University of British Columbia
Records in the Chain Project

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Contents

Abstract

This document reports on a project, carried out between January 2017 and December 2017, concerning the development of an application of Blockchain technology for the data sharing process for participants in health research. The University of British Columbia's "Records in the Chain" Project had a Ph.D. student, Darra Hofman, embedded in this project.

A. Overview

This case study has been conducted in cooperation with the Centre of Excellence for Prevention of Organ Failure (PROOF) and Deloitte. It discusses a solution developed by PROOF, a not-for-profit organization that develops biomarker tests. PROOF co-hosted by the University of British Columbia and Providence Health Care in Vancouver, British Columbia, Canada, the University of Nebraska Medical Center, a public academic health sciences centre in Omaha, Nebraska, United States, Genome British Columbia, a non-profit genomic research organization in Vancouver, British Columbia, Canada, and Deloitte Inc., the Canadian branch of an international professional services firm.

The case study reports on the development of a Proof-of-Concept (PoC) blockchain solution for managing the sharing of health data for participants in health research. The PoC has provided insight into steps that will need to be taken and issues that will need to be addressed before the solution can be piloted. This paper concentrates on the development of the PoC. Data on the solution was gathered between May 2017 to January 2018.

During the period during which the solution was developed, Darra Hofman, a doctoral student at the School of Library, Archival and Information Studies at the University of British Columbia, was embedded into the PoC development team and participated in three sprints (scrum development cycles), as well as the examination of documentation and reports about the project.

The report uses a version of the InterPARES case study report template specifically adapted for the Records in the Chain Project. The report summarizes the current state of the areas covered in the case study template related to the case study goals. It could also function as a base for further cooperation or studies. Information about the architecture of the system presented in this case study has been validated by PROOF and Deloitte.

Case study goals

The case study has several broad goals, which are to describe:

- How the Blockchain solution is to be used;
- What Blockchain platform is being used for the solution;
- How the Blockchain solution is using information;
- How the Blockchain solution operates;
- How the blockchain solution works under the law;
- How the Blockchain solution affects users, including institutions, researchers, and patients, as well as the broader research community; and
- How the blockchain solution affects the trustworthiness and long-term preservation of records.

B. Statement of Methodology

The research was carried out under the overall direction of Dr. Victoria Lemieux of the University of British Columbia. Dr. Lemieux was first contacted about the project in November 2016 by Dr. Raymond Ng, Chief Information Officer of the PROOF Centre for Excellence (PROOF). Dr. Ng was interested in the possibility of collaborating on a proof of concept to explore the use of blockchain for secure and transparent sharing of clinical and genomic data across borders for which PROOF had received funding from Genome BC under a Can-SHARE New Initiatives Program.[1] The project, which was led by PROOF brought together Providence Health Care, the University of Nebraska Medical Center (UNMC) and Genome British Columbia (Genome BC). It was agreed that the archival perspective provided by the Records in the Chain Project would be useful throughout the development of the PoC; Darra Hofman, a Ph.D. student with the Records in the Chain Project joined the PROOF team (and representatives of the other participating organizations) in meetings and sprints pertaining to the development of the PoC beginning in May 2017. Over the course of 12 weeks, which included 4 development sprints of 3 weeks each, the project and development teams developed a blockchain-based PoC on the Nuco Ethereum platform (described *infra*). The scrums were all led by developers from Deloitte, who came on board for the technical development of the PoC in August 2017. During the meetings, Ms. Hofman, an active participant-observer, took notes including: observations, dialogues and points for further research.

Data gathering for development of the PoC also included holding a "Blockathon" (hackathon for blockchain technology) on August 4, 2017 to generate ideas about design patterns and approaches to implementation relating to the use case from Blockathon participants.[2]

The Deloitte team produced two reports, a high level "Final Report" as well as a more detailed "Technical Documentation" at the conclusion of the PoC, as well as posting the solution code on Github, a version-control repository for storing, sharing, reviewing, managing and developing code. These notes and documents have all been consulted in the process of developing this case study.

[1] PROOF Centre of Excellence. 16 January 2017. "PROOF is awarded a 'New Initiatives' CanSHARE grant to improve data-saring in healthcare research." Accessed February 3, 2018, at: http://www.proofcentre.ca/proof-is-awarded-a-new-initiatives-canshare-grant-to-improve-data-sharing-in-healthcare-research/

[2] The Blockathon was organized by the University of British Columbia's Blockchain@UBC research and education cluster, under the direction of Dr. Victoria Lemieux. Ms. Hofman did not participate in the Blockathon because at the time she was studying for her PhD qualifying examination. For details about the Blockathon, see https://blockchainubc.ca/2017/05/30/blockathon/.

C. Description of Context

1. Provenancial

Test-bed Name

• Prevention of Organ Failure Centre of Excellence, Vancouver, BC, Canada

• Providence Health Care, Vancouver, BC, Canada

• University of Nebraska Medical Centre, Omaha, NE, United States

Location

• Vancouver, BC, Canada and Omaha, NE, United States

Origins of the Test Bed

The three test bed institutions are health research institutions that share clinical and genomic data in furtherance of their research studies. PROOF is a non-profit research organization that "develops biomarker tests to better predict, diagnose, manage and treat a range of diseases."[3] Established by the Networks of Centres of Excellence Secretariat under the Centres of Excellence for Commercialization and Research (NCE CECR) Program, PROOF is co-hosted by the University of British Columbia, a public university, and Providence Health Care. Providence Health Care, one of PROOF's co-hosts, is a non-profit organization which provides health care services in Vancouver, BC, Canada, in partnership with Vancouver Coastal Health and the Provincial Health Services Authority. The University of Nebraska Medical Center is the only public academic health center in Nebraska, and is one of four campuses of the University of Nebraska, a public university in Omaha, NE, United States.

2. Juridical-Administrative

The three testbed sites all perform health research. Providence Health Care and UNMC also provide clinical services. UNMC provides medical education as part of the University of Nebraska. The health research performed in the test bed sites utilizes extremely sensitive clinical and genomic health data. Onboarding study participants into this research is currently a slow, laborious process that requires significant amounts of institutional staff time and paperwork to ensure informed patient consent and protect patient privacy. This is particularly true in the case of data sharing across the border. The test bed sites initiated the PoC to explore the potential of a blockchain solution to improve the efficiency of participant onboarding and data sharing, and to allow participants greater control over and access to their data.

[3] PROOF Centre of Excellence. "About." Accessed February 3, 2018 at http://www.proofcentre.ca/about/s.

3. Legal

The two jurisdictions involved in this study, British Columbia, Canada and the Nebraska, United States, have very different regimes for the management and protection of health data. Canada has omnibus legislation (primarily, but not exclusively, the Personal Information Protection and Electronic Documents Act[4] (PIPEDA)), as well as provincial omnibus and sectoral legislation (in British Columbia, where PROOF and Providence Health Care are located, some laws regulating health data include the Personal Information Protection Act[5], the Freedom of Information and Protection of Privacy Act[6], the Electronic Transactions Act[7] the E-Health Act[8], the Ministry of Health Act[9], the Public Health Act[10], and the Health Authorities Act[11]). UNMC, by contrast, is under the sectoral legislation of the United States and the state of Nebraska, including the Health Insurance Portability and Accountability Act (HIPAA)[12], the Health Information Technology for Clinical and Economic Health (HITECH)[13] Act, the Electronic Signatures in Global and National Commerce (ESIGN) Act[14], and a variety of provisions in the Nebraska Revised Statutes and Nebraska Administrative Code.

A number of standards must be considered in future development of the solution. Relevant standards include:

- Government of British Columbia Information Management/Information Technology Standards.[15]
- Government of Canada Guideline on the Management of Public Key Infrastructure in the Government of Canada.[16]

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[4] *Personal Information Protection and Electronic Documents Act*. S.C. 2000, c. 5. Accessed 12 February 2018 at: http://laws-lois.justice.gc.ca/eng/acts/P-8.6/

[5] *Personal Information Protection Act*. S.B.C. 2003, c. 63. Accessed 12 February 2018 at: http://www.bclaws.ca/Recon/document/ID/freeside/00_03063_01

[6] *Freedom of Information and Protection of Privacy Act*. R.S.B.C. 1996, c. 165. Accessed 12 February 2018 at: http://www.bclaws.ca/Recon/document/ID/freeside/96165_00

[7] *Electronic Transactions Act*. S.B.C. 2001, c. 10. Accessed 13 February 2018 at: http://www.bclaws.ca/Recon/document/ID/freeside/00_01010_01

[8] *E-Health (Personal Health Information Access and Protection of Privacy) Act*. S.B.C. 2008, c. 38. Accessed 12 February 2018 at: http://www.bclaws.ca/Recon/document/ID/freeside/00_08038_01

[9] *Ministry of Health Act,* R.S.B.C. 1996, c. 301. Accessed 12 February 2018 at: http://www.bclaws.ca/civix/document/id/complete/statreg/96301_01

[10] *Public Health Act*. S.B.C. 2008, c. 28. Accessed 12 February 2018 at : http://www.bclaws.ca/civix/document/id/complete/statreg/08028_01

[11] *Health Authorities Act*. R.S.B.C. 1996, c. 180. Accessed 12 February 2018 at: http://www.bclaws.ca/civix/document/id/complete/statreg/96180_01

[12] *Health Insurance Portability and Accountability Act of* 1996. 104 Public Law 191. Accessed 13 February 2018 at https://www.gpo.gov/fdsys/pkg/PLAW-104publ191/html/PLAW-104publ191.htm

[13] *Health Information Technology for Clinical and Economic Health Act.* 42 U.S.C. §300jj; 42 U.S.C. §17921 et seq. 111 Public Law 5. Accessed 13 February 2018 at https://www.healthit.gov/sites/default/files/hitech_act_excerpt_from_arra_with_index.pdf

[14] *Electronic Signatures in Global and National Commerce Act.* 15 U.S.C. §§7001 – 7031. Accessed 13 February at: https://www.law.cornell.edu/uscode/text/15/chapter-96

[15] *See, e.g.,* British Columbia Office of the Chief Information Officer, Ministry of Technology, Innovation, and Citizens' Services. 2014. Information Management/Information Technology Standards Manual. Accessed 13 February 2018 at https://www2.gov.bc.ca/assets/gov/government/services-for-government-and-broader-public-sector/information-technology-services/standards-files/standards_manual.pdf.

[16] Government of Canada. 2011. "Guideline on the Management of Public Key Infrastructure in the Government of

- Government of Canada Common Services Policy.[17]
- Government of Canada Cloud Adoption Strategy.[18]
- Genome Canada Data Release and Sharing Policies.[19]
- The Uniform Electronic Transactions Act.[20]
- Information and Communication Technology (ICT) Final Standards and Guidelines.[21]
- United States Federal Public Key Infrastructure Guides.[22]
- OAuth 2.0.[23]

Funding

The PoC is funded by a "New Initiatives" Canadian International Data Sharing Initiative (Can-SHARE) grant, funded by Genome British Columbia and Health (Genome BC), awarded to and administered by PROOF to explore how "[u]sing Blockchain technology for healthcare data has the potential to streamline data-sharing between researchers, while also giving patients oversight of their own data." [24]

Resources (Physical)

PROOF occupies a suite in an office building in downtown Vancouver, BC. The physical resources of Providence Health Care (which includes three hospitals, a dialysis facility, a clinic, a hospice, and residential care facilities) or UNMC (which includes a College of Medicine College of Nursing, College of Pharmacy, College of Dentistry, College of Public Health, Graduate College, College of Allied Health Professions, cancer research and treatment institutions, and a hospital partner, Nebraska Medicine) were not examined for this study. However, from discussion of workflows with researchers in Providence Health Care's St. Paul's Hospital and UNMC, each site has a mix of paper and electronic health records, as well as a staff of health information professionals, filing clerks, and other records professionals.

Human Resources

PROOF is overseen by an eight member board of directors. There are six members of the management team, six members of the operations team, and six trainees.

4. Procedural

Although there are a number of records processes related to research data, the PoC

Canada." Accessed 13 February 2018 at https://www.tbs-sct.gc.ca/pol/doc-eng.aspx?id=20008&section=html.

[17] Government of Canada. 2006. "Common Services Policy." Accessed 13 February 2018 at: https://www.tbs-sct.gc.ca/pol/doc-eng.aspx?id=12025

[18] Government of Canada. 2016. "Cloud Adoption Strategy." Accessed 13 February 2018 at: https://www.canada.ca/en/treasury-board-secretariat/services/information-technology/cloud-computing/government-canada-cloud-adoption-strategy.html

[19] Genome Canada. 2016. "Genome Canada Data Release and Sharing Policies." Accessed 13 February 2018 at: https://www.genomecanada.ca/sites/default/files/publications/gcdatasharingpolicies16-09-23.pdf

[20] National Conference of Commissioners on Uniform State Laws. 1999. Uniform Electronic Transactions Act. Accessed 13 February 2018 at: http://www.uniformlaws.org/shared/docs/electronic%20transactions/ueta_final_99.pdf

[21] 36 C.F.R. §§1193 – 1194. Accessed 13 February 2018 at: https://www.federalregister.gov/documents/2017/01/18/2017-00395/information-and-communication-technology-ict-standards-and-guidelines

[22] Government of the United States of America. General Services Administration. Accessed 13 February 2018 at: https://fpki.idmanagement.gov/

[23] Accessed 13 February 2018 at: https://oauth.net/2/

[24] Op. cit., *supra* fn 1.

focused on processes of registration and enrollment which are necessary for onboarding participants into a research study. Currently, the process of accessing clinical data requires a number of points of contact, and is largely done manually, through phone calls and emails among research coordinators. A researcher will seek participants for a program. The potential participant's informed consent must be sought and documented. If the patient consents to the use of his/her/their data in the study, the site holding this data (such as a hospital), then forwards the requested records to the researcher.

5. Documentary

There is no archivist within PROOF. Providence Health Care and UNMC employ a number of records and health information professionals, however, none of those were directly involved with this project. Clinical and genomic data are stored in systems deemed to be compliant with regulations, including paper record keeping systems and electronic health data systems. The onboarding system is largely managed on paper by the Clinical Research Director in conjunction with the researchers.

6. Technological

The existing electronic health records systems and clinical data management systems meet regulatory requirements and other standards, however, these systems are not currently used for managing the patient enrollment and onboarding process. Instead, that process is managed manually.

Answers to the Project's Applicable Set of Questions:

- *How is/will the Blockchain be used?*

The PoC discussed in this case study examined the use of a blockchain based system for enrolling study participants in healthcare-related research programs in order to address three challenges:

- The role of the researcher as intermediary between their research unit, hospitals, and potential study participants. Currently, researchers must serve as intermediaries to coordinate among study participants, their research centre, and institutions such as hospitals in order to receive consent to use clinical or genomic patient data. This makes the research process slow and cumbersome. Blockchain-based consent could be a key enabler of a single-window research centre solution for consent management.
- Participants' limited ability to see how their data is used in studies and their challenges in accessing their data. Blockchain-based consent could give participants a greater window into how their data are being used.
- The time-consuming, resource-intensive nature of the current manual system, which takes, on average, sixty days to complete (i.e., onboard a participant into a study). Blockchain-based solutions could use digital artifacts and smart contracts to introduce efficiencies into the process of onboarding and enrolling study participants.

Budin-Ljosne, et al., in their article advocating "Dynamic Consent," outline some of the challenges that make consent so time-consuming and resource-intensive:

> [R]esearch participants often do not understand the content of the information sheet or the consent form […] [some] may want to go through the information several times and may have additional questions or concerns. […] If new research needs arise that were not foreseen and included in the original consent document, collecting new consent from research participants may be expensive and burdensome […] If multiple consents are collected over time, keeping records of these consents can be complicated, particularly in cohort studies, or in projects spanning several years and multiple iterations where paper consent forms are stored in several institutions.[25]

As articulated in the Deloitte Final Report on the development of the PoC, the solution team broadly sought to evaluate the use of blockchain technology in driving process efficiency and creating a trust mechanism across research entities so as to provide for near real-time tracking of privileges to study participant data and understand how blockchain technology would help provide participants with control over their data.[26] In some ways, this is a reimagining of consent, from "a one-time event [to a process that] is ongoing, dynamic, and granular, allowing

[25] Budin-Ljosne, Isabelle, Harriet J.A. Teare, Jane Kaye, Stephan Beck, Heidi Beate Bentzen, Luciana Caenazzo, Clive Collett, Flavio D'Abramo, Heike Felzmann, Teresa Finlay, Muhammad Kassim Javaid, Eric Jones, Visnja Katic, Amy Simpson, and Deborah Mascalzoni. 2017. "Dynamic Consent: a potential solution to some of the challenges of modern biomedical research. *BMC Medical Ethics* 18

[26] Deloitte, "Enabling Secure & Transparent Sharing of Clinical and Genomic Data Across Borders: Blockchain-based Proof-of-Concept (PoC)", Final Report, December, 2017.

participants to change their minds."[27] Such a solution could, in theory, address the issues raised by Budin-Ljosne et al., allowing patients to spend as much time as they need reviewing the consent documents on their own, allowing new consents to be collected in a relatively timely and low cost manner, and providing a centralized repository for consents that could be made accessible even if researchers and projects moved to different institutions.

The PoC used the Blockchain to build a single decentralized, disintermediated system to serve as an interface between participants, researchers, and hospitals. The system allows participants to enroll and consent through a webportal, and access timestamped audit trails of their interactions with the system. It allows researchers to create studies and invite participants, and also allows researchers to request patient data from other institutions within the system; the data sharing user journey, below, shows how the system integrates and coordinates the steps and participants in the previously manual process of researchers requesting data from other institutions.

