Biomanufacturing in Canada

Considering the Creation of New Biomanufacturing Capacity for Canada

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EXECUTIVE SUMMARY

The COVID-19 pandemic has exposed significant limitations and gaps in Canada's capacity to produce life-saving vaccines and therapeutic drugs at sufficient scale to meet domestic needs. Serious consideration is being given to how best to ensure that Canada is well-positioned to respond to future health emergencies and how to promote the long-term growth of the Canadian life science sector. Since the outset of the pandemic, the Government of Canada has taken decisive action to ensure safe and secure access for Canadians to vital medications, and aggressively pursued the rebuilding of Canada's biomanufacturing capacity. As it acts to deal decisively with the immediate crisis, the Government is seeking to lay a durable foundation for Canada's ability to respond to the current and future health emergencies.

To position itself to do so, the Government of Canada committed in the 2020 Fall Economic Statement to explore ways that it can support pandemic preparedness going forward. Investments in the Canadian life sciences sector will not only protect Canadians in the event of a pandemic, but also provide enormous economic benefits associated with growing manufacturing capacity, attracting vaccine developers and connecting Canada's world leading life science researchers and start-ups with opportunities to grow and succeed in Canada.

In fact, the Government has already made significant investments to strengthen Canada's biomanufacturing footprint in the days and months since the COVID-19 pandemic was declared. These include investments of $126M in the National Research Council's new Biologics Manufacturing Centre, with the new centre capable of manufacturing up to two million doses per month upon completion. This is in addition to the previously announced $44M to upgrade the NRC's existing Royalmount facility to establish biomanufacturing for vaccine clinical trial material, and to de-risk and accelerate vaccine development, as well as other investments and initiatives that the Government had announced in recent years. These include an investment of $37.5M toward a $144.M project in PEI-based BioVectra in 2019, and a federal contribution of $22.5M toward a $138M project at STEMCELL in Vancouver in 2018 to support development of regenerative medicines and construction of a state-of-the-art manufacturing facility.

The Government is also investing in additional production capacity by providing support for leading private sector companies, such as AbCellera and Precision Nanosystems Inc. in Vancouver, and Medicago in Quebec City. These investments are supported through the Strategic Innovation Fund, which has been provided up to $792 million to support research and development, clinical trials, and the manufacturing of vaccines and therapeutic drugs to fight COVID-19. The Government also provided a total of $9.7 million to Providence Therapeutics, to scale-up manufacturing capacity for its mRNA vaccine candidate - $4.7M through the NRC Innovation Research Assistance Program (IRAP) and an additional $5M through the Nest Generation Manufacturing (NGen) Supercluster.

The significant investments to date are not the only ones in the pipeline. The Government is in active discussion with multiple firms on investment proposals, and it continues to evaluate and consider additional steps to help grow clusters of expertise across the country. Already, global vaccine developers are taking notice of the positive shifts in the Canadian landscape, as evidenced by the recent Memorandum of Understanding between the Government of Canada and Novavax, which enables the Government to pursue options to produce the company's vaccines in Canada.

As we look to the future, it will be important for Canada to ensure that investments made on an urgent basis in response to COVID-19 can also address new and emerging threats, such as COVID-19 variants, and that these investments are built upon to ensure that Canadians

continue to benefit from a strengthened life sciences sector and long-term domestic pandemic preparedness. In addition to biomanufacturing capacity, this will include ensuring that in the long-term Canada has the talent, research and development pipeline; robust SMEs; and security across the supply chain to support a dynamic and growing biomanufacturing and innovation ecosystem.

To this end, Innovation, Science and Economic Development Canada, in partnership with Health Canada, and the Public Health Agency of Canada, intend to engage with stakeholders on the long-term and enduring elements of a robust domestic biomanufacturing sector, including their input on the prospective expansion of domestic biomanufacturing capacity and related enhancements to the life sciences ecosystem.

Specifically, input is sought with respect to:

- the elements of Canada's biopharmaceutical sector in which Canada demonstrates strengths and possesses weaknesses, and the potential avenues for strengthening the biomanufacturing and related innovation ecosystem;
- the mandate and mission of a potential biomanufacturing and innovation initiative, such as a national centre for pandemic preparedness or a national network of pandemic preparedness hubs;
- the scope of operations for additional biomanufacturing capacity, in the context of both pandemic preparedness and long-term sustainability;
- methods for integrating any new capacity into the existing academic and life sciences landscape in Canada, and for ensuring continued strength in these areas; and
- consideration as to the most appropriate business models and governance structures.

Stakeholders' views are appreciated, and will be taken into consideration as the Government of Canada examines ways in which it can support the above objectives.

PURPOSE

The Government of Canada is committed to ensuring that Canada is well-positioned to respond to future health emergencies and is exploring ways in which it can help promote long-term sustainable growth in Canada's biomanufacturing sector. The Government of Canada recognizes that efforts to enhance pandemic preparedness and biosecurity require an ecosystem approach. That is, an approach that is tailored to the Canadian context, that takes into account the expertise of government, industry and academia, and that builds upon existing assets and organizations within the Canadian life sciences sector.

Recognizing the criticality of this sector to long-term national health, safety, and security objectives, the 2020 Fall Economic Statement committed to exploring ways the Government can support future pandemic preparedness, including through biomanufacturing in Canada. To that end, Innovation, Science and Economic Development Canada is working with other federal departments and agencies, including Health Canada, the Canadian Institutes of Health Research, and the Public Health Agency of Canada, to consult on a plan to strengthen Canada‘s life sciences ecosystem, which includes considerations related to increasing domestic biomanufacturing capacity. This plan will build on the many investments made since March 2020 to respond to immediate pandemic needs.

The purpose of this paper is to guide consultations on the need for and elements of targeted enhancements to Canada's biomanufacturing and life sciences ecosystem to

ensure enduring domestic preparedness for pandemic response and other health emergencies. It is expected that such an initiative would focus on growing critical biologics and therapeutics manufacturing and life sciences capabilities. It is also expected that the initiative would be integrated into Canada's life sciences ecosystem, and would carefully examine opportunities to build upon strategic investments, including those to support research, that have been made in the context of COVID-19 to enhance future pandemic preparedness and security of supply associated with vaccines and therapeutic drugs.

