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Vaccine Industry Committee

Injecting Success: The Future of Vaccines in Canada

Investir dans le succès: L'avenir des vaccins au Canada

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This paper is from the *Building on the Legacy of Vaccines in Canada: Value, Opportunities, and Challenges* Series. To read the series, visit www.biotech.ca/vaccines.

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10.1 Executive Summary / Sommaire

10.1.1 Executive Summary

Since the discovery of modern vaccination more than 200 years ago, vaccines have proved to be one of the most successful and cost-effective public health interventions. Globally, investment in research and development (R&D) has resulted in a broad range of vaccines targeting over 25 infectious diseases. Building on past momentum, renewed investment in the vaccine enterprise has been fuelled by numerous factors, including unmet medical need in preventing major diseases such as malaria, hepatitis C, and acquired immunodeficiency syndrome, AIDS; concerns regarding emerging infectious diseases as well as recurring threats of pandemic influenza and bioterrorism; and the recent growth and “blockbuster” revenues observed in the global vaccine market. Looking to the future, current estimates suggest there are approximately 150-200 vaccines in the clinical-stage development pipeline worldwide, and intensified interest in vaccine R&D is anticipated to generate a three-fold increase in available vaccines over the next few decades.

Exciting new advances in immunology and molecular biology techniques have enabled the application of multiple innovative strategies in vaccine development, which in turn have advanced the ability of researchers to create both preventive and therapeutic vaccines (or target new diseases) not thought possible before. In contrast to traditional preventive vaccines, emerging therapeutic vaccines are intended to treat an existing disease, rather than provide prophylactic protection (see Paper 3). At present, therapeutic vaccines are being evaluated to treat a diverse range of human disorders, including certain chronic infectious diseases (AIDS, hepatitis C, chlamydia), as well as non-infectious diseases such as cancer; metabolic diseases (hypertension, diabetes); neurodegenerative diseases (stroke, Alzheimer’s); and autoimmune diseases (multiple sclerosis, rheumatoid arthritis). Other recent advances in vaccine technology include the development of new adjuvants (which enhance the immune response to an antigen) and novel vaccine delivery methods, i.e. via oral, intranasal, transdermal (e.g. patch), or intradermal (e.g. microinjection) routes that may help to minimize the pain and logistical constraints associated with current needle-based delivery. The intranasal influenza vaccine, FluMist (AstraZeneca/MedImmune) is expected to be approved in Canada in 2010.

Given the recent boom in vaccine technology, it is expected that new vaccines will have a significant impact on the delivery of immunization programs and the epidemiology of vaccine-preventable diseases in Canada in the near-term future. Indeed, several new vaccines have been approved since mid-2006 and are already offering new disease prevention opportunities for Canadians. These new vaccines target rotavirus, shingles, additional strains of bacteria that cause pneumococcal disease, and clinical disease caused by human papillomavirus (HPV) – primarily cervical cancer. Many innovative vaccine technologies are also in development by global pharmaceutical and Canadian-owned companies, with several vaccine candidates currently in preclinical and clinical trials. Across the country, the pipeline is bulging, and continued innovation is anticipated to generate a new wave of preventive vaccines (e.g. against influenza, hepatitis A & B, HIV/AIDS) as well as cutting-edge therapeutic vaccines (e.g. targeting breast, ovarian and prostate cancers, and prion-mediated diseases such as Lou Gehrig’s and Alzheimer’s disease). While Canada continues to make strong contributions to the development of next-generation vaccines, collectively, these research initiatives are poised to extend the current benefits of immunization – particularly to adolescent and adult populations. In addition, on the international horizon, impressive advances are being made in targeting leading global killers, especially those endemic in developing countries, such as pneumonia, malaria, tuberculosis, AIDS, dengue, and rotaviral disease.

As technology innovation continues to drive the discovery of revolutionary new vaccines and delivery methods, the range of immunization program options also widens, with the consequent need for updated, improved governance and funding systems. At present, emerging vaccines are being introduced by manufacturers, yet the interval between Health Canada approval and immunization program implementation is undesirably long (e.g. three to six years), including lengthy reviews by the National Advisory Committee on Immunization (NACI) and the Canadian Immunization Committee (CIC). In addition, patient access to recently approved vaccines is currently impeded by a lack of sustained federal funding for public sector programs. Unfortunately, the net result is that Canadians are denied timely, consistent access to approved vaccines – and thus left at

unnecessary risk, due to lack of optimal protection from vaccine-preventable diseases. Overall, despite well-recognized successes in decreasing the incidence of infectious diseases, Canada's current immunization system can still be characterized as lacking harmonization and transparency, resulting in unacceptable duplication, inequities and delays.

In particular, the recent Canadian experience with introducing the novel quadrivalent vaccines Gardasil (which targets HPV-related clinical disease) and Menactra (which targets meningitis) – both licensed in 2006 – serves as a convincing platform to articulate the need for improvement in reshaping our national immunization landscape. In essence, realizing the full promise of vaccination will demand significant attention to developing new models for cohesive, transparent immunization governance systems (including predictable evaluation/recommendation procedures), sustainable funding and procurement mechanisms, and ultimately, timely access to innovative vaccines – with a clear vision by all stakeholders in terms of placing patient needs explicitly at the forefront.

In responding to requests made by BIOTECanada's Vaccine Industry Committee (VIC), the Public Health Agency of Canada (PHAC) hosted an International Forum in December 2008, with the preliminary goal of evaluating immunization systems in other higher income countries, i.e. to shed light on best practices (for vaccine recommendation, funding, procurement and program-related research) that might be adaptable to Canada's decentralized health governance system. To build on the key themes and challenges identified during this forum – and in working toward an improved vaccine environment conducive to meeting both industry and public health objectives – the VIC has also put forth preliminary recommendations for future models to help streamline vaccine program development and funding mechanisms (see below). In proposing such models, the VIC will continue to proactively argue the case that immunization programs provide excellent value, particularly in terms of their broad medical, societal and economic impact. The VIC will also continue to advocate for greater financial support of immunization resources across all federal/provincial/territorial (F/P/T) decision makers, and intends to work in partnership with the PHAC and F/P/T jurisdictions to help shape a reinvented National Immunization Strategy (NIS).

Collectively, in leveraging past achievements in improving Canada's vaccination system, stakeholders at all levels will be required to develop innovative collaborative approaches to strengthen the existing immunization infrastructure, with the goal of securing the quality, harmonization and sustainability of national vaccination programs as critical cost-effective solutions in protecting public health. Moreover, the imminent arrival of therapeutic vaccines underscores the need to develop appropriate, efficient models for recommendation, financing and procurement of next-generation vaccines. In the spirit of collaborative partnership – and to help ensure that when the next breakthrough vaccine arrives, patient access will not be hindered by undesirable discrepancies or delays in vaccine program adoption – the VIC has put forward the following recommendations for consideration by F/P/T governments and other key immunization stakeholders (see further details presented in Papers 3, 5, 6, 7 and 9).

Federal/Provincial/Territorial Recommendations

1. Policy approaches to developing an efficient vaccine marketplace should encourage long-term investment in R&D in the vaccine sector. These initiatives should assist in sustaining and enhancing vaccine research in Canada, thus driving future innovation in the development of next-generation preventive and therapeutic vaccine technologies.
2. To minimize duplicative, bureaucratic efforts in evaluating and recommending new vaccines, the federal government should aim for increased efficiencies (and minimal redundancy across Health Canada/NACI/CIC mandates), including the provision of adequate financial and human resources. Canadian immunization authorities (including NACI/CIC officials) should also endeavour to leverage the substantial financial/human resources currently in place in other developed countries, e.g. through more frequent, formal collaboration with the U.S. Advisory Committee on Immunization Practices (ACIP) and/or other national vaccine advisory bodies.

3. To facilitate the timeliness and predictability of vaccine adoption and patient access to new immunization programs, NACI should issue recommendations on the use of new vaccines within 90 days of Health Canada approval. This will require enhanced NACI/industry collaboration, including ongoing dialogue, and formal definition of points of engagement (e.g. pre- and post-licensure) for data presentation/submission to NACI as recommendations are being developed.
4. To build on the success of the NIS, a sustainable federal funding mechanism should be established for immunization programs (potentially in the form of a permanent trust fund of \$100 million per year minimum) to ensure new vaccine technologies can be incorporated into public vaccine programs.
5. The federal government should work with the provinces/territories to establish a standardized, sustainable funding mechanism to ensure adoption of new, recommended vaccines in public health programs within approximately six months of their approval by Health Canada.
6. To minimize disparities and gaps in Canada's immunization programs, the provinces and territories should aim to work towards a national immunization schedule that is followed across the country.
7. With the imminent launch of therapeutic vaccine technologies in Canada, Health Canada should work in a transparent manner with manufacturers and other relevant stakeholders to determine the most appropriate route(s) of evaluation and financing for therapeutic vaccines.
8. In working towards an optimal, modern, fair and transparent vaccine procurement system, revisions should be made to specific terms/conditions in improving current bulk contract flexibility (e.g. to increase vaccine delivery lead times and decrease vaccine waste) – to help build long-term manufacturing capacity to ensure the stability of the domestic vaccine supply.
 - Implementation of more favourable pricing structures is required, i.e. to reflect the full intrinsic value of vaccines as both high-technology products and effective primary prevention tools.
9. To support timely, accurate, and comprehensive vaccine program-related research and evaluation, F/P/T governments should allocate significant additional funds to strengthen Canada's multi-faceted (currently fragmented) disease surveillance and post-marketing safety surveillance infrastructure(s).

Stakeholder Recommendations

10. To discuss common critical issues in immunization, meetings of all relevant stakeholders (including F/P/T government and public health officials, regulators, policy makers, medical professionals, vaccine manufacturers/developers and researchers, investors, payers, and the general public) should be convened on a regular basis – potentially by the PHAC, in conjunction with the VIC. Urgent matters that require transparent dialogue encompass, but are not limited to, the following topics:
 - Potential new governance/funding models to encourage predictable recommendation procedures and sustained financing mechanisms, i.e. to support timely, equitable patient access to vaccines.
 - Continued identification of best practices for vaccine program development and delivery in other higher income nations that merit consideration in the context of the Canadian vaccine landscape.

10.1.2 Sommaire

Depuis la découverte de la vaccination moderne il y a plus de 200 ans, la vaccination s'est révélée l'une des interventions de santé publique les plus efficaces et les plus rentables. Sur la scène internationale, les investissements dans la recherche et le développement (R et D) ont mené à la découverte d'une vaste gamme de vaccins visant plus de 25 maladies infectieuses. Misant sur le regain d'intérêt manifesté au cours des années passées, les investissements renouvelés dans l'industrie des vaccins sont alimentés par de nombreux facteurs, dont l'absence de vaccins contre d'importantes maladies, telles le paludisme, l'hépatite C et le sida, les préoccupations que suscite l'apparition de nouvelles maladies infectieuses et de menaces récurrentes de pandémie de grippe et de bioterrorisme, de même que la croissance récente du marché mondial des vaccins et des recettes faramineuses qu'il génère. Si l'on jette un regard vers l'avenir, les chiffres actuels indiquent qu'entre 150 et 200 vaccins en sont au stade de développement clinique dans le monde et, d'après l'intérêt accru que suscitent les activités de R et D liées aux vaccins, on prévoit que le nombre de vaccins disponibles triplera au cours des prochaines années.