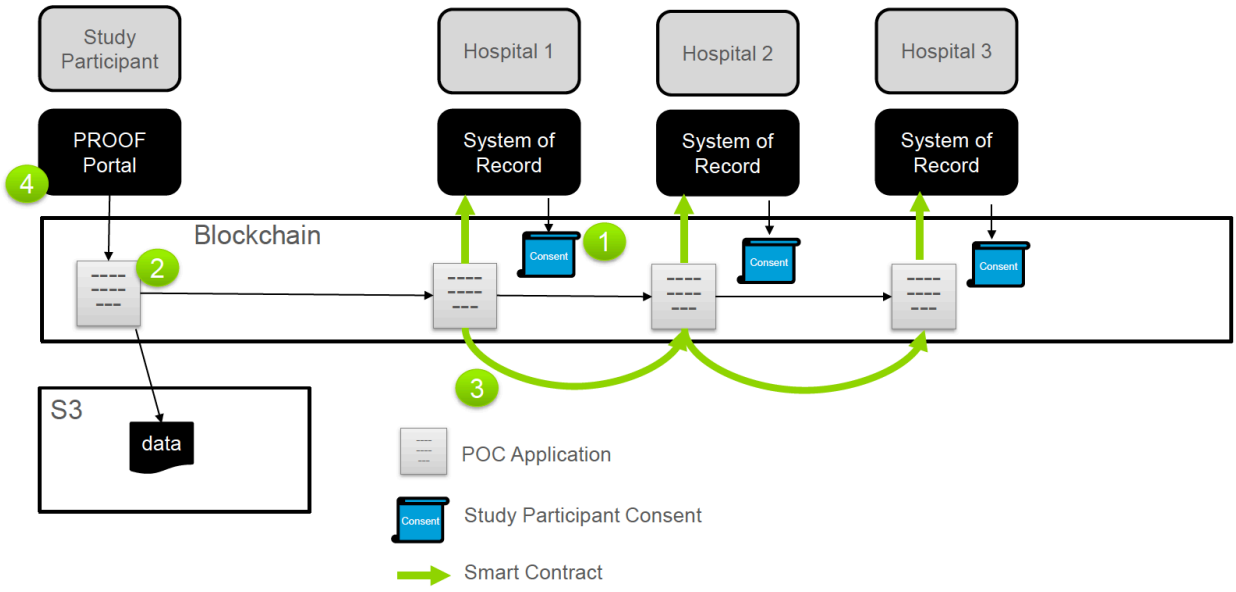

Figure 1: Overview of the Proof-of-Concept (PoC) [Source: Deloitte, "Final Report"]

- *What Blockchain platform is being used? How is the Blockchain using information? How*

[27] Kirby, Emily, Ma'n H. Zawati, and Bartha Maria Knoppers. 2013. "Electronic Consent to Health Research in Canada." *The Canadian Bar Review* 91: 417, at 432.

is the Blockchain run?

The solution uses a Nuco Ethereum private blockchain kernel with a custom ReactJS front-end Graphical User Interface (GUI), a Play (JS/Java) middleware application, and an Amazon S3 file server, with Amazon Web Services (AWS) providing the infrastructure as illustrated below:

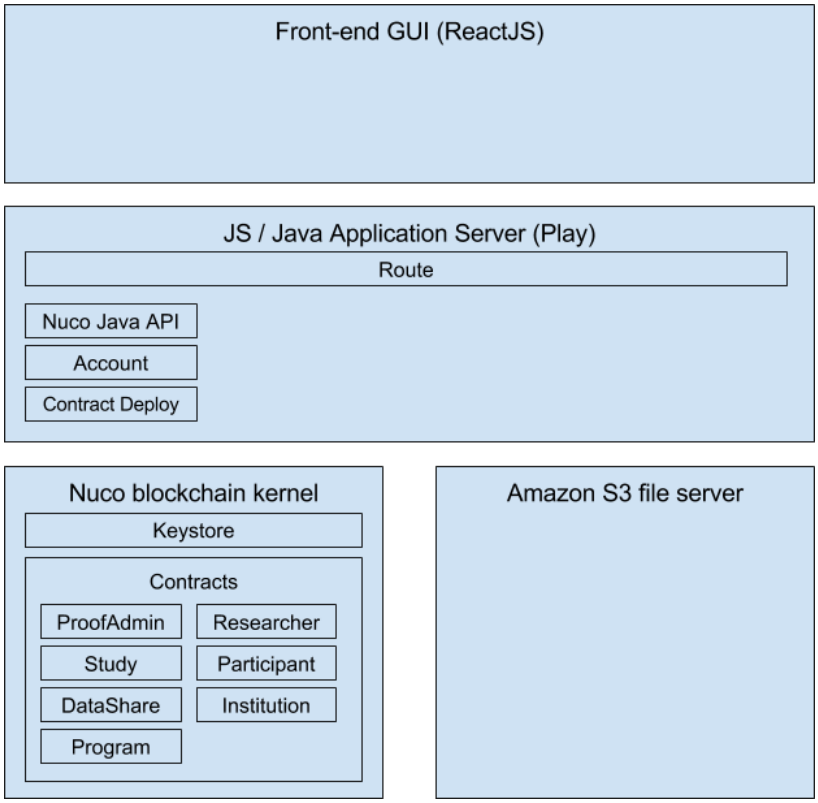

Figure 2: Logical Architecture from Deloitte Technical Report

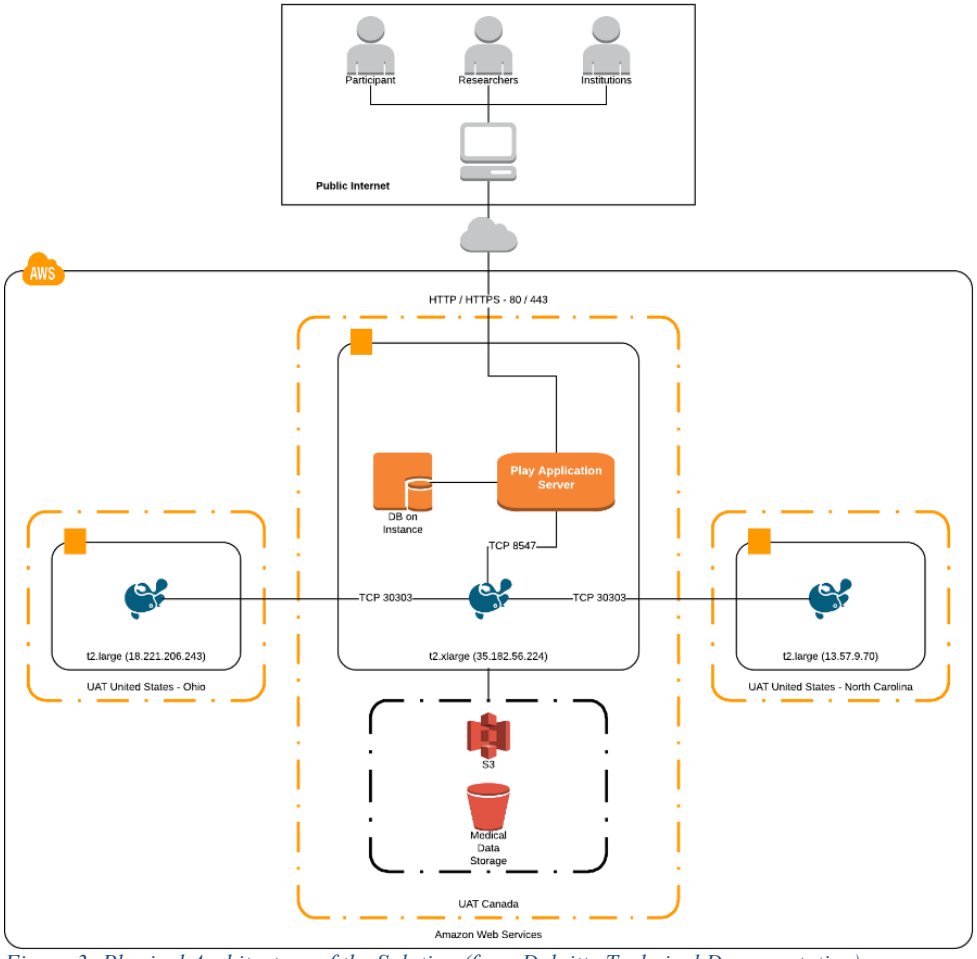

Figure 3: Physical Architecture of the Solution (from Deloitte Technical Documentation)

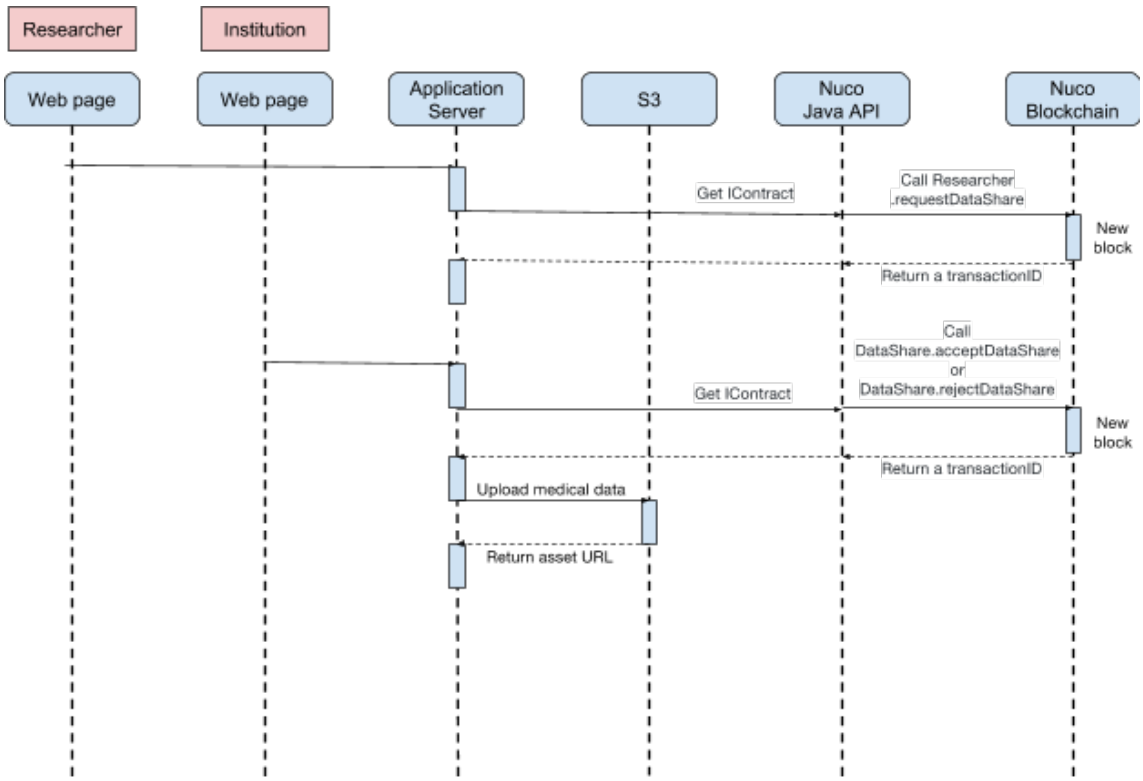

Figure 4. "Data Share" User Journey from Deloitte "Technical Documentation"

Nuco is a blockchain platform that is an extension of Ethereum. Ethereum is an open source blockchain protocol suite originally designed as an alternative to the Bitcoin blockchain platform. Beginning in 2016, Nuco built a general-purpose designed, high performance, scalability, high-modularized and enterprise-centric blockchain infrastructure (see Figure 5). The Nuco enterprise blockchain had been introduced into several enterprise PoC projects already at the start of the PROOF PoC project. The Nuco blockchain is implemented in Java, a powerful programming language that has complete, robust, well-maintained libraries, and strong community and enterprise support. Nuco owns a software license and released the binary installer and gave authorized use to Deloitte for the purposes of developing the PoC. For this project, Deloitte deployed version 1.0.3.17-08-18.61d070e build as a private network on the Amazon cloud server.[28] This choice was made for the following reasons:

- "**Scalability**: The Nuco blockchain can deploy a maximum of 64 nodes as a blockchain network under Byzantine Fault Tolerance (BFT) consensus algorithm. Additionally, the Amazon cloud server can easily duplicate, relocate and enlarge the server instance.
- **Application**: Only expose the application server to the end-users. This decreases the risks of the blockchain kernel being attacked by unfriendly connection or DDoS.
- **Maximize the system's performance**: As of the time of this report, the Ethereum public network can only handle an average of 4 transactions per second. This throughput does not meet the needs of most enterprise environments. However, the Nuco blockchain can handle an average of 500 transactions per second when there are less than 16 nodes

[28] Deloitte, Technical Report

distributed in the network."[29] The Nuco blockchain uses a customized version of the Practical Byzantine Fault Tolerance consensus algorithm (NBFT) to confirm blocks in the chain using a "single-vote consensus which any node in the network can submit, rather than relying upon mining power.

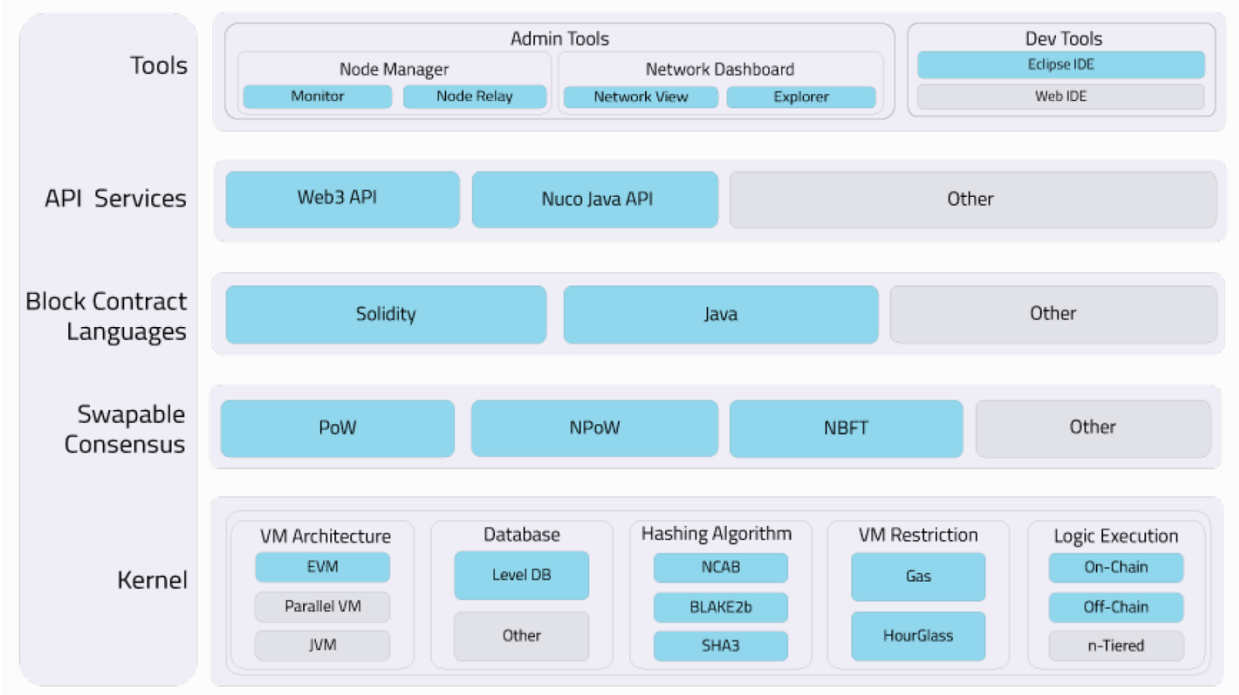

Figure 5: Nuco Architecture [Source: Deloitte Technical Report]

Nuco Ethereum was chosen because it is enterprise oriented, scalable, and modularized, with an out-of-the-box Nuco-customized Byzantine Fault Tolerance consensus mechanism (NBFT) that is well suited to a project where the participants in the Blockchain are known and semi-trusted. A detailed comparison with other blockchain platforms that may be suitable to use (e.g., Ethereum Geth or Hyperledger Fabric) remains to be completed.

Nuco's Java Application Interface (API) is designed to bridge the Nuco blockchain network with Java specific applications (see Figure 6). The main purpose of the API implementation is to increase transaction throughput and allow for customization of enterprise-specific APIs. It uses multi-threading TCP/IP daemon and binary protocol to alleviate network traffic pressure and deliver high-performance throughput.[30] It reduces network congestion between client and network through holding a persistent connection when events, when triggered, are pushed to the client. It is also customized to function in an NBFT consensus environment and exposes more kernel-specific information to the user. This is said to make it ideal for small-to-medium sized private blockchain implementations. The Nuco Java API was integrated into the Play framework in order to bridge the front-end user web interface to the back-end Nuco blockchain kernel.[31]

[29] Deloitte, "Blockchain Clinical and Genomics Data Sharing: Technical Documentation" [hereinafter referred to as Deloitte. Technical Report], December 2017, p. 11
[30] Ibid.
[31] Op. Cit.