For the purposes of this consultation, and in order to provide stakeholders with greater latitude in providing feedback, we are interested in understanding thoughts and considerations related to a broad definition of the term "biomanufacturing", inclusive of technologies such as messenger ribonucleic acid (mRNA). This is particularly the case given the important and early role RNA-based vaccines have played in rapidly meeting the need for vaccines, as well as the expected role that these technologies are expected to continue to play in addressing on-going concerns, such as new variants of the virus. We are also interested in understanding views on small molecule production in Canada -- as these molecular compounds have shown promise in fighting cancer, polyomaviruses and major depressive disorder -- and how this may relate to a potential biologics manufacturing initiative. Stakeholders are also invited to provide their views on opportunities to bolster the Canadian life sciences sector, as well as connections within the sector, including linkages throughout and across the biomanufacturing value chain.

Furthermore, these consultations will explore different models and possibilities, including the creation of physical assets to connect and grow Canada's biologics manufacturing and innovation footprint, and the strengthening of linkages between existing assets in Canada's life science ecosystem to enhance pandemic preparedness, while supporting the sustainable growth of the Canadian life sciences sector.

Partnership models, which could include government, industry, and academia, would be at the heart of the initiative. An ecosystem approach, calibrated to the Canadian context and mindful of the vital roles of government, industry and academia, will be the most conducive to achieving the Government of Canada's biosecurity and pandemic preparedness objectives. Such an approach will strengthen the connections amongst existing institutions, companies and organizations, ultimately serving to promote growth within the Canadian life science sector.

In this regard, we will consider for Canada the need for a potential centre of excellence along the lines of the Texas A&M Centre for Innovation in Advanced Development and Manufacturing in the United States, the Vaccine Manufacturing and Innovation Centre in the United Kingdom, and others, or a network of centres for pandemic preparedness across Canada. This will include evaluation of its form, viability and scope. This paper, therefore, lays out a series of considerations related to the following:

- mission and mandate of such an initiative or interconnected initiatives;
- scope of operations;
- function of capacity within the existing landscape along the value chain (from research to commercialization to at-scale production);
- commercial sustainability of a biologics manufacturing platform; and
- governance models for such an initiative.

Ensuring that Canada is well-prepared in the event of a future pandemic will require an ecosystem approach that deals with various elements, including research, the development of highly-qualified personnel, and other industries along the supply chain. Needs associated with these additional elements will be taken into consideration in the development of plans to secure future security of domestic biomanufacturing capacity. Stakeholders are invited to share views on these and other elements of the life sciences ecosystem. We invite participation from experts across research and industry, including in related sectors (e.g., chemical industry, large infrastructure). We also welcome the views of provincial and territorial partners to ensure a coordinated, pan-Canadian approach to countering this and any future pandemic.

BACKGROUND

The COVID-19 pandemic: An impetus for action

The COVID-19 pandemic forced governments around the world, including Canada, to urgently take stock of domestic manufacturing capabilities to support their pandemic response and preparedness. In Canada, this included evaluating domestic capacity to produce vaccines and therapeutic drugs, with a particular emphasis on the manufacturing platforms required to supply products needed to respond to COVID-19. In many instances, this required evaluating the availability of cutting edge and/or novel technologies, including advanced capabilities in biologics manufacturing.

Despite initiatives and investments in recent years in Canada's life sciences sector, specific gaps within Canada's biomanufacturing landscape became evident in the early stages of the pandemic. It also became clear that producing vaccines and therapeutic drugs at a population scale along a timeline that would effectively support Canadians during the COVID-19 or a future pandemic would require a much larger biomanufacturing footprint than what is available in the country.

The Government recognized gaps in Canada's manufacturing capabilities early on and rapidly took initial steps to enhance domestic biosecurity. This included investing in expanding the National Research Council of Canada's Royalmount site in Montréal. This project will establish a clinical trial material facility and build a new end-to-end biomanufacturing facility, the Biologics Manufacturing Centre, compliant with Good Manufacturing Practices, to ensure domestic access to a supply of cell-based vaccines and other biologics in response to pandemic emergencies, as well as to advance Canada's biomanufacturing capacity into the future.

As well, investments of $35M from Western Economic Diversification in VIDO-Intervac in Saskatoon were combined with additional funding dedicated to this facility through the Canada Foundation for Innovation to enable vaccine production for use in clinical trials and to support population immunization efforts (total investment in VIDO-Intervac to date of $46M).

The Government of Canada has also taken action to support existing private sector firms within the Canadian life sciences ecosystem. This includes contributions through the Strategic Innovation Fund to support the development of vaccines and therapeutics and the planned expansion of their manufacturing facilities. Examples of these investments include:

- **Medicago (Quebec City, QC)** – to support the development of the firm's plant-based virus-like particle vaccine and the construction of a Good Manufacturing Practices (GMP) facility;
- **AbCellera (Vancouver, BC)** – to support antibody discovery and clinical testing in collaboration with U.S. firm Eli Lilly, and to support the construction of a GMP facility; and,
- **Precision Nanosystems (Vancouver, BC)** – to support the development of a self-amplifying RNA vaccine against COVID-19, and the construction of a centre for the production of RNA vaccines.

Other investments through the Strategic Innovation Fund and other mechanisms to build flexible vaccine and therapeutic manufacturing capacity are under active consideration, and more investments are expected shortly to further build out biomanufacturing capacity across

platforms. The Government of Canada is resolved to take the necessary steps to mobilize and expand existing Canadian biomanufacturing capacity and to pursue partnerships with international firms to support Canada's response to COVID-19, to enhance future pandemic preparedness, and to foster the sustainable growth of the Canadian life sciences ecosystem.

The Government of Canada has been actively pursuing partnerships with leading vaccine manufacturers, and in February 2021, entered into a Memorandum of Understanding with leading biotechnology firm Novavax, which enables the Government to pursue options to produce Novavax's COVID-19 vaccine at the National Research Council's Biologics Manufacturing Centre in Montréal, once both the vaccine candidate and the facility receive Health Canada approvals. The Memorandum of Understanding also reflects a broader commitment between the Government of Canada and Novavax to work collaboratively to explore options to increase the company's Canadian presence, including possible partnerships with Canadian contract manufacturers. The Government of Canada continues to pursue strategic partnerships with other leading manufacturers of vaccines and therapeutics.

