Accelerating pandemic response and biomanufacturing through integrated biorepositories

Biobanks are a cornerstone of translational research and integral to modern drug, vaccine and assay development. Access to diverse biological samples underpins fundamental research, understanding host-pathogen mechanisms, and identifying targets for vaccines, drugs, and assays. The COVID-19 pandemic dramatically underscored the critical importance of biobanks when worldwide biobanks provided viral samples, blood samples, and human tissues, leading to the sequencing of the COVID-19 virus and a better understanding of its pathogenic mechanisms, host-pathogen response, and effects on host tissues. Ultimately this led to the rapid development of effective vaccines—an unprecedented achievement in the annals of vaccine development. The value of clinical samples in a biobank directly correlates with the associated clinical data. Capturing clinical data using traditional (manual) methods is time-consuming, expensive, and subject to human-introduced errors. Pandemic preparedness requires a faster and more efficient strategy addressing concerns regarding maintaining patient privacy. The digital transformation of health opens opportunities for more efficient and safe Methods.

Objectives: B-PREPARED:

1) Expand biobanking capacity and security - to meet expanding demand for pandemic preparedness, biomanufacturing, the objectives of the PRAIRIES Hub, and the overarching objectives of the Biomanufacturing and Life Sciences Strategy (BLSS). We will expand the site by twenty -80 $_{o}$C freezers - each with appropriate backup systems in the event of power loss. Each site requires modest renovations to ensure ventilation systems are appropriate. Additional security safeguards will be implemented at each site to meet and exceed security standards.
2) Further develop and enhance existing biobanking database software; will be achieved by partnering with Amazon Web Services (AWS, who have experience creating data infrastructure for UK Biobank) to enhance and improve the security of the open-source sample management system developed by the Canadian BioSample Repository (CBSR; UAlberta). By leveraging cloud services, the integrated biobank network will have the highest standards for security.
3) Leverage the single province-wide laboratory management system (LIMS) to identify and request consent to use remnant samples; will develop an application interface to facilitate obtaining an electronic consent to use remnant samples from Alberta Health Services (AHS) and Alberta Precision Laboratories (APL)
4) leverage the single province-wide electronic medical record (EMR), LIMS, and expertise in artificial intelligence (AI) for curation of clinical data from the health record; will require the development of an application interface for AHS's cloud-based enterprise data warehouse. The interface will be queried to pull relevant data from the patient health record, with individual informed consent, to be curated and included in the associated clinical data. Much of the data stored in the EMR is challenging to access as it was recorded as unstructured text notes. Our AI expertise will facilitate data abstraction from unstructured text notes using an open-source large language model already deployed in our high-performance computing environment - the Data and Analytics Research Core (DARC, UAlberta). An electronic research data capture system (REDCap) is already integrated into the provincial EMR and can pull data, with permission, from the EMR using the Fast Healthcare Interoperability Resources standard. We will leverage this platform to achieve
5) leverage the integrated research electronic data capture systems within the EMR; requiring no additional infrastructure investment (i.e. using REDCap)
6) develop an integrated repository for clinical trial data and biological samples;
7) create a portal for researchers to discover, request, and access clinical samples and data, while preserving stakeholder interests, privacy, and security, and for participants to actively participate in the research process and support dynamic consent processes ensuring that individual autonomy and diversity are respected in biobank activities; will create a portal for researchers to discover and request samples while ensuring that all released data and samples meet the owners' requirements and for participants to receive ongoing information, employing a dynamic consent model. Similar concepts have been used in highly successful biobank like the UK Biobank.

Anticipated Outcomes: The requested research infrastructure shall facilitate the PRAIRIE Hub's 3 key research programs (1) self-amplifying mRNA biomanufacturing; (2) diagnostics and assay development platform; and (3) drug discovery focussed on interrupting viral pathogenic mechanisms and manipulating host proteins to enhance recovery from infection. Well-characterized and diverse

samples will be a fundamental resource for these programs. Efficient and faster collection of, and an increased capacity to store samples and alternate sources (i.e. remnant samples) will enable PRAIRIE (and other) Hub researchers to improve future responsiveness to emerging pathogens. The biobank network will improve inter-provincial collaboration and create opportunities for collaboration with existing biobank networks in Canada and the world.