Solidity smart contracts control the workflow, hold key timestamps and status information. A total of 7 smart contracts were developed for the PoC as follows:

1. contract Researchers: Stores institutional researchers' information, settings and involved programs;
2. contract Participant: Stores participants' information, settings, involved programs (represented as the studies) and audit history:
3. contract Program: Stores programs' information, settings and involved people;
4. contract Study: Stores status, action and data sharing of enrolled participant:
5. contract DataShare: Assists in recording all data share entities on the Proof system, including which studies are part of the request, and if it was accepted/rejected;
6. contract Institution: Assists in generating an institution specific entity that represents the part that interacts with data shares;
7. contract ProofAdmin: Used for the data preload, creating researcher, participant and program.[32]

The data model in Figure 6 illustrates the data elements involved in the Solidity smart contracts, as well as their fields and relationships.

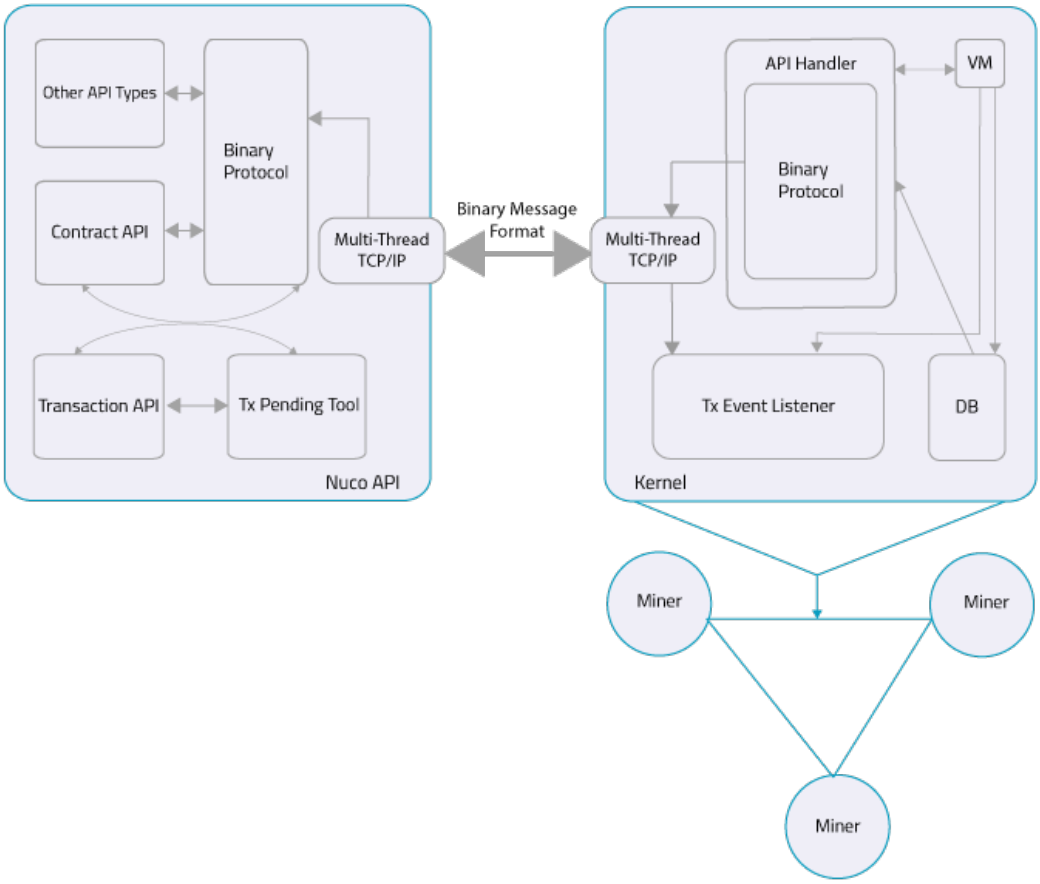

Figure 6: Nuco's Java API Architecture [Source: Deloitte Technical Report]

[32] Ibid.

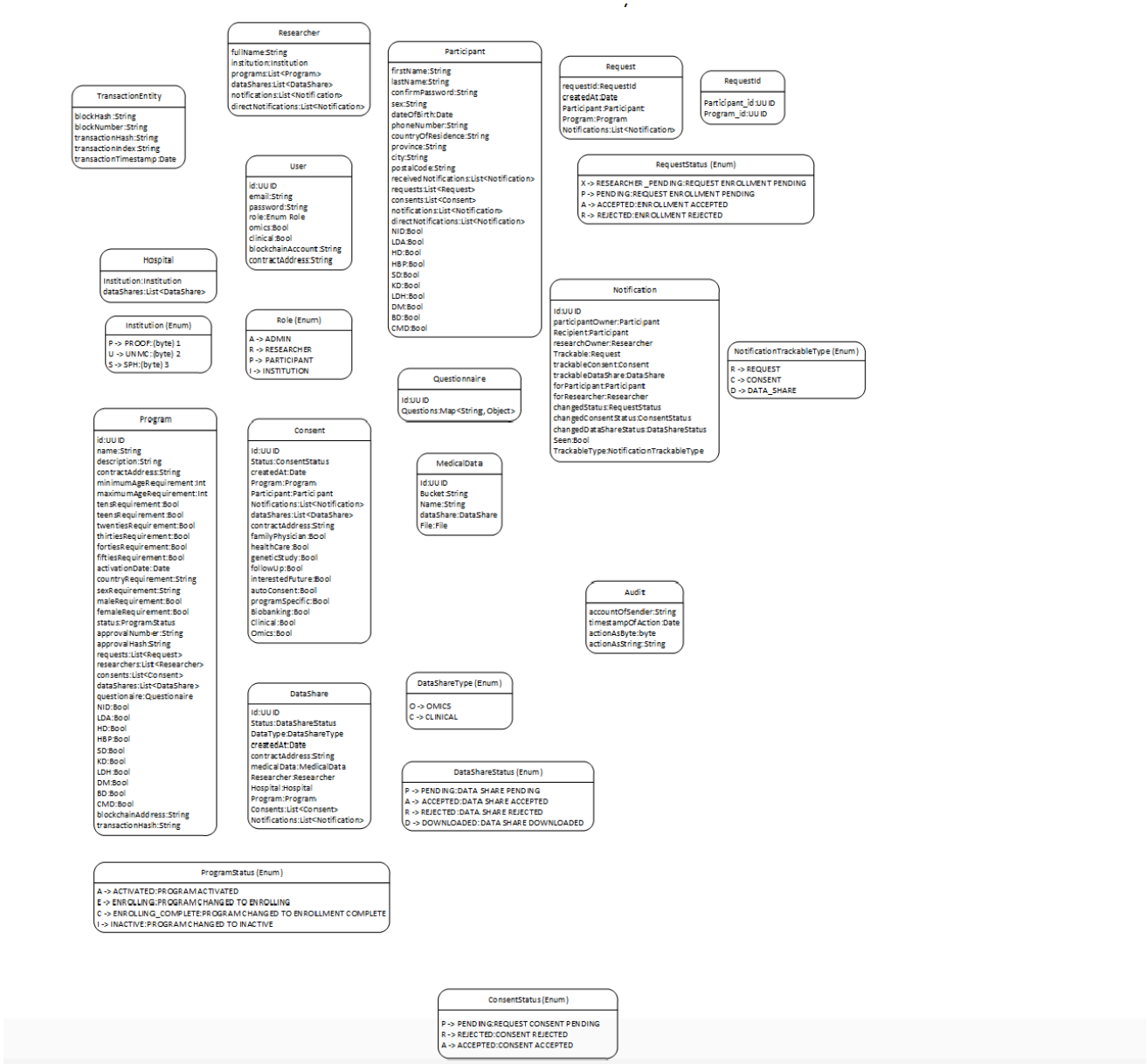

Figure 7: Solidity Smart Contract Data Elements [Source: Deloitte Technical Report]

Amazon S3 was chosen for the PoC because it permits choice of region with regard to where clinical/genomic data is hosted. Due to data localization laws in British Columbia (discussed in greater detail *infra*), personally identifiable information (including health information) must be hosted within the province. Although this solution is currently only a PoC, the ultimate off-chain storage solution will be an important factor in the solution's build, because the clinical and genomic data, which will not be stored on chain, must be secure for data transfers between research and clinical sites.

The user interacts with the ReactJS web interface (study participant mockup in Figure 4, below). The front end is split into components or widgets, such as a header, navigation bar, and main area. The interface the user encounters depends upon the user's role (participant, researcher, clinical site). ReastJS was chosen to help render reusable components and hold HTML code and JS logic. This allows for dynamic display of content and updates to the GUI whenever updates occur. Redux was used for the architecture to manage application states and statement management and wraps around JS components. This helps simplify applications with complicated data scenarios and chains of events, such as this PoC, with the following attributes:

- **Store:** Centralizes all states in one big JavaSrcript object
- **Actions**: Handles/dispatches actions, has payload of data
- **Reducers**: Multiple reducers that modify pieces of data off of store immutably.[33]

ReactJS was cho

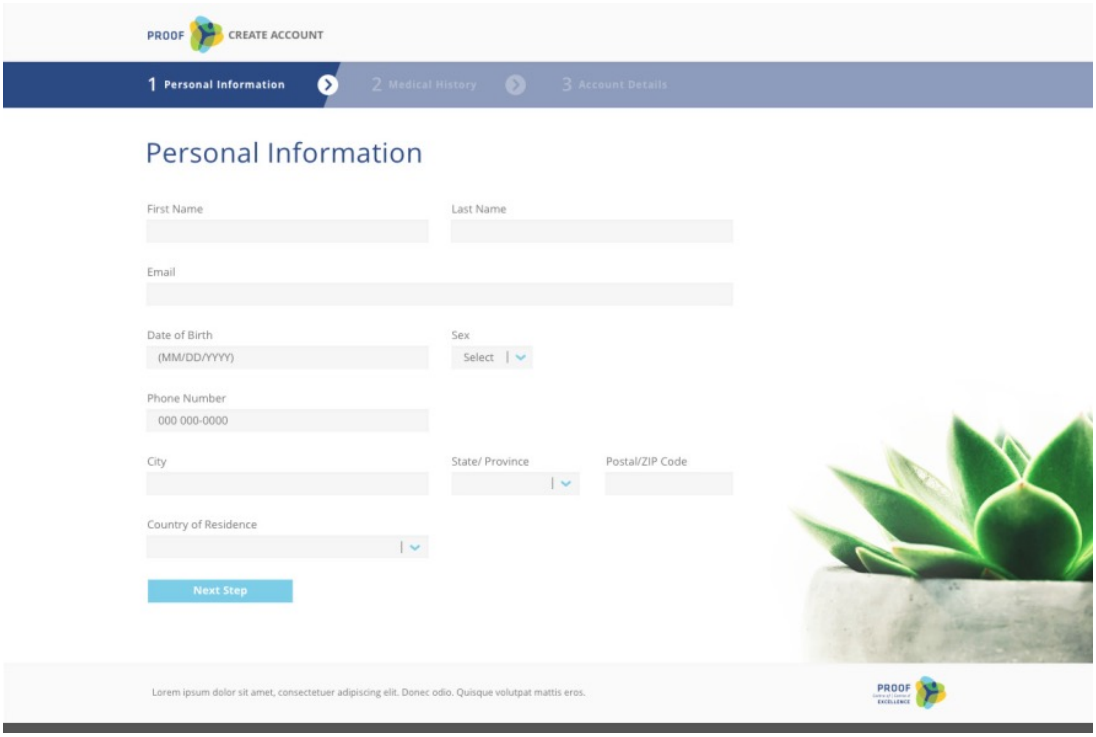

Figure 8. Patient Registration Screen from Deloitte Report on Study Participant Screens

Transaction signing is done using the Nuco client. Key pairs for signing are stored within the Nuco kernel, and accessed when there is a need to sign (e.g., user would like to grant consent for use of their data). In order to know which keys to use, the platform maintains a list of key

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pairs matched to a user or an entity, and their relative addresses. There is also an extra piece of data needed to use the keys, which is the passphrase. All of this information is stored on a database. With this information, the application can then unlock a user key pair, and sign any transaction.

If the mapping between users and key pairs is done correctly, and no compromise of the platform has occurred, then it is safe to assume that the business logic related transactions signed by any user, where performed by that user, provides for non-repudiation (i.e., that a user has given consent for use of their data).

Another consideration is how key signing should be handled for purposes of future integrations. In such cases, account management must be implemented to associate keys to integrated applications. Alternatively, integrating systems can manage their own keys and send transactions already signed. This has the advantage of reducing the trust that must be placed in the middleware code, but transaction signing must be implemented there since Nuco relies upon local wallets (i.e., keys) in the middleware. The Deloitte Technical Report also recommends future implementation of a Hardware Security Module (HSM) for key management, as discussed in more detail *infra.*

Additional features of the solution that may be included in a post-PoC release include:

- Extension of data models to include other stakeholders (e.g., Research Ethics Board, other research groups, government, and family doctors)
- Development of detailed access control matrix
- Onboarding/integration toolkits (registration, administration panels, etc)
- Contract registry
- Administration pages
- Additional APIs
- Development tools
- Consent wallet for participant to manage all consents
- "Smart" recommendations of study and participants based on attributes
- Mobile app for study participants (Researchers and Hospitals would use web app)
- Listener as part of middleware or off-chain components to listen for events that happen on chain
- Hardware Security Module for key management

- *How does the blockchain work under the law?*

Health data, including clinical data and genomics data, is subject to significant legal and regulatory controls. The following analysis focus primarily on the legal context in Canada and specifically, British Columbia. This is due in part to the fact that both the Department of Health and Human Services (HHS) and the Food and Drug Administration (FDA) in the United States have stated in their guidance[34] that a variety

[34] U.S. Department of Health and human Services Office for Human Research Protections (OHRP) and Food and Drug Adminstration Center for Drug Evaluation and Research (CDER), Office of Good Clinical Practice

of electronic informed consent (eIC) approaches are acceptable to meet informed consent requirements under the statutes governing those bodies' approval of human subject research (45 CFR §46 and 21 CFR §11, §50, and §56, respectively). Although the guidance is non-binding, it is indicative of general acceptance of eIC in the United States. The legal status of eIC in Canada is less settled. The discussion of data localization laws focuses exclusively on British Columbia, as there are currently no data localization laws in the United States.

Legal recognition, admissibility and weight

In order to have legal effect, records must have legal recognition. The legal status of blockchain based records is evolving quickly and jurisdiction dependent. In British Columbia, for example, the Electronic Transactions Act, which is meant to provide for the use and enforceability of electronic records[35], provides that "A requirement under law that a record be in writing is satisfied if the record is (a) in electronic form, and (b) accessible in a manner usable for subsequent reference."[36] This drafting can be interpreted to include blockchain records, although this interpretation has not been tested in the courts given the novelty of this technology. According to this interpretation of the law, the consents anchored in the PoC Blockchain would be enforceable due to their electronic nature. The Electronic Transactions Act further provides that, "If there is a requirement under law for the signature of a person, that requirement is satisfied by an electronic signature."[37][38] Furthermore, the courts have been fairly broad in their interpretation of what constitutes an "electronic signature," explicitly rejecting the argument that such signature needs to rise to the level of a digital signature and accepting as informal a signature as a name written in an email.[39] Thus, both consent forms and participant signatures obtained and preserved electronically are likely to be legally enforceable. Indeed, given the ongoing nature of consent, the blockchain's timestamped consent, and a digital system's ability to permit participants to revoke consent at any time, could be considered an improvement on traditional consent processes (and records) from the perspective of protecting and ensuring participants' rights.

This presumption of legality is further strengthened by the language in the Personal Information Protection and Electronic Document Act (PIPEDA). PIPEDA contemplates both "electronic signatures" and "secure electronic signatures" in Part 2, which provides for:

> the use of electronic alternatives […] where federal laws contemplate the use of paper

(OGCP), Center for Biologics Evaluation and Research (CBER) and Center for Devices and Radiological Health (CDRH). 2016. "Use of Electronic Informed Consent Questions and Answers; Guidance for Institutional Review Boards, Investigators, and Sponsors". Accessed 13 February 2018 at: https://www.fda.gov/downloads/drugs/guidances/ucm436811.pdf

[35] The act excludes from its application wills, trusts created by wills, power of attorney, documents that create or transfer interests in land and that require registration to be effective against third parties, and other records prescribed in the regulations. *Electronic Transactions Act,* SBC 2001, c.10, s. 2(4).

[36] *Electronic Transactions Act*, SBC 2001, c. 10, s. 5.

[37] *Electronic Transactions Act*¸ SBC 2001, c. 10, s. 11(1)s.

[38] It should be noted, however, that individual institutions may require "wet" signatures. The University of Victoria Research Ethics Board, for example, explicitly excludes electronic signatures as enforceable on their applications for ethics approval.