D'intéressantes percées réalisées dans les domaines de l'immunologie et de la biologie moléculaire ont permis d'utiliser des stratégies innovatrices pour développer des vaccins, ce qui, en retour, a accru la capacité des chercheurs de créer des vaccins préventifs et thérapeutiques (ou de cibler de nouvelles maladies) qu'on ne pensait pas possibles il y a quelques années. Contrairement aux vaccins préventifs traditionnels, les nouveaux vaccins thérapeutiques visent à combattre des maladies existantes plutôt qu'à conférer une protection prophylactique (voir le document 3). On en évalue actuellement l'efficacité contre un vaste éventail de troubles humains, y compris certaines maladies infectieuses chroniques, dont le sida, l'hépatite C et l'infection à Chlamydia, et des maladies non infectieuses comme le cancer, les troubles métaboliques (hypertension, diabète), les maladies neurodégénératives (accidents vasculaires cérébraux, maladie d'Alzheimer) et les maladies auto-immunes (sclérose en plaques, polyarthrite rhumatoïde). Le développement de nouveaux adjuvants (qui améliorent la réaction immunitaire à un antigène) et méthodes d'administration des vaccins, notamment par voie orale, intranasale, transdermique (p. ex., les timbres) ou transcutanée (p. ex., la micro-injection), pouvant contribuer à réduire la douleur et les contraintes logistiques causées par la méthode actuelle d'administration à l'aide d'une seringue, fait aussi partie des percées récentes de la technologie vaccinale. L'approbation du vaccin intranasal FluMist (développé par MedImmune, société acquise par AstraZeneca) contre la grippe saisonnière est attendue au Canada en 2010.

Compte tenu de l'essor récent des technologies vaccinales, on prévoit que les nouveaux vaccins auront une incidence importante sur la prestation des programmes d'immunisation et l'épidémiologie des maladies évitables par la vaccination au Canada, dans un avenir prochain. En effet, plusieurs nouveaux vaccins approuvés depuis le milieu de 2006 offrent déjà à la population canadienne la possibilité de prévenir de nouvelles maladies. Ces nouveaux vaccins sont utilisés contre le rotavirus, le virus zona-varicelle, d'autres souches bactériennes à l'origine d'infections pneumococciques et les maladies cliniques liées au virus du papillome humain (VPH), notamment le cancer du col de l'utérus. Beaucoup de nouvelles technologies vaccinales sont également en cours de développement dans des sociétés pharmaceutiques mondiales et des sociétés appartenant à des intérêts canadiens, alors que plusieurs candidats-vaccins sont actuellement soumis à des essais précliniques et cliniques. D'un bout à l'autre du pays, la recherche s'active, et l'on prévoit que l'innovation continue produira une nouvelle génération de vaccins préventifs (notamment contre la grippe, l'hépatite A et B, et le VIH/sida) et de vaccins thérapeutiques de pointe (notamment contre le cancer du sein, de l'ovaire et de la prostate, et contre des maladies à prions, comme la maladie de Lou-Gehrig et la maladie d'Alzheimer). Alors que le Canada continue de contribuer de manière importante au développement de vaccins de nouvelle génération, ensemble, ces activités de recherche vont accroître les avantages actuels de l'immunisation et en faire profiter notamment les adolescents et les adultes. Sur la scène internationale, en outre, d'étonnantes percées sont réalisées en vue de combattre d'importantes maladies mortelles dans le monde, notamment les maladies endémiques qui affligent les pays en développement, comme la pneumonie, le paludisme, la tuberculose, le sida, la dengue et l'infection par le rotavirus.

À mesure que l'innovation technologique continue de stimuler la découverte de nouveaux vaccins révolutionnaires et de nouvelles méthodes pour les administrer, la diversité des programmes d'immunisation s'élargit également, donnant lieu à la nécessité d'actualiser et d'améliorer les systèmes de gouvernance et de financement. Bien qu'actuellement, de nouveaux vaccins fassent leur entrée sur le marché, le délai qui sépare l'approbation de Santé Canada et la mise en œuvre des programmes d'immunisation est encore trop long (p. ex., de trois à six), si l'on tient compte aussi de la lenteur des évaluations effectuées par le Comité consultatif national de l'immunisation (CCNI) et le Comité canadien d'immunisation (CCI). En outre, l'accès des patients aux vaccins approuvés récemment est actuellement entravé par l'absence d'aide financière soutenue de la part du gouvernement fédéral pour les programmes publics. Cela revient malheureusement à priver la population canadienne d'un accès opportun et uniforme aux vaccins approuvés – et à l'exposer à un risque inutile, compte tenu de l'absence d'une protection optimale contre des maladies évitables par la vaccination. En général, malgré les percées notoires qui ont été réalisées en vue de réduire l'incidence des maladies infectieuses, on peut néanmoins affirmer que le système d'immunisation actuel du Canada comporte des lacunes sur le plan de l'harmonisation et de la transparence, ce qui entraîne un chevauchement des tâches, des injustices et des délais inacceptables.

La situation qu'a connue récemment le Canada quand les nouveaux vaccins quadrivalents Gardasil (contre les maladies cliniques liées au VPH) et Menactra (contre le méningocoque) – tous deux homologués en 2006 – ont fait leur apparition sur le marché est un argument convaincant pour faire valoir la nécessité d'améliorer le portrait de notre système national d'immunisation. Pour réaliser pleinement les objectifs de la vaccination, il faudra, essentiellement, prêter une attention particulière à l'élaboration de nouveaux modèles propices à des systèmes de gouvernance cohérents et transparents en matière d'immunisation (y compris des méthodes d'évaluation et de recommandation prévisibles), à des mécanismes de financement et d'approvisionnement durables, et, en bout de ligne, à un accès opportun aux nouveaux vaccins – et s'assurer que tous les intervenants partagent une vision claire pour ce qui est de mettre les besoins des patients au premier plan.

En réponse aux demandes du Comité de l'industrie des vaccins (CIV) de BIOTECanada, l'Agence de la santé publique du Canada (ASPC) a tenu un forum international en décembre 2008, dont l'objectif préliminaire était d'évaluer les systèmes d'immunisation dans d'autres pays à revenu élevé, notamment pour jeter de la lumière sur les pratiques exemplaires (relatives à la recommandation, au financement et à l'approvisionnement des vaccins, de même qu'à la recherche sur les programmes de vaccination) qu'on pourrait adapter au système décentralisé de gouvernance de la santé au Canada. Afin de donner suite aux principaux thèmes et défis abordés durant ce forum – et de travailler à améliorer le contexte de la vaccination pour qu'il réponde aux objectifs de l'industrie et de la santé publique – le CIV a également formulé des recommandations préliminaires en faveur de modèles futurs contribuant à simplifier l'élaboration des programmes de vaccination et les mécanismes de financement (voir ci-contre). Préconisant l'adoption de ces modèles, le CIV continuera de soutenir, de façon proactive, que les programmes d'immunisation représentent un investissement rentable, notamment en ce qui a trait à leurs répercussions générales sur le plan médical, social et économique. Le CIV continuera également d'exhorter tous les décideurs fédéraux, provinciaux et territoriaux à augmenter leur aide financière aux programmes d'immunisation, et entend travailler en collaboration avec l'ASPC pour revigorer la Stratégie nationale d'immunisation (SNI).

Ensemble, tous les intervenants, misant sur les réalisations antérieures visant à améliorer le système de vaccination du Canada, seront tenus d'élaborer de nouvelles approches coopératives en vue de renforcer l'infrastructure d'immunisation et ainsi assurer la qualité, l'harmonisation et la viabilité des programmes de vaccination nationaux – solutions rentables essentielles à la protection de la santé publique. L'arrivée imminente de vaccins thérapeutiques au Canada souligne également la nécessité d'élaborer des méthodes adéquates et efficaces de recommandation, de financement et d'approvisionnement des vaccins de nouvelle génération. Dans un esprit de collaboration et pour s'assurer qu'à l'arrivée du prochain vaccin innovateur, l'accès des patients ne sera pas entravé par des écarts et des délais indésirables dans l'adoption des programmes de vaccination, le CIV a formulé les recommandations suivantes à l'intention des gouvernements fédéral, provinciaux et territoriaux, et d'autres intervenants clés du secteur de l'immunisation (pour plus de renseignements, consulter les documents 3, 5, 6, 7 et 9).

Recommandations à l'intention des gouvernements fédéral, provinciaux et territoriaux