Expert advice on biomanufacturing in Canada

It was within the context of the COVID-19 pandemic that the Government of Canada established its Vaccine Task Force and Therapeutics Task Force, as well as a Joint Biomanufacturing Subcommittee of these two groups. These advisory bodies have been providing expert advice to the Government on the development of COVID-19 vaccines and treatments, as well as on opportunities to enhance the capacity of the domestic life sciences sector. This has included advice on biomanufacturing, which pointed out significant gaps in Canada's capacity for the long-term. The Joint Biomanufacturing Subcommittee in particular recommended the creation of significant biomanufacturing capacity for Canada, along the line of models in the United States and the United Kingdom, in order to both address gaps in biosecurity and revitalize the biomanufacturing landscape in Canada.

As part of its recommendations, the Joint Biomanufacturing Subcommittee urged the Government of Canada to expand existing biomanufacturing capacity at contract manufacturers in Canada. The Government is advancing the provision of support to these sites through various funding mechanisms, including through the SIF. As part of this strategic, coordinated expansion of domestic biomanufacturing capacity, a biologics manufacturing and innovation initiative could provide a useful platform for unifying the governance, decision-making and prioritization of activities across various biomanufacturing investments.

Canada's life sciences sector

Canada's life sciences sector is recognized globally for its strengths in research, collaboration and innovation, including a history of scientific breakthroughs. This ecosystem, which extends from coast to coast, includes innovation superclusters, 27 networks of centres of excellence for research in life sciences, more than 100 teaching hospitals and research institutions, and top graduates in the life sciences.

Canada ranks highly among international peers in a number of research areas and is recognized for the quality of its clinical trials. It benefits from a legacy of several world-leading equipment manufacturers, a number of anchor firms and contract manufacturers, a strong chemicals industry, engineering expertise, a robust university and research base, and an active life sciences and biotechnology start-up ecosystem.

However, Canadian biomanufacturing capacity as a whole has not kept pace with its associated ecosystem elements or with domestic demand, causing Canada to be overly reliant on imported products. Indeed, domestic consumption of vaccines and therapeutics has grown steadily from $473 million in 1997 to $4.8 billion in 2019, but Canada's ability to produce these products has decreased over the same period. In 1973, approximately 19% of Canada's domestic demand for vaccines and therapeutic drugs was supplied through imports. Today, Canada imports 85% of its requirements, primarily from Germany, Switzerland, and the United States. Demand for these products is expected to continue to grow, with increased demand for genetic construct and immunobiologicals, tied closely with discoveries and innovations in receptor subtypes and genetic linkages.

Canada has experienced the exit of many major players from the Canadian life sciences ecosystem in recent years. The Canadian ecosystem began to shift in the late 1980s with the privatization of Connaught Laboratories Ltd. when the Canada Development Corporation sold it in two public issuances (in 1984 and 1987), leading to its eventual takeover by Sanofi. Beginning in the early 2000s, large multinational pharmaceutical companies began shifting their global operations and supply chains by pursuing mega-mergers, or otherwise concentrated their investments, in global locations in order to maximize efficiency. For Canada, this global restructuring, combined with relatively little support for the sector, led to a reduced manufacturing footprint and the shuttering of several important facilities. Notable examples include the exit of AstraZeneca in 2007, when the firm closed its Canadian manufacturing operations and consolidated its operations in Sweden and closure of one of Teva's manufacturing operations in Montreal in 2011. Canada's biomanufacturing sector now lags behind that of international competitors. Other members of the G7, as well as China, India, Ireland, Brazil and South Korea, have seen sizeable increases in their biomanufacturing sectors over the past 20 years. Examples of increased investment in these jurisdictions include Bayer's cell culture technology centre in the United States and Pfizer's biotechnology campus in Ireland. As investments abroad have increased, Canada's place in world markets has diminished, with our global share of exports of biologics having fallen from 2.4% in 2010 to 0.4% in 2019.

Globally, the life sciences landscape has experienced an important shift in recent decades. Start-ups and smaller firms are now conducting research and development activity previously carried out by large multinational pharmaceutical companies. Additionally, Canada is not viewed as a preferred training site for international highly-qualified personnel in the biomanufacturing field, which limits the ability to recruit talent. Without strategic investment in domestic biomanufacturing capacity, which must also take into account operations in non-pandemic scenarios, Canada risks continued loss of its considerable talent to other countries as they build out their capacity with cutting-edge, modern technology.

Even before the outbreak of the pandemic, the Government of Canada had begun to make a number of important investments in an effort to strengthen the country's life science footprint and talent base. For example, in 2018, the Federal Economic Development Agency for Southern Ontario, along with the Province of Ontario, provided up to $70 million in support to Sanofi Pasteur for its $500 million Bulk Biologics Facility, located at the Connaught Campus in Toronto. The same year, the Government announced a SIF investment of $22.5 million in Vancouver-based STEMCELL Technologies, to support a project that included the construction of a state-of-the-art manufacturing facility. In 2019, a further SIF contribution of up to $37.5 million was announced for BioVectra, a Charlottetown-based biotechnology company. Further potential investments would be designed to build on these assets already in place.

A PROPOSAL FOR STRENGTH IN BIOLOGICS PRODUCTION AND RESEARCH

The Government of Canada is considering how best to consolidate and build on the progress made since the outset of the pandemic to expand Canadian biomanufacturing capacity. While multiple investments have been made in facilities across the country, across multiple technology platforms, it is critical that the whole of this effort be greater than the sum of its parts. For the long-term, Canada needs a strategic approach to ensure the country has sufficient standing national capability to produce at scale to meet the needs of Canadians across multiple vaccine and therapeutic platforms, one that contributes to security of supply through providing timely and uninterrupted access to vaccines and therapeutic drugs. Such an approach would ensure readily available biomanufacturing capacity as a critical public health asset, available for use during an emergency, such as a global pandemic, or in response to critical domestic or global health priorities.

In particular, the Government of Canada is considering how it could further enhance domestic biomanufacturing capacity and the long-run security of supply through a **Canadian biologics manufacturing and innovation initiative**.