[39] See *Johal v. Nordio,* 2017 BCSC 1129.

to record or communicate information or transactions."[40] Under s. 48(1) of PIPEDA, regulations have been made which define a "secure electronic signature" as "a digital signature that results from completion of the following consecutive operations:

(a) Application of the hash function to the data to generate a message digest;

(b) Application of a private key to encrypt the message digest;

(c) Incorporation in, attachment to, or association with the electronic document of the encrypted message digest;

(d) Transmission of the electronic document and encrypted message digest together with either

  i. A digital signature certificate, or

  ii. A means of access to a digital signature certificate; and

(e) After receipt of the electronic document, the encrypted message digest and the digital signature certificate or the means of access to the digital signature certificate,

  i. Application of the public key contained in the digital signature certificate to decrypt the encrypted message digest and produce the message digest referred to in paragraph (a),

  ii. Application of the hash function to the data contained in the electronic document to generate a new message digest,

  iii. Verification that, on comparison, the message digests referred to in paragraph (a) and subparagraph (ii) are identical, and

  iv. Verification that the digital signature certificate is valid.[41]

The secure electronic signature regulations are meant to provide an electronic alternative for records which require a high degree of trustworthiness under PIPEDA, such as "sworn statements (section 44), statements declaring truth (section 45), witnessed signatures (section 46), originals (section 42), documents under seal (section) and documents as evidence or proof (section 36)."[42] These records are some of those that require the highest degree of formality and proof of reliability. Although there is no statutory language addressing the requirements for informed consent documentation, it is a reasonable assumption, given how such documents are currently treated, that any formalities imposed would not exceed those placed on sworn statements.

Data localization, protection and privacy

[40] *Personal Information Protection and Electronic Documents Act*. S.C. 200, c.5, s. 31, s. 32.
[41] *Secure Electronic Signature Regulations*. SOR/2005-30, s. 2.
[42] McIsaac, Barbara and Howard R. Fohr. "Legal update, Canada: PIPEDA's Secure Electronic Signature Regulations have been published". *Digital Evidence and Electronic Signature Law Review* 6(2): 1-2 at 1. Accessed 13 February 2018 at http://sas-space.sas.ac.uk/5262/1/1752-2369-1-SM.pdf

As mentioned *supra*, the Amazon S3 File Storage solution was chosen in part because of British Columbia's data protection and privacy laws. In particular, s.30.1 of the Freedom of Information and Protection of Privacy Act[43] (FIPPA) provides that, "a public body must ensure that personal information in its custody or under its control is stored only in Canada and accessed only in Canada," absent an exception. Although the Office of the Information and Privacy Commissioner for British Columbia has held that Providence Health Care Society is not a public body under FIPPA,[44] the University of British Columbia, which co-hosts PROOF, is a public body for purposes of FIPPA. A safe, albeit conservative, assumption would be that PROOF is obligated to abide by the data residency provisions of FIPPA. Thus, solutions that host the data outside of Canada may not be compliant depending on the data, use case, and other factors.

Data residency localization, in and of itself, however, i not sufficient to provide privacy protection for research data, especially genomic data. "By nature, the genome encodes a sensitive yet heritable signature of an individual that is marked by genetic variation reflecting one's ancestry and disclosing one's susceptibility to health and diseases."[45] Both Canada and the United States have passed genetic non-discrimination acts in light of the potential medical, professional, legal and social consequences that individuals might face should their genomic information be disclosed.[46] The risk of reidentification is one that requires particular attention; private data can be discerned from seemingly innocuous data within the results of genomic research. Im et al., in a study of genome-wide association studies (GWASs), found that "regression coefficients for many SNPs [single nucleotide polymorphisms] can reveal [a] person's participation and for participants his or her phenotype with high accuracy."[47] Other research has shown that research participants can be linked to a sample through "pooled SNP disease studies[48] [and] data sets of RNA expression levels in tissue samples[49]"[50] Erlich and Narayan identify a full fourteen different types of attacks for breaching genetic privacy."[51] Thus,

[43] In this particular use case, we are presuming that the participants would be treated as public bodies, obligated to comply FIPPA. By contrast, private organizations in B.C. are obligated to comply with the *Personal Information Protect Act (PIPA),* S.B.C. 2003, c. 63. However, PIPA states explicitly that the act does not apply to "personal information if the *Freedom of Information and Protection of Privacy Act* applies (s. 3(2)(c)), and therefore it has not been analysed.

[44] [2009] B.C.I.P.C.D. No. 36

[45] Shi, Xinghua, and Xintao Wu. 2017. An overview of human genetic privacy. *Annals of the New York Academy of Sciences* 1387 (1): 61-72.

[46] Genetic Non-Discrimination Act, S.C.2017, c.3; and Genetic Information Non-Discrimination Act, 29 USC §216(e), 29 USC §1132.

[47] Im, Hae Kyung, Eric R. Gamazon, Dan L. Nicolae, and Nancy J. Cox. 2012. On sharing quantitative trait GWAS results in an era of multiple-omics data and the limits of genomic privacy. The American Journal of Human Genetics 90 (4): 591-8.

[48] Homer, Nils, Szabolcs Szelinger, Margot Redman, David Duggan, Waibhav Tembe, Jill Muehling, John V. Pearson, Dietrich A. Stephan, Stanley F. Nelson, and David W. Craig. 2008. Resolving individuals contributing trace amounts of DNA to highly complex mixtures using high-density SNP genotyping microarrays. PLoS genetics 4(8): e1000167.

[49] Schadt, Eric E., Sangsoon Woo, and Ke Hao. 2012. Bayesian method to predict individual SNP genotypes from gene expression data. Nature genetics 44(5): 603-608.

[50] Weil, Carol J., Leah E. Mechanic, Tiffany Green, Christopher Kinsinger, Nicole C. Lockhart, Stefanie A. Nelson, Laura L. Rodriguez, and Laura D. Buccini. 2013. NCI think tank concerning the identifiability of biospecimens and "omic" data. Genetics in Medicine 15(12): 997-1003.

[51] Erlich, Yaniv, and Arvind Narayanan. 2014. Routes for breaching and protecting genetic privacy. Nature

the privacy protections built into any form of the solution dealing with real participant data (as opposed to dummy data for a PoC) must be built to provide the highest level of privacy protection. As built, the PoC solution does offer privacy protections. It encrypts user passwords, key pair unlocking passphrases, and study participant data shares using BCrypt server-side encrypting with Amazon S3-managed encryption keys (SSE-S3). Deloitte recommends several modifications for a live build that would enhance the privacy protecting nature of the solution, including: use of an access control matrix, use of a hardware security module, and reconsidering the choice of blockchain platform (in Deloitte's analysis, Hyperledger Fabric offers privacy out of the box, whereas Nuco and Ethereum Geth both require custom development to provide privacy protection).

- *How does the blockchain affect others?*

Participants: "The central concern of medical research ethics is to protect the interests of research participants while allowing beneficial research to proceed."[52] The primary means by which participants assert their autonomy – and their interests – in the research process is through the consent process, in which the participant gives *voluntary*, *informed* consent to the use of his/her/their data. Current systems for managing both clinical and research data, however, are problematic in how they protect participants' interests. User-centric models, such as the solution in this study, permit much more granular consent; instead of consenting once, broadly, to a myriad of potential research uses, participants can consent to each use without having to go through a time-intensive manual onboarding each time. Participants also have greater access to their data and its uses through this solution. Because participants have the option to sign up for studies, participants who might have been missed through traditional recruitment could be included through the use of this solution (although the solution carries the risk of excluding participants on the wrong side of the digital divide, a group which overrepresents elderly, low income, and ethnic and racial minority participants). Finally, because the participant, his/her/their consents, and his/her/their data (including clinical data shared from providers who participate in the system) can be seamlessly and securely linked through the system, participants can participate by sharing data that has already been collected pursuant to their care, without necessarily having to submit to further data collection.

Researchers: Researchers need good data to do good research. Currently, finding the right participants with the right data and onboarding them to the right study consumes significant amounts of time and money – if the right participants can even be found. The solution helps researchers in two ways. Firstly, it permits them to create studies in the solution, to which participants can then onboard themselves. Secondly, it greatly simplifies the process of both seeking data – be it healthcare data, biologic samples, or full datasets – from other institutions, and of obtaining and documenting consent to use that data. This permits the researchers to spend less time finding data, and more time analyzing data.

Reviews Genetics 15(6): 409-421.

[52] Kaye, Jane, Liam Curren, Nick Anderson, Kelly Edwards, Stephanie M. Fullerton, Nadja Kanellopoulou, David Lund, Daniel G. MacArthur, Deborah Mascalzoni, James Sheperd, Patrick L. Taylor, Sharon F. Terry, and Stefan F. Winter. 2012. "From patients to partners: participant-centric initiatives in biomedical research." *Nature Reviews: Genetics* 13: 371 – 376 at 371.

Research Institutions: "One of the main barriers [in heath research] is that healthcare and health research data reside in silos that do not communicate with one another."[53] This solution, by making it easier for institutions to track requests and consents in a transparent way, Furthermore, "it still takes months or years – and often thousands of dollars per patient – to locate individuals or biological samples for clinical trials that may save or improve lives."[54] Indeed, the National Research Council of the National Academies (NRC) states that the "current discovery model offers no path toward economically sustainable integration of data-intensive biology with medicine."[55] This solution offers at least some means to address two aspects of the cost problem. Firstly, it significantly reduces the inefficiencies associated with consent management, thereby reducing both staff time spent on managing consent, and the non-staff resources that must be devoted to consent management. Secondly, it will hopefully reduce the cost of participant recruitment, in part by allowing participants to self-recruit, and in part by facilitating data sharing between research and healthcare institutions.

- *How does the blockchain affect the trustworthiness and long-term preservation of records?*

This section presents an archival theoretic evaluation of the aforementioned solution.

In archival science, a record[56] is said to be trustworthy if it is assessed as being accurate, reliable and authentic. These main attributes can be decomposed as shown in Figure 9. Each of these characteristics is discussed below in relation to the solution and issues presented in the previous section.

[53] McManus, Bruce. 2016. "User-centric genomics data exchange and aggregation with BlockChain technologies." Genome BC Can-SHARE New Initiatives Program Grant Proposal.
[54] Shelton, Robert H. 2011. "Electronic Consent Channels: Preserving Patient Privacy Without Handcuffing Researchers." *Science: Translational Medicine* 69(3): 1 – 3 at 2.
[55] National Research Council (US) Committee on a Framework for Developing a New Taxonomy of Disease. 2011. *Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease.* Washington, DC: National Academies Press (US). Accessed 13 February 2018 at: https://www.ncbi.nlm.nih.gov/books/NBK91503/
[56] "Record" is a term of art in archival science and does not encompass the whole universe of documents. A record is an "intellectual object" that is "made or received in the course of an activity as an instrument or a byproduct of such activity and set aside for action or reference." International Council on Archives, *ISAAR (CPF). International Standard Archival Authority Record for Corporate Bodies, Persons, and Families 2nd Ed* (ICA 2004). Thus, the level analysis in archival science is not the level of data, but the level records.

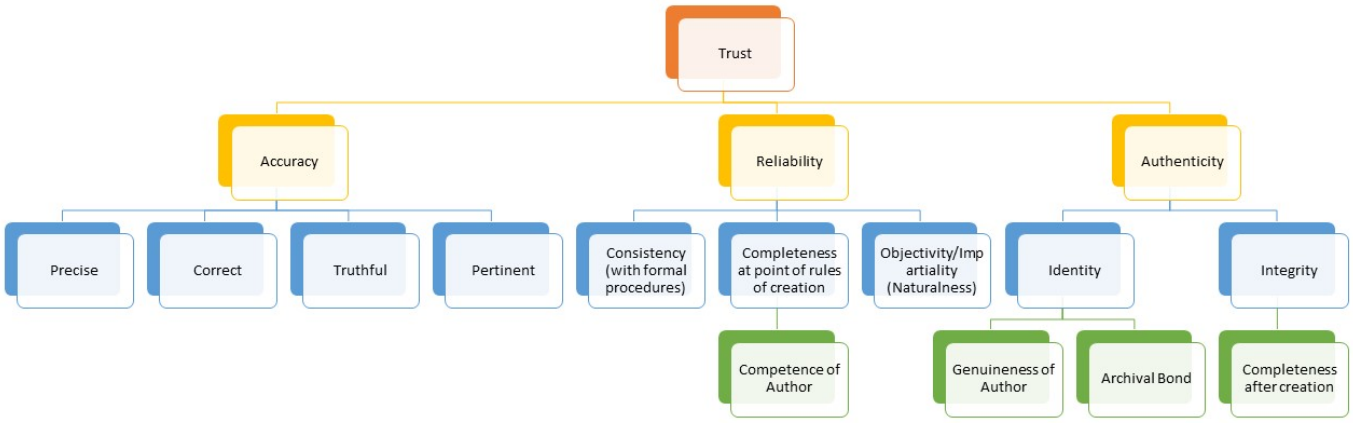

Figure 9: A taxonomy of key archival concepts and their relationship to trust[57]

In their analysis of the ethical, legal, and social implications (ELSI) of electronic consent to health research in Canada, the challenges that Kirby et al. identify are, ultimately, archival, including "concern over ensuring the integrity of electronic consent, adequate linking of electronic consents to participants through a valid electronic signature, and ensuring records of electronic consents are properly retained and accessible."[58] Indeed, their review of the statutory and common law requirements in five Canadian provinces (Quebec, Ontario, British Columbia, Alberta, and Nova Scotia) as well as the requirements at the federal level identified four requirements for electronic consent to "achieve functional equivalence" with paper, all of which are directly archival, and which this solution seeks to address through the use of blockchain technology:

1) Ensuring the *integrity* of the electronic documents;
2) Establishing a link between the participant and the electronic documents via an *electronic signature*;
3) Ensuring *accessibility* of the documents for subsequent reference; and
4) Ensuring their *retention.*[59]

[57] Rendering by Victoria Lemieux.
[58] Kirby, Emily, Ma'n H. Zawati, and Bartha Maria Knoppers. 2013. "Electronic Consent to Health Research in Canada." *The Canadian Bar Review* 91: 417, at 420.
[59] Kirby, Emily, Ma'n H. Zawati, and Bartha Maria Knoppers. 2013. "Electronic Consent to Health Research in Canada." *The Canadian Bar Review* 91: 417, at 425.

The foregoing elements are all discussed in the broader context of the archival characteristics of the solution *infra*. Integrity, along with identity, forms the authenticity of a record. The link between the participant and the documents through the electronic signature speaks to both the record's reliability and its authenticity; as Duranti explains: "By requiring a signature, bureaucracy asks writers to declare by signing that their records mirror the facts […] The signature is the fact."[60] Accessibility and retention - treated here as part of preservation, as the article makes clear the latter term is closer to the authors' meaning - both fall within the archival ambit and are discussed in their own separate sections.

Accuracy

Accuracy, in archival terms, is "the degree to which data, information, documents, or records are precise, correct, truthful, free of error or distortion, or pertinent to the matter."[61] Accuracy, then, is "straightforward, referring to the truthfulness of the content of the record."[62] Given that the PoC is designed to facilitate consent and data sharing through the system (as opposed to documenting consent and data sharing that have already happened), the records will be accurate insofar as the data from originating systems are accurate. Thus, a patient's consent will be accurate insofar that the patient inputs the correct information (if the patient hits "Yes," but means "No," the record will be inaccurate). Similarly, if a records custodian at one institution receives a data sharing request, but transfers the wrong data, the records in the solution will be accurate insofar as data was shared, but inaccurate as to which data was shared. Data entry input controls and restraints can help improve the accuracy of records in the solution. Another unresolved accuracy issue with regards to blockchain solutions in general (and applicable to this solution) is the question of how to correct inaccurate records. The immutable ledger of the blockchain is meant to be precisely that – immutable. Errors, therefore, simply cannot be overwritten. If the solution is built in such a way that the archival bond is instantiated (see authenticity, *infra*), making the relationship between records easy to find and follow, then it should be a relatively straightforward matter to correct the error with a downstream transaction that links back and refers to the earlier inaccurate transaction record, but this requires the system to be built with such functionality.

Reliability

"The reliability of a record is its capacity to be trusted as a faithful representation of the juridical fact it speaks of, that is, it is the degree to which a record 'can be treated as the fact of which it is evidence.63'" "Reliability is provided to a record by its form and procedure of creation."64 As discussed above, signatures (along with date/time notation) are often indicia

[60] Duranti, Luciana. 1989. "Diplomatics: New Uses for an Old Science (Part II)." *Archivaria* 29: 4 – 17, at 5.
[61] Pearce-Moses, Richard (ed.). 2017. "Accuracy" in InterPARES Trust Terminology Database. Accessed 14 February 2018 at http://arstweb.clayton.edu/interlex/en/term.php?term=accuracy.
[62] Duranti, Luciana, and Randy Preston. 2008. *International research on permanent authentic records in electronic systems (InterPARES) 2: Experiential, interactive and dynamic records.* CLEUP.
[63] Owen, Kevin. 2015. "Reliability." In *The Encyclopedia of Archival Science*, eds. Luciana Duranti and Patricia C. Franks (Lanham, MD: Rowman & Littlefield). Citing Duranti, Luciana. 1995. "Reliability and authenticity: The concepts and their implications." *Archivaria* 39: 5 – 10.
[64] Duranti, Luciana. 1995. "Reliability and authenticity: the concepts and their implications." *Archivaria* 39: 5 – 10.

of reliability. However, mere timestamping is not sufficient to render a record reliable. As Duranti explains: "an electronic message whose formal components are not predetermined, and whose creation is not procedurally controlled does not become reliable when electronically sealed or time stamped."65 In the case of records within the PoC, informed consent records' reliability would be a measure of how trustworthy they are as representation of the fact that the participant consented to the participation. With regards to records of data sharing, the records' reliability would be their capacity to be trusted as a representation that the data sharing actually happened.

