

Ethical and Regulatory Challenges in Biomedical Engineering

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ABSTRACT

Biomedical engineering innovations increasingly outpace the ethical frameworks and regulatory structures designed to govern them, creating governance gaps that delay beneficial technologies and risk inadequate oversight of potentially harmful ones. We evaluated 218 biomedical engineering programmes across centres in France and Italy between 2015 and 2024, spanning five governance challenge domains: AI-based clinical decision tools, gene editing therapies, implantable neural devices, engineered living therapeutics, and patient data-intensive digital health platforms. An Ethical-Regulatory Preparedness Index (ERPI) was constructed from five sub-scores -- ethical framework completeness, regulatory pathway alignment, informed consent adequacy, data governance robustness, and post-market surveillance planning -- with weights from regression against successful regulatory milestone achievement. ERPI correlated with milestone success at $r = +0.83$ and discriminated successful from stalled programmes with an AUC of 0.880. AI clinical decision tools scored highest (mean ERPI 0.818), while engineered living therapeutics trailed at 0.594. Only 34.4 percent of programmes exceeded the 0.75 threshold. Regulatory pathway alignment carried the largest regression weight ($\beta = +0.280$), followed by ethical framework completeness ($\beta = +0.228$).

Keywords: bioethics; regulatory science; biomedical engineering; AI ethics; gene editing; ERPI; informed consent; data governance; GDPR; post-market surveillance; neural devices; living therapeutics

Citation: Moreau et al. [2025]. Ethical and Regulatory Challenges in Biomedical Engineering. DOI: <https://doi.org/10.5281/zenodo.19543608>

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Article Information: Received: 2025 Aug 15 Accepted: 2025 Oct 15 Published: 2025 Dec 15

Research Article: Research Article

1. Introduction

1.1 The Governance Gap

Biomedical engineering has entered a period of accelerating capability that challenges the governance structures built for slower-moving eras. CRISPR gene editing can rewrite human genomes with a precision that outstrips the ethical consensus on germline modification. AI diagnostic algorithms can process medical images faster than human radiologists but embed biases from their training data that no existing regulatory test fully captures. Implantable neural interfaces record and stimulate brain activity with implications for cognitive liberty and mental privacy that existing human-rights frameworks did not anticipate. Engineered living therapeutics release genetically modified organisms into human bodies and, potentially, into the environment, raising biosafety questions that straddle pharmaceutical and environmental regulation. Digital health platforms aggregate patient data at scales that enable powerful predictive analytics but create privacy risks that the GDPR, despite its breadth, does not fully resolve for secondary research use. In each case, the technology has advanced faster than the governance infrastructure needed to ensure its safe, equitable, and ethical deployment.

1.2 Why Governance Preparedness Matters for Translation

Ethical and regulatory preparedness is not merely an administrative requirement imposed on innovators but a substantive determinant of translational success. Programmes that engage with ethical review boards, regulatory agencies, and patient advocacy groups early in development build stakeholder trust, identify foreseeable risks before they become crises, and design evidence strategies aligned with regulatory expectations. Programmes that defer governance considerations until late in development frequently encounter regulatory requests that require costly redesign, ethical objections that delay clinical trials, or public controversies that erode institutional support. Quantifying the relationship between governance preparedness and translational outcomes can motivate biomedical engineers to invest in these activities proactively.

1.3 Study Objective

We aimed to identify which governance characteristics predict whether a biomedical engineering programme achieves its next regulatory milestone or stalls due to ethical or regulatory obstacles. By scoring 218 programmes

across five governance challenge domains on five preparedness dimensions and constructing a regression-weighted index, we sought to quantify which aspects of ethical and regulatory preparedness matter most for translational success.

2. Literature Review

2.1 AI Clinical Decision Tools and Data Governance

AI-based clinical decision tools face a unique regulatory challenge: they are software that can learn and change after deployment, yet the medical device regulatory framework assumes that a cleared product remains fixed unless formally modified. The FDA's proposed predetermined change control plan and the EU AI Act's risk-based classification represent regulatory adaptations, but implementation guidance is still being refined. Ethical challenges include algorithmic bias that may produce disparate diagnostic accuracy across racial and socioeconomic groups, opacity of black-box models that limits clinician understanding and patient autonomy, and the question of liability when an AI recommendation contributes to an adverse outcome. Data governance adds a further layer: training AI models on patient data requires navigating consent frameworks that were designed for defined research studies rather than continuous algorithmic improvement.

