is the common ground on which cross-system comparison rests. Without an agreed ontological vocabulary, comparison collapses into the confusion of comparing terms rather than things.

Moment E — Epistemology. At this moment we ask: *how is this element constituted and recognised under the dual normative framework?* The dual framework operates at this moment: private international law and domestic regulatory law constitute each element as a legal fact; cross-cultural research ethics constitutes it as an ethical fact. The same ontological element is often constituted differently across legal systems and ethical traditions. This is where governance gaps originate.

Moment P — Praxeology. At this moment we ask: *what canonical practical activities in clinical research realise this element under the epistemological conditions identified at Moment E?* Here the governance gap becomes operationally visible: a praxeological activity that satisfies the requirements of one jurisdiction may be invalid, inadequate, or technically impossible in another.

Definition 1 (Governance Gap). A *governance gap* arises when the praxeological activity required to realise an ontological element under normative order N_1 (jurisdiction A , or ethical tradition T_1) is inconsistent with the praxeological activity required under normative order N_2 (jurisdiction B , or ethical tradition T_2), and both N_1 and N_2 simultaneously apply to that element in a given international collaborative study.

Gaps are classified by the moment at which they arise: an *ontological gap* (no shared concept exists); an *epistemological gap* (contested or inconsistent constitution); or a *praxeological gap* (mutually inconsistent required activities).

6.2. Formal Tabular Presentation of the Six Ontological Elements

Tables 1–3 present the six ontological elements systematically. Table 1 provides formal definitions and paradigm instances. Table 2 maps each element through the full $O \rightarrow E \rightarrow P$ movement under the dual normative framework. Table 3 summarises the primary governance gap for each element by moment and by normative order.

Table 1: Formal Definitions and ICR Instantiations of the Six Ontological Categories. The rightmost column follows the distinction between *continuants* (entities that persist whole through time) and *occurrents* (entities that have temporal parts, i.e. unfold over time).

Category	Formal Definition	Paradigm ICR Instances	Type
Entities	An independently existing object that persists through time, can be referred to, bears attributes, and stands as the relatum of relations. Entities endure whole at each moment of their existence; they have no temporal parts.	Sponsor; principal investigator (PI); research participant; investigator site; contract research organisation (CRO); ethics committee / IRB; study dataset; biological specimen; protocol document; study registration record.	Continuant
Relations	A structured, durable connection between two or more entities that generates normative entitlements and obligations for its relata. Some relations are partially constitutive of the entities they connect (role-relations); others are purely external.	Sponsor–PI contractual relation; PI–participant fiduciary / benevolent-authority relation; sponsor–CRO delegation relation; site–IRB oversight relation; data controller–data subject relation; sponsor–regulatory authority notification relation.	Continuant

Continued on next page. . .

(Table 1 continued)

Category	Formal Definition	Paradigm ICR Instances	Type
Attributes	A property inhering in an entity or relation that determines, in conjunction with applicable norms, the obligations and entitlements attaching to its bearer. Attributes are not self-interpreting: their normative significance varies across legal systems and ethical traditions.	Participant's legal capacity; degree of vulnerability; investigational product's risk classification; study's scientific validity; site's GCP qualification status; data's sensitivity classification; sponsor's domicile; participant's habitual residence.	Continuant
Events	A spatiotemporally bounded occurrence involving one or more entities that changes the state of at least one entity or relation. Events are punctual: they occur at a time (or over a short bounded interval) and do not persist once completed.	Informed consent signing; serious adverse event (SAE) occurrence; protocol amendment execution; cross-border data transfer; regulatory approval notification; randomisation; database lock; contract execution; close-out notification.	Occurrent
Processes	A temporally extended, teleologically structured sequence of causally connected events that transforms an initial state into a target final state. Processes have normative structure: sub-events are ordered; some must precede others; the whole sequence is directed toward a goal state.	Informed consent process; ethical review process; regulatory approval process; pharmacovigilance and safety monitoring process; randomised controlled trial; prospective cohort follow-up; biobank establishment and operation; federated genomic analysis pipeline.	Occurrent

Continued on next page...

(Table 1 continued)

Category	Formal Definition	Paradigm ICR Instances	Type
States	A stable, persistent configuration of one or more entities or relations that obtains over a period and is susceptible to change through events or processes. States provide the “snapshot” perspective on the governance situation at a given moment.	Protocol approval status (<i>pending</i> / <i>approved</i> / <i>suspended</i>); participant enrolment status (<i>screened</i> / <i>consented</i> / <i>enrolled</i> / <i>withdrawn</i> / <i>completed</i>); data residency state; study active / suspended / completed; IP ownership state.	Continuant

Table 2: O→E→P Mapping of the Six Ontological Categories Under the Dual Normative Framework. Left epistemology column: PIL and domestic regulatory law. Right epistemology column: cross-cultural research ethics. Praxeological column: canonical activities realising the element in clinical research practice.

Category	PIL / Dom. Law Epistemology (E)	Cross-Cultural Ethics Epistemology (E)	Canonical Praxeological Activities (P)
Entities	Constituted through <i>legal personality</i> and connecting factors (domicile, nationality, habitual residence, <i>lex incorporationis</i>). The same natural person is simultaneously located in different legal systems for different purposes. The study-as-entity acquires public identity through registration, but no unified legal personality exists. The CRO is constituted as a delegate of the sponsor's regulatory obligations under written agreement.	<i>Principlist</i> : participant as pre-relational autonomous individual. <i>Confucian</i> : participant as node in relational network; personhood constituted through relationships, not prior to them. <i>Ubuntu</i> : personhood as inherently communal (<i>umuntu ngumuntu nga-bantu</i>). <i>Islamic bioethics</i> : body as <i>amānah</i> (divine trust), generating constraints on specimen use and genomic analysis.	Participant screening and eligibility confirmation; site qualification (entity-level GCP assessment); sponsor delegation documentation (delegation log); CRO agreement execution; study registration in a WHO-recognised primary registry.

Continued...

(Table 2 continued)

Category	PIL / Law	Domestic	Cross-Cultural Ethics	Canonical Praxeological Activities
Relations	PIL characterises relations by legal category (contract, tort, status, property) and applies the corresponding choice-of-law rule. Key problems: <i>characterisation conflict</i> (investigator–participant is contractual in common law, a status relation in civil law, a public-law relation where the site is a state hospital); <i>mandatory rules</i> overriding chosen law; <i>multi-party conflict</i> with no settled choice-of-law doctrine.		<i>Fiduciary</i> (common law bioethics): non-waivable duties of loyalty and care owed by investigator to participant. <i>Confucian benevolent authority</i> : legitimate deference to the investigator’s clinical judgment; not a manifestation of coercion but an expression of care. <i>Feminist ethics of care</i> : relational accountability as primary normative anchor, preceding rule-based constraints.	Clinical trial agreement (CTA) negotiation and execution; regulatory notification and application constituting the sponsor–authority relation; IRB/EC submission constituting the oversight relation; data processing agreement (controller–processor) execution.

Continued...

(Table 2 continued)

Category	PIL / Domestic Law	Cross-Cultural Ethics	Canonical Praxeological Activities
Attributes	<p>The <i>reference-norm problem</i>: which legal system determines whether an attribute meets a legally relevant threshold? <i>Capacity</i>: governed by habitual residence (most systems), threshold 18 or 20 years or cognitive standard. <i>Vulnerability</i>: no uniform PIL rule; ICH GCP §1.61 defines without specifying governing law. <i>Data sensitivity</i>: categorical (GDPR Art. 9: health data always sensitive) vs. enumerated (China PIPL Art. 28; Japan APPI special category).</p>	<p>CIOMS (2016) seven-dimensional vulnerability taxonomy (cognitive, juridical, deferential, medical, allocational, infrastructural, social), plus the under-recognised <i>relational vulnerability</i> dimension (familial and communal obligations constraining individual choice) prominent in Confucian and Ubuntu scholarship. <i>Scientific validity</i>: purely factual (principlist) vs. partially ethical (adequate population representation as an ethical, not merely epistemic, requirement).</p>	<p>Eligibility assessment (confirmation of inclusion/exclusion attributes; source-data documentation); IRB/EC scientific review; vulnerability assessment and enhanced-protection protocol design; data sensitivity classification and corresponding technical and legal processing controls.</p>

Continued. . .