Developing the network in Alberta builds on opportunities that currently exist only in Alberta, including the single provincial EMR and LIMS. It will build on provincial strengths related to AI, natural language processing, and integrated research data capture systems. B-PREPARED will be proof of principle indicating that biobanks can tightly integrate with clinical information systems and AI can improve the quality and efficiency of data curation. Our platform of interoperability and integration in Alberta will entice and facilitate the development of similar systems in other provinces and Hubs within the BLSS mandate.

Patients' needs are central to B-PREPARED, and leveraging the advanced capacity and expertise of the Strategy for Patient-Oriented Research will ensure participant engagement in biobanking. We will improve equity in health research by deploying a dynamic consent process and portal for participants to track their sample usage and learn research outcomes resulting from their participation.

Expected Applications: B-PREPARED will support all PRAIRIE Hub research objectives in pandemic preparedness and biomanufacturing. Expanded biobank capacity and efficient data collection will improve pandemic research programs (including vaccine-related adverse outcomes) and support archiving completed trials and new clinical trials of drugs, diagnostics, or vaccines related to new and existing pathogens. B-PREPARED biobanks will be sustained through supporting other therapeutic areas and industry clinical trials.

Section 1. Proposal

Biobanks are integral to modern drug, vaccine and diagnostics development and biomanufacturing, offering diverse biological samples necessary for fundamental research, understanding host-pathogen mechanisms, and identifying targets for vaccines, drugs, and assays. The critical role of biobanks was apparent during the recent COVID-19 pandemic. When the SARS-CoV-2 virus emerged, biobanks globally shared blood, viral, and human tissue samples, which enabled scientists to quickly develop an effective mRNA-based vaccine—an unprecedented achievement in the annals of vaccine development. The UK Biobank, which holds genetic and health data from half a million UK residents, contributed serology data from 20,000 participants, their children and grandchildren (aged over 18) (1) . These contributions began in the first four weeks of the pandemic and continue supporting studies. *We aim to build on existing biobanking capacity in Alberta and the PRAIRIE Hub, deploy novel methods to curate clinical samples and data and leverage an integrated provincial health system to maximize the efficiency in collecting and storing diverse clinical samples with associated rich phenotypic data to support the objectives of the PRAIRIE Hub, pandemic preparedness, and biomanufacturing.*

Excellence in Biobanking and Relevance to Research Hubs

The *University of Alberta (UAlberta) and the University of Calgary (UCalgary) have a long-standing record of excellence* in translational research and biobanking. The **UAlberta Canadian BioSample Repository (CBSR) has been a leader in biobanking for over 20 years.** The CBSR was founded and is led by Co-Director Dr. Bruce Ritchie, and for the last two decades, he has been an innovator in developing sample management software, deploying automation, and supporting biobanking needs across a broad range of disciplines. CBSR is registered with the Canadian Tissue Repository Network (CTRNet) , maintaining operating and quality assurance procedures that meet national and regulatory standards across various health research disciplines, including regulatory studies with Health Canada oversight. The CBSR *houses over 1 million samples* , including cryotubes and FTA paper DNA blood spots. The samples, collected from 26,676 participants and 48,340 collection events, originate from 78 studies that require long-term storage and another 46 clinical trials, many of which aim for regulatory approval. The biobank has twenty-four -80ºC freezers and 3 liquid nitrogen dewars (-170ºC), with space for 500,000 cryotubes at vapour phase nitrogen. The CBSR uses automated sample-handling robotics, funded through a prior Canada Foundation for Innovation (CFI) infrastructure grant (Tonelli M, Fedorak R). The biorepository has extensive experience supporting infectious disease and immunity studies, including the National Blood Borne Pathogens Surveillance Project (BBPSP; Ritchie B) and the COVID-19 Surveillance Collaboration (CoCollab; Ritchie B, Richer L). The study continues to enrol a prospective cohort creating a repository of samples from both COVID-19 positive and negative participants.

