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Ethics Governance Outside the Box: Reimagining Blockchain as a Policy Tool to Facilitate Single Ethics Review and Data Sharing for the 'omics' Sciences

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Section: Use Cases/Pilots/Methodologies

Clinical research and health information data sharing are but ripples in a growing wave of reimagined applications of distributed ledger technologies beyond the digital marketplace for which they were originally created. This paper explores the use of distributed ledger technologies to facilitate single institutional ethics review of multi-site, collaborative studies in the data-intensive sciences such as genetics and genomics. Immutable record-keeping, automatable protocol amendments and direct connectivity between stakeholders in the research enterprise (e.g., researchers, research ethics committees, institutions, funders and regulators) comprise several of the conceptual and technological advantages of distributed ledger technologies to research ethics review. This novel-use proposal dovetails recent policy reforms to research ethics review across North America that mandate a single ethics review for any study that takes place across more than one research site. Such reforms in the United States, Canada and Australia replace prior institution-by-institution approval mechanisms that contributed to significant research delays and duplicative procedures for collaborative research worldwide. While this paper centers on the Common Rule revision in the United States, the single ethics review mandate is a noteworthy example of regulation evolving in parallel with advances in the data-intensive sciences it governs. The informational exchange capacities of distributed ledger technologies align well with the procedural goals of streamlining the ethics review system under the new Common Rule ahead of its official

implementation on January 19, 2020. The ethical, legal and social implications of applying such technologies to ethics review will be explored in this concept paper. Namely, the paper proposes how administrative data from research ethics committees (REC) could be protected and shared responsibly, as well as inter-institutional cooperation negotiated within a centralized network of research ethics committees using the blockchain.

Keywords: *Blockchain, Data Sharing, Ethics Review, Governance, IRB, Research, Single Mutual Recognition*

In January 2017, the United States National Institutes of Health finalized what is arguably the most significant reform to policies of ethics review for research involving humans and their data.[1] In the revised Common Rule, nonexempt multi-site research will undergo a mandated single research ethics review. That is, collaborative research studies that span data collection and participant recruitment across multiple institutions and state jurisdictions will no longer require separate ethics approval from each collaborating site named in the study.

A policy artifact of post-Nuremberg consensus, this institution-by-institution approval process served its purpose well until a few landmark scientific advances in the early 2000's. The Human Genome Project, for one, systemically challenged the notion of scientific discovery built on the singular contributions of 'lone scientists' in biomedicine.[2] The current demands for data of adequate volume, veracity and validity to make sound scientific associations between the human genome and disease are far greater than any one scientist or institution can meet alone.[3–5] An ethical imperative to share genomic and associated clinical data complements this scientific rationale. Participants accept informational risk(s), albeit minor, as part of their involvement in genetic/genomic research.[6–11] It is therefore the charge of research ethics committees (REC) to determine whether the study strikes an appropriate balance between these risks and the knowledge benefits anticipated from the collaborative study. Increasing recognition of the need to marry clinical research and care in what the Institute of Medicine termed the 'learning healthcare system,'[12] further underscores the direct involvement of research ethics review to facilitating innovation in standards of care.[13]

As noted elsewhere, the "same ethics review procedures have historically applied to single-site biomedical studies as for multi-site[i], data-only studies despite their internationalization and data intensification."[14] The pronounced emphasis on collaboration and data sharing motivated by the Human Genome Project (HGP) accentuated the growing incoherence between traditional models of ethics governance—namely the institution-by-institution approach to research ethics approval—and the norms of collaborative research practice in the 'omics' disciplines in particular e.g., genomics, proteomics as well as broader biomedical research endeavors e.g., precision medicine of cancer[15–18] and dementia.[19,20] to name two.

Growing anecdotal and empirical evidence in the years preceding reform suggested the extent of this incoherence.[21–27] Taken together, the procedural inefficiency, inconsistency, high administrative burden and increasing cost of the ethics approval process under the institution-by-institution model prompted transition to a single institutional review board (sIRB) approach for multi-site studies within the United States by 2020[1] and in other international jurisdictions.[28–30] The sIRB model is purported to better respond to the contemporary realities and practices of collaborative, data-intensive research typified by the emerging 'omics' disciplines.[31] It subscribes to a principle of mutual recognition, or the ethical, legal and social legitimacy of ethics review(s)

conducted by an external institution named in a multi-site study.[31,32] Motivating adoption of the sIRB model is the hope that centralizing ethics review will reduce—if not eliminate outright—the redundancies and inefficiencies that previously delayed the ethics approval step on the bench-to-bedside continuum for genetic and genomic research.