(Table 2 continued)

Category	PIL / Law	Domestic	Cross-Cultural Ethics	Canonical	Praxeological Activities
Events	<i>Event localisation:</i> where did the event “occur” for PIL purposes? Consent: place of signature (formal) vs. habitual residence of participant (substantive validity of capacity and voluntariness). SAE: occurrence, assessment, and sponsor-reporting sites may be in three different jurisdictions, each triggering simultaneous domestic reporting obligations. Data transfer: contested legal location of data in transit and in distributed cloud storage.	<i>Principlist:</i> informed consent event as discrete moment of autonomous decision; documented by ICF signature. <i>Confucian / Ubuntu:</i> the ICF signature is the culmination of an extended relational process; its validity depends on the adequacy of the preceding process. SAE disclosure: principlist—full and immediate disclosure to participant. East Asian: <i>beneficent non-disclosure</i> in terminal illness contexts as a legitimate clinical and ethical practice.	in-	Informed consent activities (jurisdiction-specific forms and procedures); SAE detection, assessment, and multi-portal multi-language reporting; cross-border data transfer event management; protocol amendment execution and notification to each national approval system.	

Continued. . .

(Table 2 continued)

Category	PIL / Domestic Law	Cross-Cultural Ethics	Canonical Praxeological Activities
Processes	Procedural mandatory rules specify how legally significant activities must be conducted, regardless of chosen governing law. <i>Temporal asynchrony</i> : approval processes in Japan, China, EU, and US operate on different statutory timelines with no legal synchronisation mechanism. A study may exist in different regulatory states in different jurisdictions simultaneously.	<i>Principlist</i> consent process: bounded information-transfer sequence, terminated at the consent event. <i>Confucian / Ubuntu</i> : open-ended constitutive process involving the participant's relational network; not terminated by the ICF signature; revisable as relational context changes. Ethics review: Western IRB/EC as bureaucratic-procedural gate; East Asian relational model as collegial accountability dialogue between committee and institution.	Ethical review process (jurisdiction-specific procedures and composition requirements); regulatory approval process (parallel national submissions); pharmacovigilance and safety monitoring process; study-type canonical processes: RCT, prospective cohort, biobank, federated genomic analysis.

Continued. . .

(Table 2 continued)

Category	PIL / Domestic Law	Cross-Cultural Ethics	Canonical Praxeological Activities
States	<p><i>Asynchronous regulatory states</i>: same study simultaneously “approved” in one jurisdiction and “pending” in another; no automatic mutual recognition. <i>Data residency state</i>: constituted by data sovereignty law (China DSL/PIPL localisation; GDPR Chapter V transfers); contested for cloud-distributed data. <i>Participant withdrawal state</i>: retained data has heterogeneous legal state (right to erasure: GDPR Art. 17; PIPL Art. 47; Japan APPI— none straightforwardly applicable cross-border).</p>	<p><i>Principlist</i>: enrolled state creates bounded obligations defined by the consent document and applicable regulation; post-protocol moral residue is minimal. <i>Confucian / Ubuntu</i>: enrolled state creates an <i>ongoing relational bond</i>; obligations extend beyond formal study close-out; post-trial access and result disclosure are relational obligations, not merely regulatory ones.</p>	<p>State transition activities (ethics-pending → approved; screened → consented → enrolled → withdrawn); compliance monitoring (continuing review; monitoring visits; regulatory inspections); close-out and post-trial activities (results registration; data archiving; post-trial access programme).</p>

Table 3: Primary Governance Gaps Arising from Epistemological Divergence for Each Ontological Category. “Gap moment” identifies the $O \rightarrow E \rightarrow P$ moment at which the gap originates. E = epistemological; P = praxeological; $E+P$ = gap arises at both moments.

Category	Primary Gap	PIL	Primary Gap	Ethics	Gap Moment	Operative Consequence
Entities	No unified concept of the registered study as a legal person; multiplicity of connecting factors for participant rights across purposes.	legal	Incompatible ontologies of personhood (individual vs. relational vs. communal).	on-	E	Legal vacuum for study-level liability allocation; consent procedures designed for one personhood ontology are ethically invalid in another.
Relations	Characterisation conflict for the investigator-participant relation; mandatory rules not mapped against contractual choice-of-law; multi-party PIL doctrine underdeveloped.		Fiduciary benevolent-authority constitution creates different assessments of the same consent procedure.	vs. con-	E	CTA clauses may be overridden by mandatory rules the sponsor did not anticipate; consent procedures may be simultaneously legally compliant and ethically coercive (or paternalistic).

Continued...

(Table 3 continued)

Category	Primary Gap	PIL	Primary Gap	Ethics	Gap Mo- ment	Operative Consequence
Attributes	Reference-norm problem: multiple legal systems claim authority to determine legal significance of the same attribute.		Vulnerability taxonomy incomplete; relational dimension absent from CIOMS framework.	tax-	E	Risk of enrolling participants who lack legal capacity under applicable domestic law; vulnerable populations inadequately identified and protected.
Events	Localisation indeterminate for consent, SAE, and data transfer events; simultaneous multi-jurisdictional public-law reporting obligations.	in-	Temporal constitution of consent event: document-moment vs. relational-process culmination.	consti-	E + P	A single SAE may trigger five simultaneous reporting obligations in three languages through four portals; events legally valid in one system may fail ethical validity tests in another.

Continued...

(Table 3 continued)

Category	Primary Gap	PIL	Primary Gap	Ethics	Gap Mo- ment	Operative Consequence
Processes	Temporal asyn- chrony of national approval processes; no legal synchroni- sation mechanism; partial-jurisdiction commencement creates unequal risk exposure.	asyn- chrony of national approval processes; no legal synchroni- sation mechanism; partial-jurisdiction commencement creates unequal risk exposure.	Process- constituting norms (adequate de- liberation) not cross-culturally validated; pro- cess duration contested.		E + P	Trials cannot be commenced uniformly across sites; parallel partial acti- vation creates unequal risk exposure and fragmented safety monitor- ing.
States	Asynchronous regulatory states; contested data residency; het- erogeneous data- retention obli- gations (5–25 years).	Bounded (prin- cipalist) vs. re- lational (Con- fucian/Ubuntu) constitution of the enrolled and post-trial states.			E + P	Same study simultaneously lawful in one jurisdiction and in violation in another; post-trial ac- cess obligations unenforceable across systems; data governance in a persistent grey zone.

7. Private International Law as Intermediate Language

7.1. The Intermediate-Language Thesis

The methodological heart of this paper is the claim that private international law performs a distinctive *intermediate-language* function in the governance of international collaborative clinical research. The claim is both descriptive and normative: descriptively, PIL currently functions as the principal legal instrument for routing cross-border research relationships to applicable domestic systems; normatively, the paper argues that a well-functioning PIL framework should perform this function

more completely, consistently, and transparently than the current fragmented landscape allows.

The thesis can be stated with precision. Each of the six ontological categories, when it arises in a cross-border setting, must be *routed* from the universal vocabulary of the research relationship to a domestic legal system that will give it concrete normative content. This routing cannot be performed by domestic law itself: domestic law presupposes that it has already been identified as applicable. It cannot be performed by ethics: ethical principles are normatively binding but do not, of themselves, resolve conflicts between two or more domestically valid but mutually inconsistent legal rules.

PIL occupies precisely this functional position. Its connecting factors and choice-of-law rules translate each ontological element from the *source vocabulary*—in which “consent” is a cross-cultural concept and “vulnerability” is a property of a research participant—into the *target vocabulary* of the applicable domestic legal system, in which consent has a determinate formal validity test and vulnerability has a specific juridical definition.

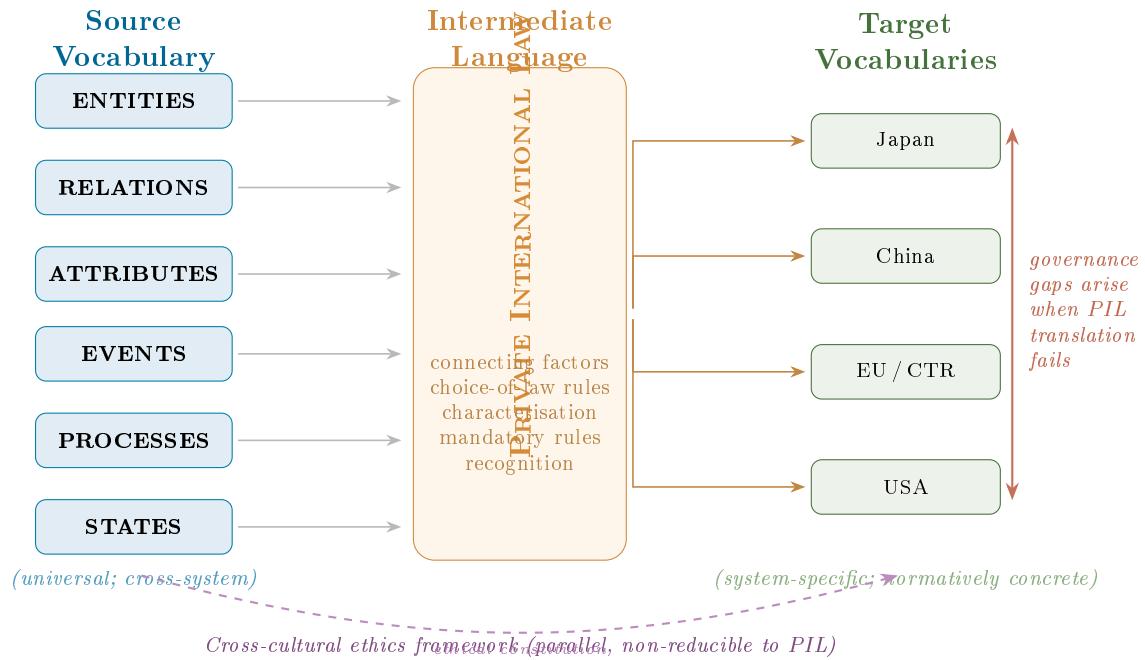


Figure 1: PIL as intermediate language in ICR governance. The six ontological categories form a universal *source vocabulary*. PIL’s connecting factors and choice-of-law rules constitute the *translation mechanism* routing each element to the applicable domestic legal system that gives it normative content. The cross-cultural ethics framework operates in parallel: it constitutes the same elements ethically, independently of the PIL translation. Governance gaps (right margin) arise when the PIL translation is absent, ambiguous, or produces conflicting translations for the same element in two jurisdictions simultaneously.