1. *Les approches politiques à l'égard du développement d'un marché des vaccins efficace doivent viser à encourager les investissements à long terme en R et D dans l'industrie des vaccins. Ces initiatives doivent contribuer à soutenir et à améliorer la recherche sur les vaccins au Canada, pour ainsi stimuler l'innovation future dans le développement des vaccins préventifs et thérapeutiques de nouvelle génération.*
2. *Afin de minimiser le chevauchement des tâches et la bureaucratie qui caractérisent le processus d'évaluation et de recommandation des nouveaux vaccins, le gouvernement fédéral doit aspirer à augmenter l'efficacité (et réduire le chevauchement des mandats de Santé Canada, du CCNI et du CCI), et à allouer des ressources humaines et financières suffisantes.*
3. *Afin d'accélérer l'adoption des vaccins, d'en favoriser la prévisibilité et de faciliter l'accès des patients aux nouveaux programmes d'immunisation, le CCNI doit diffuser des recommandations sur l'utilisation des nouveaux vaccins dans les 90 jours suivant l'approbation de Santé Canada. Cette mesure nécessitera une collaboration accrue entre le CCNI et l'industrie, y compris la tenue d'un dialogue continu et l'établissement officiel de points de contact (p. ex., avant et après l'homologation) où les parties s'engagent à présenter des données au CCNI au fur et à mesure que des recommandations sont formulées.*
4. *Afin de donner suite aux réalisations accomplies dans le cadre de la SNI, le gouvernement fédéral doit établir un mécanisme durable de financement des programmes d'immunisation (peut-être sous la forme d'un fonds permanent d'affectation spéciale d'au moins 100 millions de dollars par année) pour que les nouvelles technologies vaccinales puissent être intégrées aux programmes publics de vaccination.*
5. *Le gouvernement fédéral doit travailler en collaboration avec les provinces et territoires afin de mettre en place des mécanismes de financement uniformisés et durables, qui favoriseront l'adoption de nouveaux vaccins (recommandés) par les programmes de santé publique dans les six mois suivant l'approbation de Santé Canada.*
6. *Afin de minimiser les écarts et les lacunes observés dans les programmes d'immunisation au Canada, les gouvernements provinciaux et territoriaux doivent aspirer à établir un calendrier national d'immunisation, respecté dans tout le pays.*
7. *Devant le lancement imminent de vaccins thérapeutiques au Canada, Santé Canada doit travailler en collaboration avec les fabricants et autres intervenants concernés d'une manière transparente afin de déterminer les modes d'évaluation et de financement des vaccins thérapeutiques qui conviennent le mieux.*
8. *Afin de créer un système d'approvisionnement en vaccins qui soit optimal, moderne, équitable et transparent, il conviendrait d'apporter les améliorations suivantes aux conditions particulières des marchés cadres actuels en vue d'en accroître la souplesse (p. ex., pour accélérer les délais d'administration des vaccins et diminuer le gaspillage) – afin de contribuer à renforcer la capacité de fabrication à long terme en vue d'assurer la stabilité des réserves nationales de vaccins.*
 - *L'application de structures plus favorables de fixation des prix des vaccins, qui tiennent compte notamment de la pleine valeur des vaccins, considérés comme des produits de haute technologie et des outils de prévention primaire efficaces.*
9. *Afin de contribuer à la mise en place de mécanismes opportuns, précis et complets de recherche sur les programmes de vaccination et d'évaluation de ces programmes, les gouvernements fédéral, provinciaux et territoriaux doivent allouer des sommes supplémentaires importantes en vue de renforcer l'infrastructure canadienne de surveillance des maladies et de surveillance de l'innocuité des vaccins après leur commercialisation, laquelle, bien que polyvalente, est actuellement fragmentée.*

Recommandations à l'intention d'autres intervenants

10. Afin de débattre des enjeux importants liés à l'immunisation, tous les intervenants concernés (y compris les représentants des gouvernements fédéral, provinciaux et territoriaux, les responsables de la santé publique, les organismes de réglementation, les décideurs, les professionnels de la santé, les fabricants de vaccins et les développeurs et chercheurs, les investisseurs, les payeurs et le grand public) doivent être conviés régulièrement à des réunions – peut-être par l'ASPC, en collaboration avec le CIV. Ces enjeux, qui nécessitent un dialogue transparent, comprennent, sans en exclure d'autres :

- De nouveaux modes possibles de gouvernance et de financement, qui encouragent l'utilisation de méthodes de recommandation prévisibles et de mécanismes de financement soutenus, notamment pour favoriser l'accès opportun et équitable des patients aux vaccins.
- Le recensement continu de pratiques exemplaires relatives à l'élaboration et à la prestation de programmes de vaccination dans d'autres pays à revenu élevé, qui méritent d'être prises en compte dans le cadre du système de vaccination du Canada.

10.2 Vaccines for the 21st Century

10.2.1 Recent Rejuvenation of the Vaccine Enterprise

Since the discovery of modern vaccination more than 200 years ago, vaccines have proved to be one of the most successful and cost-effective public health interventions.¹ Globally, investment in research and development (R&D) has resulted in a broad range of vaccines targeting over 25 infectious diseases.² Building on past momentum, the vaccine enterprise has been undergoing a major renaissance in recent years, particularly as health care authorities increasingly acknowledge the medical, societal, and economic benefits of vaccination. Recent rejuvenation within the vaccine sector has been fuelled by several factors, including unmet medical need (e.g. vaccines are not currently available for several major infectious diseases, such as malaria, hepatitis C, and acquired immunodeficiency syndrome, AIDS);³ concerns regarding emerging infectious diseases as well as recurring threats of pandemic influenza and bioterrorism;^{4,5} and the recent growth and “blockbuster” revenues observed in the global vaccine market.⁶

The bright future prospects of the vaccine enterprise have been echoed by several experts in the field, who assert that we are entering into a “new golden era of vaccinology”, and that we are experiencing a “wave of optimism in medical science”, in which vaccine research and manufacturing is considered an art form.^{7,8} Such optimism – based in large part on recent scientific advances in immunology and molecular biology – has also encouraged a resurgence of investment in the sector. Indeed, big pharma companies currently view vaccine technologies as a crucial path to diversification and growth, i.e. to replace aging drug products now poised to lose patent protection, and are hence eager to purchase promising vaccine assets.⁹ For example, while analysts have highlighted the importance of Wyeth’s vaccine research pipeline in its recent takeover by Pfizer (which closed in late 2009),¹⁰ other vaccine-driven deals announced in 2009 include Abbott’s acquisition of the Belgian company Solvay,¹¹ sanofi pasteur’s acquisition of Indian-based Shantha,¹² and Johnson & Johnson’s purchase of an 18% stake in Dutch-based Crucell.¹³ This latest spate of global deals testifies to the renewed interest by big pharma companies in gaining entrance (or further expansion) into the burgeoning vaccine sector; the current trend toward corporate mergers and acquisitions is expected to continue.¹⁴ Moreover, in the wake of the recent concerns regarding the spread of H1N1ⁱ influenza, vaccine development is becoming a more attractive venture for smaller biotech firms.¹⁵

According to the World Health Organization (WHO), the global vaccine market has almost tripled in size since the year 2000, and continues to be one of the most dynamic and fastest growing sectors of the biopharmaceutical industry.¹⁶ Looking to the future, current industry estimates suggest there are approximately 150-200 candidates in the vaccine pipeline worldwide (in various stages of clinical development), and intensified interest in vaccine R&D is anticipated to generate a three-fold increase in available vaccines over the next few decades.^{17,18,19} Well recognized as a global leader in vaccine research, Canada continues to make significant contributions to global vaccine research and development – to help save lives, increase life expectancy, decrease human suffering, and reduce health care costs – and ultimately to protect the well being of individuals and societies in Canada and abroad (see Paper 3). Indeed, in its Strategic Plan for 2007-2012, the Canadian Institutes of Health Research Institute of Infection and Immunity (CIHR-III) has identified “Vaccines of the 21st Century” as a top research priority.²⁰

ⁱ H1N1 refers to hemagglutinin sub-type 1, neuraminidase sub-type 1 (of the influenza A virus); H1N1 flu is referred to as the “swine flu”.

10.2.2 Emerging Vaccine Technologies

As alluded to above, the recent revival in vaccine innovation has been propelled by the rapidly expanding body of knowledge in the fields of microbial pathogenesis and immunology, which in turn has advanced the ability of researchers to create both preventive and therapeutic vaccines (or target new diseases) not thought possible before.²¹ In contrast to traditional preventive vaccines, emerging therapeutic vaccines are intended to treat an existing disease, rather than provide prophylactic protection. Hence therapeutic vaccines can be administered after infection or disease onset, with the (typical) goal of enhancing the body's immunity against a specific biological target, thereby reducing the burden of disease and/or enhancing quality of life (refer to Paper 3).²²

With regard to the underlying mechanism of action of therapeutic vaccines, these novel vaccines are “able to act against a disease by inducing a specific immune response to a micro-organism, a protein or other substance, or a class of cells”,²³ i.e. in a manner roughly analogous to that in which a preventive vaccine may induce the immune system to attack a viral or bacterial pathogen. Thus an immune response – when correctly targeted – can be used to eliminate cells with aberrant behaviour or aberrant genomic function, or to reduce the extent of inflammation affecting a specific organ. It is this general approach that raises the possibility of extending the application of vaccines outside their conventional (preventive) areas of use; for example, therapeutic vaccines can be used to target diseases not known to be related to infectious agents, including cancer and autoimmune disorders.²⁴

More broadly, therapeutic vaccines are currently being evaluated to treat a wide range of human disorders, including certain chronic infectious diseases (AIDS, hepatitis C, chlamydia), as well as non-infectious diseases such as cancer (melanoma, colorectal, breast, ovarian, prostate, leukaemia); metabolic diseases (atherosclerosis, hypertension, diabetes); neurodegenerative diseases (stroke, Alzheimer's, amyotrophic lateral sclerosis, ALS); and autoimmune diseases (multiple sclerosis, rheumatoid arthritis).²⁵ In addition, therapeutic vaccines are presently in development to treat allergies, asthma, and drug addictions (e.g. to nicotine and cocaine), and to maintain contraception (by immunization against specific hormones).²⁶

Interestingly, a new therapeutic cancer vaccine (Provenge, developed by U.S.-based Dendreon Corp.) awaits imminent approval by the Food and Drug Administration (FDA) for use in treating prostate cancer.²⁷ The Provenge vaccine targets a protein found in most prostate cancer cells; it represents the first in a new class of “active cellular immunotherapies” that engage the patient's immune system to help fight such cancer cells. In the treatment of prostate cancer, this novel therapy involves mixing the vaccine with the patient's infection-fighting white blood cells – followed by injection of the combination – to help attack aberrant tumour cells. If licensed by the FDA, as anticipated in the first half of 2010,²⁸ Provenge would become the first therapeutic cancer vaccine to enter the U.S. market, representing a revolutionary vaccine breakthrough in the treatment of new classes of devastating (non-infectious) disease. However, such personalized, cell-based vaccine approaches are expected to be costly.

In addition to the emergence of therapeutic vaccines, innovative adjuvant technology is also driving the development of another wave of new vaccines. Adjuvants are critical components of vaccines; they enhance the immune response to an antigen and help trigger specific types of immune responses. Until recently, adjuvants contained in human vaccines licensed in North America were limited to mineral (e.g. aluminum) salts.²⁹ However, vaccine and adjuvant developers are currently looking to new adjuvants for a range of potential benefits, not only to heighten immune responses, but also to lengthen the effectiveness of vaccines and to trigger a different set of protective responses beyond the traditional antigen/antibody approach.³⁰ Emerging adjuvant technologies currently encompass oil-in-water emulsions (including MF59, used in Novartis' seasonal and pandemic influenza vaccines), liposomes, toll-like receptor (TLR) agonists (such as monophosphoryl lipid A, known as MPL that targets TLR4; and CpG oligodeoxynucleotides that target TLR9), cytokines, and other substances that help stimulate a T helper type 1 (T_H1) immune response.^{31,32} An effective adjuvant may also decrease vaccine manufacturing costs, since less of the expensive active ingredient is needed to generate the desired immune response. This can be vital in cases where vaccines are in short supply, since adjuvants act to efficiently “extend” the limited vaccine stock.³³ Certain adjuvants may also help reduce overall health care costs by decreasing the number of required visits to physicians or clinics for booster

immunizations, i.e. due to heightened immune response and immunological memory subsequent to initial vaccination.