UCalgary , a second key PRAIRIE Hub member, also has extensive biobanking experience, including the **Foothills Medical Center** (Hirota S) **, Arnie Charbonneau Cancer Institute** (Chan J) **, and the Alberta Children's Hospital (ACH) BioCORE** (Esser M), which supports relevant COVID-19 surveillance and biobanking initiatives: the Alberta Childhood COVID-19 Cohort Study (AB3C), the CIHR-funded Pediatric Outcome Improvement through Coordination of Research Networks (POPCORN), and a global study - PERN–COVID-19 (2) (Freedman S) - a prospective cohort study of the outcomes for youth tested for SARS-CoV-2 infection at one of 41 emergency departments across ten countries (Argentina, Australia, Canada, Costa Rica, Italy, New Zealand, Paraguay, Singapore, Spain, and the United States). Collectively, UCalgary received over $65 million in research funding and contracts. UAlberta and UCalgary biobank assets form an ideal ground zero for a pandemic-ready integrated biobank resource for the province and beyond.

UAlberta and UCalgary have the experience and expertise in biobanking and are immediately available to facilitate innovative research programs such as the linked CBRF proposals. Existing infrastructure can immediately respond to Hub research requirements in biobanking. Still, the **requested infrastructure is critical to meet expanding needs for local, regional, and national research and surveillance to accelerate future responses to pathogens with pandemic potential and biomanufacturing.** Linked PRAIRIE Hub research programs include self-amplifying mRNA vaccine development (Houghton; CBRF2-2023-00113), a comprehensive strategy to develop broad-spectrum small-molecule therapeutics for emerging viral pathogens (Lemieux; CBRF2-2023

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00102), diagnostic assay development (Le; CBRF2-2023-00103), PRAIRIE CMAPS (Nezhad; CBRF2-2023-00092), and integration with large-scale diagnostic labs for disease surveillance (Lewis; CBRF2-2023-00106). The requested infrastructure will host and support many research and biomanufacturing programs in the PRAIRIE Hub and other hubs nationwide. **National linked proposals** outside of the PRAIRIE Hub include CBRF2-2023-00225 translational and targeted therapeutics centre from the HI3 Hub (Bhat M) and other national initiatives, including the Coronavirus Variants Rapid Response Network (CoVaRR-Net) Biobank and Data Platform (see letter of support). The related Canadian COVID-19 Biobank and Data Alliance , which aims to link several COVID-19 biobanks in Canada to collectively support a national effort to share data and biological materials, will be enhanced by our proposed expanded local and regional sample and data repository. In leveraging a federated data model, our proposal will integrate well with the Alliance's efforts to develop common data standards to support harmonization across partner biobanks while overcoming the legal and ethical barriers to sharing.

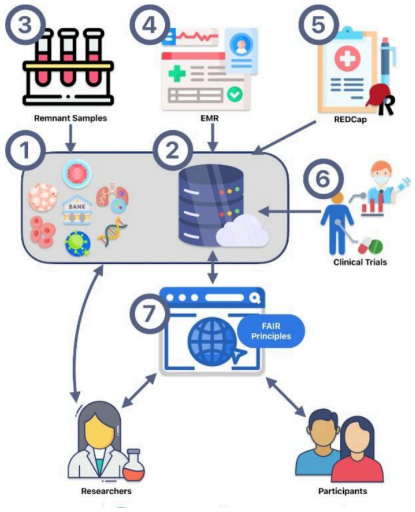
Research Objectives Enabled by the Requested Infrastructure (see Figure 2)

Local and provincial data and sample collection, given the privacy and legal restrictions across provinces, is the most efficient approach to expanding the availability of relevant samples and deploying innovative approaches to data curation or consent. A unique opportunity exists in Alberta to significantly improve the efficiency, diversity, and volume of clinical samples and data curated to accelerate future responses to pathogens with pandemic potential. *Our proposal aims to leverage Alberta's integrated health information systems and laboratory management systems to maximize the use of remnant clinical samples while creating an innovative system to efficiently curate data using state-of-the-art artificial intelligence and to obtain and maintain dynamic consent from diverse participants for storing and using samples and linked health information.* The requested infrastructure will build on the biobank infrastructure at UAlberta and UCalgary and create the **Integrated Biobanks for pandemic PREPAREDness and biomanufacturing in Alberta (B-PREPARED)** . The integrated, secure, and participatory biobank network B-PREPARED will significantly expand capacity while developing an innovative data infrastructure to leverage **population-level data sources available only in Alberta** . The proposed approach will maximize the diversity and representativeness of stored data and samples. B-PREPARED will also leverage extensive expertise in biomanufacturing (MacIsaac A), artificial intelligence (Mitchell R), and strong institutional commitment (Tonelli M, Richer L, Freedman S) to ensure the success and sustainability of the network. Figure 2 outlines the specific objectives described in more detail below.