7.2. Formal Characterisation of the Translation Operation

More formally, denote the set of six ontological elements as $\mathcal{O} = \{E_1, \dots, E_6\}$ (entities, relations, attributes, events, processes, states). Denote the set of domestic legal systems relevant to a given study as $\mathcal{D} = \{D_1, \dots, D_n\}$. A PIL framework $\mathcal{F}$ is a partial function:

$$\mathcal{F} : \mathcal{O} \times \mathcal{R} \rightarrow \mathcal{D}$$

where $\mathcal{R}$ is the set of connecting factors (domicile, habitual residence, place of harm, lex incorporationis, etc.) characterising the specific research relationship. For a given element E_i and connecting factor profile $r \in \mathcal{R}$, $\mathcal{F}(E_i, r) = D_j$ designates the domestic system whose substantive rules govern E_i in that relationship.

A *gap* of the first kind (incomplete translation) arises when $\mathcal{F}(E_i, r)$ is undefined: no PIL rule resolves the question. A *gap* of the second kind (conflicting translation) arises when $\mathcal{F}$ is not a function but a relation: two domestic systems D_j and D_k both claim authority over E_i under their respective connecting-factor analyses, and their substantive rules conflict. A *gap* of the third kind (mandatory-rule override) arises when $\mathcal{F}(E_i, r) = D_j$ by choice-of-law, but D_k 's mandatory rules claim application to E_i regardless, producing a residual normative conflict that $\mathcal{F}$ cannot resolve.

The policy task of Part V is, in this framework, to extend $\mathcal{F}$ so as to eliminate or minimise gaps of all three kinds within the ICR domain.

7.3. Limits of the Intermediate-Language Function

The intermediate-language thesis has three precise limits that must be stated.

Limit 1: Ethics is not PIL. PIL translates ontological elements into domestic *legal* vocabularies. It does not translate them into ethical vocabularies. The cross-cultural ethics dimension requires a separate analytical operation not governed by PIL rules. This is why the paper maintains a dual framework: PIL and ethics are complementary but irreducible to each other. An informed consent procedure may satisfy its applicable domestic law and still fail cross-cultural ethical validity tests—or vice versa.

Limit 2: Mandatory rules as translation failures. Where mandatory rules of a domestic system override the PIL-designated applicable law, the intermediate-language function breaks down: two legal systems each claim exclusive authority to constitute the same ontological element. These mandatory-rule conflicts are the most intractable governance gaps diagnosed in Part IV.

Limit 3: PIL lexical gaps. For certain ICR elements—notably the multi-party research relation, the study-as-entity, and the federated-analysis process—there are no well-developed PIL rules. The intermediate language has lexical gaps. Part V proposes specific instruments to fill them.

8. Comparative Legal Method

8.1. The Functional Approach

The comparison of domestic legal frameworks in Part III follows the *functional method* [?]. The functional method structures comparison by the social and governance *function* that a legal institution performs, rather than by formal legal category. Applied to ICR governance, this means: rather than comparing “informed consent law” as a formal category across systems—which risks importing the assumption that different systems are attempting to achieve the same formal structure—we ask what governance problem informed consent solves (protecting participant autonomy; constituting the research relationship as voluntary; providing an audit trail of authorisation) and compare how different systems solve that problem.

8.2. Tertium Comparationis

The standard against which all systems are compared—the *tertium comparationis*—is the six-element ontological framework supplemented by the four evaluative criteria of §12. This choice is methodologically significant: it is derived from no single legal system, and therefore avoids the charge of implicit legal imperialism, while remaining concrete enough to generate determinate comparisons.

9. Cross-Cultural Ethics Analysis Method

9.1. The Problem of Incommensurability

A persistent challenge in cross-cultural bioethics is incommensurability: whether frameworks grounded in different ontologies of personhood, different accounts of moral authority, and different institutional practices can be compared at all.

This paper takes a pragmatic position calibrated to governance needs. Full metaphysical commensurability is not required. What is required for governance purposes is: (i) identification of the dimensions of divergence that are *governance-relevant*—that generate conflicting praxeological requirements; and (ii) identification of con-

vergent substantive requirements across traditions that can anchor a cross-culturally valid governance minimum.

9.2. Three-Step Analytical Procedure

For each ontological element, the cross-cultural ethics analysis in Part III proceeds in three steps:

1. *Reconstruction*: reconstruct the ethical tradition’s account of the element from authoritative sources within the tradition, in its own terms.
2. *Comparison*: identify points of convergence and divergence with other traditions and with the dominant international ethics framework (Declaration of Helsinki / CIOMS Guidelines 2016).
3. *Governance implication*: derive the specific praxeological requirement that the tradition imposes on ICR practice, and identify the resulting governance gap where this requirement conflicts with another tradition’s.

10. Evidence Collection

10.1. Evidence Typology

The evidence base of Part III is classified according to the typology in Table 4. Each evidence type is assessed against four quality criteria: *authority* (normative status of the source), *recency* (whether the source reflects current law/practice), *representativeness* (whether jurisdictions covered are adequate to the paper’s scope), and *verifiability* (whether the claim can be independently confirmed).

Table 4: Evidence Typology, Role in Analysis, and Quality Standards.

Evidence Type	Examples	Role in Analysis	Quality Standard
International instruments	Declaration of Helsinki (WMA 2013); CIOMS Guidelines (2016); ICH GCP E6(R2) and E17; Rome I/II; Brussels I Recast; Hague Judgments Convention (2019).	Establishes global governance baseline and universal minimum standards.	Official text; current revision in force.
Domestic legislation	Japan CRA (2018); China PIPL (2021), DSL (2021), Drug Administration Law (2019); EU CTR 536/2014; US Common Rule (2018).	Establishes jurisdiction-specific mandatory requirements and public-law obligations.	Authenticated, post-amendment consolidated text.
Regulatory guidance	PMDA, NMPA, EMA, FDA guidance on international and multi-regional studies.	Operationalises legislative requirements; reveals implementation gaps between statute and practice.	Dated official publication; superseded guidance noted.
Institutional practice	EFPIA/PhRMA model CTA (2018); MRCT Center operational tools; GA4GH data governance framework; European Health Data Space framework.	Documents current practice; reveals aspirational vs. operational gaps.	Source organisation and date of issue identified.

Evidence Type	Examples	Role in Analysis	Quality Standard
Doctrinal scholarship	PIL: Dicey, Morris & Collins; Calliess & Reisenhuber. Bioethics: Beauchamp & Childress; Fan Ruiping; Tangwa; Shabana.	Provides interpretive framework for contested questions; identifies doctrinal debate.	Peer-reviewed; established authority in field.
Empirical case material	Japan–China NCNP collaborative neurological research (EEG-based seizure prediction study).	Provides operational grounding; reveals governance gaps invisible from documentary analysis alone.	Treated as paradigm case; not as probative evidence for general claims.

10.2. Scope Limitations

The evidence base has two acknowledged limitations. First, geographic coverage is weighted toward East Asian (Japan, China) and European / North American jurisdictions. Sub-Saharan African, South Asian, and Latin American regulatory frameworks are engaged for ethical analysis but not subject to equivalent depth of legal analysis. Second, prescriptive claims are calibrated to the governance landscape as of the date of writing; particularly rapid regulatory developments in China’s data-governance framework and the EU Health Data Space may require updating.

11. State Inference Methodology

The transition from the evidentiary record of Part III to the gap diagnosis of Part IV requires a formal inference procedure. The paper adopts a *normative state inference* method comprising four steps.