New routes of vaccine delivery (e.g. oral, intranasal, transdermal) are also playing an important role in the development of future vaccine technologies – and may be useful in administering new adjuvanted³⁴ or combination vaccines.³⁵ Although injections into the skin (subcutaneous) and muscle (intramuscular) have traditionally served as the means to deliver vaccines into humans, there are limitations to the feasibility of numerous injections. In addition to pain reduction, there are several theoretical reasons for preferring other routes of immunization, including minimization of logistical constraints associated with needle disposal, storage, and mass immunization strategies.^{36, 37} Hence alternative routes of immunization are being introduced, e.g. FluMist, the new live, attenuated influenza vaccine is given intranasally (see Section 10.2.3), thus inducing both systemic and local responses and providing broader protection against antigenically drifted strains. Other promising technologies in the development pipeline include aerosol administration (inhalation) of measles and rubella vaccines, oral delivery of vaccines (e.g. against hepatitis B surface antigen), and transcutaneous administration (via adhesive patches, microneedles or powder applied to the skin) of hepatitis B and anthrax vaccines.³⁸

As one excellent example of breakthrough vaccine delivery technology, sanofi pasteur's intradermal (ID) seasonal influenza vaccine, Intanza, has been licensed in Europe in 2009 for adult/elderly patients.³⁹ The ID administration of Intanza provides direct access to the immune system through the dermal skin layer, where there is a high concentration of specialized immune cells. This convenient, pre-filled microinjection system uses a very short needle that enables rapid, accurate, safe and reliable delivery into the dermis.

Further confirming the allure of novel vaccine delivery technologies, it should be noted that in late 2009, GlaxoSmithKline purchased a 5% share in the Austrian firm Intercellⁱⁱ to gain marketing rights for the Company's experimental (needle-free) vaccine patch technology.⁴⁰ Intercell is currently developing a vaccine patch to protect against *E. coli* that causes traveller's diarrhea (in Phase III clinical testing), as well as a pandemic influenza vaccine patch (in Phase II trials). In the latter case, a vaccine against H5N1 avian influenza is delivered as a single-dose shot, and a "vaccine enhancement patch" containing a proprietary adjuvant (booster) is then placed on the skin for six hours to enhance the vaccine's effectiveness. For both indications, the vaccine or adjuvant is initially formulated as a liquid, and then applied to the patch matrix, which permits rapid water evaporation. The thermo-stability profiles of the two products suggest the possibility of multi-year refrigerated storage and cold chain-free shipping.⁴¹ Hence, while this innovative transdermal patch technology offers the advantage of simplified logistics (which may be particularly important for use in underdeveloped countries, where refrigeration is not always available), it also provides (in the case of the diarrhea patch) the benefit of eliminating injection-site pain.

ⁱⁱ Intercell intends to remain independent, but has licensed marketing rights to some of its other injectable vaccines to partners including Merck & Co., Sanofi Aventis, and Novartis AG (Novartis currently owns a 15% share of Intercell).

10.2.3 Recently Approved and Emerging Vaccines in Canada

Given the recent boom in vaccine research and technology within the past decade, it is expected that new vaccines will have a major impact on the delivery of immunization programs and the epidemiology of vaccine-preventable diseases in Canada in the near-term future.^{42, 43} Indeed, several new vaccines have been approved since mid-2006 and are already offering new disease prevention opportunities for Canadians (Table 10.1). These new vaccines target rotavirus, shingles, additional strains of bacteria that cause pneumococcal disease, and clinical disease caused by human papillomavirus (HPV) – primarily cervical cancer. For several of these recently approved vaccines, recommendations from the National Advisory Committee on Immunization (NACI) are still pending,ⁱⁱⁱ and these vaccines are generally not yet part of publicly-funded immunization programs in Canada.^{iv}

Table 10.1 – Recently Approved Vaccines in Canada^{44,45,46,47,48,49,50}

Vaccine Tradename	Approved Indication	Manufacturer	Health Canada Approval	NACI Statement
Rotateq	Rotavirus gastroenteritis	Merck ^v	August 2006	January 2008 Update Anticipated Spring 2010
Rotarix	Rotavirus gastroenteritis	GlaxoSmithKline	October 2007	Anticipated Spring 2010
Zostavax	Herpes zoster/shingles	Merck	August 2008	January 2010
Synflorix	Pneumococcal strains 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F	GlaxoSmithKline	December 2008	Pending
Pevnar 13	Pneumococcal strains 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23	Pfizer	December 2009	Pending
Cervarix	Human papillomavirus strains 16 and 18 (primarily targeting cervical cancer)	GlaxoSmithKline	January 2010	Pending

ⁱⁱⁱ Table 10.1 may be considered an update to Table 5.2 presented in Paper 5.

^{iv} In Canada, publicly-funded immunization programs are not vaccine specific, but rather, disease-state specific. However, the status of public funding for newly approved vaccines targeting HPV and pneumococcal disease (which target different serotypes than those vaccines already covered under publicly-funded programs) has generally not yet been clarified.

^v Merck and Schering-Plough announced their intention to merge in March 2009, with deal closure completed in late 2009. The merger was not considered to be vaccine-driven; the combined Company will have a diverse portfolio across several key therapeutic areas, including cardiovascular, respiratory, oncology, neuroscience, infectious disease, immunology, and women's health.

In the context of newly approved vaccines for human use in Canada, it is interesting to note that Bioniche Life Sciences Inc., based in Belleville, Ontario, has developed Econiche, the world's first cattle vaccine that prevents animal-to-human transmission of *Escherichia coli* (*E. coli*) disease – by reducing the shedding of *E. coli* O157:H7. Econiche was licensed by the Canadian Food Inspection Agency (CFIA) in October 2008, and is currently available for unrestricted use by Canadian cattle producers and their veterinarians.⁵¹

In addition to those vaccines recently licensed in Canada, at least one other innovative vaccine has been filed with Health Canada, with anticipated approval in 2010. For example, in August 2009, AstraZeneca Canada (working in partnership with its biologics subsidiary MedImmune), filed a New Drug Submission (NDS) for FluMist, a live attenuated influenza vaccine (LAIV), which is administered intranasally.⁵² The proposed indication for this novel, needle-free vaccine delivery technology (which is anticipated to circumvent the pain and potential fear of intramuscular injection) is the prevention of seasonal influenza.

Many innovative vaccine technologies are also in earlier-stage development by Canadian-owned vaccine companies, with several vaccine candidates currently in clinical trials and in preclinical (animal) testing, as highlighted in Tables 10.2 and Table 10.3, respectively. While these tables are not intended to represent comprehensive summaries of current vaccine R&D in Canada, they provide a flavour of the diverse array of exciting research and clinical initiatives currently underway. Across the country, the vaccine pipeline is bulging, and continued Canadian innovation is anticipated to lead to the development of a wide range of preventive vaccines (e.g. against influenza, hepatitis A & B, HIV/AIDS, cryptosporidiosis, *Candida albicans*, and other infectious targets) as well as therapeutic vaccines (e.g. targeting breast, ovarian and prostate cancers, and prion-mediated degenerative diseases such as ALS and Alzheimer's disease). These companies are also advancing enabling technologies to enhance vaccine design (e.g. through the use of virus-like particles, VLPs,^{vi} and liposomes) and to improve antigen presentation, as well as to facilitate vaccine manufacturing (e.g. via plant-based methods).

Apart from the broad range of vaccine R&D programs currently underway by Canadian companies to counter infectious disease, continued investment and progress is also being made in vaccine innovation by leading big pharma companies in Canada (including GlaxoSmithKline Canada, Merck Canada, sanofi pasteur, Pfizer Canada, and Novartis Canada). These efforts include both preclinical and clinical research (see Paper 3, Section 3.4.1), e.g. to develop seasonal and pandemic influenza vaccines, therapeutic vaccines for the treatment of cancer and Alzheimer's disease, and a new quadrivalent meningococcal vaccine,⁵³ Menveo, which has received U.S. FDA approval (in late February 2010) to prevent invasive meningococcal disease caused by serogroups A, C, Y, and W-135 in individuals 11 to 55 years of age.⁵⁴ Collectively, these research initiatives are poised to extend the current benefits of vaccination – particularly to adolescent and adult populations – with promising potential to improve Canada's future immunization programs.

Finally, an impressive roster of early-stage vaccine research programs is also underway across many Canadian academic, hospital, and government laboratories and research institutions; current activities and advances at these organizations are showcased in a recent report published by the Canadian Institutes of Health Research (CIHR).⁵⁵ Notably, a unique and relatively new organization within the Canadian vaccine research landscape is the Pan-Provincial Vaccine Enterprise (PREVENT), established in February 2008 as a federally-funded Centre of Excellence for Commercialization and Research (CECR) at the University of Saskatchewan.⁵⁶ As summarized in Paper 3, the broad goal of PREVENT is to leverage existing vaccine expertise through partnerships with other key Canadian research organizations,⁵⁷ i.e. to help bridge the gap between basic science and licensed vaccines – and to accelerate patient access to essential new vaccines within the Canadian marketplace.

^{vi} Virus-like particles (VLPs) are designed as macromolecular structures that look like viral protein shells (capsids), allowing them to be recognized readily by the body's immune system. However, they lack the core viral genetic material, making them non-infectious and unable to replicate.

Table 10.2 – Vaccine Candidates in Clinical Trials^{58,59,60}

Vaccine Candidate	Target Indication(s)	Developer	Regulatory Status
DPX-0907 [Therapeutic cancer vaccine, based on DepoVax™ platform]	Breast, ovarian and prostate cancer	Immunovaccine Inc.	Phase I to be initiated in 2010 [FDA approved]
AE37 [Therapeutic cancer vaccine, based on synthetic peptide]	Prostate cancer	Generex Biotechnology Corporation	Phase I
	Breast cancer		Phase II
H5N1 pandemic vaccine [Adjuvanted plant-made H5 virus-like particle (VLP) vaccine]	H5N1 avian influenza	Medicago Inc.	Phase I completed in 2009 Phase II anticipated in 2010

Table 10.3 – Vaccine Candidates in Preclinical Trials^{61,62,63,64}

Vaccine Technology Platform/Approach	Target Indication(s)	Developer
Variosite™ Technology (synthetic peptide technology)	Broadly reactive seasonal and pandemic influenza, HIV	Variation Biotechnologies Inc. (VBI)
Proprietary oral formulation technology	Influenza, hepatitis A/B, and intestinal disorders	
Plant-based subunit vaccine	Cryptosporidiosis (fatal diarrheal disease)	Platform Corporation
Synthetic Candivax vaccine	<i>Candida albicans</i> yeast infection	TheraCarb Inc.
Therapeutic vaccines (targeting misfolded protein superoxide dismutase, SOD1)	Amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease), Alzheimer's disease	Amorfix Life Sciences Ltd.