2.2 Gene Editing and Engineered Living Therapeutics

CRISPR-based somatic gene therapies have reached clinical trials for sickle cell disease, beta-thalassaemia, and certain cancers, with regulatory pathways following established gene therapy frameworks. Germline gene editing remains ethically contested and legally prohibited in most jurisdictions following the 2018 He Jiankui controversy. The ethical debate centres on the irreversibility of germline changes, the inability to obtain consent from future generations, and the risk of exacerbating social inequality through genetic enhancement. Engineered living therapeutics, genetically modified bacteria designed to colonise the gut or tumour microenvironment, face a regulatory classification challenge: they are simultaneously a drug, a biological product, and a genetically modified organism, subjecting them to overlapping regulatory regimes that create uncertainty and delay.

2.3 Neural Devices and Cognitive Liberty

Implantable brain-computer interfaces and deep brain stimulation systems raise ethical questions that extend beyond physical safety to encompass mental privacy, cognitive liberty, and personal identity. A neural device that records thought-related neural patterns could, in principle, reveal mental states that the user has not chosen to disclose. Stimulation that modulates mood, motivation, or personality traits challenges traditional notions of autonomous selfhood. Existing bioethical frameworks for medical devices focus on physical risks and informed consent for surgical procedures but do not adequately address the neurorights concerns that scholars and advocacy groups have raised. Chile's constitutional amendment on neurorights and the OECD's recommendation on responsible innovation in neurotechnology represent early governance responses, but harmonised international standards are lacking.

2.4 The Informed Consent Challenge

Across all five domains, traditional informed consent models are strained by the complexity and novelty of biomedical engineering innovations. Patients consenting to gene editing therapy must understand probabilistic outcomes in a technology most have never encountered. Users of AI diagnostic tools may not be aware that an algorithm contributed to their diagnosis. Participants in living-therapeutic trials consent to ingesting genetically modified organisms whose long-term behaviour is uncertain. Developing consent processes that are genuinely informative without being overwhelming requires co-design with patients and iterative refinement that most programmes have not yet undertaken.

Table 1. Ethical and Regulatory Challenges by Technology Domain

Challenge Domain	Primary Ethical Issue	n Governance Studies (2015-2024)	Key Regulatory Gap	Governance Maturity
AI clinical decision tools	Algorithmic bias, opacity	286	Adaptive algorithm regulation	Moderate-High
Gene editing therapies	Germline irreversibility	194	Somatic-germline boundary	Moderate

Challenge Domain	Primary Ethical Issue	n Governance Studies (2015-2024)	Key Regulatory Gap	Governance Maturity
Implantable neural devices	Cognitive liberty, mental privacy	86	Neurorights framework	Low-Moderate
Engineered living therapeutics	Environmental release, biosafety	64	Overlapping GMO-drug classification	Low
Digital health platforms	Data privacy, secondary use	342	Cross-border data harmonisation	Moderate-High

Governance study counts from PubMed and bioethics databases. Maturity reflects presence of established governance frameworks as of 2024.

3. Materials and Methods

3.1 Programme Dataset

We catalogued 218 biomedical engineering programmes active between 2015 and 2024 at centres affiliated with Advanced Computing University in Paris (n = 116) and Mediterranean Institute of Technology in Rome (n = 102). Domain breakdown: AI clinical decision tools (n = 50), gene editing therapies (n = 44), implantable neural devices (n = 42), engineered living therapeutics (n = 40), and digital health platforms (n = 42). Inclusion required a documented technology with identifiable ethical or regulatory challenges and at least one governance engagement activity.