One element of reliability is consistency with formal rules of creation. Although there are no legal requirements, at least in British Columbia, as to the formalities of informed consent or data sharing, consent and its documents has a number of rules embedded in the regulations and ethical rules of research institutions themselves and of external bodies such as Research Ethics Boards and Institutional Review Boards. A number of bodies involved with health research – the Government of Canada[66], the Tri-Council[67], the University of British Columbia Office of Research Ethics[68], and Providence Health Care[69] - all provide extensive guidance, templates, and procedures for obtaining and documenting informed consent. The B.C. Common Clinical Informed Consent Template – designed to meet the requirements of UBC-affiliated and BC regional health authority Research Ethics Boards and attached hereto as Appendix 1 – provides an overview of the procedures for informed consent. As an example, the procedures for informing a participant about the risks of a Phase I Study, as outlined in the B.C. Common Clinical Informed Consent Template, are different from those for a Phase IV study. Although the PoC examined some of the procedures involved in clinical data sharing, the Deloitte Technical Report notes that "Post-PoC [such review] should be extended to cover the full spectrum of processes and also [to] be more thorough/quantitative. Part of the consideration should be the requirements found in guidance such as the B.C. Common Clinical Informed Consent Template, and the best way to integrate those requirements into post-PoC records.

Another element of reliability is completeness. Completeness – "the property of having all physical and intellectual component required by the process or laws regulating the system that created the record"[70]. For example, the B.C. Common Clinical Informed Consent Template dictates that one of necessary persons involved in the creation of the record, the author – the Principal Investigator – be identified at the top of the informed consent forms, with information such as the investigator's degrees, institution, and department which attest to the author's competence. For the post-PoC solution to provide reliable records, analysis of the physical and intellectual form of complete informed consent and data sharing records would

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[65] *Id.*

[66] https://www.canada.ca/en/health-canada/services/science-research/science-advice-decision-making/research-ethics-board/requirements-informed-consent-documents.html

[67] http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/chapter3-chapitre3/

[68] https://ethics.research.ubc.ca/sites/ore.ubc.ca/files/documents/SOP%20701%20GENERAL%20REQUIREMENTS%20OF%20INFORMED%20CONSENT.pdf

[69] http://www.providenceresearch.ca/research-ethics/forms-guidance

[70] Society of American Archivists. "Completeness." *Glossary of Archival and Records Terminology.* Accessed 13 February 2018 at: https://www2.archivists.org/glossary/terms/c/completeness.

help identify the necessary form of the records created using the solution.

Finally, reliability must also be examined in regard to the competence of the document's author to carry out a transaction. If the author does not possess the power to give effect to the transaction's intended outcome, the record is unreliable. In the case of the PoC, for example, someone who is not the participant or the participant's surrogate decision maker would not be *competent* to consent to participation in a study. Thus, any such consent record would be unreliable. Establishing this aspect of records' reliability requires that the identity of the person giving consent be linked to the record of consent in order to help establish their competence to give consent, which highlights the importance of an identity management layer for effective operation of the system in regard to production of trustworthy records.

It must also be noted that potential security threats to the system can undermine records reliability. For example, "[t]he current architecture depends on an application server and data base […these] serve as single points of failure."[71] Given that one of the strengths of blockchain technology is the elimination of single points of failure, the reintroduction of this weakness through the middleware between the client and the blockchain lessons the benefits of using a blockchain-based approach. Utilizing a third party service such as Amazon for key management also could prove problematic. If keys are compromised, any records signed using the compromised keys are per se unreliable, as the author of records created using the compromised keys lacks the necessary competence. As Deloitte suggests in its Technical Report, the post-PoC solution should, at a minimum, use a Hardware Security Module for key management. Furthermore, the post-PoC solution should use end-to-end encryption to protect any personally identifiable information (PII) be sent to the blockchain. Given the sensitivity of the type of data being shared between the institutions, both server side and client-side encryption should be implemented on authorized data shares.

The choice of consensus mechanism should also be considered in terms of security as an aspect of reliability of records. Although Byzantine Fault Tolerance is one of the most common consensus mechanisms in permissioned blockchains, due in part to its energy efficiency, it is not necessarily the most secure of the available consensus mechanisms, as shown in the figure[72][73] below:

[71] Deloitte. 2018. "Technical Report."
[72] Lemieux, Victoria. "Blockchain Technology: Technical Deep Dive." Executive Women's Forum on Information Security, Risk Management and Privacy. 25 October 2017.
[73] It should be noted, however, that other sources disagree with this assessment of the secure of Byzantine Fault Tolerance. See, e.g., Garay, Juan, Aggelos Kiayas and Nikos Leonardos. 2015. "The Bitcoin Backbone Protocol: Analysis and Applications." *Annual International Conference on the Theory and Applications of Cryptographic Techniques*. Berlin, Heidelberg: Springer.

Property	PoW	PoS	PBFT	DPOS	Ripple	Tendermint
Node identity management	open	open	permissioned	open	open	permissioned
Energy saving	no	partial	yes	partial	yes	yes
Tolerated power of adversary	$< 25\%$ computing power	$< 51\%$ stake	$< 33.3\%$ faulty replicas	$< 51\%$ validators	$< 20\%$ faulty nodes in UNL	$< 33.3\%$ byzantine voting power
Example	Bitcoin	Peercoin	Hyperledger Fabric	Bitshares	Ripple	Tendermint

This might be acceptable, given the other security features in a post-PoC build, but it should be explicitly considered nonetheless. Although a full security analysis is beyond the scope of this report, other security risks must, of course, be considered in the design and implementation of a full post-PoC solution in order to ensure that the records produced will not be unreliable due to security compromises.

Authenticity

Authenticity, in archival terms, is "the trustworthiness of a record as a record; i.e., the quality of a record that establishes that it is what it purports to be and that it is free from tampering or corruption."[74] It should be noted that a record can be authentic without being reliable: "[p]roving a record's authenticity does not make it more reliable than when it was created. It only warrants that the record does not result from any manipulation, substitution, or falsification occurring *after the completion of its procedure of creation*, and that is therefore what it purports to be."[75] (emphasis added) In other words, how reliable a record is depends on the circumstances of its creation; how authentic a record is depends on the circumstances of its preservation. Trustworthy records must be both reliable and authentic.

There are two elements to authenticity: identity and integrity. The identity of the record is determined based on the genuineness of its author (authorial identity) and its archival bond (record identity). The integrity of a record is a matter of its completeness after creation. As noted above, signatures are associated with both reliability and authenticity. This is because signatures, when they serve as the attestation of the author, countersigner, or witness, are among those documentary components of a reliable record that can create a presumption of authenticity.[76] In particular, signatures of authors are important, because the genuineness of the creator of the record must be established in order to assess the record's authenticity. In the case of the PoC (and post-PoC solution), identity management within the system is critical to ensure that records are authentic in the sense that their author can be established. When an individual uses their private key to digitally sign their consent, it is important to be able to

[74] Duranti, Luciana. 1995. "Reliability and authenticity: the concepts and their implications." *Archivaria* 39: 5 – 10.
[75] *Id.*
[76] The other such elements are "seals, special signs, and stamps affixed by delegates of the public authority." *Id.*

determine that consent cannot be repudiated or denied. To that end, the system in the PoC uses public key infrastructure and role-based access control. However, for a full build, as Deloitte notes, identity for internal information systems requires that the public key infrastructure meet the technical standards required for recognition by the Canadian Bridge Certificate Authority, operated by the Communications Security Establishment of Canada. It is also necessary to establish controls on access to accounts; one suggestion from the Deloitte Technical Report, the use of hardware wallets (possession authentication) or mobile phone authentication (mobile two-factor authentication, rejected by NIST) to increase non-repudiation could also increase the likelihood of a record's author being genuine, especially if used in conjunction with knowledge authentication. The Deloitte technical report also recommends the use of a Hardware Security Module, a physical computing device, in order to better manage and control keys, since loss of custody or control of individual's private keys could comprise both reliability and authenticity of ledger-based consent records.

A record's identity is also dependent upon its "archival bond." The archival bond is "the network of relationships that each record has with the records belonging in the same aggregation. The archival bond is *originary*, because it comes into existence when a record is created […], *necessary,* because it exists for every record […] and *determined*, because it is qualified by the function of the record in the documentary aggregation in which it belongs."[77] In short, it is not possible to have information or data serve as a record, i.e., evidence of a business transaction or agreement, unless it is possible to link it back to the business transaction or agreement it was created to prove and to other records associated with the same business transaction or agreement. The archival bond serves as "the primary identifying component"[78], turning a document into a record, and permitting a dozen identical documents to become a dozen unique records, depending upon their relationship to other records. The archival bond is central to the identity – and authenticity – of records because it "expresses the network of relationships that each record has with the records resulting from the same activity."[79]

An important pre-determinant of establishing the archival bond is that each ledger record be uniquely identified in the first place. This is easily achieved in a blockchain-based system via the unique hash code associated with each transaction. It may not be as easily achieved for records that need to be logically linked to ledger records, such as those stored in the S3 Fileshare, so thought has to be given in the further development of the PoC as to how to ensure unique identities to these records as well. In some systems, records stored off chain are also hashed to create a unique identity, and then the hash link to the off-chain record is embedded in the on-chain ledger transaction[80]

Instantiating the link from the ledger record to its transactional context needs to be explicitly

[77] Duranti, Luciana. 1997. "The Archival Bond." *Archives and Museum Informatics* 11: 213 – 218.
[78] *Id.*
[79] Victoria Lemieux and Manu Sporny. 2017. "Preserving the Archival Bond in Distributed Ledgers: A Data Model and Syntax." 2017 International World Wide Web Conference. April 3 – 7, 2017, Perth, Australia.
[80] See for example, Daniel Flores et al., 2018, **"Real Estate Transaction Recording in the Blockchain in Brazil (RCPLAC-01) – Case Study 1",** Records in the Chain Project, http://blogs.ubc.ca/recordsinthechain/files/2018/01/RCPLM-01-Case-Study-1_v14_English_Final.pdf

designed into the architecture and operating model of the system. In a paper recordkeeping context, the archival bond is implemented in the classification code, explicitly linking all records participating in the same activity and preserving, through the simple operation of arithmetic, "the direction of the cause-effect relationship."[81] The archival bond can also be seen through file structure; records participating in the same activity are typically placed in the same file together. Preserving the archival bond in electronic records requires more deliberateness; it can be done through metadata (including classification codes).

Instantiating and preserving the archival bond in blockchain technologies must be purpose-built. It must link records to the transactions that give rise to them, and other records that form part of the same relationship. This can be quite challenging when ledger records, and associated records, are created, stored and processed in a distributed computing environment, as is the case with the Deloitte PoC (see Figure 10). In Figure 10, the archival bonds between records are captured in red, while the link between authors and their records are captured in blue. The archival bond and link back to the authors of transactional records must both be preserved if the records are to be proven authentic.

[81] Duranti, Luciana. 1997. "The Archival Bond." *Archives and Museum Informatics* 11: 213 – 218.

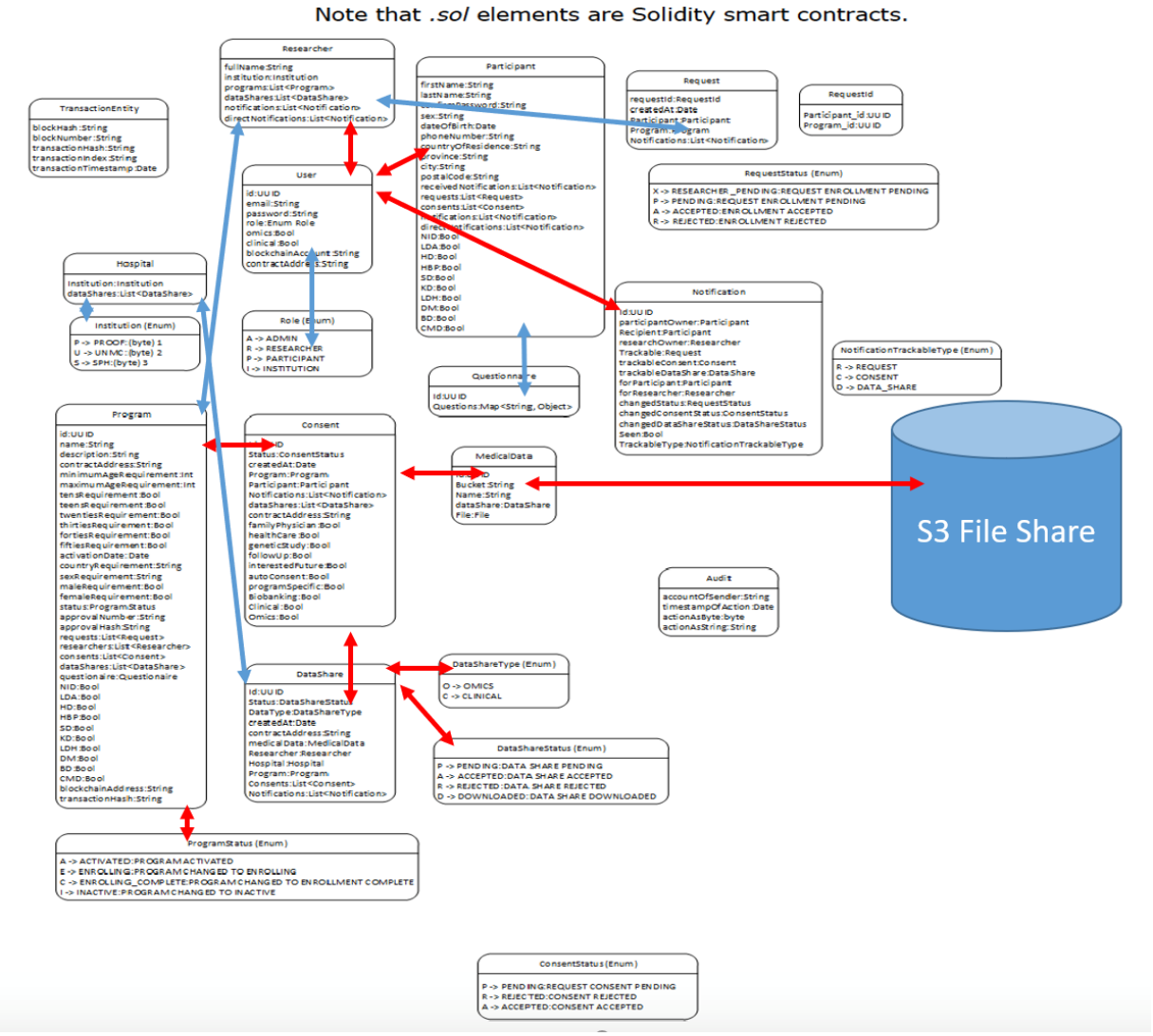

Figure 10: PoC Blockchain smart contract data Model, indicating places where archival bond is needed

One of the recommendations from Deloitte for the full implementation of the solution in this study is the implementation of a consent wallet for participants to manage all of their consents. Similar wallet structures could be used to establish the relationship between any records and their creators within the solution. The design of such a wallet must be carefully considered. For example, a custodial hierarchical distributed wallet structure comprised of sub-wallets for system users offers convenience and easier recovery of records, if, for example, the patient loses his/her/their private key. However, if a custodial wallet structure is compromised, all of the records may be compromised. It will also be necessary to ensure that any links between those portions of the record stored off chain, which could be significant, and the transactions on-chain remain live and unbroken.

In addition to establishing the identity of a record, in order to show that the record is authentic, one must also establish the record's integrity. In other words, one must assure that

the record is "free from tampering or corruption." While the blockchain is helpful with this in some ways – any tampering will change the record's hash, for example – it is not, in and of itself, a panacea. Controls including access controls and security system controls to prevent tampering must still be in place to protect the records from tampering. Particularly in the case of a blockchain using a Byzantine Fault Tolerance-type consensus mechanism, such as this one, the blockchain cannot guarantee integrity in and of itself. Because the solution assumes participants are known and semi-trusted, and utilizes a single-vote consensus in which any node can submit a transaction, an adversary who gains access to any single node could greatly undermine the integrity of the records in the system. The PoC also relies on Amazon's S3 for off-chain document storage and management. Such an arrangement has inherent risks. First, by relying upon Amazon, the institutions have very limited ability to audit the system in relation to how well it works to preserve records' integrity. Evidence law in a number of jurisdictions, including Canada, treats individual records as having integrity as long as the system producing those records has integrity. Although legal and archival integrity are not synonymous, the problems of verifying the integrity of the recordkeeping system are common to both. While the blockchain provides some assurances of integrity, such as offering automatic audit trails, a solution using Amazon's S3 is ultimately reliant upon Amazon to demonstrate the normal functioning, regular maintenance, and frequency of upgrades of those aspects of the system under their control. Governance of the blockchain itself (such as how forks will be handled in the case of disagreement between nodes) must also be considered in designing the system in order to protect records integrity. Second, record handling and storage processes in Amazon's S3 may alter the bit structure of the record. This would render any earlier hash produced based on a previous bit structure invalid. Even minor alterations in the record could make it impossible to check the integrity of a record by comparing its hash with a hash stored on chain.

Accessibility

Understanding who may access their information and under what circumstances is important to participants in deciding whether or not to participate in research. "[W]hen individuals do not understand who is accessing their information or how it might be used, they are less willing to share these valuable resources when the information is not being used directly for their care."[82] For patients who are less technologically savvy, or simply prefer personal reassurance from a professional, an electronic consent system may discourage participation if they do not understand the accessibility of their data. Another accessibility issue that must be considered is key management. One of the factors to be balanced in key management is non-repudiation versus the need to permit access. The use of an escrow account should be examined for use in the post-PoC solution. Currently, institutional personnel serve as a default escrow account, managing and providing access to records as needed by participants, regulatory bodies, and others. In a full implementation of a blockchain system, records will need to be accessible, even if the individual participants lose their private keys.