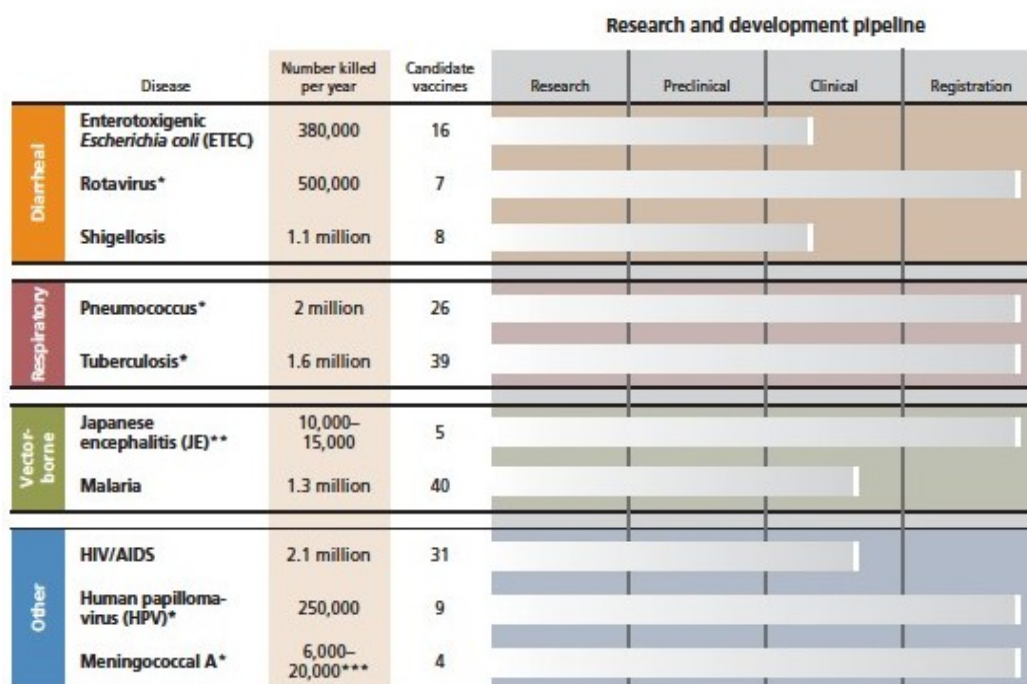
Overall, Canada continues to make strong contributions to the development of next-generation vaccines to improve the future health of Canadians. Against the backdrop of this positive momentum in generating exciting new disease prevention opportunities, it should be noted that the abrupt cancellation (announced in February 2010) of plans to build an AIDS vaccine facility in Canada has come as a severe blow to the vaccine R&D community.⁶⁵ Unfortunately, although \$88 million had been earmarked for the plant through a partnership between the federal government and the Gates Foundation – as a non-profit venture intended to produce small lots of vaccine for clinical trials – the sudden reversal in the request for proposal (RFP) process was allegedly based on the government's perception that North America and Europe currently have sufficient vaccine manufacturing capacity to meet research needs. Also, according to a recent announcement on the website of the Canadian HIV Vaccine Initiative, none of the applicants "were found to be successful in meeting the pre-established criteria", although the criteria were not specified.⁶⁶

This recent withdrawal of the RFP process has raised serious questions regarding government decision-making; the rationale for project cancellation is suspected to involve factors other than those claimed publicly by the federal government, and is believed to be unrelated to Canada's high quality research and scientific capabilities. For Canada's broader vaccine R&D community, the disappointing outcome serves as powerful motivation to redouble efforts in proactively promoting the value of vaccine innovation, not only to ensure future development of lifesaving vaccines, but also to secure the vaccine supply, and to encourage additional investment to help sustain Canada's economic growth and global competitiveness.

10.2.4 Emerging Vaccines on the Global Horizon

Although a comprehensive review of new vaccines arriving on the global horizon falls outside the scope of this paper, Figure 10.1 provides a snapshot of the extensive international vaccine pipeline targeting a wide range of infectious diseases, including leading global killers such as pneumonia, tuberculosis, AIDS, malaria, and diarrheal disease due to rotavirus. Introduction of these vaccines, as well as a vaccine against dengue,⁶⁷ has the potential to save millions of lives, particularly in the developing world. At present, major international vaccine research programs are funded through the World Health Organization (WHO), the Global Alliance for Vaccines and Immunization (GAVI), and the United Nations Children's Fund (UNICEF). In addition, an unprecedented donation announced in January 2010 by the Bill and Melinda Gates Foundation will allocate a further \$US 10 billion over the next decade to study, develop and distribute vaccines to developing countries, with the goal of boosting vaccination rates to prevent 90% of children in developing countries from contracting diarrhea, pneumonia and other diseases.⁶⁸

Figure 10.1 – Lifesaving Vaccines on the Global Horizon



* Vaccines currently exist for these diseases. However, due to unique challenges that exist in immunization in the developing world, it is necessary to continue R&D for new, appropriate vaccines for those most in need.

** Due to limited supply and options of existing JE vaccines, research and development for new, appropriate vaccines for the developing world are needed to succeed in the fight against JE.

*** Estimate of meningococcal A deaths per year in 21 African countries specified by the World Health Organization. The range represents an estimate of the mortality in a normal year to that of an epidemic year.

Source: Fact Sheet, Lifesaving Vaccines on the Horizon, PATH, June 2009; www.path.org.

10.2.5 Pandemic H1N1 Influenza: Preliminary Lessons Learned

Although the global H1N1 pandemic that erupted in early 2009 has proven milder to date than initially anticipated, the recent outbreak of novel influenza A (H1N1) has yielded some valuable (albeit early) lessons that may help shape the future of influenza immunization practices in Canada. Most importantly, the H1N1 outbreak has underscored the importance of rapid and sufficient vaccine supply, and has clearly demonstrated that traditional vaccine manufacturing capabilities fail to satisfy demand in a timely fashion.^{69,70} To date, Canada has relied on GlaxoSmithKline (GSK) as the sole domestic supplier of H1N1 vaccine, based on a 10-year supply contract in place since 2001.⁷¹ However, federal government officials have announced that when this contract is renegotiated, the Canadian government will consider a multiple-supplier tender for the production of future pandemic vaccines,⁷² i.e. to avoid the production delays seen during the H1N1 vaccination campaign, and to ensure maximum production flexibility.^{vii}

While long production lead times continue to represent a challenge in vaccine manufacturing (see Paper 7), future opportunities to reduce development/production cycle times (and increase the predictability and/or scalability of vaccine production) include the use of: i) modern molecular techniques such as recombinant and plant-based technologies; ii) cell cultures to replace egg-based methods; iii) common platforms to produce more than one antigen; and iv) disposable bioreactors in place of fixed equipment.^{73,74,75,76} As described in Section 10.2.3, several Canadian companies are currently developing innovative manufacturing methods for future influenza vaccines, targeting both pandemic and seasonal strains. Notably, Medicago, Generex and Variation Biotechnologies Inc. are advancing proprietary VLP and synthetic peptide technologies (now in preclinical and clinical testing) to provide safe, efficacious alternatives to conventional influenza vaccines.

Overall, significant work lies ahead in improving influenza vaccine technology, and a far-reaching global goal is to develop a universal influenza vaccine (e.g. targeting an intracellular protein) that would not have to be reformulated as the virus mutates every season.⁷⁷ Fuelled by the recent H1N1 pandemic, new research may also be directed towards the development of new pandemic vaccine or drug targets, e.g. based on the evaluation or use of novel cytokines (such as interleukin 17)⁷⁸ or immunoglobulins (such as IgG2)⁷⁹ – both of which have been reported to be associated with severe H1N1-related illness. Furthermore, future research to evaluate the use of antiviral drugs (such as Tamiflu, Relenza and other emerging antivirals) is expected to provide new hope for optimizing treatment (and prevention/chemo-prophylaxis) of illness caused by future influenza strains.⁸⁰

Moreover, the recent pandemic outbreak may also help to lay a more solid foundation in strengthening global influenza surveillance systems, i.e. to enable early warning systems to efficiently detect circulating flu strains – and to maximize critical lead times for large-scale vaccine production.⁸¹ Finally, as described in Paper 8, a key lesson of the H1N1 outbreak – termed the “*epidemic of confusion*” – is that communication by government and public health officials must be significantly improved;⁸² the outbreak serves as a sober reminder that the Canadian public requires (and deserves) timely, clear direction regarding the value and benefits of immunization, i.e. as a prerequisite for rebuilding trust in future vaccination programs.

^{vii} As a point of reference, the United States has had five H1N1 vaccine suppliers during the 2009/2010 influenza season, although most of these suppliers operate production plants outside the United States.

10.3 Future Models for Vaccine Governance and Funding in Canada

10.3.1 The Need for Change in Canada's Immunization System

As detailed in Section 10.2, several new vaccines have recently been approved, and technology innovation continues to drive the discovery of new vaccines that will transform the future of public health in Canada.⁸³ As the number of new vaccines and delivery methods continues to increase, the range of immunization program options also widens, with the consequent need for updated, improved governance and funding systems. Furthermore, with the imminent arrival of leading edge therapeutic vaccines, innovative models for vaccine governance and financing may also be required (see Section 10.3.6). In reflecting on possible areas for future improvement, it should be considered whether all new vaccines should fit within a single process, and whether it is time for a comprehensive, system-wide review of vaccine programs and development processes in Canada, with input from a full range of immunization stakeholders.⁸⁴ Indeed, during an International Forum on National Immunization Programs held in December 2008, the Public Health Agency of Canada (PHAC) has taken initial steps to evaluate immunization governance structures and funding mechanisms in eight “higher income” countries for the purpose of identifying key lessons and best practices that merit consideration in the Canadian context (see Section 10.3.4).⁸⁵

From a research and scientific perspective, Canada's current immunization programs are considered world-class, based on a tradition of excellent leadership and collaboration among key scientists and opinion leaders.⁸⁶ According to the PHAC, Canada is also recognized as having a strong base to build upon in terms of future vaccine program development. For example, the ongoing development of the National Immunization Strategy (NIS) has provided an initial framework (and mechanism, through the newly established Canadian Immunization Committee, CIC) for federal, provincial and territorial (F/P/T) collaboration on key immunization issues, including consensus building on national goals and objectives. Canada also has an analytical framework in place for assessing new vaccines across a variety of scientific and other dimensions in developing national program recommendations.⁸⁷ Finally, recent federal funding, as well as collaborative work to facilitate vaccine procurement and supply management, e.g. through the F/P/T bulk purchase program, have yielded positive results – also contributing to the success of Canada's immunization programs.⁸⁸ Thus in general, Canada's present immunization infrastructure is believed to provide a strong foundation for future improvement, building on the success of current approaches.⁸⁹

While recent successes in improving immunization programs in Canada should be celebrated,⁹⁰ further improvements and initiatives will be necessary in continuing to advance vaccine program development. Given that a common, over-arching goal across all immunization stakeholders is to increase vaccine coverage rates (i.e. to further decrease the burden of vaccine-preventable diseases), an ongoing challenge is to strengthen and accelerate vaccine evaluation, recommendation, and funding mechanisms – to enhance patient access to innovative vaccine technologies through public sector programs. At present, emerging vaccines are being introduced by leading manufacturers, yet the interval between Health Canada approval and ultimate immunization program implementation is undesirably long (e.g. three to six years), including lengthy review times by NACI and the CIC.⁹¹ In addition, patient access to recently approved vaccines is currently impeded by a lack of sustained federal funding.⁹² Hence – despite recent achievements in certain areas – overall, the Canadian immunization system can still be characterized as lacking harmonization and transparency, resulting in unacceptable duplication, inequities and delays.⁹³ Unfortunately, the net result is that Canadian citizens are denied timely, consistent access to approved vaccines – and thus left at unnecessary risk, due to lack of optimal protection from vaccine-preventable diseases. Clearly, Canada must strive to continue to strengthen its national immunization structure(s).