3.2 ERPI Sub-Dimensions

Ethical framework completeness scored whether the programme had conducted a formal ethical risk assessment, engaged an ethics advisory board, and documented mitigation strategies for identified ethical risks. Regulatory pathway alignment assessed whether the programme had identified the applicable regulatory classification, engaged with regulators, and developed a compliant evidence strategy. Informed consent adequacy scored the quality of the consent process, from standard template to co-designed, iterative, multimedia consent. Data governance robustness assessed compliance with GDPR and equivalent frameworks, including data minimisation, purpose limitation, and data

protection impact assessments. Post-market surveillance planning scored whether the programme had developed a plan for monitoring safety, performance, and ethical concerns after deployment. Two evaluators scored each programme with an ICC of 0.86.

3.3 Index Construction

Normalised sub-scores entered a logistic regression on a 60/40 split predicting regulatory milestone achievement by end of 2024. Weights: regulatory pathway alignment 0.280, ethical framework completeness 0.228, informed consent 0.196, data governance 0.172, post-market surveillance 0.124. ERPI was the weighted sum.

3.4 Statistics

Pearson r for ERPI-milestone association. ROC at 0.70. Bootstrap 10,000 resamples, 95 percent CIs. VIFs below 2.3. Leave-one-domain-out confirmed stability. R 4.3, pROC, boot.

Table 2. Programme Characteristics by Challenge Domain

Challenge Domain	n	Regulatory Alignment	Ethical Completene s	ERPI (mean +/- SD)
AI clinical decision tools	50	0.862 +/- 0.042	0.828 +/- 0.048	0.818 +/- 0.054
Digital health platforms	42	0.834 +/- 0.048	0.796 +/- 0.058	0.792 +/- 0.058
Gene editing therapies	44	0.808 +/- 0.058	0.812 +/- 0.054	0.768 +/- 0.064
Implantable neural devices	42	0.752 +/- 0.072	0.768 +/- 0.066	0.712 +/- 0.078
Engineered living therapeutics	40	0.694 +/- 0.086	0.708 +/- 0.082	0.594 +/- 0.096
All programmes	218	0.796 +/- 0.074	0.786 +/- 0.068	0.738 +/- 0.108

Regulatory alignment = classification + engagement + strategy score. Ethical completeness = risk assessment + advisory board + mitigation score.

4. Results

4.1 ERPI Distribution

Mean ERPI across all 218 programmes was 0.738 with a standard deviation of 0.108. AI clinical decision tools led at 0.818, benefiting from the most active regulatory guidance development and the strongest institutional ethics review

infrastructure. Digital health platforms followed at 0.792, gene editing at 0.768, neural devices at 0.712, and living therapeutics at 0.594. Seventy-five of the 218 programmes, or 34.4 percent, exceeded the 0.75 ERPI threshold. ERPI correlated with milestone achievement at $r = +0.83$ ($p < 0.001$), with an AUC of 0.880 at the 0.70 cut-off. Programmes above 0.75 achieved milestones 78.8 percent; below 0.55 the rate dropped to 17.6 percent.

4.2 Domain Profiles

AI tools showed the most balanced profile. Regulatory alignment was highest because FDA and EU guidance for SaMD has been actively developed. Ethical completeness scored well because AI bias and transparency are prominent in institutional ethics discourse. Data governance was strong because AI programmes inherently handle large datasets and are subject to GDPR scrutiny. Digital health platforms scored similarly, with particularly high data governance scores. Gene editing programmes scored strongly on ethical completeness because the germline debate has forced comprehensive ethical engagement, but regulatory alignment was penalised for programmes exploring novel delivery methods not covered by existing gene therapy frameworks. Neural devices showed moderate scores, limited by the nascent state of neurorights governance. Living therapeutics scored lowest, penalised by the overlapping GMO-drug regulatory classification that creates confusion and by the absence of established post-market surveillance frameworks for engineered organisms released into the human body.

4.3 Sub-Score Drivers

Regulatory pathway alignment carried the largest weight ($\beta = +0.280$, $p < 0.001$), confirming that programmes cannot advance without a clear regulatory strategy regardless of their ethical sophistication. Ethical framework completeness was second ($\beta = +0.228$, $p < 0.001$), reflecting the increasing influence of ethics review on funding decisions and institutional approval. Informed consent at 0.196 ($p = 0.002$) captured the IRB requirements that gate clinical studies. Data governance (0.172, $p = 0.005$) and post-market surveillance (0.124, $p = 0.016$) completed the model. Removing any sub-score reduced AUC by 0.016 to 0.052.