Persistence and Preservation

[82] Shelton, Robert H. "Electronic Consent Channels: Preserving Patient Privacy Without Handcuffing Researchers". *Science: Translational Medicine* 69(3): 1 -3 at 1. DOI: 10.1126/scitranslmed.3002037

It is not enough for records to be authentic at one point in time, nor is it sufficient for evidence of reliability to be produced and then discarded. For records to remain trustworthy, they must remain accurate, reliable, and authentic across time and space. Preservation encompasses "those activities and functions designed to provide a suitable and safe administrative context and environment that enhances the usable life"[83] of records. Preserving digital records requires addressing data integrity (both bit structure and semantic integrity), format and media sustainability, and information security. It would be difficult to overstate the need to ensure the importance of preserving the semantic integrity of records; if the semantic integrity, achieved mainly through instantiation of the archival bond and the affixing of records metadata, of a record is compromised, it may well be that the record will lose its capacity to serve as evidence of past acts and facts. Loss of bit integrity, on the other hand, such as through bit rot, might be problematic from the perspective of using hashes as a measure of integrity, but could well occur without compromising the record's trustworthiness as a record. In order to ensure that digital preservation is successful, it should be built into systems, as opposed to being imposed on legacy systems when records may well have already been compromised. In the case of the PoC, preservation both on-chain and off-chain must be considered. In particular, should the Amazon S3 (or other third party vendor) solution be chosen for off-chain storage going forward, guarantees such as S3's guarantee of "99.99% data durability" should be evaluated against the actual preservation needs for such storage (.01% is critical if it's the wrong .01%. Also, what other strategies – erasure coding or deduplication, for example – would make the most sense to meet the preservation needs of the system?). Preservation of blockchain-based consent records remains challenging, since there is as yet no model of distributed records preservation and standard models (e.g., OAIS) may be insufficient.

D. Conclusions

The solution in this study seeks to utilize some of the unique features of the Blockchain – its immutability, automatic timestamping, and distributed architecture – to solve some of the pain points in study participant enrollment, consent gathering, and data sharing in health research. The study to date has produced a Proof of Concept system, utilizing a Nuco Ethereum blockchain with off-chain storage, a user interface that permits users to view an audit trail of all activities on the blockchain, and an access control framework for managing data access and encryption. The full implementation, if designed correctly, could reduce the work and cost of consent management and data sharing. However, a number of archival, technical, and ethical aspects of the system must be better understood before the system moves from Proof of Concept to fully functioning solution. An examination of the formal procedures controlling the creation of the records associated with the system, as well as a full diplomatic analysis of such records to identify their required physical and intellectual forms, is necessary to ensure that the systems can create reliable records. The smart contracts must be tested to ensure that they support the instantiation of the archival bond, without which records cannot be shown to be authentic. Key management must be examined to ensure the continuing accessibility of records, even if a user loses his/her/their private key, and keys must be linked to system users identities to ensure reliability and authenticity of records. Given the extraordinarily sensitive

[83] Ritzenhaler, Mary Lynn. 2010. *Preserving Archives and Manuscripts*, 2nd edition. Chicago: Society of American Archivists.

nature of the data that will be stored and shared through the system, privacy protections including end-to-end encryption should be implemented. Because of the light regulatory hand applied to health research (at the level of statute, as opposed to ethics board oversight), this use case offers an opportunity to explore the use of a blockchain solution in a high-impact, high-requirement, yet relatively free environment.

E. Acknowledgements

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F. Appendices

1. Appendix 1: BC Common Clinical Informed Consent Template

How to use this document

This document is intended to assist investigators in producing consent forms that meet the requirements of the following UBC-affiliated and BC regional health authority REBs/RRC:

- BC Cancer Agency REB
- Children's & Women's REB
- Providence Health Care REB
- UBC Clinical REB (CREB)
- Fraser Health REB (including studies involving SFU-affiliated investigators)
- Interior Health REB
- Northern Health Research Review Committee (not currently a constituted REB)
- Vancouver Island Health Authority Clinical REB

Adherence to these guidelines may not be sufficient, however, and investigators should also refer to the guidance notes and policies of the individual REBs (see Appendix I).
All Information required by the potential participant to make a free and informed decision to participate in the research must be included in the consent form. If any of the required sections have not been included, a consent document may be returned to the applicant for amendment.

The appendices provide more detail on specific aspects of the consent form creation.
Appendix I includes links to REB guidance notes, policies, and forms.
Appendix II includes general style and formatting guidelines.
Appendix III includes general directions to those responsible for obtaining consent.

Before you begin

1. To ensure you are using the most current version of this template, download a new copy each time you create consent forms. To use the template, you may copy this and use it as a guideline.
2. Required wording is highlighted in yellow.
3. Recommended wording is in regular font.
4. Instructions are provided in *italics*.
5. Once you have completed your draft:
    a. Delete all italic content
    b. Remove colour highlighting from the remaining text
    c. Finalize the footers and remove the headers.
    d. Remove template appendices
6. Consent forms must be saved on the appropriate letterhead, as follows:
    a. BCCA REB requires BCCA letterhead.
    b. C&W REB requires UBC and/or Hospital/Program Department letterhead.
    c. PHC REB requires UBC and Providence Health Care/Providence Clinic Letterhead.
    d. UBC CREB requires UBC Department letterhead or VCH or VCHRI letterhead, if appropriate.
    e. FH REB requires Fraser Health Authority letterhead.
    f. IH REB requires Interior Health Authority letterhead if the study will be carried out by an IH site investigator. If the study is multi-jurisdictional, addition of the IH logo to another site's letterhead is acceptable.
    g. NH prefers not to have its logo on the letterhead; the consent form should be on the principal investigator's institutional letterhead.
    h. VIHA REB requires VIHA letterhead.

Consent Form Elements

(Click on the element to move to the corresponding section.)

Template content and instructions begin on the next page.

Participant [Subject] Information and Consent Form

An individual *recruited into a study should be referred to as the "participant." "Subject" may be used, but "participant" is preferred in TCPS2 (see chapter 2.A.).*

The chosen *term must be used consistently throughout the document, including in the Title of Study.*

[insert Title of Study]

The title *must be the exact title of the research protocol and include (if applicable) the protocol number.*

A short *simplified title may accompany the title if it is too difficult for a layperson to understand. The title should convey that the proposed intervention is for research rather than for educational, treatment, or other purposes.*

Study personnel
For BCCA and VIHA REB:
Principal Investigator must be identified.
One lead Principal Investigator for each additional participating BCCA or VIHA centre must be identified.
Co-Investigators are not required to be listed.
For IH REB: All co-investigators must be listed.
All other REBs require at least the PI to be included; listing other study personnel is optional.

Principal Investigator: [insert name, degrees held]
[insert UBC/PHC/CW/BCCA/IHA/NHA/VIHA Department]
[insert institution/centre]
[insert contact phone number(s)]

Co-Investigator(s): [insert name(s), degrees held]
[insert UBC/PHC/CW/IHA/NHA/VIHA Department]
[insert institution/centre]
[insert contact phone number(s)]

Sponsors: [insert names of all sponsors, granting agencies, and coordinating groups.]

Emergency Telephone Number

A 24-hour*, 7-day a week phone number is required for all studies that include non-minimal risk research procedures or interventions. Ideally, a person needing emergency assistance should not be required to go through a switchboard. If using a switchboard, ensure that requisite information is available and is kept current regarding referrals.*

Refer *to local REB policies for further guidance.*

Required wording for BCCA REB**. Note that the researcher is responsible for ensuring that emergency numbers are provided and correct. For non-emergency contact numbers, insert the appropriate contact information from Sections 19 and 20 (Who do I contact…?).**

For emergencies only: Call the centre nearest you and ask for your study doctor or, if he or she is not available, ask for your usual oncologist or the oncologist on-call.

Vancouver Centre	(604) 877-6000
Vancouver Island Centre	(250) 370-8000
Fraser Valley Centre	(604) 581-2211
Abbotsford Centre	(604) 851-4700
Centre for the Southern Interior	(250) 862-4000
Centre for the North (Prince George)	(250) 645-7300

For non-emergency contact numbers: [insert contact numbers].

***For pediatric studies**: Place the following bolded text above the Invitation.*

If you are a parent or legal guardian of a child who may take part in this study, permission from you and the assent (agreement) of your child may be required. When we say "you" or "your" in this consent form, we mean you and/or your child; "we" means the doctors and other staff.

***For studies that recruit adults who lack capacity**: Place the following bolded text above the Invitation.*

If you are a substitute decision-maker for someone who may take part in this study, permission from you and the agreement and the assent (agreement) of the potential research participant may be required. When we say "you" or "your" in this consent form, we mean the research participant; "we" means the doctors and other research staff.

1. Invitation

***Describe** the characteristics of the sample population that are important for the study, e.g. you have been diagnosed with high blood pressure.*

Recommended Text

You are being invited to take part in this research study because [insert details].

2. Your participation is voluntary

This section *should stress the voluntary nature of participation.*

Procedures *for study withdrawal are described in Section 14: What happens if I decide to withdraw my consent to participate?*

Recommended Text

Your participation is voluntary. You have the right to refuse to participate in this study. If you decide to participate, you may still choose to withdraw from the study at any time without any negative consequences to the medical care, education, or other services to which you are entitled or are presently receiving.

You should be aware that there is a difference for both you and your doctor between being a patient and being a research participant. As a patient all medical procedures and treatments are carried out for your benefit only according to standard accepted practice. As a research participant you and your doctor also must take into account the requirements for the research study. These may include procedures and treatments that are not part of standard practice or are not yet proven. This consent form describes the diagnostic and treatment procedures that are being carried out for research purposes. Please review the consent document carefully when deciding whether or not you wish to be part of the research and sign this consent only if you accept being a research participant.

If you wish to participate in this study, you will be asked to sign this form.

Please take time to read the following information carefully and to discuss it with your family, friends, and doctor before you decide.

3. Who is conducting this study?

Name *all agencies contributing funds, including grants-in-aid, resources, and drugs and other products.*

Declare *any actual or potential conflicts of interest regarding remuneration received from the sponsor that are above or beyond reimbursement for costs to conduct the study, such as additional payment for conducting or being involved with any part of the study (e.g., study design) and/or possible benefits from commercialization of research findings.*

Recommended Text

This study is being conducted/sponsored by the [name of research group, e.g. industry sponsor/granting agency].

Or,

This study is not receiving funds from an external agency or sponsor.

BCCA REB conflict of interest statement is required if applicable.

The sponsors of this study may reimburse the BC Cancer Agency for all or part of the costs of

conducting this study or they may provide the BC Cancer Agency some or all of the standard or experimental medications being used in this study. However, neither the BC Cancer Agency nor any of the investigators or staff conducting this study will receive any personal payments for conducting this study.

For all other REBs, the conflict of interest statement is required if applicable.

The Principal Investigator [insert study personnel and/or institution] has received financial compensation from the sponsor [name the sponsor] for the work required in doing this clinical research and/or for providing advice on the design of the study/travel expenses/etc. Financial compensation to researchers for conducting the research is associated with obligations defined in a signed contractual agreement between the researchers and the sponsor. Researchers must serve the interests of the participant and also abide by their contractual obligations. For some, the payment of financial compensation to the researchers can raise the possibility of a conflict of interest. You are entitled to request any details concerning this compensation from the Principal Investigator.

4. Background

The background *section should be different from the "purpose" section below that will describe the specific goals of the study.*

Provide *a brief explanation of why the research is being done (explain the basis for the experimental intervention) so that the participant can understand why a particular health problem/intervention needs to be studied.*

Include *non-technical information on the prevalence or incidence of a disease, the problems associated with a disease, the poor outcomes for other treatment methods, previous studies, etc.*

This section *must include the standard/usual treatment(s) or care for participants who are eligible for this study and the likelihood of the known therapeutic effect and the duration of that effect, so that the participant can compare this to what is being proposed in the study.*

Include *a brief explanation of participants' involvement in the study.*

When applicable*, address the following key points:*

- *If placebo controls are being used, explain what a placebo is (i.e. explain that a placebo is an inactive substance, that it looks identical to the test drug/intervention but that it contains no therapeutic or experimental ingredients) and explain and why it is appropriate to use such controls*
- *Whether the research is being carried out for the first time in humans*
- *If the research is part of a larger multi-site clinical trial, indicate whether there are other Canadian sites and/or countries where the study will be conducted*
- *The total number of participants that will be recruited and the expected number at the local site*

***For drug** or device studies, include the following Health Canada information, modified as necessary.*

Recommended Text

Health Canada has not approved the sale or use of [insert study drug/device] to treat [insert disease, including stage of disease where relevant, for example, for cancer], although they have allowed its use in this clinical study.

Or,

Health Canada has approved the sale or use of [insert study drug/device] to treat [insert type of disease], although they have not approved its use for [this disease/stage of disease, or at this dose, etc.], they have allowed its use in this clinical study.

5. What is the purpose of the study?

***This section** should be distinguished from the "Background" section so that the participant can easily identify the specific goal(s) of this research project. The goal statement should specify exactly what the study hopes to find out.*

***In addition**, the purpose of Phase I, II, III, or IV clinical trials, pilot studies, extension studies, etc., must be explicitly explained in lay terms to participants, so that they can understand the current stage of scientific investigation of the therapy, and therefore, what scientific question(s) the study is trying to answer.*

***Note**: Only descriptive statistics are appropriate. Neither the project description nor the consent document should imply that a definitive answer will result.*

***Refer** to the TCPS2 Chapter 11 for information on clinical trial phases.*

[Insert goal statement]

For a pilot or feasibility study
***For BCCA** REB applications, please also follow the guidelines in the document "Elements Required for a Pilot or Feasibility Study.pdf" also posted on the BCCA REB webpage for New Applications.*

Recommended Text

A "pilot study" or "feasibility study" is done to test the study plan and to find out whether enough participants will join a larger study and accept the study procedures. This type of study involves a small number of participants and so it is not expected to prove safety or effectiveness. The results may be used as a guide for larger studies, although there is no guarantee that they will be conducted. Participation in a pilot study does not mean that you will be eligible to participate in a future larger study. Knowledge gained from pilot or feasibility studies may be used to develop future studies that may benefit others.

For a Phase I Study

The language *used throughout the study should make it clear that this is NOT a study in which efficacy will be determined. Phase I studies are neither expected nor intended to provide personal benefit.*

This is a Phase I study. A Phase I study is a trial of an experimental study drug or treatment which is tested in a small group of people for the first time to evaluate its safety, determine a safe dosage range, and identify side effects. Phase I studies are neither expected nor intended to provide a direct personal benefit to participants.

Include the following if applicable and modify accordingly.

The purpose of this study is to find the highest dose of a new drug [insert agent] that can be tolerated without causing very severe side effects. This is done by starting at a dose lower than the one that does not cause side effects in animals. Participants are given [insert agent] and are watched very closely to see what side effects they have and to make sure the side effects are not severe. If the side effects are not severe, then more potential participants are asked to join this study and are given a higher dose of [insert agent]. Participants joining this study later on will get higher doses of [insert agent] than participants who join earlier. This will continue until a dose is found that causes severe but temporary side effects. Doses higher than that will not be given.

For a Phase II Study

This is a Phase II study. A Phase II study is undertaken after preliminary safety testing on a drug or treatment. It is usually conducted on a small number of individuals (100-300 persons), and its goal is to begin to find out what effect it has on your [insert disease or condition] and to further evaluate its safety.

For a Phase III Study

This is a Phase III study. A Phase III study is a study of an experimental drug or treatment which is given to large groups of people to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information to determine whether the experimental drug or treatment can be used safely.

For a Phase IV Study

This is a Phase IV study. A Phase IV study is a study of an approved drug or treatment (also called "a post marketing study") which is conducted to obtain additional information regarding the drug's or treatment's, benefits and optimal use.

For Expanded Access Protocols (EAP): See BCCA REB guidelines posted on the web page for New Applications.

6. Who can participate in this study?

***List**, in point form, the major characteristics indicating eligibility to participate in this study. This list should be limited to inclusion criteria that the potential participant is likely to be aware of.*

Recommended Text

You may be able to participate in this study if*:*

- [insert criteria]

7. Who should not participate in this study?

***List**, in point form, the major characteristics indicating ineligibility to participate in this study. This list should be limited to exclusions that the potential participant is likely to be aware of (e.g., illnesses and medical conditions).*

***Exclusion criteria** should not be the opposite of inclusion criteria. They address the question: of those who meet ALL of the inclusion criteria, what characteristics/criteria/features are there ANY ONE of which would make an otherwise eligible participant ineligible?*

***If specific** medications must be avoided by participants, indicate here and list them.*

***If participants** must live within a certain distance of the centre, indicate this restriction and why it is necessary (e.g., because participants receiving experimental drugs must be able to come back to the hospital or center quickly if any severe or unexpected problem develops.)*

***If excluding** due to reproductive risks specify. E.g., "If you are pregnant or of childbearing potential and/or a man who is able to father a child, you must agree to avoid pregnancy (and clarify for how long)." See details under Reproductive risks in Section 10, and PHC required wording below.*

***If breastfeeding** is an exclusion, indicate here and for how long, (e.g. only while on treatment, or longer).*

***Further** details regarding reproductive risks will be required under Section 10 of the consent.*

Recommended Text

You will not be eligible to participate in this study if:

- [insert criteria]

***Required wording** for PHC REB studies (recommended wording for other REBs):*

Because we do not know if or how an unborn baby/fetus could be harmed, you should avoid becoming pregnant. Talk to your study doctor about the risks to your unborn baby/fetus if you did get pregnant. Work with your study doctor to find the best solution to make sure you do not get pregnant, if you wish to be in the study.