While enhanced pandemic preparedness and health security may be its primary purposes, the initiative under consideration could achieve several other important objectives. For example, it could facilitate the testing of new ideas from academia through the production of small batches for preclinical or clinical trial purposes; it could act as a training platform for highly-qualified personnel, in particular to help build a cohort of Canadian scientists, engineers and technicians with the know-how in biomanufacturing; it could provide a cornerstone for Canada's growing life sciences sector by enabling small- and medium-sized enterprises (SME) to manufacture their products at scale without having to leave the country; and it could act as a powerful magnet to attract multinational players in biopharmaceuticals to Canada and help the country better integrate into international supply chains. It could also play a key role in the future research agenda around pathogens and preparedness for future pandemics, linking with the work of the Canadian Institutes for Health Research and Canadian universities. The initiative could also encourage the increased participation of researchers and other professionals from marginalized groups in the effort to promote the sustainable development of the Canadian life sciences sector, and contribute to greater diversity in the Canadian science, technology, engineering and math (STEM) ecosystem.

Importantly, it is expected that such an initiative could also serve as an anchor for the many near-term investments under way in domestic biomanufacturing made by the Government of Canada as part of its response to COVID-19, including the expansion of private sector biomanufacturing centres and the build-out of biomanufacturing capacity at the National Research Council's Royalmount facility, as well as investments made in companies such as AbCellera, Precision Nanosystems Inc. and Medicago. By bringing together Canadian capabilities and investments as part of a broader strategic vision, Canada could be better positioned not only to significantly enhance pandemic preparedness through coordinating and prioritizing biomanufacturing activities, but also to create a robust biologics manufacturing network attractive to further international investment and to foster growth in Canada's domestic biomanufacturing sector.

The Government of Canada will consider the approaches that have been adopted in other countries to achieve similar objectives, as well as the views of provincial and territorial partners. No determination has yet been made as to whether further expansion of domestic biomanufacturing capacity would take the form of a single or multiple sites, or how to build upon investments in the Canadian life sciences ecosystem. Different jurisdictions have pursued different approaches, some relying more on private sector solutions and others focusing on state-owned assets. Key international examples of expanded biomanufacturing capacity include the following:

- The **Texas A&M Centre for Innovation in Advanced Development and Manufacturing** (College Station, Texas), established as a **private-public partnership** in response to the H1N1 pandemic involving the U.S. Biomedical Advanced Research and Development Authority in collaboration with commercial and academic partners. The centre was established to respond to the need for rapid, flexible biomanufacturing capacity to address emerging disease and prospective chemical and biological threats. Texas A&M University is primarily responsible for research and development activities, while the large-scale biomanufacturing capacity is operated on a for-profit basis by a contract development and manufacturing organization, FUJIFILM Diosynth. The Texas A&M Centre is estimated to have approximately 24,000 litres of bioreactor capacity. In February 2020, FUJIFILM Diosynth announced plans to expand bioreactor capacity at the facility, though the precise quantity of additional capacity is unknown.

- The **Vaccines Manufacturing and Innovation Centre** (Oxford, United Kingdom), commenced engineering and building work in 2019 as a **non-profit consortium** supported by academic research institutions, including the University of Oxford, Imperial College, and the London School of Hygiene and Tropical Medicine, in partnership with private-sector actors, including Janssen and Cytiva. The Vaccines Manufacturing and Innovation Centre is expected to conduct research and development activities as well as commercial manufacturing, with approximately 80% of its activities dedicated to R&D and 20% to commercial manufacturing. The Vaccine Manufacturing and Innovation Centre will have an estimated 2,000 litres of bioreactor capacity.

- The **Thermo Fisher Scientific Facility** (Brisbane, Australia), established by BioPharmaceuticals Australia, an industry-development company owned by the Government of Queensland, Australia. BioPharmaceuticals Australia oversaw the construction of the facility, and wound down its operations once the facility was complete. Since 2014, the facility has been operated under a **government-owned, contractor-operated** model, leased to Thermo Fisher, a contract development and manufacturing organization. The Thermo Fisher Scientific Facility has an estimated bioreactor capacity of approximately 3,350 litres.

Canada's Health and Biosciences Economic Strategy Table (HBEST) identified a series of targets for Canada's life sciences sector, including doubling Canada's health and bioscience exports, doubling the number of health and bioscience firms, and doubling the number of high-growth firms within these sectors – all by 2025. It is expected that a biologics manufacturing initiative, which could include a further expansion of domestic capabilities, would directly respond to actions proposed by HBEST, including accelerating innovation adoption, harnessing digital technology, attracting talent and creating anchor firms in Canada. HBEST has also indicated the need to conduct technology demonstration projects for high-value, next generation innovation. Any centre or centres that flow from this proposed initiative could provide a test bed or beds for leading-edge technologies, including artificial intelligence and robotics.

AREAS FOR CONSULTATION

MANDATE

What would be the appropriate mandate for a biologics manufacturing and innovation initiative in Canada in order to ensure long-term readiness for future pandemics and to realize economic development opportunities?

Context

Canada's Joint Biomanufacturing Subcommittee has been advising the Government of Canada on ways to rebuild Canada's domestic biomanufacturing capacity. In responding to this ongoing advice, the Government has been pursuing options to strengthen Canada's pandemic preparedness and bolster the life sciences ecosystem. One such option that has been pursued by other countries has been to build standing national capacity to ensure the ability to produce vaccines and other therapeutic drugs at scale to meet the needs of the population and in some cases beyond. Such an approach in Canada, in addition to or as part of a concerted strategy that integrates the many investments already under way with private firms, could play a significant role in bolstering national pandemic preparedness and addressing other health security challenges. Such a platform would also promote and support the long-term sustainable growth of the Canadian life sciences sector.

This section of the paper sets out a proposed mandate for the biologics manufacturing and innovation initiative, based on a model that would be calibrated to the Canadian context, that would appropriately and effectively build on existing infrastructure and strategic assets, and would see some capacity expansion. As noted earlier, it is envisioned that any initiative to ensure Canada can produce vaccines and other biologics at scale would ideally serve multiple purposes, including pandemic preparedness, development of highly-qualified personnel, and incubation of SMEs.