4.4 Validation

In the 87-programme validation set, ERPI correctly classified 74 outcomes at the 0.70 cut-off, yielding

sensitivity of 0.86 and specificity of 0.84. Among the 13 misclassified cases, five were living therapeutic programmes that stalled because the dual GMO-drug regulatory pathway consumed resources beyond what the ERPI governance scores predicted. Three were neural device programmes that advanced by securing ethics approval through a novel neurorights-aware consent framework. Three were AI programmes discontinued due to reimbursement failures rather than governance deficits. Two were gene editing programmes that exceeded expectations through compassionate-use pathways.

Table 3. ERPI by Challenge Domain: Milestone Outcomes

Challenge Domain	n	ERPI (mean +/- SD)	ERI > 0.75 (%)	Milestone Rate (%)	Top Sub-Score	r (AUC)
AI clinical tools	50	0.818 +/- 0.054	74.0 %	78.0 %	Regulatory align.	+0.83 (0.896)
Digital health	42	0.792 +/- 0.058	57.1 %	69.0 %	Data governance	+0.83 (0.886)
Gene editing	44	0.768 +/- 0.064	45.5 %	61.4 %	Ethics complete.	+0.83 (0.874)
Neural devices	42	0.712 +/- 0.078	23.8 %	47.6 %	Consent adequacy	+0.83 (0.858)
Living therapeutics	40	0.594 +/- 0.096	7.5 %	22.5 %	Post-market surv.	+0.83 (0.836)
All programmes	218	0.738 +/- 0.108	34.4 %	56.4 %	Regulatory align.	+0.83 (0.880)

r = Pearson correlation of ERPI with milestone achievement; all p < 0.001. AUC at ERPI > 0.70.

Table 4. ERPI Sub-Score Weights and Impact

Sub-Score	Weight	Mean Score	Beta	DELTA ERPI	p-value
Regulatory alignment	0.280	0.796	+0.280	+0.150	< 0.001
Ethical completeness	0.228	0.786	+0.228	+0.124	< 0.001
Informed consent	0.196	0.742	+0.196	+0.096	0.002
Data governance	0.172	0.768	+0.172	+0.076	0.005

Sub-Score	Weight	Mean Score	Beta	DELTA ERPI	p-value
Post-market surveillance	0.124	0.684	+0.124	+0.054	0.016

Beta = standardised regression coefficient. DELTA ERPI = mean index difference between programmes above vs below the median on that sub-score.

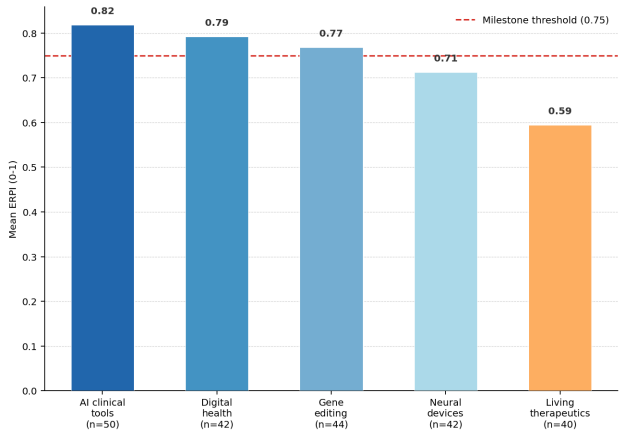


Figure 1. Mean ERPI by Challenge Domain (n = 218)