8. What does the study involve?

Explain *in lay terms exactly what will happen to a participant who enrols in the study. Participants should be able to understand the extent of their involvement in the research and each step of their participation in it (e.g., screening procedures, treatment procedures, follow-up).*

Describe *the overall design of the study first, with respect to the different treatment arms/groups (should this apply), followed by a detailed description of the specific steps of the research, including the screening phase. A reference to the availability of any optional parts of the study can be included with an explanation that a separate optional consent will be provided with the details that they will need to sign if they wish to take part in the optional study.*

It is also helpful *to have a separate sub-heading for screening procedures used to determine eligibility for enrolment and to distinguish them from procedures that are part of the conduct of the study. This can follow the initial description of the overall design.*

Research-related *procedures may include standard or common investigations that would not normally be done in routine clinical care for the particular problem being investigated or that are done more frequently during the research than in routine clinical care for that particular problem. These should be distinguished from standard care. Standard care and related tests do not normally need to be disclosed unless they are being investigated as part of an experiment.*

The following *sections describe specific information that can be included in the consent form when applicable to the individual study.*

Overall design of the study

This first section should include, as applicable, a description of the following specific information:

- ***Any specific testing*** *which may be required to determine eligibility for the research (e.g. biopsy results, psychological tests, blood work, etc.)*
- ***The research*** *intervention: i.e. testing a new drug, undergoing surgery, review of records, undergoing specific diagnostic procedures (e.g. X-rays, MRI, taking blood), completing a questionnaire, answering questions in an interview, etc.*
- ***The different*** *treatment "arms" (i.e. study groups). Ensure that the description of each is presented in such a way (e.g. separate paragraphs with sub-headings) that participants can discern the differences among the arms. A diagram of the different arms is often helpful.*
- ***The differences*** *between standard therapy and the experimental procedures and whether or not the participant will continue to receive standard therapy.*
- ***How participants*** *will be assigned to specific treatment arms (i.e. randomization – explain that this is like the flip of a coin so that there is an equal chance of being in any of the groups; double-blinding – neither the researcher nor the participant will know which*

group they are in). Note that a description of a placebo arm in lay terms should have been given earlier in the consent form – see Section 4).

- ***Double-blinding** should include an explanation that the code can be broken in the case of an emergency so that the study drug can be identified;*
- ***The overall** duration of the study and how this would differ from that of standard care, the number of visits, and the length of each visit (use a sub-heading to make this information easy for the participant to find);*
- ***The number** of questionnaires and/or interviews, the period of time over which these would be administered, and the length of time it may take to fill out questionnaires or participate in interviews. Include a statement that participants do not need to answer questions that they are not comfortable answering.*

If You Decide to Join This Study: Specific Procedures

This section should describe in detail the research procedures that the participant would experience.

- ***Use sub-headings** for each step in the participant's involvement, including screening.*
- ***Ensure that** specific tests are spelled out initially before using acronyms.*
- ***Describe** the dosages of all study drugs.*
- ***If applicable**, specify the amount of blood/tissue to be taken each time as well as the total amount of blood/tissue to be taken (i.e. state the amount of blood to be taken in teaspoons/tablespoons NOT millilitres).*
- ***Charts** are often helpful to summarize procedures and time commitments, especially for complex or long-term studies.*

Recommended Text

If you agree to take part in this study, the procedures and visits you can expect will include the following: [Insert procedures]

Additional recommended text for Blinded Studies

This study is double-blinded, meaning that neither you nor your doctor will know which study medication you take. However, this information is available in case of an emergency.

Sub-Headings

***If there** is more than one part to the screening visit, use sub-headings for each.*

Screening Visit/Initial Visit/Before You Begin the Study
[insert details]

Randomization Visit
[insert details]

Study Visits

These can be described in a variety of ways depending on the research procedures, e.g.: Day 1, 2, 3; During the First Year of Your Participation in the Study; During the Remaining Years of Participation in the Study; First/Second/Third Visit; For Participants in Group 1/Group 2.

Expected Follow-up

Describe the number of follow-up visits and their duration.

Use of Data from Secondary Data Sources

***If data** is collected from secondary data sources for the purposes of the study, the consent form must meet the requirements of TCPS2 Ch.5 section D.*

***See also** local REB Guidance Notes (links in Appendix I).*

Optional Studies

A separate section should be used to explain briefly about the availability of any optional studies that are not part of the main study and for which separate consent must be obtained, for example, tissue and blood banking studies, pharmacokinetic studies, use of individual data, records, or personally identifying information in another study, and analysis of secondary data from linked databases.

Recommended Text

The following studies are optional. For each optional study, you will be provided with a separate consent that describes the details, and which you will be required to sign if you wish to participate. You can take part in the main study and not take part in these optional studies. If you decide not to take part in any or all of the optional studies, your care will not be affected.

Mandatory/Optional Blood or Tissue Collection and/or Biobanking

***Mandatory tissue**/blood collection must be limited to what is required for the conduct of the current study. Otherwise, it is considered optional and separate consent must be obtained.*

***See local REB** policies and guidance notes for further information regarding consent requirements and tissue/biobanking consent templates.*

***For BCCA** REB studies – see BCCA REB Interim Guidance on Mandatory Consent for Tissue Acquisition in Clinical Trials*

If mandatory tissue*/blood collection is applicable, its use must be explained and assurance given that biobanking for unspecified, unrelated or genetic research will not occur.*

Use *lay language to explain the scope of the research.*

Explain *how the samples will be identified, where they will be stored and for how long.*

Explain *that once these tests have been completed, any leftover samples will be returned to the facility from which they were obtained if needed, or destroyed (or if applicable; that they will be given an option to allow these to be used for other future research purposes, in which case they will be given a separate optional consent form to sign.)*

If the tissue *sample will be obtained from previously collected tissue, explain that no additional biopsy will be required.*

Explain *that the samples will only be used for the purposes described in this consent document and will not be sold.*

Explain *who will/will not receive reports about any research tests done on these samples and whether the reports will or will not be put in their health records.*

Consider *the use of flow charts or some form of graphic display to illustrate the handling and use of specimens; e.g. from initial collection of specimens, to banking, to distribution for future research. The chart could indicate when de-identification of specimens occurs and could show involvement of REBs in reviewing the use of specimens for future research.*

If optional *specimens will be obtained (tissue, blood, other material) for research, refer to the local REB's consent form template for tissue and/or blood collection or other additional optional testing. Only tests that are required for participation in the main study should be described in the main consent. A statement may be made to indicate that an optional component is available and that a separate consent document will be provided and reassure the participant that they may choose not to participate in the optional part of the study and still participate in this main study.*

9. What are my responsibilities?

This section should list and specify any requirements of the study that the participant must comply with in order to participate, but avoid language of a contractual or legal nature. This may include requesting that the participant contact their research doctor before taking any medication other than the study drug. Avoid placing redundant information in this section. For example, if birth control responsibilities are described elsewhere in the consent, they do

not need to be repeated in detail here, although a brief reminder "to avoid pregnancy" may be included.

- [insert list]
-

10. What are the possible harms and discomforts?

The following information (and any other relevant information) should be included in this section where applicable:

***Explain** the risk that the participant's condition may worsen.*

***Disclose** all known risks and discomforts associated with study procedures, including social and psychological risks/discomforts, risks to others, reproductive risks (see recommended wording below), genetic risks (see required wording below), risks that require counselling (describe whether counselling will be made available), and risks related to testing for reportable diseases, and risks related to use of placebo or associated with drug washout periods.*

***Indicate whether** the harms of the study drug may be severe, disabling, irreversible, or may cause death.*

***Indicate** whether the risks are fully known and whether there may be unexpected harms/side effects, including unexpected effects of novel drug combinations or because the study drug is in an early stage of development.*

***Quantify** the risks/discomforts in percentages, or use an appropriate numerical estimate, wherever possible. Arrange by groups of likelihood. For example: "Very Common (approximately 50% or greater)…Common (20-50%)…Less Common (5-20%) Uncommon (2-5%)…Rare (less than approximately 1%-2%)…."*

***Clarify** the risks to women should they become pregnant as well as any risks to potential fathers (see recommended wording below);*

***Instruct** participants that they should immediately inform their study doctor of any side effects they experience, if applicable;*

***Instruct** prospective participants to discuss the known side effects with their study doctor prior to their decision to participate in the study;*

***Clarify** that participants assigned to the placebo group may experience worsening of their condition since they will not have their condition treated.*

***List** in bold text any medications, supplements, or foods that should not be taken while on the study.*

***Disclose** the role of any data safety monitoring board or committee (i.e., explain that an independent group of experts will be reviewing the data for safety at intervals throughout the study).*

***Disclose** any potential loss of opportunity to receive standard care or the related known benefits from standard care.*

***For further** information regarding describing risks to participants, refer to the local REB's guidance notes (links in Appendix I).*

***For FH REB** format for inclusion of risk information see FH REB's Guidance notes for Initial Ethical Review Section #13, Harms.*

Risks and Discomforts from Standard Treatment

Risks and discomforts of standard treatment(s) are not normally listed, unless safety and/or efficacy of standard treatment(s) are being studied or standard treatment(s) is (are) being compared to experimental therapy, or if the standard treatment (drug) is being given in combination with an experimental treatment (drug). Side effects and other issues related to standard interventions should be explained following usual clinical practice. However, a statement should be included in the consent to explain this.

Recommended Text

The risks and side-effects of the standard or usual treatment of [insert details] will be explained to you as part of your standard care.

Reproductive Risks

If a pregnant partner consent is required, this should be submitted to the REB. This can be submitted later as an amendment, should a pregnancy occur.

Recommended Text

Because the effects that [insert study drug] may have on an unborn child are unknown, you should not become pregnant or father a baby while on this study. An effective method to avoid pregnancy should be used while you are on study treatment. [Explain if this extends for a period of time after treatment has stopped and specify how long it should continue.] Ask the study doctor about counseling and more information about preventing pregnancy. You should not breastfeed your baby while on this study [explain if this is only while taking the experimental treatment or extends for a period of time after treatment has stopped and specify how long] because it is possible the drugs used in this study may be present in your breast milk. [Include a statement about possible sterility when appropriate (e.g., "Some of the drugs used in the study may make you unable to have children in the future. Your study doctor will discuss this with you."]. If you (or your partner) become pregnant while you are on this study, you should notify your study doctor.

Genetic Risks

***Insert** if applicable. Disclose other genetic risks as applicable to the study.*

In addition to the risks of physical harms outlined in this consent form, there are also possible non-physical risks associated with taking part in this study. For example, disclosure of genetic or tissue marker research data could result in discrimination by employers or insurance providers toward you or your biological (blood) relatives. The chance that research data would be released is estimated to

be small.

11. What are the potential benefits of participating?

State *that the participant may not benefit from being in the study.*

Include *relevant information about the nature of the potential benefits (how important are these benefits?) and the likelihood of these benefits occurring.*

In research *projects where there may be anticipated benefits to society or to a specific group, these potential benefits must be explained in a separate paragraph so as not to confuse potential benefits to others with potential benefits to the research participant.*

Clarify *– in addition – whether or not the investigators can provide the participant with their results from certain tests that would not otherwise be done if they were not participating in the study, which might be construed as a benefit.*

Recommended Text

No one knows whether or not you will benefit from this study. There may or may not be direct benefits to you from taking part in this study.

We hope that the information learned from this study can be used in the future to benefit other people with a similar disease.

12. What are the alternatives to the study treatment?

Describe, if applicable, any alternatives (i.e. other standard treatments) to the treatment that participants would receive in the study.

State *if there are no such alternative therapies available.*

Where applicable*, palliative or best supportive care should be included as an alternative (see recommended wording below).*

Describe *alternative therapies, if they are available.*

Recommend *in the consent form that the participant discusses the alternative therapies with the study doctor or their personal physician before deciding whether or not to join this study.*

Ensure *that the participant understands clearly what treatment they may receive should they not participate in the study.*

Recommended Text

If you choose not to participate in this study or to withdraw at a later date, the following treatment options may be available to you:

- [Insert]
-

If applicable, include in the list of alternatives:

- Palliative Care or Best Supportive Care (BSC). This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the disease. It does not treat the disease directly, but instead tries to improve how you feel. Best Supportive Care tries to keep you as active and comfortable as possible.

You can discuss these options with your doctor before deciding whether or not to participate in this research project.

13. What if new information becomes available that may affect my decision to participate?

Insert required text if applicable.

If you choose to enter this study and at a later date a more effective treatment becomes available, it will be discussed with you. You will also be advised of any new information that becomes available that may affect your willingness to remain in this study.

14. What happens if I decide to withdraw my consent to participate?

Indicate *that the participant may withdraw at any time without giving reasons, including withdrawal from optional study components. Participants cannot be required to submit a request for withdrawal in writing.*

Include *the following when applicable:*

Explain *that participants have the option to withdraw from treatment but remain in the study for follow-up purposes. Describe what this will involve.*

Explain *that participants may remain in any optional studies.*

Explain *that examinations (e.g. physical, blood pressure, blood tests) may be recommended for or requested of the participant if they decide to withdraw from the study and that these would occur after the participant has been released from the study; explain why these examinations may be recommended or requested.*

For double-blind *studies, explain whether participants will be able to find out what treatment they were receiving.*

Disclose *if it will not be possible to undo the research-related intervention (e.g., somatic cell gene transfer, implantation of medical device [e.g. stent]). However, the participant may be able to withdraw from participation in the research (e.g. the ongoing evaluation) even though the procedures already performed cannot be undone.*

Explain *what will happen to any data collected up to the point of the participant's withdrawal from the study. For studies that are regulated by Health Canada or the US FDA, include the statement that such data will be retained and cannot be withdrawn. For studies not regulated by Health Canada or US FDA, the investigator must outline the factors that would lead to the participant's request to withdraw their data being denied.*

Remove *text in square brackets [ ] if biological samples (e.g., blood, tissue, etc.) are not being collected.*

For research that is regulated by Health Canada or US FDA: Amended July 2014

Recommended Text

You may withdraw from this study at any time without giving reasons. If you choose to enter the study and then decide to withdraw at a later time, all information about you collected up to the point of your withdrawal [including, where applicable, information obtained from your biological samples] will be retained for analysis in order to protect the integrity of the research, which may benefit future research participants and patients. However, no further information will be collected.

[If samples have been collected before you withdraw, they will be destroyed or returned to the facility from which they were obtained. There may be exceptions where the samples will not be able to be withdrawn for example where the sample is no longer identifiable (meaning it cannot be linked in any way back to your identity).] If your participation in this study includes enrolling in any optional studies or long term follow-up, you will be asked whether you wish to withdraw from these as well.

For research NOT regulated by Health Canada or US FDA: Amended July 2014

Recommended Text

You may withdraw from this study at any time without giving reasons. If you choose to enter the study and then decide to withdraw at a later time, you have the right to request the withdrawal of your information [and/or samples] collected during the study. This request will be respected to the extent possible. Please note however that there may be exceptions where the data [and/or samples] will not be able to be withdrawn for example where the data [and/or sample] is no longer identifiable (meaning it cannot be linked in any way back to your identity) or where the data has been merged with other data. If you would like to request the withdrawal of your data [and/or samples], please let your study doctor know. If your participation in this study includes enrolling in any optional studies, or long term follow-up, you will be asked whether you wish to withdraw from these as well.

15. Can I be asked to leave the study?

Describe *under what circumstances the study investigator would take the participant off the study, e.g. the study may be stopped by the sponsor or regulatory agency if knowledge of any unexpected or unexplained serious adverse events that affect participant safety become known.*

Include *any specific instructions to the participant regarding what they need*

to do should they be withdrawn from the study.

Recommended Text

If you are not able to follow the requirements of the study or for any other reason, the study doctor may withdraw you from the study and will arrange for your care to continue. On receiving new information about the treatment, your research doctor might consider it to be in your best interests to withdraw you from the study without your consent if they judge that it would be better for your health. If you are asked to leave the study, the reasons for this will be explained to you and you will have the opportunity to ask questions about this decision.

16. How will my taking part in this study be kept confidential?

Procedures *for coding participant information that are different from the required wording below (e.g., use of participants' initials, PHN, etc.), and any related consent wording changes, will need to be explained and justified to the REB on the application.*

If there is planned disclosure *of personal identifiers (e.g. names, date of birth, or initials) outside the local study site, or if such personal identifiers are used on study documents or any research-related information or are part of the unique identifier, this must be justified to the REB on the application and, if permitted, the required wording below must be amended as necessary.*

Placement *of any research data or results in the participant's health records must be disclosed to participants, and justified to the REB on the application.*

Your confidentiality will be respected. However, research records and health or other source records identifying you may be inspected in the presence of the Investigator or his or her designate by representatives of [insert here, if relevant, the name of the sponsoring company or cooperative group conducting the study,] Health Canada, [insert here, if relevant, the U.S. Food and Drug Administration,] and [insert name of your REB] for the purpose of monitoring the research. No information or records that disclose your identity will be published without your consent, nor will any information or records that disclose your identity be removed or released without your consent unless required by law.