10.3.2 Canada's Current Immunization System Structure

To provide appropriate background perspective in setting the stage for a discussion of potential new models for vaccine program development, Table 10.4 presents an overview of the infrastructure underlying Canada's current immunization system, as recently summarized by the PHAC.

Table 10.4 – Canada's Current Immunization System: Governance, Funding, Procurement & Program-Related Research^{94,95,96}

System of Government	Health System	Decentralized administration of health care; federal government establishes national legislation and regulations; 13 P/T jurisdictions have primary responsibility for health service delivery
	Health Funding	Publicly-funded through taxes
Immunization Program Governance	Pre-market Assessment and Authorization for Use	Federal: Health Canada, BGTD
	New Vaccine Recommendations	Federal: NACI provides scientific and technical advice to the PHAC; the CIC (with representatives from F/P/T levels) provides advice on program planning
		P/T: Ministries of Health make the final decision for individual jurisdictions
Harmonization of Immunization Schedules Across Jurisdictions	P/Ts have their own immunization schedules that may or may not be completely in alignment with national recommendations	
Funding	Funding for Vaccine Purchases	P/T: Individual jurisdictions are responsible to provide funding for vaccine purchases
	<i>*In 2009, the federal government also committed to funding 60% of the cost of 50 million doses of pandemic H1N1 vaccine; P/Ts were to pay for the remaining 40%.</i>	Federal*: Since the introduction of the NIS in 2003, the federal government has provided time-limited funding to P/Ts; the Canadian Immunization Trust fund provided \$300 million in 2004 to support immunization programs for four new vaccines (acellular pertussis, meningococcal C conjugate, pneumococcal conjugate and varicella) and \$300 million in 2007 for HPV vaccination programs
Procurement	Vaccine Procurement Process	F/P/T: The federal bulk purchase program, coordinated by the PWGSC on behalf of the VSWG, uses P/T funds and a tender process to establish contracts with manufacturers
		P/T: Jurisdictions may also purchase vaccines directly from manufacturers

Program-Related Research	Evaluation of Immunization Program Safety and Effectiveness	Conducted independently by some P/Ts; manufacturers also play a role in monitoring post-market vaccine safety and effectiveness
<p>BGTD = Biologics and Genetic Therapies Directorate CIC = Canadian Immunization Committee F/P/T = Federal/Provincial/Territorial HPV = human papillomavirus NACI = National Advisory Committee on Immunization NIS = National Immunization Strategy PHAC = Public Health Agency of Canada PWGSC = Public Works and Government Services Canada VSWG = Vaccine Supply Working Group</p>		

10.3.3 Recent Case Studies as a Platform for Change: Gardasil and Menactra

Of those vaccines introduced recently in Canada, Merck’s Gardasil, a quadrivalent vaccine against HPV types 6, 11, 16 and 18 – which targets primarily cervical cancers, but also vaginal and vulvar cancers as well as genital warts – represents an excellent example that illustrates the need for greater predictability in Canada’s immunization system. As detailed in Papers 5 and 6, Gardasil was approved by Health Canada in July 2006, and a positive recommendation was made by NACI⁹⁷ in February 2007.^{viii} Based on the favourable recommendations put forward by Health Canada, NACI, as well as other medical societies in Canada and abroad, the federal government subsequently announced \$300 million in financing for HPV immunization programs across Canada (over three years) in March 2007; this funding represented an extension to previous federal financing for national vaccine programs under the NIS.⁹⁸ In response to this federal funding, between mid-2007 and mid-2008, all 10 provinces announced they had initiated (or would initiate) HPV vaccination programs.^{ix}

It was not until mid-2008 that the CIC publicly issued recommendations from its newly established joint CIC-NACI HPV Vaccine Expert Working Group – a full two years after Health Canada had approved Gardasil, and subsequent to the implementation of HPV programs in some jurisdictions. Notably, the joint committee represented the first working group of its kind, and was viewed as a pilot program to help ensure the rollout of HPV programs in Canada by developing operational/programmatic plans (e.g. target cohorts) by which vaccines recommended by NACI might be made available to the public. However, the exact role of the joint committee has never been clarified or publicized to date, and there is still no clear confirmation that the CIC and/or the pilot committee will (or should) address funding issues. Indeed, the creation of such working groups has been criticized in terms of injecting further duplication, unpredictability and delay into the system, and ultimately, lacking the ability to make timely decisions on behalf of the Canadian public.⁹⁹

^{viii} In February 2007, NACI issued a positive recommendation that all Canadian females nine to 13 years of age (prior to sexual debut for most Canadian females) as well as females 14–26 years, particularly those with no evidence of past or current HPV infection, should receive Gardasil.

^{ix} As of February 2010, all Canadian provinces and territories now offer school-based HPV vaccination programs.

Interestingly, a recent comparison of HPV program development across four countries (i.e. the U.S., the United Kingdom, Australia and Canada) has raised further questions regarding potential weaknesses in Canada's current immunization governance and funding structures.¹⁰⁰ Although the introduction of the HPV vaccine was unquestionably supported by several positive elements that underlie Canada's immunization system (including priority review by Health Canada, and the high-quality, evidence-based NACI review using the newly proposed analytical framework to encourage objective program analysis), the post-licensure review process was nonetheless viewed to be one of the most complicated, without clear procedures or performance parameters, and lacking transparency in decision-making. In addition, Canada was deemed to have the least clear policies and procedures pertaining to federal funding, i.e. within the broader context of announcing national (NACI/CIC) recommendations. Moreover, regarding program outcomes, Canada was slow to provide a full-country program start, was least uniform in both the start date and the age of routine cohorts across jurisdictions (e.g. Grade 4 in Québec through to Grade 8 in Ontario), and has not uniformly addressed or implemented catch-up programs.^{101,102,103} Finally, the *number* of targeted cohorts also varies across P/Ts, i.e. Québec is unique in targeting four distinct cohorts (girls in Grades 4 and 10, and ages 17 and 18 years), versus a single cohort in several P/Ts (e.g. Ontario).¹⁰⁴

With regard to vaccine funding, a critical concern is that beyond the renewed trust fund of \$300 million to support the introduction of the HPV vaccine (from March 2007 to March 2010), there has been no further commitment to NIS funding in the future. Hence, there is an urgent need to establish a permanent, predictable, and timely federal financing solution (potentially as a larger trust fund for other new and/or forthcoming vaccines) to maintain the momentum presently achieved under the NIS. For HPV vaccines in particular, it should be noted that, as of February 9, 2010, Health Canada has approved a second vaccine – GlaxoSmithKline's Cervarix, which targets HPV strains 16 and 18 (see Table 10.1).¹⁰⁵ With the introduction of Cervarix into the Canadian market, as well as the recent approval by Health Canada for the use of Gardasil to prevent genital warts in males,¹⁰⁶ renewed efforts will be required for HPV vaccine evaluation and recommendations. In addition, potential new funding mechanisms will need to be explored to optimize and sustain patient access to approved HPV vaccines – with priority given to maximizing protection from HPV-related clinical disease for all Canadians.

Apart from the challenges pertaining to HPV vaccine introduction in Canada, it is noteworthy that the CIC has recently issued its statement, “in concurrence with NACI”, regarding sanofi's Menactra (which targets meningococcal strains A, C, Y, and W-135) as of January 2010.¹⁰⁷ Adding weight to the argument that the CIC has created further delays in vaccine program development, it should be emphasized that this statement was issued more than three and a half years following licensure of the quadrivalent meningococcal vaccine in May 2006, and more than two and a half years after the initial NACI statement^x in May 2007.^{108,109} Unlike Gardasil, Menactra is not currently funded as a national public sector (F/P/T) program. At present, since CIC program recommendations are not formally linked to funding decisions, and P/T jurisdictions are not bound to implement CIC recommendations, individual jurisdictions must continue to seek funding (e.g. for Menactra and other newly approved vaccines) within their respective Ministries of Health, i.e. in light of CIC recommendations.¹¹⁰ As a result, as of March 2010, only Ontario, New Brunswick, Prince Edward Island, Newfoundland and the Northwest Territories have adolescent programs which provide protection against all four vaccine-preventable meningococcal serogroups (about 50% of Canada's population).¹¹¹ Thus, in general, while it was initially hoped that the introduction of the CIC (as part of broader NIS initiatives) would assist in harmonizing P/T immunization schedules, the national CIC evaluation process has instead been a disappointment to date; this “second-step review” appears to have added further complications – by introducing new misunderstandings, barriers or delays that may hinder patient access to innovative vaccines.

^x While the initial NACI statement issued in 2007 did not make any recommendation for routine public health use of Menactra, NACI later issued an update in April 2009 regarding invasive meningococcal disease, with more favourable recommendations regarding the use of Menactra.

As a striking U.S. example for comparison, recommendations regarding Pfizer's Prevnar 13 (i.e. to incorporate the newly approved pneumococcal vaccine into to the U.S. immunization schedule) were announced by the Advisory Committee on Immunization Practices (ACIP) – the advisory body analogous to Canada's NACI – on the same day (February 24, 2010) as the approval of Prevnar 13 by the Food and Drug Administration (FDA).^{112,113} This thought provoking example demonstrates the tangible results of achieving synchronized, efficient mechanisms for recommending novel vaccines in higher income countries; Canada should strive to emulate such best practices in accelerating access to enhanced and emerging vaccine technologies for all Canadians.