B-PREPARED seeks to fulfill seven KEY OBJECTIVES:

(1) Expand and enhance biobanking infrastructure capacity at UAlberta and UCalgary to meet expanding needs related to pandemic preparedness. Current biobank facilities, developed in response to other specified objectives, are near capacity. B-PREPARED will (1) expand critical freezer

capacity by 200% at both sites, (2) provide increased and properly ventilated physical space, (3) enhance electrical and cooling backup systems to mitigate catastrophic risks and improve the physical and digital security, and (4) update sample processing equipment to respond to researcher sample requests rapidly. The enhanced Biosafety Level (BSL) 2 capacity will allow for the safe storage of blood, cells, tissues, organoids, pathogens, and genetic material. Universal precautions are applied to all sample handling, and centrifugation is performed in enclosed centrifuge buckets with capped tubes, which are only opened in a flow hood. When needed upgraded BSL 3 facilities are available at UAlberta (BRIF Phase 1, Hobman T), supported by Li Ka Shing Institute of Virology (LKSIoV) and Li Ka Shing Applied Virology Institute (LKS AVI) and upgraded BSL3 facility at UCalgary, hosted by the Snyder Institute (BRIF Phase 1, Kubes P), an initiative supported through its alignment with UCalgary's VPR strategic research priorities. BSL 3 facilities are essential for culturing certain organisms. The requested equipment and resources will integrate with established cores and biobanking facilities at both sites, providing sustainability through the support of existing staff and operational budgets.



The availability of samples and clinical data will facilitate the rapid, integrated and coordinated response to emerging pathogens and complement UAlberta's robust biomanufacturing infrastructure, including the Alberta Cell Therapy Manufacturing facility (ACTM) , with fill-finish production capabilities and the Canadian Critical Drug Initiative (CCDI) . The CCDI project (MacIsaac A) is a collaboration led by Applied Pharmaceutical Innovation (API) in partnership with UAlberta and the LKS AVI to create an integrated research, development and manufacturing cluster in Edmonton. CCDI is supported by an $80 million grant from the Government of Canada, PrairiesCan. In alignment with both Canada's Biomanufacturing and Life Sciences Strategy (BLSS) and PRAIRIE Hub's strategic objectives, biobanking will contribute uniquely to accelerating translational research and biomanufacturing from pre-clinical research, early and late-phase clinical trials, and post-market evaluation of drugs or vaccines. B-PREPARED will also be accessible to support other PRAIRIE Hub members, including USask, UManitoba, VIDO, and the National Microbiology Laboratory, in future vaccine and therapeutic development.

(2) Integrate biobanking facilities in Alberta through a federated and secure digital infrastructure in alignment with nationally accepted data models (e.g. Coronavirus Variants Rapid Response Network (CoVARR-Net) Biobank and Data Alliance). The requested database development will leverage existing CBSR software (UAlberta), developed as an open-source platform called BioBank, to improve the discoverability of clinical samples between sites. The 'BioBank' platform is a comprehensive client-server Java application that allows multiple users operating at different stations and locations to process and log thousands of specimens simultaneously daily. The platform supports a federated data model across biobank sites, making it ideal for B-PREPARED. B-PREPARED will also access CBSR-developed open-source tools to produce and read machine-readable labels (barcodes, radio-frequency identification or RFID); barcode-reading software for flatbed scanners; software to link samples to results from high-throughput assay systems; and a platform to monitor storage status through automated, internet-accessible temperature and security monitoring. Researchers can enter specimens into the system, technicians can process and transfer specimens, and specimens can be requested based on the inventory information. The platform provides detailed audit logs, ensuring that BioBank conforms to 21 CFR Part 11 regulatory requirements for electronic data storage.