1. **Current-state description.** For each ontological element, the evidence base is used to characterise the current normative state: which rules, practices, and institutions currently govern this element, under which normative order, with what degree of completeness and consistency.

2. **Target-state specification.** For each element, the four evaluative criteria of §12 specify what an adequate governance framework would look like. The target state is the state the element would be in if governed by a framework satisfying all four criteria.
3. **Gap identification and classification.** The gap is the difference between the current state and the target state, characterised with maximal specificity. Gaps are classified by the $O \rightarrow E \rightarrow P$ moment at which they arise (ontological, epistemological, or praxeological) and by the formal gap type of §7 (incomplete translation, conflicting translation, or mandatory-rule override).
4. **Gap severity assessment.** Each gap is assessed against the four criteria. A gap is “critical” when it is: *systemic*—not addressable through individual party workarounds within the current normative framework; and *cross-jurisdictional*—not addressable through unilateral domestic regulatory reform. Only critical gaps generate Part V recommendations.

12. Evaluation Framework

The four evaluative criteria that define the target normative state for ICR governance are now formally specified. Each criterion is stated as a definition, operationalised through indicators, and assigned a benchmark where one exists.

12.1. Criterion 1: Efficiency (*E*)

Definition. An ICR governance framework satisfies *Efficiency* to the extent that it minimises the administrative, temporal, and resource costs of cross-border compliance, without compromising the substantive participant protections that justify those costs.

Indicators. (i) Time elapsed from protocol finalisation to first participant enrolment across all participating jurisdictions. (ii) Number of distinct regulatory and ethics submissions required for a single protocol. (iii) Degree of substantive information duplication across parallel submissions. (iv) Existence of mutual recognition mechanisms reducing redundant review.

Benchmark. The EU CTR’s centralised single-application authorisation across member states provides the current best-available efficiency benchmark. The paper uses it as an aspirational reference, not a template.

12.2. Criterion 2: Operationality (*Op*)

Definition. An ICR governance framework satisfies *Operationality* to the extent that its requirements can be implemented by research institutions with reasonable resources, without requiring specialist legal expertise that is unreasonably scarce or costly in the participating jurisdictions.

Indicators. (i) Availability of standardised forms, model contract clauses, and operational guidance for cross-border research activities. (ii) Clarity of applicable law for each governance activity in a multi-site international study. (iii) Accessibility of dispute resolution mechanisms to research participants and non-sponsor institutions. (iv) Existence of validated operational guidance for cross-cultural informed consent procedures.

12.3. Criterion 3: Controllability (*C*)

Definition. An ICR governance framework satisfies *Controllability* to the extent that: (i) the governance state of a study can be determined with reasonable certainty at any given moment; and (ii) deviations from required governance states can be detected and corrected through systematic, cross-border oversight mechanisms.

Indicators. (i) Existence and completeness of audit trails for cross-border activities (data transfers, protocol amendments, SAE reporting). (ii) Existence of unified safety monitoring signals aggregating data from all sites regardless of jurisdiction. (iii) Determinacy of the regulatory state of a study across all participating jurisdictions simultaneously. (iv) Existence of a designated governance authority with explicit cross-border oversight mandate.

12.4. Criterion 4: Ethical Adequacy (*Ea*)

Definition. An ICR governance framework satisfies *Ethical Adequacy* to the extent that it: (i) meets the requirements of the cross-culturally validated minimum ethical standard established in §9; and (ii) establishes transparent procedures for managing legitimate cross-cultural divergence without reducing all governance to any single tradition's requirements.

Indicators. (i) Informed consent procedures validated as ethically adequate in each participating cultural and legal context. (ii) Post-trial access obligations specified, included in research agreements, and practically enforceable. (iii) Benefit-sharing obligations addressed in standard research contracts. (iv) Vulnerability assessment procedures inclusive of the relational vulnerability dimension.

12.5. Summary: Evaluation Matrix

Table 5 maps each evaluative criterion to its primary ontological targets, its primary gap types under the dual framework, and the class of policy instrument best positioned to address identified gaps.

Table 5: Evaluation Criteria: Ontological Targets, Gap Types, and Best-Fit Policy Instruments.

Criterion	Primary Ontological Targets	Primary PIL Type	Primary Gap Ethics Gap Type	Best-Fit Instrument	Policy
<i>Efficiency</i> (<i>E</i>)	Processes; Events	Procedural asynchrony; duplica- tive review obligations; incompatible timelines.	Divergent deliberation norms inflat- ing process duration.	Multilateral IRB/EC tual recognition; harmonised regu- latory timelines; single-portal multi- jurisdiction submis- sion.	mu-
<i>Operationality</i> (<i>Op</i>)	Relations; Attributes	Absence of standard- ised model contracts; unclear appli- cable law for cross-border activities.	Inadequate cross-cultural consent guid- ance; no validated multi-cultural vulnerability assessment tool.	Model clinical trial agreement clauses with jurisdiction an- notations; ICH GCP E6(R3) amendment on consent process.	
<i>Controllability</i> (<i>C</i>)	States; Events	Asynchronous regulatory states; in- complete or fragmented audit trails for cross-border activities.	Contested state- transition norms (en- rolled vs. withdrawn; post-trial state).	Unified safety mon- itoring protocol for multi-regional trials (supplement to ICH E17); standardised audit trail require- ments.	

Criterion	Primary Targets	PIL Gap	Ethics Gap	Policy Instrument
<i>Ethical Adequacy (Ea)</i>	Entities; Attributes; States	Post-trial access obligations un-enforceable across systems; benefit-sharing not addressed in standard instruments.	Personhood ontology mismatch; relational vulnerability dimension excluded from operative frameworks.	Declaration of Helsinki implementing guidance; CIOMS Guideline expanded commentary; post-trial access clause.

Part III

The Present Situation: Normative Landscape and Current Practice

The six ontological categories introduced in Part I are simultaneously governed by three normative orders: private international law and domestic regulatory law, and cross-cultural research ethics. Each order applies different instruments, reaches different ontological targets with different degrees of coverage, and operates according to different institutional logics. Part III constitutes the primary evidentiary base for the gap analysis of Part IV. The evidence typology and quality criteria governing source selection are set out in §10.

13. International Collaborative Research Under Private International Law

13.1. Jurisdiction Over Disputes

Private International Law provides the meta-legal rules by which national courts and authorities determine which legal system's substantive rules govern a dispute or transaction with cross-border elements. When a participant suffers harm in a multi-site international trial, the question of jurisdiction is governed by domestic

rules that vary substantially across systems.

Within the European Union, Regulation (EU) No 1215/2012 (*Brussels I Recast*) provides a coherent framework: in matters of tort, jurisdiction lies with the court of the place where the harmful event occurred (Art. 7(2)). Outside the EU, the position is more fragmented. Japan’s civil jurisdiction rules under the *Minji Soshō Hō* do not provide clear guidance for pharmaceutical liability in cross-border settings. China’s *Civil Procedure Law* (2021 revision) adopts a territorialist approach but is silent on multi-site coordination.

No multilateral convention allocates jurisdiction over clinical-trial disputes. The result is a system in which forum shopping is both possible and strategically rational for well-resourced sponsors, while research participants face systemic barriers to effective remedies.

13.2. Choice of Law for Research Contracts

Freedom of parties to choose the governing law is widely recognised, most explicitly in the EU’s Rome I Regulation (EC) No 593/2008 (Art. 3) [5]. In practice, sponsors typically designate the law of their home jurisdiction, creating an asymmetry: principal investigators and institutions in less legally powerful positions are bound by foreign law they may not know and whose courts they cannot practically access.

Even where choice-of-law clauses are valid, mandatory rules of the participant’s state of habitual residence may override the chosen law. The scope of these mandatory rules in the clinical-research context remains under-theorised in both academic literature and regulatory guidance.

13.3. Applicable Law for Non-Contractual Obligations

Research-related torts are governed by non-contractual conflict-of-laws rules. Within the EU, Rome II (Regulation (EC) No 864/2007) applies the law of the country where the damage occurs as the default rule (Art. 4(1)) [6]. Outside the EU, analogous domestic rules range from strict place-of-injury rules (China, Japan) to more flexible most-significant-relationship tests in common law jurisdictions.

13.4. Recognition and Enforcement of Judgments

No general multilateral convention on recognition and enforcement is in force between major ICR jurisdictions. The 2019 Hague Judgments Convention provides some framework, but its ratification base remains limited [8]. Arbitration, governed

by the New York Convention (1958), offers more reliable enforcement but is costly and inaccessible to individual research participants [9].

14. Domestic Law Frameworks for Clinical Research

14.1. Japan

Japan regulates clinical research through two primary statutes: the *Pharmaceutical and Medical Devices Act* (PMD Act) and the *Clinical Research Act* (2018) [17]. The latter, enacted in response to the Diovon clinical data manipulation scandal, imposes mandatory registration, protocol disclosure, and monitoring requirements on specified clinical research. International collaborative studies involving Japanese sites must comply with these requirements regardless of the law chosen to govern the research contract.