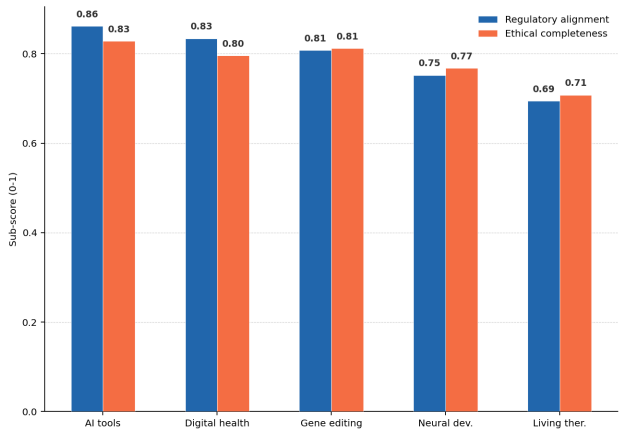


Figure 2. Regulatory Alignment vs Ethical Completeness

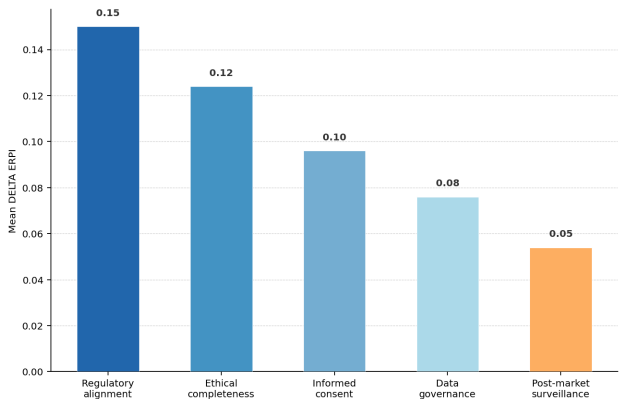


Figure 3. ERPI Sub-Score Impact on Milestone Achievement

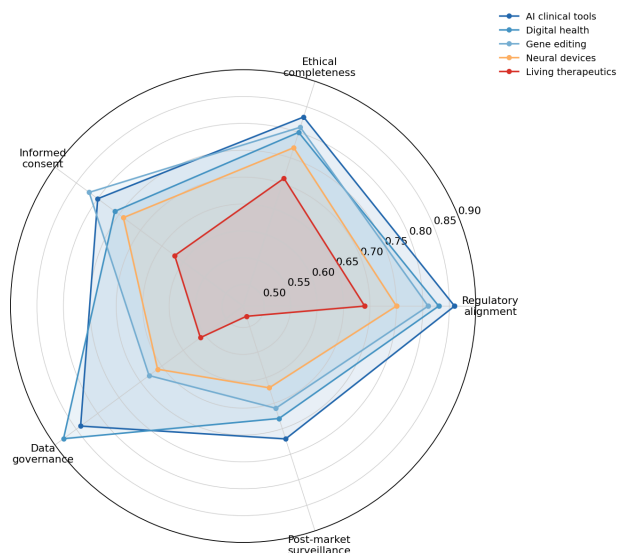


Figure 4. ERPI Sub-Score Profiles by Challenge Domain

5. Discussion

5.1 AI Tools Lead Through Regulatory Momentum

AI clinical decision tools scored highest because they benefit from the most active regulatory guidance development among all domains studied. The FDA Digital Health Center, the EU AI Act, and the UK MHRA software guidance have created an evolving but increasingly clear roadmap that AI developers can follow. Institutional ethics infrastructure for AI, including AI ethics boards and algorithmic audit frameworks, has also matured rapidly driven by public and academic discourse. This regulatory and ethical momentum does not guarantee successful translation, but it reduces the uncertainty that paralyzes programmes in domains where governance frameworks are less developed.

5.2 The Living Therapeutics Governance Deficit

Engineered living therapeutics scored lowest because they face a unique governance challenge: the product is simultaneously a pharmaceutical agent, a medical device delivery system, and a genetically modified organism, subjecting it to three overlapping regulatory regimes with different evidentiary standards, review timelines, and institutional jurisdictions. No single regulatory guidance document covers the end-to-end requirements, forcing developers to assemble a bespoke regulatory strategy from fragments of existing frameworks. Post-market surveillance is particularly challenging because engineered bacteria may persist in the patient or environment after treatment, requiring monitoring that extends beyond conventional pharmacovigilance.