For its intuitive simplicity, the sIRB model poses several challenges to implementation. Without practical guidance and infrastructural support, these challenges could negate any improvement in quality and efficiency that drove the model's adoption in the first place[ii]. First, RECs can be bureaucratically complex.[33] They involve relational hierarchies both within and external to the institution. Klitzman supports this in his claim that the relationship between a leading REC for a multi-site study and the local institutions at which the lead REC's decision applies will "profoundly shape the costs and effectiveness of future multi-site research involving human research participants."[24] Cultures of (mis)trust in the procedures, competencies and approaches between participating RECs hint at some of the relational complexities that face institutions in successfully operationalizing the sIRB model.

The mutual, yet secure network exchange capacities of the blockchain offer innovative solutions for meeting the procedural as well as relational complexities of a centralized sIRB system based on mutual recognition. This paper proposes how the blockchain could enable e-governance with respect to ethics review approvals, particularly for multi-site studies in genetics and genomics. The technological virtues of the blockchain—including immutable documentation, timestamping and automatable updating for protocol amendments, to name but a few examples—can moreover help committees achieve the performance goals that centralizing ethics review promises for researchers and institutions alike.

Distributed ledger technologies (DLT) generally, and the blockchain specifically, present several solutions to some of the systemic challenges RECs face in centralizing ethics review under the new Common Rule. This paper explores the ethical, legal and social implications of adopting the blockchain to facilitate such e-governance of ethics review in the multi-site research context. Namely, it proposes how the blockchain could enable administrative REC data exchange and broker inter-institutional cooperation across research sites or jurisdictions that will participate in a sIRB system. The blockchain furthermore affords new opportunities for improved decision reporting, transparency and accountability to stakeholders in the research enterprise e.g., researchers, institutions, funders and research participants for whom REC decisions chiefly impact. Lastly, the paper nuances several conceptual tensions that sIRB powered by the blockchain could pose for U.S. regulatory bodies moving forward.

THE BUILDING BLOCKS FOR BLOCKCHAIN IN ETHICS REVIEW

Blockchain is best recognized as the technological backend for cryptocurrencies, securely recording in a distributed and mutually transparent ledger (or database) all informational transactions in a peer-to-peer network. These transactions and the data parameters that enable them are stored as 'blocks.' Each block is timestamped and added to a chain of blocks, whereby its addition is contingent on the parameters and codes set by the blocks before it. Each block is validated by a third party 'miner' by solving a computational problem. Once successfully executed, validated and timestamped, information contained in the block is immutable, incorruptible and digitally historicized on every node server. A private ledger comprised of participating institutions named in a multi-site study, using Ethereum Smart Contracts to execute regulatory permissions and consent is proposed. Figure 1 depicts a typical research

ethics review workflow, from initial investigator application through to data safety monitoring and study closure. Figure 2, in contrast, identifies various points where Ethereum smart contracts can potentially intervene to execute regulatory permissions in the sIRB workflow via the blockchain. Smart contracts are proposed to replace three requisite approval documents needed during the review process, including inter-institutional reliance agreements between collaborating research sites, participant consent forms and data sharing/access agreements. Not only would the blockchain serve as a common platform upon which individual RECs could better oversee collaborative research studies, it could dramatically improve the consistency of REC decisions and reporting.

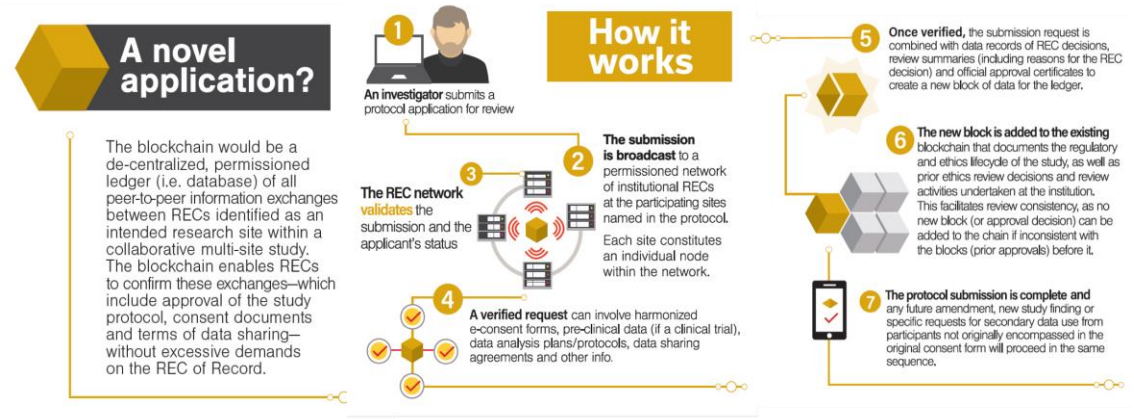

Figure 1. Proposed blockchain application for enhancing mutual recognition of institutional ethics review for research involving humans