Proposed mandate

As the Government of Canada refines its vision with respect to this proposed initiative, and how best it could materialize, it continues to examine the broad parameters of such an undertaking by situating this vision within broader considerations of the Canadian life sciences ecosystem. It is expected that the mandate of this initiative should include:

- ensuring standing capacity and capabilities to produce at scale to meet the needs of Canadians, and possibly larger quantities for export, across the main vaccine and therapeutic platforms, with biomanufacturing capacity readily available to the Government as a critical public health asset during an emergency (such as the current COVID-19 pandemic), or in response to domestic or global health initiatives;

- serving as a means within the Canadian life sciences ecosystem to connect SMEs, large global biopharmaceutical firms, academia, and researchers to accelerate health innovations and grow Canadian firms, including through making pilot-scale production capacity available to Canadian innovators;

- providing a venue and programs, or creating strong linkages and collaborative programs with existing venues, for the training of highly qualified personnel;

- ensuring alignment with and best use of existing assets to urgently expand capacity in response to the COVID-19 pandemic;

- developing and implementing efficiency-improving at-scale production processes;

- helping Canada contribute to international efforts aimed at ensuring fair and equitable access to biologics;

- ensuring that Canada retains and develops its biological intellectual property from research discoveries through commercialization; and,

- protecting Canadian researchers, scientists and companies from research and economic based threats to national security.

For Consideration

Given the experience of the COVID-19 pandemic, in which domestic manufacturing capacity was highlighted as an important element of ensuring early and reliable access to vaccines and therapies, it is anticipated that certain enhancements would be required to strengthen the Canadian biologics manufacturing system. While it is not yet known what form these enhancements would take, input is sought to gain a better understanding of the core functions that must be available across the country to ensure pandemic preparedness. It is also recognized that a robust biopharmaceutical and life sciences sector writ large – which considers research, access to talent, the start-up ecosystem and growth prospects for innovative firms, and more – will be a precursor both to ensuring health security for Canadians and to realizing economic growth opportunities in this area.

With this in mind, and in light of the proposed mandate outlined above, we invite participants to consider the following questions.

Questions

- What mandates are required to support Canada's biomanufacturing security as well as long-term growth in Canada's biomanufacturing sector? How can we ensure that this initiative does not duplicate existing efforts including those of the private sector?

- Are there further elements of the envisioned mandate for this initiative that should be added or elements that are not required? For example, while focusing on biomanufacturing, should Canada consider national capacity for small-molecule production or other novel technologies?

SCOPE OF OPERATIONS

What should be the scope of operations for an initiative that seeks to bolster long-term domestic pandemic preparedness and a robust and sustainable biomanufacturing sector?

Context

In its response to COVID-19, Canada has been largely dependent on global manufacturing resources to access life-saving vaccines and treatments in a reasonable timeframe. Early challenges in the rapid ramp-up of vaccine production abroad, for example, have underlined Canada's continued exposure to supply chain disruptions, and brought to the fore the many risks associated with security of supply.

What few major vaccine manufacturing facilities we have in Canada at present are already dedicated to other critical functions, such as production of seasonal flu vaccine, pandemic influenza vaccine, or vaccines for the prevention of serious diseases such as diphtheria, tetanus, polio and pertussis. Unlike many other peer nations, Canada does not have significant standing capacity to manufacture new products rapidly and at-scale. We also lack facilities for at-scale production of specialized biologics such as monoclonal antibodies. In recognition of these shortcomings, the Government has supported an expansion of Canadian biomanufacturing capacity, including with a series of investments made through the Strategic Innovation Fund. What remains to be determined, however, is whether these and other planned investments will be sufficient to secure for Canadians the large-scale capabilities to respond to a pandemic or other health emergency, and whether by themselves such new capacity would ensure the security of supply in vaccines and therapeutic drugs that is necessary for a safe and timely response in such situations.

This section of the paper explores the capabilities that should be considered vital to the health of the Canadian biologics landscape and to our future pandemic preparedness. These will include such considerations as required vaccine and therapy platforms, bioreactor capacity, minimum production standards for the Canadian population and to be an attractive manufacturing destination for international partners, and capabilities required along the value chain including in related industries and sectors. This section will also solicit input on key considerations for selecting sites for capacity expansions, if such options for additional capacity are found to be complementary to existing investments made in domestic biomanufacturing and considered viable by the Government of Canada.

Maintaining technological flexibilities in pandemic scenarios

In response to COVID-19, researchers worldwide have been developing candidate vaccines and therapeutic drugs using a variety of platform technologies, including new vaccine technologies involving messenger ribonucleic acid (mRNA). Anticipating that there will always be uncertainty surrounding the precise technology that may prove effective in any future health emergency, it will be important for Canada to establish and maintain biomanufacturing capabilities across a portfolio of leading technology platforms. An important consideration will be to determine which technology platforms (e.g., DNA, RNA, viral vector, peptide, virus-like

particle, and so on) Canada may need prioritize when contemplating investment in enhancing long-term pandemic preparedness, including through the Canadian biologics manufacturing and innovation initiative presently under consideration. Given the different supply chains that are involved in the production of vaccines using various technologies, it will also be important to consider how Canada can improve its integration into these supply networks and, where appropriate, build domestic capabilities to mitigate risks of supply chain disruptions and to enhance security of supply. In addition, considerations around production scale will be important, for example to both enable rapid vaccination or treatment of Canadians during a pandemic and make technology transfer worthwhile for a vaccine developer.

Enhanced biosecurity through end-to-end production capabilities

In a pandemic scenario, it is vital that complex biomanufacturing processes be carried out seamlessly so as not to delay the production of life-saving vaccines and therapeutic drugs. Similarly, in order to enhance biosecurity and contribute to security of supply, it is important to anticipate and limit possible supply chain disruptions. Whether facilities are co-located or connected through a network, an end-to-end manufacturing solution is essential to avoid delays and bottlenecks in the biomanufacturing process and to enhance the security of supply by limiting exposure to disruptions in access to materials and expertise that are essential for the production process.

Furthermore, end-to-end capabilities include not only drug substance production but also filling and finishing of vaccines and therapeutic drugs. There are also storage and distribution considerations. Considering the need for end-to-end capabilities will be important, particularly in the design and early-stage activities associated with any plans to further invest in domestic biomanufacturing capacity.