You will be assigned a unique study number as a participant in this study. This number will not include any personal information that could identify you (e.g., it will not include your Personal Health Number, SIN, or your initials, etc.). Only this number will be used on any research-related information collected about you during the course of this study, so that your identity will be kept confidential. Information that contains your identity will remain only with the Principal Investigator and/or designate. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected. You also have the legal right of access to the information about you that has been provided to the sponsor and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request to your study doctor.

If planned disclosure of personal identifiers (e.g. birth date) is approved by the REB, amend the details in the required wording above:

Your [insert personal identifier/s] will also be provided if requested by the sponsor or responsible regulatory agency.

US FDA Regulated Study

***For US FDA**-regulated studies only, include the following wording in separate paragraphs. The first paragraph is mandatory US FDA wording and cannot be amended.*

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Recommended Text

Because this study also falls under U.S. regulation, in the event of certain types of investigations of the study the U.S. Food and Drug Administration (US FDA) may need to copy and take away records that contain your personal information. By signing this consent form you are agreeing to this. In the event that this occurs, the study doctor will attempt to notify you. You should be aware that privacy protections of personal information may differ in other countries. Any study related data (or samples) sent outside of Canadian borders may increase the risk of disclosure of information because the laws in those countries dealing with protection of personal information (for example the Patriot Act in the United States) may not be as strict as in Canada.

If data is being transferred out of Canada

***Include** the following information if data is being transferred out of Canada.*

1. *The participant information that will be sent outside of Canada.*
2. *A description of the coding of the data, if different from the coding described elsewhere in the consent form.*
3. *To whom the information will be sent (e.g. individuals, organizations, regulatory agencies).*
4. *Where the information will be sent (e.g. USA, UK, Australia).*

***Clarify** whether data and/or samples will be sent outside of Canada, and include the following wording:*

Any study related data [and/or samples], sent outside of Canadian borders may increase the risk of disclosure of information because the laws in those countries, [insert (for e.g.) the Patriot Act in the United States] dealing with protection of information may not be as strict as in Canada. However, all study related data [and/or samples], that might be transferred outside of Canada will be coded (this

means it will not contain your name or personal identifying information) before leaving the study site. By signing this consent form, you are consenting to the transfer of your information [and/or samples], to organizations located outside of Canada.

- [Insert organization/s]
-

Reportable Diseases

Disclose *to participants if positive tests for communicable diseases are reportable to provincial health authorities (e.g. hepatitis B or C, Human immunodeficiency virus (HIV), West Nile virus, etc.).*
Insert *examples of any foreseeable instances where such reporting of communicable diseases may be required.*
See BCCDC List of Reportable Diseases

Your personal information or information that could identify you will not be revealed without your express consent unless required by law. If facts become known to the researchers which must be reported by law to public health authorities or legal authorities, then your personal information will be provided to the appropriate agency or authority.

- [Insert example/s]
-

Primary Care Physician(s)/Specialist(s) Notification

For BCCA REB and VIHA REB insert a statement in the consent that as a part of the study requirements the investigator will notify the participant's GP of the participant's participation in the study.

Your family physician will be notified of your participation in the study so that your study doctor and your family doctor can provide proper medical care.

For all other REBs, include the following (optional) notification section. This component cannot be used for BCCA REB or VIHA REB

Recommended Text

Please indicate, by checking the applicable box, whether you want us to notify your primary care physician(s) or specialist(s) of your participation in this study. This is not a consent to release medical information.

☐ Yes, I want the study investigator to advise my primary care physician(s) or specialist(s) of my participation in this study. My primary care physician(s) and/or specialist(s) name(s) is/are: _____

The name of the medical clinic I attend is: _____

Participant Initials: _____

☐ No, I do not want the study investigator to advise my primary care physician(s) or specialist(s) of my participation in this study.

Participant Initials: _____

☐ I do not have a primary care physician or specialist.

Participant Initials: _____

☐ The study investigator is my primary care physician/specialist.

Participant Initials: _____

I understand that if I choose not to advise my primary care physician(s) or specialist(s) of my participation in this study, there may be potential medical consequences which may affect my comprehensive medical care or treatment. I understand that the study investigator may not be responsible for these consequences.

You may wish to discuss the consequences of your decision with the study staff.

Disclosure of Race/Ethnicity

If applicable, collection of data on demographic features such as race/ethnicity, birthplace, gender, and sexual orientation must be justified in the ethics application and the reason for the collection explained to participants and that providing this information is voluntary. (Note that the UBC Behavioural REB guidance notes may be helpful; see Sections 5.2 and 6.3.)

Recommended Text

Studies involving humans now routinely collect information on race and ethnic origin as well as other characteristics of individuals because these characteristics may influence how people respond to different medications. Providing information on your race or ethnic origin is voluntary.

17. What happens if something goes wrong?

***If the person** signing consent is doing so on behalf of a participant who lacks capacity add, "or the participant's" after "any of your."*

***The study** sponsor must be prepared to cover the cost of medical treatment required for illness or injury as a result of the research if patient is uninsured.*

***The name** of the Sponsor is not necessary for non-regulated studies or unfunded studies.*

For the definition of "Sponsor" refer to ICH Good Clinical Practice Guidelines (ICH GCPs), article 1.53.

By signing this form, you do not give up any of your legal rights and you do not release the study doctor, participating institutions, or anyone else from their legal and professional duties. If you become ill or physically injured as a result of participation in this study, medical treatment will be provided at no additional cost to you. The costs of your medical treatment will be paid by your provincial medical plan and/or by the study sponsor [insert name of sponsor].

Recommended text

In case of a serious medical event, please report to an emergency room and inform them that you are participating in a clinical study and that the following person can then be contacted for further information: Dr. [insert doctor's name] at telephone number: [insert doctor's telephone number].

18. What will the study cost me?

> ***When applicable**, begin this section with a general statement that research-related care and treatment will be provided at no cost to the participant.*

Recommended Text

All research-related medical care and treatment and any related tests that you will receive during your participation in this study will be provided at no cost to you.

Reimbursement

> ***Stipulate** whether the participant will incur any personal expenses as a result of participation.*
>
> ***State** whether their expenses will be reimbursed, which expenses, and how they should claim for reimbursement.*
>
> ***Otherwise**, provide an explicit statement that there will be no reimbursement for study related expenses, if that is the case.*
>
> ***Researchers** are encouraged to cover participants' expenses such as parking, meals, travel, supportive care medications or other incidental costs over and above those needed for standard care they would not otherwise have been required to purchase.*

[insert details]

Remuneration

> ***State** whether the participant will be paid for their participation (e.g. "You will not be paid for participating").*
>
> ***If participants** will be paid for participation, include the details of any honoraria/incentives to be provided.*
>
> ***Such payments** must not be weighted toward the end of the study, as an incentive to complete participation.*
>
> ***State** that payments will be pro-rated if the participant withdraws from the study.*

[insert details]

19. Who do I contact if I have questions about the study during my participation?

Recommended Text

If you have any questions or desire further information about this study before or during participation, or if you experience any adverse effects, you can contact [insert PI or his/her representative] at (xxx) xxx-xxxx, ext. xxxx.

> ***BCCA REB** required wording*
> *For the Head of Program contact information, include only the telephone number of the applicable main switchboard, do not include this person's name or telephone extension.*

In the event of a research related injury, please speak to your doctor (indicated above) or (after hours) call the BCCA centre nearest you and ask for your study doctor or, if he or she is not available, your usual oncologist or the oncologist on call.

Or, you can speak to the doctor who is the principal investigator, [insert name of PI] at (xxx) xxx-xxxx ext. xxxx.

Or, you can speak to the Head of [insert program name, e.g. the Systemic Therapy or Radiation Therapy] Program of the BC Cancer Agency. That person can be reached at (xxx) xxx-xxxx.

20. Who do I contact if I have any questions or concerns about my rights as a participant?

For UBC-affiliated REBs (BCCA REB, C&W REB, PHC REB, UBC CREB)

If you have any concerns or complaints about your rights as a research participant and/or your experiences while participating in this study, contact the Research Participant Complaint Line in the University of British Columbia Office of Research Ethics by e-mail at RSIL@ors.ubc.ca or by phone at 604-822-8598 (Toll Free: 1-877-822-8598).

For FH REB

If you have any concerns about your rights as a research participant and/or your experiences while participating in this study, contact the Fraser Health Research Ethics Board co-Chair by calling 604-587-4681.

For IH REB

If you have any concerns about your rights as a research participant and/or your experiences while participating in the study, we would be interested in hearing from you. Please feel free to contact the Chair of the Interior Health Research Ethics Board at (250) 870-4602 with your concerns.

For VIHA REB

If you have any concerns about your rights as a research participant and/or your experiences while participating in this study, or if you wish to verify the ethical approval of this study, you may contact Karen Medler, Research Ethics Coordinator, or Dr. Marie-Térèse Little, Chair of the Clinical Research Ethics Board for the Vancouver Island Health Authority (250-370-8620).

21. After the study is finished

Describe *any information that may be given to the participant once their participation is concluded.*

For example*, this could include whether or not the participants will be able to continue treatment on the study drug. If not, include the following recommended wording below.*

Provide *participants – where possible – with a lay summary of the study results.*

Describe *when the study and/or individual results are likely to be available and how they will be disseminated.*

Inform *participants, where relevant, of procedures for accessing those results.*

Recommended Text

You may not be able to receive the study treatment after your participation in the study is completed. There are several possible reasons for this, some of which are:

- The treatment may not turn out to be effective or safe.
- The treatment may not be approved for use in Canada.
- Your caregivers may not feel it is the best option for you.
- You may decide it is too expensive and insurance coverage may not be available.
- The treatment, even if approved in Canada, may not be available free of charge.

Future Contact

If researchers wish to contact participants later to participate in other studies, include this request with an appropriate yes/no tick box. Researchers are encouraged to include this request if there is any chance that they may wish to ask participants to participate in future studies.

22. Signatures

This section *of the consent form should start on a new page and include the full study title.*

The participant *is signing the form to indicate that he/she has read, understood and appreciates the information concerning the study. As such,*

use the first person pronoun ("I") for this section.

***Include** a checklist of the issues most critical to making an informed decision.*

***Required** and suggested checklist items appear below.*

***Ensure** that the checklist fits on the page with the signatures of the participants. The signatures should never be on a page by themselves.*

***Provide** a copy of the signed and dated consent form to the participant.*

***Where third party consent** is being obtained and participants have capacity to assent/dissent: refer to the local REB guidance notes (links in Appendix 1) for clarification of assent policies and guidelines.*

[Insert full study title]

Participant Consent

My signature on this consent form means:

- I have read and understood the information in this consent form.
- I have had enough time to think about the information provided.
- I have been able to ask for advice if needed.
- I have been able to ask questions and have had satisfactory responses to my questions.
- I understand that all of the information collected will be kept confidential and that the results will only be used for scientific purposes.
- I understand that my participation in this study is voluntary.
- I understand that I am completely free at any time to refuse to participate or to withdraw from this study at any time, and that this will not change the quality of care that I receive.
- I authorize access to my health records [insert if applicable and samples] as described in this consent form.
- I understand that I am not waiving any of my legal rights as a result of signing this consent form.
- I understand that there is no guarantee that this study will provide any benefits to me.
- [Insert any other research specific clauses that may be important to reiterate.]

Required wording *where participants who lack capacity are capable of assent.*

The parent(s)/guardian(s)/substitute decision-maker (legally authorized representative) and the investigator are satisfied that the information contained in this consent form was explained to the child/participant to the extent that he/she is able to understand it, that all questions have been answered, and that the child/participant assents to participating in the research.

I will receive a signed copy of this consent form for my own records.

I consent to participate in this study.

"Participant's Signature" should be replaced with "Participant's or Substitute Decision-maker's Signature" if third party consent may be obtained from a legally authorized representative.

_____	_____	_____
Participant's Signature	Printed name	Date

_____	_____	_____	_____
Signature of Person Obtaining Consent	Printed name	Study Role	Date

Where *applicable include the following elements:*

If this consent process has been done in a language other than that on this written form, with the assistance of an interpreter/translator, indicate:

Language: _____

Was the participant assisted during the consent process in one of ways listed below?

☐ Yes ☐ No [Note: For typical situations where the person conducting the consent discussion simply reads the consent with the participant to ensure that informed consent is properly obtained, check "no".]

If yes, please check the relevant box and complete the signature space below:

☐ The consent form was read to the participant, and the person signing below attests that the study was accurately explained to, and apparently understood by, the participant (please check if participant is unable to read).

☐ The person signing below acted as an interpreter/translator for the participant, during the consent process (please check if an interpreter/translator assisted during the consent process).

_____ _____ _____

Signature of Person Assisting in the Consent Discussion | Printed Name | Date

Witness Signature

> ***Optional, except*** *where an oral consent is necessary such as when the participant is illiterate or blind, or disabled, or for cultural reasons so that they either cannot or will not sign the consent form. In such circumstances, the witness must be independent of the Principal Investigator or designate. For blind or illiterate participants, an REB approved summary of what is to be said to the participant or his or her authorized representative must be signed by both the person providing the consent and the witness. In such circumstances, the signature of the witness is intended to attest to the fact, and to state, that what is included in the summary was actually said to the participant or legally authorized representative.*

Investigator Signature

> ***Some REBs*** *may require an investigator signature for all consent forms. Check local REB requirements. As well, a signatory line for "investigator signature" (example below) must be added if required by the sponsor, but*

this may not replace the line for the "person obtaining consent" if this is a different person:

Investigator Signature	Printed name	Date

My signature above signifies that the study has been reviewed with the study participant by me and/or by my delegated staff. My signature may have been added at a later date, as I may not have been present at the time the participant's signature was obtained.

Appendix I

Links to REB sites providing guidance notes, policies, and/or forms for UBC-affiliated, SFU, and BC regional health authority REBs/RRC

UBC-affiliated Clinical REBs

BC Cancer Agency REB (BCCA REB)

Children's & Women's REB (C&W REB)

Providence Health Care REB (PHC REB)

Clinical REB (CREB)

Simon Fraser University ORE and REB (SFU ORE and REB)

Fraser Health REB (FH REB)

Interior Health REB (IH REB)

Northern Health Research Review Committee (NH RRC)

Vancouver Island Health Authority REB (VIHA REB)

Appendix II

General style and formatting guidelines for consent forms

1. Consent forms should be written at a Grade 7 level of understanding.
   In Microsoft Word, you can display the Flesch-Kincaid Grade Level Score by clicking on "Spelling and Grammar" in your tool bar. If the option to check for readability statistics is not viewable, ensure it is enabled. In Word 2013: Click the File tab, and then click Options. Click Proofing. Ensure "☑ Show readability statistics" is selected.
2. Type size: no smaller than the type on this page (12 point).
3. Improve readability by using headings, short paragraphs, and spaces between paragraphs.
4. Use plain language; explain medical terms and jargon. Use non-scientific terminology. For assistance with finding lay language substitutes, refer to the Canadian Cancer Society Glossary of Terms: http://info.cancer.ca/glossary/
5. Acronyms should be avoided. If they must be used, they should be written out the first time they appear, e.g., Peculiar Acronym for General Use (PAGU).
6. Number the pages in the following manner: "1 of 3", "2 of 3", "3 of 3," etc.
7. Include a footer ON EACH PAGE with the version number and date. Also include a brief reference to the study such as the protocol number or REB number or nickname of the study.
8. All information required by the participant must be included in the informed consent form, with the exception of ancillary drug information sheets, if applicable.
9. The consent form submitted for review should be in its final form and on letterhead (as it will be seen by the participant).
10. Spelling, grammar and formatting must be corrected before submission to the REB.
11. Use second person pronouns for the participant information part of the consent form (you/your). Use first person pronoun ("I") only for the final Participant Consent portion of the form.
12. References to "doctor" should be clarified to identify who is being referred to, e.g., the family doctor, study doctor, oncologist.

Appendix III

General directions to those responsible for obtaining consent

1. The "person obtaining consent" must be sufficiently familiar with the study, the disease being treated and the process of informed consent to be able to obtain properly informed consent and, thus, will usually be the investigator or a designated research assistant.

   If a study doctor is also the treating doctor for the potential research participant, this must be clearly stated in the application to the REB. Include an explanation of efforts that will be made to mitigate the potential for undue influence over a potential participant when obtaining their consent to participate. In such cases best practice has been identified as having someone other than the study/treating doctor obtain consent, or receive the participant's answer regarding their final decision. This does not preclude the study/treating doctor from providing information to the participant or answering any of their questions. See TCPS2-Chapter 11.A: Duty of Care.

2. The investigator should independently document the obtaining of informed consent in the medical record, noting the date, the participant's full understanding of the risks and benefits of enrollment and the voluntary nature of participation.

3. Translated Consent Documents: A translated consent document cannot replace the English language version but it can serve as an additional aid in the consent process. A translated consent document also does not replace the requirement for a translator/interpreter to be present during the consent process and throughout the study. The investigator should ask for the translated version to be independently reviewed for accuracy. The final version of the translated consent document must be submitted to the REB for approval along with a statement signed by the interpreter confirming that the translation is accurate, stating the name and version date of the document they translated and their qualifications. These documents may be submitted as an amendment after the REB has approved the English version. The participant will sign the translated consent.

4. A translator/interpreter should be a PHSA/BCCA or other such certified or qualified translator/interpreter. They should be impartial, that is, not a relative, study team member, or a person who might have influence over the participant. For more information see the PHSA Provincial Language Services site.