Japan has implemented ICH GCP E6(R2) [3], but domestic requirements in certain areas exceed the ICH standard, notably regarding IRB composition, the recording of informed-consent explanation sessions, and re-consent procedures for protocol amendments.

14.2. China

China's *Drug Administration Law* (2019 revision) [18] and its implementing regulations establish the regulatory framework for clinical research. Recent reforms have aligned China's requirements more closely with ICH GCP, facilitating multi-regional trials. However, data localisation requirements under the *Personal Information Protection Law* (PIPL, 2021) [19] and the *Data Security Law* (2021) have introduced new complexity for cross-border data flows from Chinese sites, requiring government-approved standard contracts or security assessments for outbound transfers of important data.

14.3. European Union

The EU Clinical Trials Regulation (EU) No 536/2014 (CTR), fully applicable since January 2023 [20], introduced a centralised authorisation procedure through the Clinical Trials Information System (CTIS), enabling single-application approval across all participating member states. The CTR represents the most advanced multilateral harmonisation of clinical-trial governance currently in force.

14.4. United States

The U.S. framework rests on the *Common Rule* (45 CFR Part 46, 2018 revision) [21] and FDA regulations (21 CFR Parts 50 and 56). The extraterritorial reach of FDA requirements, which apply to all trials intended to support FDA marketing applications regardless of where they are conducted, makes the U.S. framework a de facto global standard in pharmaceutical research.

15. Multi-Regional Clinical Trial Practice

ICH guideline E17 (2017) [4] provides principles for the design and conduct of multi-regional clinical trials (MRCT). E17 focuses on statistical and pharmacological considerations and does not address the legal and governance issues with which this paper is concerned. The MRCT Center at Harvard and the Global Alliance for Genomics and Health (GA4GH) have produced operational tools for cross-site governance [16], but these are voluntary and lack legal force.

16. Cross-Cultural Research Ethics

16.1. The Principlist Framework and Its Limits

The four-principle framework of Beauchamp and Childress, comprising autonomy, beneficence, non-maleficence, and justice, remains dominant in Anglo-American bioethics and has been incorporated into the Declaration of Helsinki and the CIOMS Guidelines (2016 revision) [11, 1, 2]. The framework's universalist aspirations sit in tension with documented cross-cultural variation in the moral weight assigned to individual autonomy relative to family or community decision-making authority.

16.2. East Asian Relational Ethics

A substantial literature in East Asian bioethics argues that the principlist framework inadequately reflects Confucian conceptions of personhood, in which the individual is constituted through relations rather than prior to them [12]. In this tradition, informed consent is not merely an individual transaction but a relational event involving the participant's family network. Japan's research ethics system reflects this tension: while formally adopting individual informed consent, the clinical practice of *nemawashi* (prior consensus-building among relevant parties before formal decision) persists and interacts with consent procedures in ways that ICH GCP does not address.

Self-determination and family-determination represent, in Fan’s analysis, two incommensurable but both legitimate principles of autonomy [12]. Their coexistence in cross-cultural research settings cannot be resolved by stipulating that one principle overrides the other. Governance frameworks must instead accommodate legitimate procedural pluralism within a minimum shared ethical floor.

16.3. Ubuntu and African Communitarian Ethics

Ubuntu ethics, expressed in the Nguni axiom *umuntu ngumuntu ngabantu* (a person is a person through other persons), holds that individual identity and moral standing are constituted through communal relationships rather than prior to them [13]. Applied to clinical research, this ontology generates several governance-relevant positions.

First, community-level authorisation is not a procedural supplement to individual consent but a constitutive precondition: the individual participant’s consent derives part of its moral validity from the community’s endorsement of the research relationship. Governance frameworks that treat community engagement as optional good practice are therefore ethically inadequate from an Ubuntu perspective.

Second, the enrolled state creates obligations not only to the individual participant but to the community whose collective health and, in the case of genomic research, whose genetic heritage is implicated by the study. Post-trial obligations including results disclosure and benefit sharing cannot be discharged through individual compensation alone [13, 2]. The CIOMS Guidelines (2016), Guidelines 7 and 8, partially reflect this position in their requirements for post-trial access and community-level benefit-sharing, but the mechanisms for enforcement across jurisdictions remain underdeveloped.

Third, the governance implication at the praxeological level is that research ethics committees in settings where Ubuntu norms are operative must include community representatives with genuine decision-making authority, not merely advisory standing, and that community engagement processes must precede, rather than accompany, individual recruitment.

16.4. Islamic Bioethics

Islamic bioethical reasoning operates within a framework defined by the primary sources (*Qur’an* and *Sunnah*), the classical juridical tradition (*fiqh*), and the principle of *maslaha* (public interest or welfare), which permits departure from strict literal rules where significant human benefit can be achieved and harm avoided [14].

Three principles are directly relevant to clinical research governance.

First, the body as *amānah* (divine trust). The human body is understood in Islamic jurisprudence as a trust given by God and not owned by the individual as a matter of autonomous will. This has the consequence that individuals cannot consent to procedures involving irreversible bodily alteration, or to the permanent alienation of biological specimens including genetic material, simply on the basis of autonomous choice. Consent in clinical research must therefore be grounded in a demonstration of expected benefit and must be accompanied by safeguards against commercialisation or misuse of biological samples [14].

Second, the communal dimension of consent. While Islamic jurisprudence recognises individual legal capacity (*ahliyyah*), decisions bearing on bodily integrity are appropriately made within a framework of family consultation, particularly for decisions with long-term or irreversible consequences. This does not amount to a family veto right, but it does imply that consent procedures designed exclusively around individual autonomous decision-making may be culturally and ethically inadequate in Islamic-majority research contexts.

Third, the principle of *la darar wa la dirar* (no harm shall be inflicted or reciprocated) generates a precautionary requirement in research involving uncertain risk that goes beyond the standard risk-benefit calculus of principlist ethics. First-in-human studies and research involving vulnerable populations are subject to heightened scrutiny under this principle.

The governance implication is that ethics committees in settings where Islamic bioethical reasoning is operative must include members with competence in *fiqh*-based analysis, and that research contracts should contain explicit provisions governing the handling, storage, and permitted uses of biological specimens collected from Muslim participants.

16.5. Towards Cross-Cultural Convergence

Despite their differences, the major ethical traditions converge on a set of substantive requirements: scientific validity as a condition of ethical permissibility; special protection for vulnerable populations; obligations of post-trial access; and the need for independent oversight [2]. A governance framework operationalising these convergent requirements, while establishing transparent procedures for managing legitimate divergence, can claim cross-cultural validity without requiring cultural homogenisation.

Part IV

Analysis: Diagnosing the Governance Gap

Part III constitutes the evidentiary record. This part applies the four-step state inference methodology of §11: for each of the six ontological categories, the current normative state is described, the target state is specified by the evaluative criteria of §12, the gap is identified by $O \rightarrow E \rightarrow P$ moment, and severity is assessed. A gap is **Critical** when it is both systemic (not addressable through individual party workarounds) and cross-jurisdictional (not addressable through unilateral domestic regulatory reform). It is **Significant** when it is structurally entrenched but addressable, at least in part, through domestic action.

17. Structured Gap Analysis by Ontological Category

Tables 6–11 present the gap analysis for each of the six ontological categories. For each category, the table records: the current normative state under the dual framework; the target state as defined by the evaluative criteria; the $O \rightarrow E \rightarrow P$ moment at which the gap arises; and the gap’s severity and primary evaluative criterion.

Table 6: Gap Analysis: Entities. E = epistemological moment; P = praxeological moment.

Dimension	Current State	Target State
PIL / Domestic	No unified legal concept of the registered study as a legal person. The same natural person is simultaneously subject to different legal systems for different purposes: capacity by habitual residence; data-protection rights by the controller's establishment; tort liability by place of harm. No PIL rule resolves multi-party attribution of research obligations in studies involving sponsor, CRO, and multiple sites.	A designated legal vehicle for the study-level entity enabling unified liability attribution. Harmonised connecting-factor rules for participant rights across jurisdictions.
Cross-Cultural Ethics	Consent procedures and participant information sheets designed for an individual autonomous subject. No formal mechanism for adapting entity-level governance to Ubuntu communal personhood, Islamic <i>amānah</i> -based bodily integrity norms, or Confucian relational personhood.	Consent procedures validated for the operative personhood ontology in each participating jurisdiction.
Gap Moment	Epistemological (E): the same entity is constituted as a different legal and moral subject depending on the normative order applied.	
Severity / Criterion	Critical: systemic and cross-jurisdictional. Criteria violated: Operationality, Ethical Adequacy.	