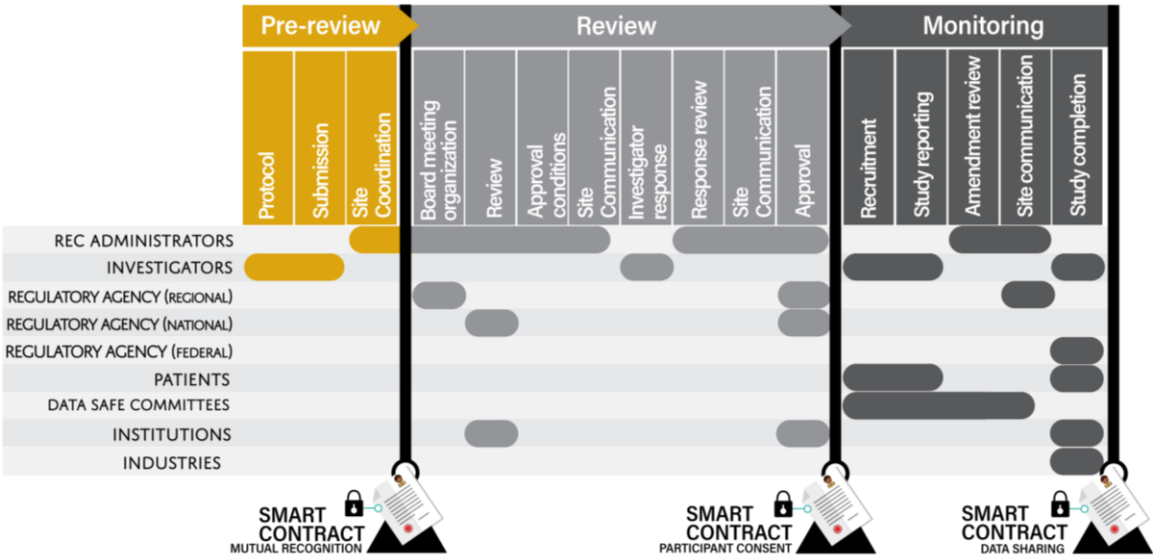

Figure 2—Model Institutional Review Board workflows using the blockchain

Consider two potential use cases of the blockchain to enhance decision-making consistency for sIRBs: "blockchain-based credentialing" and "blockchain-accountable data sharing". The former use case automates eligibility criteria for the nominated board of record, providing a transparent view of the lead REC's

credentials to be deemed lead. An REC of record, for example, could only serve as the lead REC if it met established criteria for proper representation of scientific expertise and community membership, and its membership was free of any financial or perceived conflicts of interest. In "blockchain-accountable data sharing," the single REC of record could easily monitor and hold researchers accountable for sharing their data if the study is required to do so under mandatory data sharing conditions for funding.

Many federal funding agencies including the NIH[34] and NSF[35] require researchers to make data from publicly funded projects available following a one-year publication window. Few researchers, however, are sanctioned for failing to meet these data sharing requirements despite policies proposing how they could be better held accountable (see for example the Global Alliance for Genomics and Health Accountability Policy released in 2015).[36] RECs that participate in a sIRB system could fill this important accountability gap using the blockchain. The blockchain could prevent approval of federally funded studies without a data sharing or management plan, and by automating annual study reporting. Furthermore, smart contracts executing the Accountability policy could also be integrated into the ethics review process, allowing RECs to collectively monitor researchers' data sharing activities.

Adapted from Peterson et al,[37] the benefits of the blockchain could facilitate a sIRB model insofar as three general assumptions about the participating RECs (or nodes) are true. First, data input and participation from institutional RECs should subscribe to a shared lexicon of data protection and securities (e.g., harmonized definitions of data encryption, anonymization, pseudonymization etc. to assess data management plans for multi-site studies).[37] Second, without guarantees of security and auditability outlined in sIRB reliance agreements, institutional RECs will not trust each other to share study information from other research sites named in the protocol.[37] Third, individual RECs should control their own records, authorize how these records may be accessed and by whom via a permissioned sIRB ledger.[37]

BLOCKCHAIN AND THE FOUNDATIONS FOR ETHICS E-GOVERNANCE IN RESEARCH INVOLVING HUMANS AND THEIR DATA

Beyond powering a shared infrastructural platform upon which a sIRB system could rest, distributed ledger technologies carve a space for ethics e-governance of research involving humans and their data. This e-governance system might adopt the structure of a Global Solutions Network (GSN) not unlike what Tapscott proposes as an approach to governing existing cryptocurrencies.[38] Of the ten interrelated networks that comprise the GSN, three subnetworks in particular would be key to facilitating ethics review mutual recognition internationally:

i) policy networks,
ii) knowledge networks, and
iii) global standards networks

The relationship binding each of the three subnetworks is discussed below, using the Global Alliance for Genomics and Health as an exemplar case of a GSN for ethics review mutual recognition in the data-intensive sciences.