Amazon Web Services (AWS) Professional Services will provide their innovative cloud services, imaging, while the third will focus on structural biology and the fourth on AI applications in drug discovery. These investments reflect UAlberta's commitment to AI in health research and present a remarkable opportunity in pandemic preparedness and biomanufacturing. The large dataset created through B-PREPARED will provide a unique opportunity for the new AI scientists to collaborate with a diverse group of researchers focusing on pandemic preparedness at UAlberta, UCalgary, within the

PRAIRIE Hub and beyond. Dr. Ross Mitchell, a current Amii research fellow, CIFAR Chair, and AHS Chair for AI in Health, will lead our efforts to develop an innovative approach to data curation from unstructured text notes and images . Data in unstructured text and images have traditionally been "locked" in forms that require manual and human resource-intensive approaches abstracting relevant information. We will develop a system to read text and images using artificial intelligence and large-language models similar to ChatGPT. Similar efforts developed in other jurisdictions have demonstrated the potential (3) . At UAlberta, Dr. Mitchell has deployed and piloted large language models (LLM) on our on-premise infrastructure, including the state-of-the-art Llama 2 LLM from Meta AI. He demonstrated that the LLMs can curate relevant health information from unstructured text and images without additional training. We will test and fine-tune the existing models to improve data curation relevant to infectious diseases. Traditional approaches to data abstraction require a human to review the data, which is prone to error and typically very slow while being significantly resource-intensive. The requested database and software development will build on existing high-performance computing at both UAlberta (Data and Analytics Research Core (DARC)) and UCalgary (Medically-Advanced Research Computing (MARC)).

Alberta has deployed a single electronic medical record (EMR) and integrated LIMS called Connect Care (Epic Systems, 2023). Enterprise data is housed in the cloud and accessed via an AWS cloud-native secure data platform (Snowflake). Using Alberta's provincial EMR and LIMS will also ensure a broad and fair representation of Alberta's population and be inherently inclusive of all genders, sexes, locations (rural vs. urban), languages, and cultures (4,5) . We will request data from AHS in two ways: (1) with the consent of biological sample contributors and (2) with a requested waiver of consent for provincial aggregate-level analysis from smaller targeted cohorts of non-identifying health data. We will enhance the value of biorepository samples by clinical and other data (e.g. imaging, genomic) drawn from the EMR and other sources (6,7) . In addition, the proposed model will serve to curate participant data before infection. Our team has extensive expertise in real-world and administrative health data research (Tonelli C, Freedman S, Top K, Richer L), and the proposal builds on existing analytics expertise with real-world and administrative health data through the Real-World Evidence Unit (UAlberta) and the Center for Health Informatics (UCalgary).

(5) Leverage integrated research support systems and multi-site research ethics approval. The research electronic data capture platform, REDCap, is integrated with the provincial EMR using the HL7 standard Fast Healthcare Interoperability Resources (FHIR) standard. The interoperability allows for capturing laboratory and other discrete data elements directly from the EMR, avoiding unnecessary data entry by research personnel. We use the integrated REDCap in the current COVID-19 surveillance study CoColab (Ritchie B). The embedded data collection system and application of AI (as above) will enable critical research across the spectrum of clinical care, including the intensive care units (Fiest K, Esser M), tertiary hospital wards (Ritchie B) and the emergency department (Freedman S). We will use drug administration, diagnostic imaging, and laboratory data to capture a complete picture of the clinical phenotype and samples. Samples with rich phenotypic data are of the most significant value to drug or vaccine discovery, assessment of host response, and surveillance. In addition, a provincial clinical trial management system, OnCore, is linked to Connect Care across Alberta to facilitate clinical trial enrolment. Multi-site research is also accelerated through the REB Exchange (REBx), which allows for a single ethics approval for research in multiple sites in Alberta.

security, and experience deploying the digital infrastructure for the UK Biobank to deploy the BioBank platform across sites hosted in cloud-based infrastructure and advanced physical and digital security. We will enhance the functionality of the BioBank software in the following ways (1) updated state-of-the-art digital security; (2) an overarching data management strategy and systems architecture that will ensure maximum uptime; (3) development of a distinct and private portal for researchers and participants alike (described below); and (4) develop an application interface to access cloud-based resources of Alberta Health Services (AHS) through an Amazon cloud-hosted platform (Figure 2).