In summary, the recent Canadian experience with introducing new vaccines (such as Gardasil and Menactra) serves as a convincing platform to articulate the need for improvement in reshaping our national immunization landscape. Significant work lies ahead, primarily in terms of achieving predictable recommendation procedures and sustainable funding mechanisms for immunization programs in Canada – two necessary cornerstones in realizing equitable and timely access to vaccines across the provinces and territories. Overall, Canada's system for national vaccination programs currently stands at a crossroads; we face an urgent need to revamp our immunization framework, including a major overhaul of the current public health infrastructure for vaccine adoption.¹¹⁴ In addressing this critical call to action, patient needs must be placed explicitly at the forefront, with a clear vision by all stakeholders in terms of providing consistent, timely access to new vaccine innovations developed both in Canada and abroad.

10.3.4 Potential New Models: Challenges and Recommendations

Given the urgent need for major reform within Canada's national immunization system, it has been suggested – particularly by BIOTECCanada's Vaccine Industry Committee (VIC) – that federal and P/T public health officials should do more to consider international best practices for immunization program development. In taking preliminary steps towards this end, the PHAC hosted an International Forum in December 2008, with the key goal of evaluating immunization systems in other higher income countries, i.e. to shed light on best practices and models that might be adaptable to Canada's decentralized health governance system. In addition to invited guests from each of the eight countries,^{xi} meeting attendees also included officials from the PHAC, BGTD, and individual P/T jurisdictions, as well as representatives from the CIHR and the vaccine industry (through participation by the VIC).

This two-day International Forum focused on the key themes of: i) governance structures for immunization programs; ii) vaccine funding and procurement; and iii) immunization program-related research and evaluation. While the Forum provided an excellent opportunity to benchmark global best practices to help shape the future of vaccine programs in Canada, current challenges faced specifically within the Canadian environment were identified for further consideration by the PHAC (as presented in Table 10.5). Building on these identified themes and challenges, recent recommendations for F/P/T governments to improve the current immunization infrastructure, as put forward by BIOTECCanada's VIC (and covered in detail in Papers 5, 6, 7 and 9), are also summarized in Table 10.5. As the common voice of Canada's vaccine industry, the VIC's broad mission is to work collaboratively as a reliable, trusted partner with government and public health officials to create an enabling vaccine environment – in which Canadians are ensured the availability of (and full access to) all existing and innovative new vaccines.¹¹⁵

^{xi} Participating countries included Australia, Austria, Belgium, Germany, Spain, Sweden, the United Kingdom and the United States.

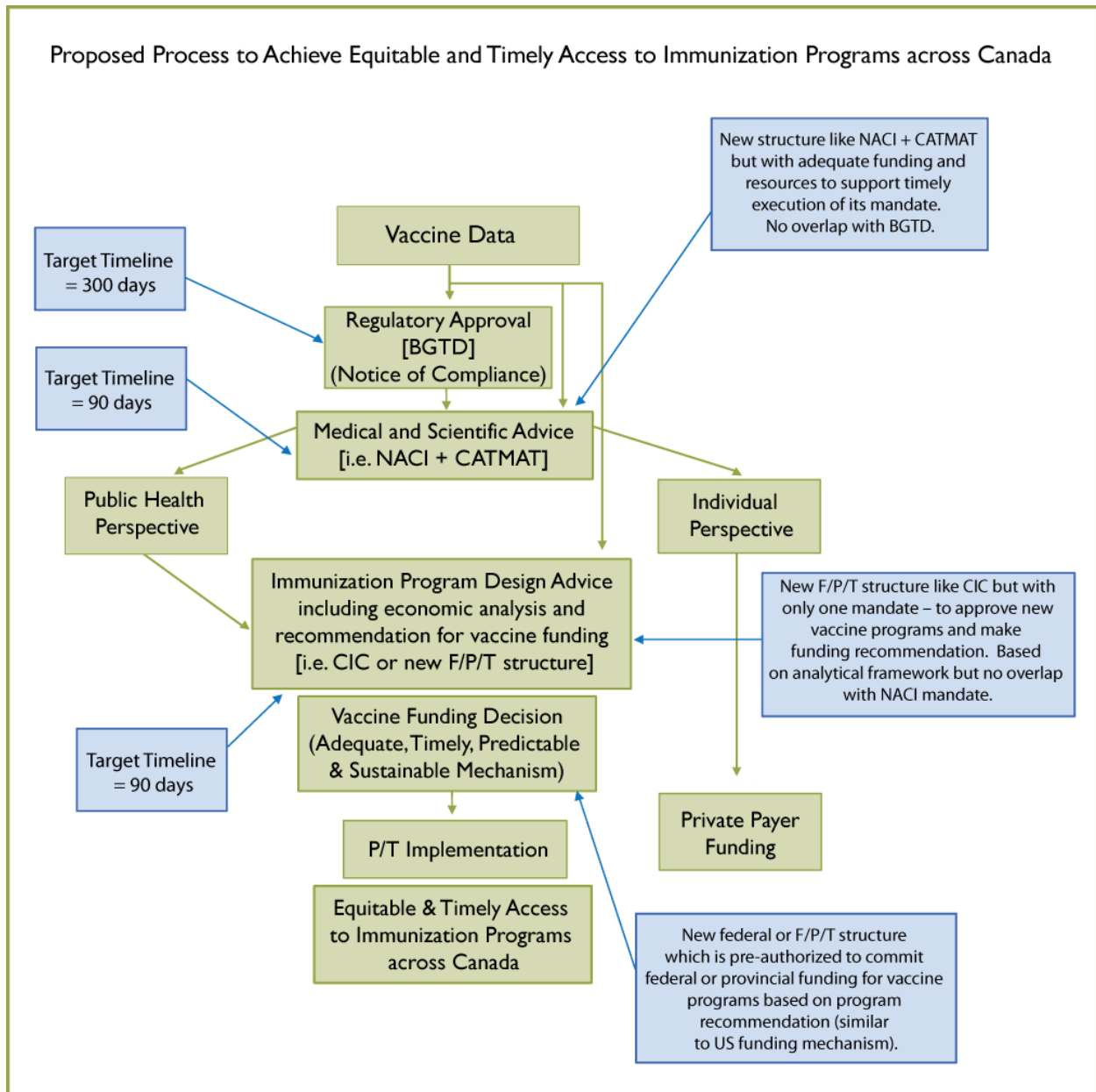
Table 10.5 – Current Challenges & Recommendations for Improving Canada’s Immunization System: Governance, Funding, Procurement & Program-Related Research^{116,117,118,119}

Key Challenges	Vaccine Industry Committee (VIC) Recommendations
Governance (see Paper 5)	
<ul style="list-style-type: none"> Increasing number of vaccines and delivery methods complicates evaluation process Inadequate NACI/CIC coordination and lack of timely evaluation/recommendations to guide Canada’s immunization programs Inequities in P/T capacities to support decision-making processes (unequal P/T participation in existing governance model) Variation in P/T schedules (inequitable patient access to publicly-funded programs) 	<ul style="list-style-type: none"> Minimize duplicative bureaucratic efforts (by streamlining authority across NACI, CIC, and P/T Advisory Committees) to optimize use of limited public health resources Develop timely, predictable evaluation/recommendation procedures, i.e. to reduce lag time to full (national) program implementation and enhance NACI credibility Define specific points of engagement for NACI/industry interactions (both pre- and post-licensure), i.e. to enhance two-way dialogue and enhance timeliness of NACI decision-making Implement a formal appeal mechanism for cases in which stakeholders do not agree with NACI recommendations Improve P/T harmonization, i.e. to align vaccine program development with intent of National Immunization Strategy (NIS) Enhance transparency, accountability, and stakeholder participation in program development, i.e. to foster collaboration/trust
Funding (see Paper 6)	
<ul style="list-style-type: none"> Increasing cost of new vaccine technologies Time-limited federal funding for specific vaccination programs (e.g. for 3 years) requires P/Ts to develop longer-term, sustainable funding solutions to maintain such programs National recommendations are not formally linked to F/P/T funding decisions (and do not bind P/T program implementation) Program delivery costs are not well understood, but should be evaluated and considered as part of total immunization program costs (e.g. for funding decisions) 	<ul style="list-style-type: none"> Develop timely, predictable, and sustainable funding mechanisms for national vaccine programs in Canada Renew federal funding commitment (e.g. by creating a permanent fund of \$100 million per year, minimum) to ensure newly recommended vaccines are accessible to all Canadians through publicly-funded immunization programs Establish clear policies that link national recommendations to federal and P/T funding decisions Deploy adequate (financial and human) resources to support both process and program elements

Key Challenges	Vaccine Industry Committee (VIC) Recommendations
Procurement (see Paper 7)	
<ul style="list-style-type: none"> • Dual-source awards promote security of vaccine supply, whereas single-source contracts may be associated with lower costs overall (difficult trade-off for PWGSC on behalf of P/T users) 	<ul style="list-style-type: none"> • Promote recognition of the full value of the vaccine supply chain (and that lowest price does not necessarily deliver greatest value) • Improve procurement environment by increasing flexibility of PWGSC/VSWG contract terms (e.g. increased lead times for initial vaccine delivery, contract extensions, and volume increases) • Decrease vaccine waste (through improved forecasting by P/T users and enhanced education/communication regarding cold chain management) to help secure vaccine supply
Program-Related Research & Evaluation (see Paper 9)	
<ul style="list-style-type: none"> • Planning of (and investment in) program-related research is often neglected • Mechanisms to fund/conduct post-market immunization research in a nationally coordinated manner are not well defined 	<ul style="list-style-type: none"> • Enhance Canada's capacity to support comprehensive, real-time, surveillance of: <ul style="list-style-type: none"> i) vaccine-preventable disease; ii) vaccination coverage; and iii) adverse events following immunization, i.e. to permit evaluation of safety, effectiveness (public health impact), and overall success of immunization program planning/delivery
Acronyms: See Table 10.4	

In working towards a more optimal immunization system for Canada – and to help build an environment conducive to meeting both industry and public health objectives in implementing future vaccine program strategies – the VIC has also clarified its vision for future program development and funding in the form of an illustrative flow chart (Figure 10.2). This flow chart, still considered an early work-in-progress, presents additional recommendations regarding target review times to support full (national) immunization program implementation, beginning with BGTD authorization, and focuses primarily on: i) medical/scientific review by NACI and the Committee to Advise on Tropical Medicine and Travel (CATMAT); ii) program recommendations by the CIC (or a new F/P/T structure); and iii) program funding by federal and P/T governments. Specifically, for each new vaccine, the VIC recommends that a NACI statement should be issued within 90 days of Health Canada approval (requiring enhanced industry/NACI engagement both pre- and post-licensure). In this context, it is noteworthy that CATMAT provides the PHAC/NACI with ongoing medical, scientific, and public health advice relating to tropical infectious disease and health risks associated with international travel – and hence makes immunization-related recommendations regarding the prevention and treatment of infectious diseases that may be encountered by travelers outside Canada.¹²⁰

Figure 10.2 – VIC Vision for Vaccine Program Development and Funding



Source: BIOTECCanada, Vaccine Industry Committee (VIC), 2010.