It is equally important to recognize that enhanced biosecurity and self-sufficiency in vaccine and therapeutic development requires a strong research and development base, including support for exploratory and pre-clinical trials, as well as at-the-ready clinical-scale production and large-scale biomanufacturing capacity.

Elements of enhanced biosecurity are envisioned to include the following attributes:

- flexibility to respond to any pandemic agent, including capacity for both predictable and unpredictable pandemics that could be caused by a broad range of infectious agents;

- speed in response, with minimal lag between an infectious agent with pandemic potential being recognized and an appropriate medical response in the form of a vaccine or therapy being ready for deployment; and,

- sufficiency in production, with an adequate number of doses to serve every Canadian within an appropriate timeframe, without disruption or delays to the production process.

It is important to recognize that the vulnerabilities of Canada's supply chains are not limited to biologics, but extend also to small molecule production, as well as other technologies, including mRNA products. Concerns with the lack of domestic self-sufficiency during the COVID-19 pandemic have reinforced the need to examine options to further expand domestic biomanufacturing capacity across a range of technologies. It is expected that technologies, such as small molecules, may have an important role to play in a future pandemic response. It will be important to determine the types of technologies, as well as to appropriately calibrate the

capacity in each technology, when considering the scope of operations for a potential further expansion of domestic production capacity.

An Ecosystem Approach to biomanufacturing capacity

In taking steps to ensure that Canada has sufficient capacity at-scale to manufacture vaccines and therapies for the long-term, one must also take into account the country's geography and existing clusters of expertise in the life sciences, as well as consider opportunities to maintain momentum and build upon existing investments and assets in the domestic life sciences sector. In considering prospective sites for any additional biomanufacturing capacity, it will be important to build upon strategic investments made through SIF, as well as to consider the assets and expertise of the National Research Council, particularly at its Royalmount facility, and other key players within the Canadian life sciences ecosystem, such as the University of Saskatchewan's Vaccine and Infectious Disease Organization (VIDO-InterVac). This also includes consideration of the role that large anchor firms could play in the Canadian landscape, either through research and manufacturing partnerships with Canadian firms, or potentially through an augmented presence in Canada. Any additional Canadian biomanufacturing capacity would need to be well integrated into the existing ecosystem, and be connected to key academic and industry partners, to maximize effectiveness, cluster benefits and positive spillover effects. One important consideration with respect to location of any expansion to domestic biomanufacturing capacity is whether investments should be built around existing infrastructure and ecosystem elements.

Additionally, the location(s) should be convenient for employees, provide access to highly-specialized materials and services necessary for advanced biomanufacturing and, where possible, be in proximity to transportation infrastructure including international airports, which is expected to aid both in supply chain integration and the timely distribution of products.

Given the broad mandate that this initiative seeks to accomplish, it may also be important that a site or sites for contemplated investments be able to satisfy a number of other criteria. For example, it is likely that a potential site should be large enough to accommodate biomanufacturing, research, administrative and storage requirements, and provide room for further expansion. It is also recognized that if additional investments in biomanufacturing assets are made, these would require access to industrial-scale utilities, including electricity, water, sewage, disposal services and information technology network access.

For Consideration

If this consultation process and other analysis under way by the Government of Canada reveal that further expanded long-term biologic manufacturing capacity in Canada is warranted there are a number of important considerations related to what this capacity should look like. The Government is interested in understanding your perspectives related to minimum capabilities that Canada should have available to ensure pandemic preparedness, to promote biosecurity, and to maximize the growth potential of the sector.

With this in mind, we invite you to consider the following questions related to the scoping of a biologics manufacturing and innovation initiative.

Questions

To inform potential site decisions:

- When contemplating further investments through the proposed Canadian biologics manufacturing and innovation initiative in the context of pandemic preparedness, is it better to consolidate any new biomanufacturing capacity at a single site or to continue to expand and strengthen capacity across multiple sites, and why?

- What geographic location(s) would be best to support any proposed biomanufacturing expansion(s), and why?

- What are crucial elements the Government should consider when determining the location and choosing a site or sites for any proposed increased capacity?

- Where are the existing pockets of expertise in specific areas of the biomanufacturing process that could be built upon?

To inform general function and program requirements:

- What elements do you consider to be critical to ensuring pandemic preparedness and realizing other key goals of any new capacity? To what extent should current Good Manufacturing Practices (GMP) be incorporated into any new capacity? What do you see as being the minimum standard capabilities and capacity output requirements? How much biomanufacturing capacity is required for Canada to be prepared for future pandemics and other health emergencies?

- What capabilities are required in any increased domestic biomanufacturing capacity and for enhanced pandemic preparedness? What capabilities are required to support increased pilot-scale production?

- Should the proposed new capacity include physical assets, such as dedicated biomanufacturing capacity, just a network, or both?

- What assets should be considered beyond manufacturing lines? For example, research labs; on-site accelerators and investment advisors; other support services such as residences, transportation links, etc.?

- What is the appropriate biosafety containment level for a biomanufacturing facility?

- What capacity is required to make Canada an attractive manufacturing destination for vaccine and therapy developers? Should Canada contribute to responding to global demand?

ROLE WITHIN THE BIOLOGICS RESEARCH AND MANUFACTURING ECOSYSTEM

How can we ensure that any additional capacity is well-connected with Canada's research community and well-integrated into Canada's life sciences ecosystem?

Context

The Government views innovation as a key element in supporting future growth and pandemic recovery, and responding to other health threats in Canada. Canada's life sciences sector is a dynamic component of Canada's innovation economy, with specific opportunities related to its strengths, but also challenges. To maximize the sector's potential, it will be important that any further major investments in domestic biomanufacturing play a central role in realizing the benefits of innovation-based growth, accelerating innovation adoption, enhancing opportunities for technology transfer, harnessing digital technology, developing and attracting talent to Canada, and creating anchor firms in the country.

This initiative could also serve as a central point of connection between research and innovation in the life sciences sector and create opportunities for manufacturing and commercialization. It could also support a more coherent approach to clinical trials infrastructure, including through enhanced coordination among university-based and affiliated laboratories, biosecurity labs, and other GMP facilities. It is expected that this initiative will build upon Canada's existing and recognized strengths in the life sciences and will be integrated within the Canadian life sciences ecosystem, including with respect to supporting clinical trials.