(3) Maximize the use of remnant clinical samples. Remnant samples for clinical diagnostic testing are destroyed at variable time points according to standard operating procedures. The provincial laboratory information management system (LIMS) can be used to identify samples of interest before destruction. The Alberta Diagnostics Ecosystem Platform for Translation (ADEPT) program has already established the approach to using remnant samples of interest for research purposes without individual consent, which is of great value to many translational research efforts. However, consent is necessary to collect identifying health data linked to the remnant samples. Leveraging Alberta's integrated health

information systems, we will develop an innovative system and approach to efficiently obtain individual patient consent to transfer remnant clinical samples to the biobank before destruction *and collect relevant health data.* Requests for patient consent can be facilitated by the provincial patient-facing apps (i.e. My AHS Connect) linked to the electronic medical record and help ensure maximum diversity of samples from all groups, including rural and urban settings. We will develop a streamlined approach to obtaining consent in collaboration with Alberta Health Services (AHS) and AWS Cloud Services. This additional pathway to well-annotated clinical samples will open new research opportunities and significantly accelerate the potential to study emerging pathogens early in their course.

(4) Leverage artificial intelligence and integrated population-based provincial data systems to maximize the curation of relevant sample annotation and data analysis . Artificial intelligence applied to health research and innovation promises to change our approach dramatically. We will leverage UAlberta's expertise in **artificial intelligence (AI) and natural language processing** to maximize the curation of relevant health data for sample annotation while reducing the risks to individual privacy. UAlberta is in the process of hiring four new AI scientists with a focus on health research. The Canadian Institute for Advanced Research (CIFAR) Pan-Canadian AI Strategy partly funds the positions. All will be fellows of the Alberta Machine Intelligence Institute - one of three CIFAR-funded institutes in Canada. One position will focus on natural language processing and applications of AI related to health data. In contrast, another will focus on AI applications in diagnostic

(6) Create clinical trial data and sample repository. B-PREPARED data systems will also serve as a repository of clinical trial data and samples, further enhancing access to well-curated biological samples and associated data. The deposition of samples collected under controlled protocols from vaccine and other antimicrobial trials will support drug development and improve the understanding of adverse events. Multiple studies, including some unrelated to infectious disease, will also provide a valuable source of uninfected control data and biological samples that would be inefficient and difficult to collect in an emerging epidemic. Over 40 industry-sponsored clinical trials have contracted CBSR to support biobanking for their regulatory trials, and the model will help support the sustainability of B-PREPARED.

(7) Support equitable access, diverse representation of participant populations, active participant engagement, and dynamic consent through novel participant-facing digital infrastructure . The integrated biobank network and related data systems, collaboration between UAlberta and UCalgary, and partnership with AHS will enable equitable access to research opportunities for Albertans, independent of where participants may live. We will maximize sample diversity when expanding the reach of the B-PREPARED network throughout the province, including rural and remote regions, and when employing a dynamic consent process (8) . According to the FAIR Guiding Principles, an integrated biobank promotes collaboration among researchers, public health agencies, and biotechnology companies and enables equitable data sharing, samples, and knowledge (9) . The requested digital data infrastructure will support data adjudication and sample access, ensuring we uphold all stakeholder and participant interests when sharing. The repository will also maximize the discoverability of available samples by researchers within the PRAIRIE Hub, other collaborating institutions, and national networks like the CoVaRR-Net Biobank and Data Alliance (letter of support provided) supporting a collective effort to be better prepared for future pandemics and enhance biomanufacturing capabilities.

Section 2. Anticipated outcomes

B-PREPARED will serve as an accelerator platform for fundamental research, translation, and the development of new commercial products. The platform will support academic and industry-led research and innovation needs. The quality standards, diversity of samples, and rich sample annotation will provide a valuable resource to all Research Hub stakeholders. The biobank platform aligns with the overarching objectives of the BLSS and the PRAIRIE Hub's primary goals of (1) increasing specialized infrastructure and capacity for multidisciplinary, applied research and (2) accelerating the translation of promising research into commercially viable products and processes. Secondarily, we will also fulfill BLSS's and PRAIRIE Hub's objectives to train and support Canadian highly qualified personnel (HQP) in health-related cyber-security, data management, and AI (via 4 new, fully funded scientist hires—refer to strategic overview document), as well as biobank-leveraged projects, through to biomanufacturing and clinical trials. **B-PREPARED is unique because it will access clinical samples and data at a population level across Alberta.** It creates a rich and well-annotated repository to facilitate local, Research Hub, and national research programs. It will leverage nationally accepted procedures to