Table 7: Gap Analysis: Relations.

Dimension	Current State	Target State
PIL / Domestic	Characterisation conflict for the investigator-participant relation: contractual in common law, a status relation in civil law, a public-law relation where the site is a state hospital. Mandatory rules protecting participants are not systematically mapped against contractual choice-of-law clauses in model clinical trial agreements. Multi-party PIL doctrine for three-or-more-party research relations is underdeveloped in all major jurisdictions.	Harmonised characterisation rule for the investigator-participant relation. Standardised mandatory-rules rider appended to all cross-border clinical trial agreements.
Cross-Cultural Ethics	Fiduciary framing (common law) versus benevolent-authority framing (Confucian) of the investigator-participant relation generates opposite assessments of the same consent procedure: what is ethically appropriate relational deference in one tradition is ethically problematic paternalism in another.	Governance instruments acknowledging legitimate procedural pluralism in the constitution of the research relation.
Gap Moment	Epistemological (E): the same relation is differently characterised across legal systems and ethical traditions.	
Severity / Criterion	Critical: systemic. Criteria: Operationality, Ethical Adequacy.	

Table 8: Gap Analysis: Attributes.

Dimension	Current State	Target State
PIL / Domestic	The reference-norm problem: multiple legal systems claim authority to determine the legal significance of the same attribute. Capacity thresholds range from 18 years (most jurisdictions) to 20 years (Japan prior to the 2022 Civil Code amendment) to cognitive-standard tests (UK Mental Capacity Act 2005). Data sensitivity classification differs structurally: health data is categorically sensitive under GDPR Art. 9; Japan APPI uses a narrower enumerated special category; China PIPL Art. 28 covers health, biometric, and genetic data under a single “sensitive personal information” category.	A harmonised connecting-factor rule designating one system’s attribute definitions as operative for each purpose.
Cross-Cultural Ethics	The CIOMS (2016) seven-dimensional vulnerability taxonomy does not include the relational vulnerability dimension prominent in Confucian and Ubuntu scholarship: the constraint that familial and communal obligations place on individual choice is not formally recognised as a vulnerability that triggers heightened protection.	A vulnerability taxonomy extended to include the relational dimension, with praxeological guidance on assessment procedures for each recognised dimension.
Gap Moment	Epistemological (E): attribute significance varies across normative orders; no meta-rule resolves conflicts.	

Dimension	Current State	Target State
Severity / Criterion	Critical: systemic. Criteria: Operationality, Ethical Adequacy.	

Table 9: Gap Analysis: Events.

Dimension	Current State	Target State
PIL / Domestic	Event localisation is indeterminate for the three most governance-critical events: the consent event (place of signature versus habitual residence of participant); the SAE event (site of occurrence, site of assessment, and sponsor domicile may all be in different jurisdictions, each triggering simultaneous public-law reporting obligations with divergent timelines and portal requirements); and the data transfer event (contested legal location of data in transit and in distributed cloud storage).	Clear localisation rules for each governance-critical event type. A single consolidated SAE reporting pathway satisfying all simultaneous national obligations.

Dimension	Current State	Target State
Cross-Cultural Ethics	The informed consent event is constituted as a discrete moment of autonomous decision in the principlist framework, but as the culmination of an extended relational process in Confucian and Ubuntu traditions, where the ICF signature is legally required but ethically insufficient evidence of genuine consent. The SAE disclosure event is subject to a “beneficent non-disclosure” norm in some East Asian clinical traditions that conflicts directly with the full-disclosure requirements of ICH GCP and GDPR data-subject notification obligations.	Process-validated consent procedures whose documentation captures relational deliberation, not merely the consent event.
Gap Moment	Epistemological and Praxeological (E+P): localisation rules are absent; constitutive norms conflict.	
Severity / Criterion	Critical: systemic and cross-jurisdictional. Criteria: Efficiency, Controllability, Ethical Adequacy.	

Table 10: Gap Analysis: Processes.

Dimension	Current State	Target State
PIL / Domestic	Procedural asynchrony is the dominant governance failure at the process level. The four major regulatory approval timelines (Japan 30-day notification; China NMPA up to 60 business days full review; EU CTR maximum 60-day coordinated review; US FDA 30-day IND clock) operate independently with no legal synchronisation mechanism. A study may therefore exist in different regulatory states in different jurisdictions simultaneously, creating unequal risk exposure across sites. The procedural renvoi problem is unaddressed: where a consent process is completed in jurisdiction A but its validity is challenged in jurisdiction B, no settled PIL rule determines which system's procedural requirements govern.	Harmonised or synchronised approval timelines. A lead-jurisdiction procedure designation rule for cross-border process validity questions.

Dimension	Current State	Target State
Cross-Cultural Ethics	The principlist informed-consent process is constituted as a bounded information-transfer sequence terminated at the consent event. Confucian and Ubuntu traditions constitute the consent process as an open-ended relational event not terminated by the ICF signature, revisable as the participant's relational context changes. The Western IRB/EC model constitutes ethical review as an adversarial gate. The East Asian collegial model constitutes it as an ongoing accountability dialogue with the research institution. These divergent process constitutions generate directly conflicting praxeological requirements.	Governance instruments accommodating legitimate process-constituting pluralism within a shared floor of minimum procedural protections.
Gap Moment	Epistemological and Praxeological (E+P): process timing rules conflict; process validity norms conflict.	
Severity / Criterion	Critical: systemic. Primary criterion: Efficiency. Secondary: Controllability, Ethical Adequacy.	

Dimension	Current State	Target State
-----------	---------------	--------------

Table 11: Gap Analysis: States.

Dimension	Current State	Target State
PIL / Domestic	<p>Three unresolved state-level conflicts. (i) Asynchronous regulatory states: the same study may be “approved” under EU CTR, “pending” under Japan CRA, and “conditionally approved” under China NMPA simultaneously, with no PIL rule designating an authoritative state. (ii) Data residency irreconcilability: China DSL Art. 31 and PIPL Art. 38 require certain data to reside in China, while GDPR Chapter V requires a legal basis for any “third-country transfer”; for cloud-distributed federated datasets these obligations may be logically irreconcilable. (iii) Post-withdrawal data state: the legal state of retained data after participant withdrawal diverges across GDPR Art. 17 (presumptive erasure), PIPL Art. 47 (deletion unless exception), and Japan APPI (narrower deletion right); no PIL rule designates the applicable system for cross-border datasets. Data retention periods diverge further: EU CTR mandates 25 years for trial master files; Japan mandates 15 years; the US requires 2 years post-marketing application.</p>	<p>A mutual recognition framework for regulatory states. An internationally validated federated analysis standard satisfying concurrent data-residency obligations. A harmonised post-withdrawal data governance protocol.</p>

Dimension	Current State	Target State
Cross-Cultural Ethics	The principlist tradition constitutes the enrolled state as creating a bounded, document-delimited set of obligations; the “study completed” state closes the moral relationship except for obligations explicitly specified in advance. The Confucian and Ubuntu traditions constitute the enrolled state as creating an ongoing relational bond: obligations of continuing care, result disclosure, and access to beneficial treatments extend beyond formal study close-out and cannot be reduced to advance contractual specification. These divergent ethical constitutions of the enrolled and post-trial states generate directly different praxeological requirements for close-out activities and post-trial access planning that current governance instruments do not reconcile.	Governance instruments specifying post-trial obligations that satisfy both the contractual-delimitation model and the relational-bond model, through minimum mandatory post-trial access and benefit-sharing requirements.
Gap Moment	Epistemological and Praxeological (E+P): states constituted differently across legal systems and ethical traditions; no reconciliation mechanism.	
Severity / Criterion	Critical: systemic and cross-jurisdictional. Primary criterion: Controllability. Secondary: Ethical Adequacy.	

18. Consolidated Gap Summary

Table 12 consolidates the six category-level diagnoses, mapping each critical gap to the evaluative criterion it primarily violates and the policy intervention best

positioned to address it.

Table 12: Consolidated Gap Summary by Criterion. E = Efficiency; Op = Operationality; C = Controllability; Ea = Ethical Adequacy.