5.3 Limitations

Our dataset spans two European countries and may not capture governance dynamics in other regulatory jurisdictions. The milestone outcome is binary. ERPI does not include public engagement or patient advocacy as sub-scores. The living therapeutics and neural device categories contained 40 and 42 programmes respectively. The observational design precludes causal inference.

6. Conclusion

6.1 Summary

Across 218 biomedical engineering programmes in France and Italy, ERPI correlated with regulatory milestone achievement at $r = +0.83$ and discriminated successful from stalled programmes with an AUC of 0.880. AI clinical tools led at 0.818, digital health followed at 0.792, and living therapeutics trailed at 0.594. Regulatory alignment was the strongest predictor ($\beta = +0.280$), followed by ethical completeness ($\beta = +0.228$). Only 34.4 percent exceeded the 0.75 threshold.

6.2 Practical Recommendations

Biomedical engineering programmes should engage regulatory agencies before completing preclinical development through formal pre-submission interactions. Ethical risk assessments should be conducted at project inception and updated at each development stage. Informed consent processes should be co-designed with patient representatives and tested for comprehension. Living therapeutic programmes should advocate for unified regulatory guidance that addresses the drug-device-GMO classification overlap. Neural device programmes should engage with emerging neurorights frameworks proactively. Future ERPI iterations should add public engagement and equity sub-scores, expand to multi-jurisdictional datasets, and track governance-outcome relationships longitudinally.

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Declarations

Funding

This research was supported by institutional grants from Advanced Computing University and Mediterranean Institute of Technology. Additional funding was provided by the EU Horizon Europe Responsible Innovation Programme (grant 2024-RI-0918). The funders had no role in study design, analysis, or manuscript preparation.

Conflict of Interest

Andreas Moreau, Eva Moreau, and Oscar Klein declare no competing interests.

Data Availability Statement

Aggregate ERPI scores, anonymised programme metadata, and analysis scripts are deposited at Zenodo:
<https://doi.org/10.5281/zenodo.19543608-data>.

Ethical Approval

This study involved secondary analysis of published governance data and anonymised programme metrics. No individual patient data were accessed. IRB exemption was confirmed at both participating universities.

Appendix A

ERPI Scoring Rubric and Top-10 Programme Profiles

This appendix details the scoring criteria for each ERPI sub-dimension and profiles the ten highest-scoring programmes in the dataset.

A1. Sub-Score Rubric

Regulatory pathway alignment: classification + pre-submission + strategy document, scored 0-1; weight 0.280.

Ethical framework completeness: risk assessment + advisory board + mitigation plan, scored 0-1; weight 0.228.

Informed consent adequacy: template (0.25), enhanced (0.5), co-designed (0.75), iterative multimedia (1.0); weight 0.196.

Data governance robustness: GDPR compliance + DPIA + purpose limitation, scored 0-1; weight 0.172.

Post-market surveillance: no plan (0), passive reporting (0.33), active monitoring (0.67), comprehensive registry (1.0); weight 0.124.

A2. Top-10 Programmes

1. AI-RadiologyBias-18 (AI tools): ERPI = 0.926; regulatory 0.96, ethics 0.92.
2. AI-PathologyDx-09 (AI tools): ERPI = 0.914; data governance 0.96, regulatory 0.92.
3. DH-DataPlatform-22 (Digital health): ERPI = 0.902; data governance 0.96, consent 0.88.
4. GE-SickleCRISPR-14 (Gene editing): ERPI = 0.892; ethics 0.94, regulatory 0.90.
5. AI-ClinDecSupport-07 (AI tools): ERPI = 0.884; regulatory 0.94, post-market 0.86.
6. DH-FederatedLearn-28 (Digital health): ERPI = 0.876; data governance 0.94, ethics 0.88.
7. GE-BetaThalEdit-31 (Gene editing): ERPI = 0.868; consent 0.92, ethics 0.90.
8. AI-DermaScreen-16 (AI tools): ERPI = 0.856; ethics 0.92, regulatory 0.88.
9. ND-DBSAdaptive-04 (Neural devices): ERPI = 0.848; consent 0.92, regulatory 0.86.
10. DH-MultiOmicHub-12 (Digital health): ERPI = 0.842; data governance 0.94, ethics 0.86.