Like those who established early finance regulations in the United States, drafters of the original Common Rule did not (and could not) anticipate how disruptive biotechnologies would revolutionize the nature and scope of biomedical research. Policy/guideline development in an era of rapid scientific advancement means regulators must often act on incomplete information to address specific ethical, legal and social implications such advances pose. Policy networks can be most effectively leveraged when relevant knowledge is both generated and used to support evidence-

based interventions. Knowledge networks achieve this aim and are the sources from which new systems-based solutions emerge. The resultant science governance policies therefore should be informed by relevant empirical evidence available to date, and subsequent technical standards developed to activate the ethical principles supporting the proposed policy/guideline.

The Regulatory and Ethics, as well as Data Work Streams that comprise part of the Global Alliance for Genomics and Health[39] exemplify how the three subnetworks (policy, knowledge and standards) can be leveraged to support ethics review e-governance of genomic and health-related data sharing. By proposing several Essential Elements, the *Ethics Review Recognition* (ERR) *Policy*[32] developed a procedural roadmap for establishing sIRB models based on mutual recognition. The ERR *Policy* further highlighted areas of unmet need, whereby other knowledge networks within the Global Alliance could subsequently contribute with new empirical research. Integrating knowledgeable stakeholders into the policy formulation process is the primary aim of well-organized policy networks according to Tapscott, that "turn decision making from the traditional hierarchical broadcast model to one of consultation and collaboration"[38(p20)]. Many contributors to the final ERR *Policy* went on to advise governmental policy bodies on how to model ethics review mutual recognition in their home jurisdictions. The Essential Elements outlined in the *Policy* complemented many of the provisions that were ultimately adopted in various centralization reforms in Canada, Australia and most recently in the United States.

CONCLUSION

Blockchain technologies powering digital cryptocurrencies still remain elusive in the scientific research (governance) arena. Awareness of distributed ledger technologies are, however, gradually taking hold in healthcare. This is particular true of health information systems[40–44] wherein distributed ledger technologies are helping overcome two competing goals: securing sensitive research and clinical data while ensuring its usefulness and responsible access among more stakeholders in the learning healthcare system. This paper draws on the conceptual and technological virtues of distributed ledger technologies to inspire new forms of ethics (e)governance that occupies an important gatekeeping step to innovation in the learning healthcare system. Improving the quality, transparency and efficiency of ethics review for collaborative multi-site studies can directly translate into quicker turn-around time. Further research is needed, however, to address several pressing ethical-legal challenges in pursuing this novel-use application. First, smart contracts have yet to be used to broker reliance agreements between collaborating institutions and RECs, nor their legal recognition formalized in a regulatory context.

Insofar as a permissioned ledger is used to enable a sIRB system, attestation of the information exchanges between participating RECs remains unclear. Whereas third party miners conduct this integrity-validation on the Bitcoin ledger, it is unlikely that the same role can be fulfilled on a permissioned ledger for sIRB purposes. That is, how and who testifies to the integrity of amendments to the protocol or smart contract terms among the individual research sites (nodes)? Future qualitative, and public perceptions research is planned to investigate the implementation potential of distributed ledger technologies and e-governance in the multi-site ethics review context.

This paper lays the conceptual foundation from which a transition to e-governance can launch. It is furthermore motivated by a pressing need to fill a practical, infrastructural gap in inter-institutional cooperation, data sharing and collaboration among existing governance mechanisms under the revised Common Rule; all areas of which distributed ledger technologies can facilitate towards a more responsible

governance system for biomedical research and innovation in the post genomic era.

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Conflicts of Interest
None

Acronyms
DLT: Distributed Ledger Technologies—
ELSi: Ethical, legal, social implications—
HGP: Human Genome Project
NIH: National Institutes of Health
NSF: National Science Foundation
REC: Research Ethics Committee
sIRB: single Institutional Review Board

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[i] A distinction between multi-site and multi-jurisdictional research should be emphasized here. Whereas multi-site research implies the project takes place across individual

research sites, multi-jurisdictional refers to participating research sites across different legal jurisdictions. Multi-jurisdictional research adds to the procedural complexity of multi-site studies, as RECs must reconcile the regulatory as well as legal differences of the jurisdictions included

[ii] I elaborate elsewhere that the sIRB mandate in the revised Common Rule mandate is more a leap of faith than evidence-based policy[14]. Although many in the ethics governance community recognize the virtues of centralizing ethics review on a conceptual basis[45,46,23,17,47] limited empirical evidence demonstrates the superiority of centralization over the existing institution-by-institution approach from either a cost- or resource-saving perspective[48].