Gap Area	Criterion	Severity	Policy Intervention
Jurisdiction fragmentation	C, Ea	Critical	Multilateral jurisdiction convention; model choice-of-court clause
Choice-of-law asymmetry	Op	Critical	Standardised CTA mandatory-rules rider
Consent event vs. process	Ea	Critical	ICH GCP E6(R3) amendment; cultural competency guidance
SAE reporting asynchrony	C, E	Critical	Harmonised multi-portal reporting standard (new ICH guideline)
IRB/EC parallel redundancy	E	Critical	Tiered mutual recognition framework
Data sovereignty conflict	C, Op	Critical	Validated federated analysis framework; model data transfer agreement
Regulatory state asynchrony	C	Critical	Harmonised activation timelines; lead-jurisdiction designation
Post-trial access unenforceability	Ea	Significant	Declaration of Helsinki implementing guidance; model CTA clause
Benefit-sharing lacuna	Ea	Significant	CIOMS expanded guideline; model benefit-sharing clause

Part V

Policy Recommendations

The nine recommendations below correspond directly to the critical and significant gaps identified in Part IV. Each recommendation specifies the addressees, the recommended instrument, the structural content, the expected outcome, and a feasibility assessment. Recommendations are classified by bindingness: (A) binding multilateral instrument; (B) voluntary model contract or operational tool; (C) guidance document amendment. Recommendations classified (B) or (C) can be implemented without treaty amendment and are therefore available in the near term; recommen-

dations classified (A) represent the long-term architecture.

19. Recommendations Addressing Efficiency Gaps

19.1. Tiered IRB/EC Mutual Recognition Framework [A]

Addressees: WHO, ICH, national regulatory authorities.

Instrument: Binding multilateral agreement modelled on the EU CTR’s centralised review mechanism, adapted for non-EU contexts through WHO coordination.

Structure: (i) A lead review country designated by prior agreement of all participating sites, selected on the basis of the largest participant population or the jurisdiction with the most stringent applicable ethical standard. (ii) Abbreviated national review by all other participating jurisdictions, limited to country-specific concerns: local consent language adequacy, site qualification, and national mandatory rules not addressed by the lead review. (iii) Automatic recognition of the lead review’s scientific assessment and overall ethical determination.

Expected outcome: Reduction in duplicative review time of 40–60% for multi-regional studies, while preserving each jurisdiction’s authority over matters specific to its participant population.

Feasibility: Medium. Analogous to the EU CTR within the EU; requires political will at WHO/ICH level and willingness of national regulators to accept qualified deference. The EU CTR experience provides a template for progressive implementation.

19.2. Harmonised SAE Reporting Protocol [A/B]

Addressees: ICH.

Instrument: New ICH guideline supplementing E17 and E6(R2), addressing safety monitoring in multi-regional trials.

Structure: (i) A single Data Safety Monitoring Board with cross-site mandate and access to aggregate safety data from all sites regardless of jurisdiction. (ii) One consolidated DSMB report, formatted to satisfy the reporting requirements of all participating national authorities through jurisdiction-specific annexes. (iii) Harmonised expedited reporting clocks: a single 7-day clock for fatal and life-threatening unexpected SAEs and a single 15-day clock for all others, satisfying the most stringent applicable domestic requirement.

Expected outcome: Elimination of the current situation in which a single SAE in a Japan-China-EU multi-site study triggers five simultaneous reporting obligations in three languages through four electronic systems with partially incompatible timelines.

Feasibility: Medium-high. Builds directly on the existing E17 framework; the technical content is largely available from current DSMB practice; political obstacles are lower than for jurisdiction-level mutual recognition.

20. Recommendations Addressing Operationality Gaps

20.1. Standard CTA Clauses with Mandatory-Rules Rider [B]

Addressees: Research institutions; professional associations including SCRA and APEC Life Sciences Forum.

Instrument: Voluntary model contract with jurisdiction-specific annotations, distributed as an open standard.

Structure: Model clauses covering six subject areas: (i) liability allocation between sponsor, CRO, and sites with caps calibrated to institutional resources; (ii) intellectual property ownership for jointly generated inventions and data, with default vesting rules; (iii) indemnification with mandatory minimum coverage for participant harm, defined by reference to local GDP per capita where relevant; (iv) data ownership and permitted uses, including secondary research and commercial applications; (v) post-trial access obligations, including a mandatory minimum period of access to a beneficial intervention at cost price; (vi) a mandatory-rules rider identifying, for each of Japan, China, the EU, and the US, the domestic rules that apply to the research relationship regardless of the chosen governing law.

Expected outcome: Reduction in negotiation time for cross-border CTAs; improved protection for non-sponsor parties; greater transparency for participants regarding applicable law.

Feasibility: High. Voluntary; builds on the existing EFPIA/PhRMA model CTA; can be implemented by professional associations without legislative action.

20.2. Culturally Adaptive Informed Consent Protocols [C]

Addressees: ICH, WHO.

Instrument: Amendment to ICH GCP E6, to be incorporated in the next revision cycle (E6(R3)).

Structure: (i) A requirement that sponsors conducting multi-site international studies conduct a pre-study cultural competency assessment for the consent process in each participating country, with documented output identifying any country-specific adaptations required. (ii) A documentation requirement for the deliberation process, not merely the consent event: sponsors must retain records demonstrating that the participant had adequate opportunity for relational deliberation consistent with the operative ethical tradition, in addition to the executed ICF. (iii) A permission for family-inclusive consent procedures as a supplement to individual consent where culturally appropriate and validated by the local ethics committee, provided that the individual participant retains an unencumbered right to decline participation regardless of family or community position.

Expected outcome: Consent procedures that are both legally valid and ethically adequate across all participating cultural contexts; reduction in post-hoc consent validity challenges.

Feasibility: High. Consistent with the current E6(R3) revision trajectory; the guidance component can be issued independently of a formal regulatory amendment.

21. Recommendations Addressing Controllability Gaps

21.1. Internationally Validated Federated Analysis Framework [A/B]

Addressees: National data protection authorities; OECD; GA4GH.

Instrument: Internationally validated technical and legal standard for federated clinical research data analysis, with mutual recognition of certification between national data protection authorities.

Structure: (i) A technical standard, developed through GA4GH's existing framework, specifying the minimum requirements for a federated analysis protocol to be certified as satisfying data localisation requirements under PIPL, GDPR, and analogous domestic regimes. (ii) A mutual recognition procedure whereby a national data protection authority's certification of a federated analysis protocol is accepted by other participating authorities, eliminating the need for separate national approval of each protocol. (iii) A model data transfer agreement for certified federated protocols, providing the contractual basis for cross-border collaboration under the certified technical standard.

Expected outcome: Legal certainty for cross-border genomic and clinical research data analysis; elimination of the current grey zone in which federated protocols operate without formal regulatory validation.

Feasibility: Medium. The technical component is mature; legal recognition by national authorities is the critical gap requiring dedicated negotiation.

21.2. Standardised Cross-Border Audit Trail [B]

Addressees: ISO; national data protection authorities; ICH.

Instrument: Technical standard for research data transfer logging, with regulatory recognition in participating jurisdictions.

Structure: A minimum logging specification for all cross-border data transfers, protocol amendments, and SAE reports in international clinical studies, designed to satisfy the audit requirements of PMDA, NMPA, EMA, and FDA simultaneously.

Expected outcome: Determinable governance state at any given moment; reduced regulatory inspection burden through pre-verified audit trails.

Feasibility: High. Primarily a technical standardisation exercise; can be initiated through ICH without treaty-level negotiation.

22. Recommendations Addressing Ethical Adequacy Gaps

22.1. Enforceable Post-Trial Access Obligations [A/B]

Addressees: WHO; research sponsor associations; national regulatory authorities.

Instrument: Declaration of Helsinki implementing guidance; model CTA clause.

Structure: (i) Declaration of Helsinki paragraph 34 should be given operational content through WHO-issued implementing guidance specifying: the minimum duration of post-trial access (not less than the period for which the benefit persists); the maximum price at which the intervention may be provided; and the mechanism for identifying participants requiring ongoing access at close-out. (ii) A model CTA clause incorporating these obligations as a contractual commitment of the sponsor, enforceable by the investigator site and, through a third-party beneficiary mechanism, by participants. (iii) A ring-fenced funding mechanism, specified in the protocol, ensuring that post-trial access obligations survive sponsor insolvency.

Expected outcome: Post-trial access obligations that are specific, contractually enforceable, and financially secured, rather than aspirational statements without legal effect.

Feasibility: Medium. Implementing guidance is within WHO's mandate and requires no treaty amendment; ring-fenced funding requires domestic legislative action in sponsor-country jurisdictions to be fully effective.

22.2. Community Benefit-Sharing Standards [C]

Addressees: CIOMS; national ethics committees.

Instrument: Expanded guidance under CIOMS Guideline 2 (Research in Low-Resource Settings) and Guideline 7 (Community Engagement).

Structure: (i) A requirement that sponsors conducting research in settings where participants' communities bear a disproportionate burden of the disease under study develop, in consultation with community representatives with genuine decision-making authority, a benefit-sharing plan specifying what the community will receive as a result of the research beyond individual participant compensation. (ii) The benefit-sharing plan should be submitted to and approved by the ethics committee as a condition of approval, and should be incorporated into the CTA as a binding obligation. (iii) CIOMS should develop indicative guidance on the range of appropriate community benefits, drawing on existing practice in genomic research and vaccine trials.