maximize the discoverability and sharing of samples through a federated model across all Hubs in Canada and other pandemic-related research programs. B-PREPARED will also support industry-led research and innovation, and biomanufacturing new vaccines, therapeutics, and diagnostics. Specific examples include the support of ongoing pandemic preparedness-related projects like CoColab and POPCORN. New repositories will be developed based on new and emerging pathogens or the research programs of the PRAIRIE Hub to ensure maximum future preparedness.

(1) Relevant PRAIRIE Hub CBRF Research Programs Enabled by the Requested Infrastructure. PRAIRIE Hub-endorsed research priorities will inform priorities for sample collection - both current and as they emerge. B-PREPARED will support the research and training needs of multiple linked CBRF applications through increased capacity and access to valuable samples. Proposals include: (1) **Self-amplifying mRNA vaccine development (CBRF2-2023-00113):** Self-amplifying mRNA (saRNA) vaccines are an innovative and promising vaccine strategy using cellular and viral replication machinery to amplify the production of antigens. Critical infrastructure for a large-scale saRNA production suite will be installed at the API (MacIsaac A, API) biomanufacturing plant under construction in Edmonton. Longitudinal samples can track critical host-pathogen immune responses in related vaccine studies, providing valuable insights into long-term efficacy and biomarkers of response. B-PREPARED will also support storing raw materials, intermediates, and finished vaccine products for future reference, analysis, and research purposes, helping maintain traceability, and providing reference materials. (2) **Diagnostic assay development (CBRF2-2023-00103) and integration with large-scale diagnostic labs for disease surveillance (Lewis; CBRF2-2023-00106):** Large-scale diagnostic reference laboratories represent a national resource for responding to epidemics by providing the data used to diagnose infections, flagging emerging outbreaks, and tracking the efficacy of public health containment efforts. The Prairies Diagnostics Consortium will leverage large-scale diagnostic labs to stimulate Canadian biomanufacturing in the Prairie region. The research program will be enhanced with access to curated clinical samples and data and the vast potential for the long-term storage of remnant samples of interest from the health system. (3) **Comprehensive Strategy to Develop Broad-Spectrum Small-Molecule Therapeutics for Emerging Viral Pathogens (CBRF2-2023-00102):** Targeting host cellular proteins rather than pathogen-encoded ones is a promising approach to developing therapeutics. Such therapies (e.g. interferons) can be effective against a wide range of pathogens if they target cellular mechanisms many viruses and bacteria use. B-PREPARED will support access to specimens from a spectrum of disease severities: mild to moderate (i.e. in the emergency department) or severe (in intensive care). Leveraging AI and the single EMR will ensure representative clinical data and samples are available on current and emerging pathogens being studied. Finally, clinical samples will support the development of organoids and other pre-clinical testing platforms. B-PREPARED will support the pipeline for small-molecule drugs and platforms with a supply of clinical samples helpful in assay development needed in the biomanufacturing process.

(2) Striving for Pandemic Preparedness - The Alberta Research Consortium (SPP-ARC). B-PREPARED's enhanced biobank capacity, developed in support of pandemic preparedness and biomanufacturing, is directly aligned with major priorities at UAlberta and the Striving for Pandemic Preparedness - The Alberta Research Consortium (SPP-ARC) initiative (Gottë M, Tyrrell L). With over $50 million in funding from the Government of Alberta, the SPP-ARC program will invest in major infrastructure, including cryo-EM, to accelerate research relevant to pandemic preparedness. The research team has identified biobanking as a critical need and has formed a biobanking sub-committee on which two team members participate (Ritchie B, Richer L). SPP-ARC will leverage the new infrastructure and help fund relevant surveillance and sample collection initiatives.