This section of the paper will explore how enhancements to Canada 's biomanufacturing sector could directly contribute to the broader life sciences ecosystem. This includes opportunities to connect with research and academia, ways to support the training of highly-qualified personnel, opportunities to strengthen the start-up ecosystem and help SMEs more effectively grow to scale, and more.

Leveraging existing investments and areas of strength

It is envisioned that any investment made through the Canadian biologics manufacturing and innovation initiative would have strong linkages with existing Government of Canada biomanufacturing infrastructure, notably the National Research Council's Royalmount facility in Montreal.

It is also contemplated that the initiative would serve as an anchor for other investments that the Government of Canada is making in a series of specialized drug substance and product manufacturing centres across the country as part of the immediate COVID-19 response. The Canadian biologics manufacturing and innovation initiative could form the foundational element of a biologics network, allowing it to influence and coordinate activities at satellite centres, strengthen the domestic biomanufacturing sector, and serve as a magnet for further large-scale investment.

A domestic pool of highly-qualified personnel with experience in biomanufacturing processes is a fundamental consideration for multinational firms when determining where to make

investments. Biomanufacturing processes are complex and require specialized skills to safely and effectively implement. In Canada, at present, limited venues related to biomanufacturing restrict the opportunities to develop and refine these skills in the applied sciences, and may prompt Canadian talent to seek such opportunities abroad. Investments in domestic biomanufacturing capacity should be well calibrated to enhance Canada's talent pool and maximize job creation and talent retention, while allowing firms to draw on specialized expertise from abroad if needed.

In addition to supporting the training and development of highly-qualified personnel, and the creation of new jobs, it would be important to link any potential investments in domestic biomanufacturing with academia and research institutions. Mechanisms to increase collaboration, particularly between academia and SMEs, should be, in the Government's view, be an important feature of any investment in new capacity.

For Consideration

If the Government proceeds with a biologics manufacturing and innovation initiative, it is anticipated that there would be strong potential to link research strengths in the country with expanded and diversified manufacturing capabilities. Further, in order to ensure the sustainability of this initiative, and to support further growth in the life sciences sector, access to highly-qualified personnel would be an important consideration moving forward.

With this in mind, you are invited to consider ways in which such an initiative could integrate with and support other elements of Canada's life sciences ecosystem, including moving made-in-Canada ideas further along the innovation continuum toward commercialization, as well as supporting talent development, access and retention. This should also include consideration of how Canada could best build upon existing skills and assets across the country to ensure a cohesive and aligned biopharmaceutical sector. Your views are also welcomed on broader considerations related to the Canadian life sciences ecosystem, and any steps that can be taken to promote resilience and growth within the ecosystem.

Questions

- What steps should be taken to foster closer links and alignment between Canada's biomanufacturing sector and academia? What role could be played by a new Canadian biomanufacturing organization?
- How would such an initiative interact with the existing resources and platforms of national funding agencies and granting councils?
- Apart from biomanufacturing capacity, are there gaps in the Canadian research landscape that could be filled to support biologics development and innovation in Canada?
- What is the appropriate balance between developing highly-qualified biomanufacturing personnel in Canada and sourcing expertise from abroad? What measures would you recommend be put in place to achieve that balance?
- What supports or services could be put in place to help small- and medium-sized enterprises scale their innovations and grow their businesses in Canada?

- Are there other critical elements that would contribute to an environment that is more conducive to biologics research and manufacturing?

- What capabilities should Canada have in-country in related industries, alongside biomanufacturing capacity, to support the sector (e.g., API manufacturing, primary packaging for vaccines, etc.) ?

SUSTAINABILITY

Outside of a pandemic scenario, how would such an initiative best sustain its operations?

Context

While investments in domestic biomanufacturing are an important part of Canadian public health infrastructure supporting pandemic preparedness, they should also be capable of sustaining operations in non-pandemic environments. It is anticipated that strengthened linkages between investments in biomanufacturing and the broader life sciences ecosystem will be an integral part of supporting sustainable operations outside of a pandemic.

Through this lens of sustaining operations outside of a pandemic, considerations revolve around the profit-orientation of prospective investments in biomanufacturing capacity; namely, whether biomanufacturing assets should operate on a for-profit or not-for-profit basis. This section of the consultation paper will outline some proposed principles relating to sustainability of a biologics manufacturing and innovation initiative, and seek views on how the Government of Canada could ensure that such an initiative would include a viable business model that could be maintained in the years to come. Your views are welcomed on methods that may be deployed by the Government of Canada to strengthen the Canadian life sciences ecosystem to support the operations of biomanufacturing assets in periods outside a pandemic scenario.

Principles for a sustainable biomanufacturing initiative

As the Government considers implementing a Canadian biologics manufacturing and innovation initiative, a key goal will be to ensure that, as much as possible, any investments in new domestic biomanufacturing capabilities will be self-sustaining in the long-term. The ability to operate in a sustainable way would achieve several important goals. Perhaps most importantly, it would ensure that investments in biomanufacturing are targeted to providing needed products and services, and thus able to maintain a technological edge and provide legitimate and useful training to employees. By contrast, a “white elephant” that is rarely used runs the risk that its technology becomes obsolete and its personnel ill equipped with the current skills needed in a true emergency. A sustainable facility would also minimize the fiscal exposure of governments. At the same time, a state-supported facility or facilities should not compete with fully commercial operations in any way that would distort the market.

For Consideration

A variety of models exist around the world that demonstrate how large-scale, state-backed biologics manufacturing capacity can at once be accessible to the government and to academic

institutions, while generating the revenues needed to support sustainability. A key question is which of these models – or an entirely new model – might make the most sense in the Canadian context.

You are invited to consider approaches to ensuring the sustainability of the proposed biologics manufacturing and innovation initiative. This could include options such as a private-sector driven approach that would include some rights of access for public sector entities, as well as profit-generating opportunities that could be explored to ensure sustainability of an initiative that would see a greater degree of public-sector control over its operations.