Expected outcome: Operationalisation of the community-level post-trial obligation recognised in Ubuntu and Confucian ethics and partially reflected in current CIOMS guidelines; improved community trust in international research.

Feasibility: High. A guidance amendment is within CIOMS's existing mandate; the substantive content builds on established practice in genomic research governance.

Conclusion

This paper has developed a governance framework for international collaborative clinical research grounded simultaneously in private international law methodology and cross-cultural research ethics. The framework's ontological foundation decomposes the research relationship into six categories, providing a principled vocabulary for identifying governance gaps with precision. Its central methodological contribution is the identification of PIL as an *intermediate language*: a translation mechanism routing each ontological element, through connecting factors and choice-of-law rules, to the domestic legal system that gives it normative content. The three limits of this translation function, identified in §7, define precisely where the current governance architecture fails and where new instruments are needed.

The gap analysis of Part IV reveals that current mechanisms are characterised by fragmentation, asymmetry, and normative under-specification across all six ontological categories. They fail the standards of efficiency, operability, controllability, and ethical adequacy in ways that are systemic and cross-jurisdictional, and there-

fore cannot be addressed by individual party workarounds or unilateral domestic regulatory reform.

The nine policy recommendations of Part V are graduated from binding multilateral instruments to guidance document amendments, reflecting an assessment of political feasibility. The long-term vision is a multilateral treaty framework for international collaborative clinical research governance comparable in structural ambition to the New York Convention for arbitration or the Montreal Convention for air carrier liability: a framework allocating jurisdiction and applicable law predictably, providing accessible enforcement mechanisms for participants, and operationalising cross-culturally validated ethical standards. Achieving this vision requires sustained engagement between the international legal community, the bioethics community, regulatory authorities, and research participants. This paper is offered as a contribution to that collective project.

References

- [1] World Medical Association (2013). *Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects*. Adopted 1964; last revised October 2013, Fortaleza.
- [2] Council for International Organizations of Medical Sciences (2016). *International Ethical Guidelines for Health-related Research Involving Humans*. Geneva: CIOMS.
- [3] International Council for Harmonisation (2016). *ICH Harmonised Guideline E6(R2): Good Clinical Practice Integrated Addendum to ICH E6(R1)*. Geneva: ICH. EMA/CHMP/ICH/135/1995.
- [4] International Council for Harmonisation (2017). *ICH Harmonised Guideline E17: General Principles for Planning and Design of Multi-Regional Clinical Trials*. Geneva: ICH.
- [5] Council of the European Union (2008). Regulation (EC) No 593/2008 on the law applicable to contractual obligations (Rome I). *Official Journal of the European Union* L 177, 4 July 2008, pp. 6–16.
- [6] Council of the European Union (2007). Regulation (EC) No 864/2007 on the law applicable to non-contractual obligations (Rome II). *Official Journal of the European Union* L 199, 31 July 2007, pp. 40–49.

- [7] Council of the European Union (2012). Regulation (EU) No 1215/2012 on jurisdiction and the recognition and enforcement of judgments in civil and commercial matters (Brussels I Recast). *Official Journal of the European Union* L 351, 20 December 2012, pp. 1–32.
- [8] Hague Conference on Private International Law (2019). *Convention of 2 July 2019 on the Recognition and Enforcement of Foreign Judgments in Civil or Commercial Matters*. The Hague: HCCH.
- [9] United Nations (1958). *Convention on the Recognition and Enforcement of Foreign Arbitral Awards*. Done at New York, 10 June 1958. 330 U.N.T.S. 38.
- [10] Zweigert, K. and Kötz, H. (1998). *An Introduction to Comparative Law*. 3rd ed. Translated by T. Weir. Oxford: Clarendon Press.
- [11] Beauchamp, T.L. and Childress, J.F. (2019). *Principles of Biomedical Ethics*. 8th ed. New York: Oxford University Press.
- [12] Fan, R. (1997). Self-determination vs. family-determination: Two incommensurable principles of autonomy. *Bioethics* 11(3–4): 309–322.
- [13] Tangwa, G.B. (2004). Between universalism and relativism: A conceptual exploration of problems in formulating and applying international biomedical ethical guidelines. *Journal of Medical Ethics* 30(1): 63–67.
- [14] Daar, A.S. and Al Khitamy, A.B. (2001). Bioethics for clinicians: 21. Islamic bioethics. *Canadian Medical Association Journal* 164(1): 60–63.
- [15] Searle, J.R. (1995). *The Construction of Social Reality*. New York: Free Press.
- [16] Global Alliance for Genomics and Health (2014). *A Framework for Responsible Sharing of Genomic and Health-Related Data*. Toronto: GA4GH.
- [17] Government of Japan (2018). *Clinical Research Act* (Act No. 16 of 2018). Tokyo: Ministry of Health, Labour and Welfare.
- [18] People’s Republic of China (2019). *Drug Administration Law of the People’s Republic of China* (revised 2019). Beijing: Standing Committee of the National People’s Congress.
- [19] People’s Republic of China (2021). *Personal Information Protection Law of the People’s Republic of China*. Beijing: Standing Committee of the National People’s Congress. Effective 1 November 2021.

- [20] European Parliament and Council (2014). Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use. *Official Journal of the European Union* L 158, 27 May 2014, pp. 1–76.
- [21] U.S. Department of Health and Human Services (2018). Federal Policy for the Protection of Human Subjects (“Common Rule”). 45 CFR Part 46. Revised rule effective 19 January 2018. *Federal Register* 82(12): 7149–7274.

A. Glossary of Key Terms

Term	Working Definition
Sponsor	The natural or legal person who takes responsibility for the initiation, management, and financing of clinical research.
Principal Investigator	The natural person who assumes primary legal and ethical responsibility for the conduct of research at a defined site.
Ethics Committee / IRB	An independent body tasked with prospective ethical review and ongoing oversight of research involving human participants.
Informed Consent	The voluntary, competent, and adequately informed authorisation by a participant to participate in research.
Serious Adverse Event	An adverse event that results in death, is life-threatening, requires hospitalisation, causes disability, or involves a congenital anomaly.
Data Controller	The entity determining the purposes and means of personal data processing; concept drawn from GDPR Art. 4(7).
Jurisdiction	The legal authority of a court or regulatory body to adjudicate or regulate a matter.
Choice of Law	The PIL rule or contractual clause designating which legal system’s substantive rules govern a cross-border relationship.
Mandatory Rules	Domestic law provisions that cannot be derogated from by party agreement and apply regardless of the chosen governing law.

Term	Working Definition
Federated Analysis	A data-processing approach in which analysis is conducted locally at each custodian's site, with only aggregated results transferred across jurisdictions.

B. Summary of Domestic Regulatory Frameworks

Jurisdiction	Primary Statute(s)	Regulatory Authority	ICH GCP Status
Japan	Clinical Research Act (2018); PMD Act	PMDA	Implemented (E6(R2))
China	Drug Administration Law (2019); Clinical Trial Measures (2020); PIPL (2021); Data Security Law (2021)	NMPA	Aligned, with deviations
EU	Clinical Trials Regulation No 536/2014	EMA / National CAs	Implemented
USA	Common Rule (45 CFR 46, 2018); 21 CFR 50, 56	FDA	Implemented
South Korea	Pharmaceutical Affairs Act; GCP Regulation	MFDS	Implemented

C. Model Contract Clause: Liability and Mandatory-Rules Rider

This clause is provided for illustrative purposes only and does not constitute legal advice.

Article [X] Liability Allocation and Mandatory-Rules Rider

[X.1] The Sponsor shall indemnify each Investigator Site and its personnel from claims arising from: (a) product liability relating to the Investigational Product; (b) the Sponsor's negligent acts or omissions in protocol design or monitoring; (c) any Sponsor breach of Applicable Law.

[X.2] Each Investigator Site shall indemnify the Sponsor from claims arising from its own negligent acts or omissions in study conduct at its site.

[X.3] “Applicable Law” means the laws and regulations of each jurisdiction in which Study activities are conducted, including any mandatory rules that cannot be excluded by agreement of the parties, notwithstanding any choice-of-law clause in this Agreement.

[X.4] Mandatory-Rules Rider

- *Japan*: Clinical Research Act (2018) Arts. 5–7 (site monitoring; adverse event reporting) cannot be waived.
- *China*: PIPL (2021) Arts. 38–43 (cross-border data transfer approval) and Data Security Law (2021) Art. 31 (important data localisation) apply regardless of chosen law.
- *European Union*: GDPR (2016/679) Arts. 44–49 (cross-border data transfer) and Art. 17 (right to erasure) apply regardless of chosen law.
- *United States*: Common Rule (45 CFR 46) and FDA IND safety reporting requirements (21 CFR 312.32) apply to studies intended to support FDA marketing applications regardless of conduct location.