(3) Promoting national and international cooperation. B-PREPARED will fuel national and international collaboration boasting improved data harmonization in alignment with nationally accepted standards. Linkage with CBRF2-2023-00225 Translational and Targeted Therapeutics Centre from the HI3 Hub (Bhat M) is one example of a national collaboration. The HI3 Hub and linked proposal (CBRF2-2023-00033) - CanTHRIVE Program: Optimized Therapeutic Strategies and Vaccine Design (Ohashi P (UHN) Yeung R (SickKids) will study vaccine efficacy in immunocompromised and other high-risk populations because their immune systems often cannot mount appropriate antibody responses. Access to rare clinical samples, such as immunocompromised, will be improved through collaboration with the diverse population-based samples available through B-PREPARED.

A common data model, shared approach to informed consent, inclusive language, ethical guidelines, and legal terms will facilitate collaboration and foster greater trust among researchers, stakeholders, and participants, as has been demonstrated in partnerships like Canadian Tissue

Repository Network (CTRNet) and the Global Alliance for Genomics and Health (GA4GH). The *infrastructure investment in Alberta will enhance participation in key national networks like CoVaRR-Net (letter of support provided)* . In addition, sharing best practices, regular communication, and adoption of standards will support training new highly-qualified personnel, including early career researchers (ECR). B-PREPARED aligns with international efforts like the Coalition of Epidemic Preparedness Innovations (CEPI) 100-day goal for delivering the next pandemic vaccine, focusing on low to middle-income countries. CEPI discusses building on previous experience with similar disease outbreaks, leveraging prior investments in rapid technologies and earlier biomarkers of robust immune protection, and utilizing advanced data and analytics to enable fast study set-up, real-time monitoring and data-sharing.
The International Network of Special Immunization Services (INSIS) (Top K) is a global platform investigating rare vaccine safety concerns (10) . INSIS is funded (USD 15.3M over four years) by the CEPI to identify biomarkers and underlying mechanisms of myocarditis and thrombosis with thrombocytopenia syndrome following COVID-19 vaccination through multi-OMICs 'adversomics' analysis of cases worldwide. INSIS can increase vaccine confidence by informing regulatory and policy decision-making regarding the benefit-risk assessment of vaccines. During the COVID-19 pandemic, Dr. Top was also the chair of the Vaccine Safety Working Group at the Canadian COVID-19 Immunity Task Force. Within INSIS, Dr. Top and her team use biorepositories of clinical trials and specimens to investigate vaccine adverse events. The local COVID-19 Surveillance Collaboration (CoCollab; Ritchie B, Richer L) continues to enrol a prospective cohort, creating a repository of samples from both COVID-19 positive and negative participants.

(4) Supporting biomanufacturing and commercialization through academic and industry channels. B-PREPARED will be a resource to support translation and commercialization for academia and industry. CBSR already supports the biobanking needs of over forty, mostly industry-sponsored, clinical trials. We will attract industry partner investment and collaboration with standardized provincial biobanking capabilities; well-annotated samples; unified policies; and publicly-available processes. We will follow the excellent example of the UK Biobank academic-industry partnership for exome sequencing (11) . B-PREPARED industry partner, AWS and its experience with developing the digital infrastructure for the UK Biobank, will be crucial to advancement in the global arena of pandemic product research and manufacturing. Biobanking can support biomanufacturing in multiple ways: (1) **Quality Control and Compliance** - biobanks can provide high-quality, well-characterized biological materials that can serve as benchmarks or controls for biomanufacturing. Biobanks also adhere to strict quality control measures, which can be incorporated into the biomanufacturing pipeline to enhance end-product quality. The extensive data accompanying biobank samples can assist in process development and optimization, helping manufacturers understand how variables like cell age or environmental factors might impact production. Detailed records associated with biobank materials can aid in maintaining the traceability of raw materials, an essential requirement in Good Manufacturing Practices (GMP); (2) **Efficiency and Supply Chain Security** - biobanks ensure a continuous supply of high-quality raw materials, which is essential for uninterrupted biomanufacturing. Biobanks can store a variety of cell lines and materials tailored to specific manufacturing needs. With ready access to samples, the time to collect new samples is minimized, potentially reducing time to market. Biobanks can facilitate high-throughput screening of biological samples for various traits, allowing for faster and more efficient production cycles. The genetic, proteomic, and metabolic data accompanying biobank samples can be invaluable for optimizing biomanufacturing processes.