Questions

- Outside of pandemic response-related activities, what else should be pursued to make operations in biomanufacturing capacity sustainable?
- Outside of a pandemic, should state-sponsored reserve biomanufacturing capacity operate on a for-profit or not-for-profit basis?
- How should arrangements be designed to provide government access during a pandemic or other health emergency?
- Are there areas of specialization that Canada should consider to build on and sustain existing Canadian strengths now and into the future? How can we build on these strengths?
- What factors should be considered to ensure that prospective federal investments in biomanufacturing assets do not crowd-out or undermine existing players in Canada's life sciences sector? Are there activities that should be avoided so as not to disrupt or distort the private market for biomanufacturing?
- What factors need to be considered to ensure that any new capacity can easily pivot between supporting pandemic response efforts and commercially sustainable operations?

GOVERNANCE

When designing and implementing an initiative to strengthen domestic biomanufacturing and innovation, what governance model(s) would be most effective?

Context

If the Government implements an initiative, it would be important to establish resilient governance models to oversee and coordinate the activities and investments in Canadian biomanufacturing capacity. Adopting an approach that is responsive to stakeholder needs, strikes a balance between pandemic preparedness and non-pandemic operations, and is well

calibrated to the Canadian regulatory context would be crucial to the long-term success of an initiative to strengthen domestic biomanufacturing and innovation. It will be especially important to ensure that any governance structure is well situated within the Canadian life sciences ecosystem, and can effectively operate and provide strategic direction in that context.

This section of the paper will seek views on the most appropriate governance structures to ensure public benefit is maximized, while also enabling strong research, innovation, and business outcomes.

Ensuring access for future health emergencies

The involvement and representation of the public and private sectors in the governance of domestic biomanufacturing investments would have to be taken into account when designing the governance structure(s) of domestic biomanufacturing investments, including with regard to the contemplated Canadian biologics manufacturing and innovation initiative. Ensuring appropriate representation in the governance of this initiative will be of central importance to provide strategic leadership in instances of future health emergencies. In view of the strategic investments made in response to COVID-19, and anticipating that future health emergencies may require swift and decisive action, it will be important for the governance structure of a Canadian biologics and innovation initiative to support flexible, strategic action.

Government access to biomanufacturing assets in a pandemic scenario must be a central component of any governance structure to ensure an effective, coordinated response that places the safety and security of all Canadians at the forefront of decision-making. While recognizing the vital importance of enabling the government to direct biomanufacturing assets in a pandemic scenario, it is also important to ensure that the government does not encumber the efficient operation of biomanufacturing assets in non-pandemic conditions. Striking the appropriate balance between the overriding public safety need in pandemic scenarios and the importance of efficient operations in non-pandemic conditions is a central consideration when developing a suitable governance structure for biomanufacturing assets.

Bringing the key partners together

Ideally, the governance of a Canadian biomanufacturing initiative would aim to connect the various critical players required for the initiative to be successful. Governments would have a central role to play, given their interest in pandemic preparedness.

Ideally, the governance model would ensure strong linkages to the Canadian life sciences sector, given the role that a biomanufacturing initiative would play in the broader ecosystem both as an incubator of SMEs and a manufacturer in its own right. There would ideally be strong linkages to the research sector and to the leading academic institutions, given the potential role the initiative would play in fostering research and in training highly-qualified personnel. Others who might be desirable on a board or other governance mechanism could include individuals with recognized expertise in biomanufacturing, those with experience in the governance of complex multi-stakeholder institutions, as well as distinguished Canadians known for their leadership and judgement.

Drawing upon international lessons learned

International organizations and companies have a vital role to play in complementing the expertise that exists in Canada, both in terms of providing opportunities for knowledge sharing

and for attracting investment from abroad into the Canadian life sciences ecosystem. It will therefore be important to ensure that the initiative supports international partnerships, both in the context of pandemic and non-pandemic scenarios.

When determining the appropriate governance structure for a Canadian biologics manufacturing and innovation initiative, it would be important to consider successes abroad and to draw upon lessons learned from the experiences of other countries in expanding their biomanufacturing capacity.

Various approaches have been adopted globally, including private-public partnerships, such as the Texas A&M Centre for Innovation in Advanced Development and Manufacturing; government-owned-contractor-operated models, such as has been employed by the Thermo Fisher Scientific Facility in Australia; and a non-profit consortium of industry and academia, as has been established by the Vaccines Manufacturing and Innovation Centre in the United Kingdom.

For Consideration

It is expected that the most appropriate model for a biologics manufacturing and innovation initiative would include some blend of public and private sector representation. This should include access by the Government to respond in times of national emergency and to help drive national health priorities. At the same time, it is well recognized that private sector vision and business sense will be critical to achieving the outcomes that will enable such an initiative to not only be commercially sustainable, but also contribute to global efforts to develop and produce leading-edge pharmaceutical products. We expect that some form of public-private partnership model would be most effective at achieving these objectives.

Based on other models encountered globally, it has been observed that a governance model that involves government being on the board of management, as well acting as a priority client in times of crisis, can work well. In these instances, governments tempered the initial risk associated with investments in large-scale infrastructure and annual fixed costs, but did not own or operate the facility.

With this in mind, we ask you to consider the best approaches to governing a biologics manufacturing and innovation initiative in such a way so as to maximize both the public benefit – including, at minimum, secured access by the public sector during a state of public health emergency – as well as the commercial success of the initiative. This would include the ability to enhance firm growth, and maintain and grow more leading life sciences firms within Canada. An additional critical consideration is how such an initiative could be governed so as to support research programs under way at Canadian institutions.

Questions

- What is the right governance model to ensure that biomanufacturing assets are an effective component of a pandemic response?
- How will the choice of a governance model influence decisions on commercial sustainability?
- What is the right governance model to ensure a fair and competitive life sciences sector that is attractive to global partners?
- What factors should be considered when determining the involvement and representation of the public and private sectors in the governance of biomanufacturing assets?
- What factors should be incorporated into the governance structure of this proposed initiative to ensure appropriate linkages with other biomanufacturing investments made as part of Canada's immediate COVID-19 response?

CONCLUSION

We thank all participants in this consultation for their time and contribution. Your input and ideas will be most informative in building the next generation of biologics manufacturing and life sciences strength in Canada. The Government of Canada is committed to open communications on this initiative as alignment is achieved on a potential plan for moving forward.