As indicated in Table 10.5, the VIC also recommends that the federal government should create a permanent trust fund (e.g. \$100 million per year minimum) to provide predictable financial support for publicly-funded immunization programs. Using such a sustained trust fund as a significant financing base, the federal government should play a leadership role in working collaboratively with P/T jurisdictions to establish a sustainable funding mechanism(s) to ensure adoption of new, recommended vaccines into public sector programs within another 90 days following NACI recommendations (i.e. within six months subsequent to vaccine licensure). Moreover, to accelerate vaccine adoption, clear policies should be established to link national recommendations to F/P/T funding decisions. Overall, coordinated, efficient recommendation processes, and timely, predictable F/P/T financial support for innovative vaccines will be essential in ensuring a strong future immunization infrastructure in Canada.

In early 2010, the VIC intends to share its preliminary recommendations (based on the concepts presented in Table 10.5 and Figure 10.2) to improve Canada's vaccine evaluation and recommendation infrastructure with the BGTD, PHAC, NACI, CIC, and all relevant stakeholders. The VIC will also continue to engage stakeholders in the development of new models for vaccine funding, i.e. by building support for sustainable financing solutions across F/P/T governments and target patient/advocacy groups. After receiving initial feedback from individual stakeholder groups, the VIC plans to modify and disseminate its recommendations more widely, with the broad goal of building Canada's capacity to develop and adopt innovative vaccines. In essence, the VIC aims to provide a stimulus to move forward by taking tangible steps towards developing future models to enhance vaccine governance, funding and timely patient access – to help ensure Canada remains among those leading countries with equitable, sustainable immunization systems that meet public health needs.

Returning to the over-arching theme of increasing vaccine coverage rates, it is hoped that implementation of VIC recommendations will also promote public confidence and participation in vaccination programs, i.e. through enhanced transparency and accountability within Canada's immunization system. However, maintaining public trust in vaccination programs will also require forceful, consistent responses from the immunization community,¹²¹ including demonstration of greater conviction by F/P/T officials in defending the pivotal beneficial role of vaccination in saving lives and scarce health care resources.¹²²

10.3.5 Building on the Success of the National Immunization Strategy (NIS)

As described in Papers 5 and 6, admirable progress has been made in strengthening Canada's immunization system since the introduction of the National Immunization Strategy (NIS) in 2003, with \$300 million in federal funding committed in 2004 to support national immunization programs for four vaccines (acellular pertussis, meningococcal C conjugate, pneumococcal conjugate and varicella), and an additional \$300 million injected in 2007 to finance HPV vaccine programs (as an extension of previous NIS funding). Indeed, virtually all jurisdictions have successfully introduced these five vaccines over the past several years.^{123,124} While the PHAC had conducted an interim review (in 2007) of progress made under the NIS,^{125,126,127} it was deemed too premature at that time to accurately evaluate the full impact of NIS initiatives, particularly with respect to assessing increases in national vaccination rates, prevention of vaccine-preventable disease, and potential economic savings within the Canadian health care system. The PHAC had also committed to undertaking a full-scale review of NIS progress by March 2010, but this has been rescheduled for completion by March 2011 (with the delay allegedly attributed to H1N1 pandemic influenza program planning and execution in 2009/2010). According to the PHAC, this process will also include a review of NACI/CIC coordination in terms of roles, responsibilities, and procedures in evaluating and recommending new vaccines.¹²⁸

To represent the vaccine industry in this critical review and renewal process, the VIC aims to help shape a reinvigorated NIS process by continuing to work collaboratively with the PHAC and F/P/T jurisdictions, i.e. to promote streamlined procedures for vaccine evaluation and recommendations, as well as to advocate for greater financial support of immunization resources and infrastructure across federal and P/T decision makers (as highlighted in Table 10.5 and Figure 10.2). In parallel with these activities, the VIC will also continue to advocate for an improved vaccine procurement environment in Canada to help secure the domestic vaccine supply. Given the importance of vaccination as a public health intervention – as well as the pressing need to enhance coordination of policies across these areas – it is in the best interest of all levels of government to ensure the long-term viability of the NIS.¹²⁹ Overall, the success of Canada's NIS will require expansion of initial goals, and will ultimately depend upon the availability of sustained federal funding. In the near-term future, it is hoped that recently approved and emerging vaccines not currently funded under national immunization programs (e.g. rotavirus, shingles, and higher-valent pneumococcal and meningococcal vaccines) will be recommended and funded under a more efficient, cohesive, and harmonized immunization structure – through continued investment in Canada's NIS programs.

10.3.6 Future Models for Therapeutic Vaccines

In building a new immunization system in Canada that anticipates new and improved vaccines, a key area that will require careful attention will be the development of governance and funding models for rapidly emerging therapeutic vaccines (see Section 10.2.3). For example, it is currently unknown whether emerging therapeutic vaccines will be integrated into public health programs, or whether public provincial drug plans (formularies) will be responsible for assessing and funding these vaccines, as for other therapeutic treatments.¹³⁰ In the latter case, as detailed in Paper 6, therapeutic vaccines could potentially be reviewed by the Common Drug Review (CDR) process, or by procedures under the Joint Oncology Drug Review (JODR) mechanism – now called the pan-Canadian Oncology Drug Review (pCODR) – quite apart from the current NACI deliberation system for preventive vaccines. Hence the imminent arrival of therapeutic vaccines in Canada underscores the need for decision makers at many levels to develop appropriate, efficient models for recommendation, financing and procurement of next-generation vaccines. It will also be important for federal and P/T officials to continue to consider best practices for vaccine regulatory, recommendation and financing procedures in other countries, e.g. to help achieve optimal clinical outcomes and economic value through adoption of therapeutic vaccine programs.

10.4 Communicating the Value of Vaccination

In Canada, as in many developed countries, concerns regarding the increasing number and cost of vaccines introduced in the past decade – and the consequent rise in overall cost of national immunization programs – have led to questions regarding the sustainability of publicly-funded vaccination programs. Hence an ongoing challenge for vaccine manufacturers (in proposing new models for future consideration) is to help change the perception by some individuals, including public health officials, that vaccines are “expensive”, and to proactively articulate the case that immunization programs provide excellent value for money spent – particularly in terms of their broad medical, societal and economic impact. Indeed, as described in Paper 6, the cost-effectiveness of immunization is well documented, and is greater than that of virtually any other preventive or therapeutic health activity;¹³¹ vaccines are widely recognized as among the best possible investments in health.¹³²

In essence, a key message that needs to be consistently communicated across all shareholder groups is that immunization leads to savings in health care costs, based on decreased incidence of vaccine-preventable disease, with concomitant reductions in mortality and morbidity (and thus health care utilization).¹³³ Specifically, when utilized as part of a primary prevention strategy, vaccines have potential to play a significant (yet currently underestimated) role in decreasing costs in those categories that represent the largest components of overall health care spending in Canada, i.e. payments for hospitals (28%), drugs (17.4%), and physicians (13.4%).¹³⁴ It should be emphasized that in 2008, total spending on vaccines in Canada represented less than 0.3% of total health care expenditures in Canada – an extremely small fraction of overall health expenses (see Paper 2). In this context, vaccines can be viewed as relatively “inexpensive” medical interventions. Simply put, immunization programs, which are central to prevention efforts, provide excellent value in offsetting costs in other areas while effectively promoting public health. Furthermore, while the emergence of therapeutic vaccines is anticipated to profoundly improve the health of Canadians, i.e. by generating novel treatment strategies for devastating diseases such as cancer and neurological disorders, the introduction of these new breakthrough technologies is also expected to yield additional cost savings in the future.¹³⁵

In general, Canadian government and public health officials (and the general public) need to more fully recognize the tremendous value of vaccines. In the specific context of allocating federal and P/T funds for immunization programs, key economic questions for consideration should include the following:¹³⁶ i) what are the expected program outcomes/benefits (in terms of disease-related cases, sequelae, or deaths averted and/or economic impact)?; ii) what does the program cost?; iii) does it deserve investment?; iv) can the program be afforded?; and importantly, v) can a jurisdiction afford **not** to implement the program? Finally, with regard to vaccine procurement, Canada's current procurement framework tends to treat vaccines as low-tech commodities; unfortunately, it does not adequately recognize vaccines as high-value biotech products, with proven value in disease prevention (see Paper 7).¹³⁷ Hence in the context of vaccine pricing, increased recognition is also required by designated users regarding the true value of the vaccine supply chain. In the future, implementation of more favourable vaccine pricing structures, i.e. under an enhanced procurement framework, will help build long-term manufacturing capacity to ensure the stability of the domestic vaccine supply – by encouraging vaccine manufacturers to remain in Canada. Moreover, enhanced pricing structures that reflect the full value of vaccines should also foster greater innovation in cutting-edge technologies for the benefit of patients worldwide.

10.5 Collaborative Partnerships Across Immunization Stakeholders

As highlighted in Sections 10.2 and 10.3, the vaccine sector is a vibrant, burgeoning field, in which the goals of industry and government often overlap, i.e. to help maximize the public health benefits of biopharmaceutical innovation. At the broadest level, vaccine manufacturers, regulators, officials representing the PHAC, NACI, CIC, and P/Ts governments, health care professionals, research scientists and the investment community all share the common vision of a healthier Canada.¹³⁸ Hence the collective, collaborative efforts of all relevant stakeholders will go a long way toward building a more stable and equitable immunization system – and in fostering patient access to both existing and innovative vaccines. Certainly, the coordinated actions of industry, academic and government researchers, along with national/international funding agencies, will be critical in harnessing existing research potential, while promoting long-term investment in R&D to drive future innovation in lifesaving (preventive) and therapeutic vaccine technologies.

To truly benefit from advanced vaccine technologies, all stakeholders in Canada must to work in partnership to develop a more favourable vaccine regulatory and policy environment; one in which predictable evaluation/recommendation procedures are combined with sustainable financing solutions, as well as adequate human resources for national immunization programs. Within the context of Canada's governance systems for immunization, significant improvement is required in achieving optimal NACI/industry relations, and BIOTECanada's VIC is firmly committed to building a strong collaborative partnership with NACI, i.e. with the vision of increasing the timeliness of NACI recommendations, and achieving greater transparency and accountability in the evaluation process – for the collective benefit of all Canadians. At the P/T level, open ongoing dialogue is also needed with vaccine manufacturers. This will require: i) appropriate recognition of the important contribution of industry in providing updates on vaccine technology and clinical trial progress; and ii) the removal of potential barriers (e.g. P/T governance protocols) that may block essential government/industry communication channels in fostering true partnership. Furthermore, all partners in Canada's immunization systems should consider new models for sustainable vaccine funding – as opportunities to optimize the medical and economic value of vaccination. Finally, continued progress towards a revitalized, fair procurement process is hoped to promote greater alignment between the interests of public health immunization programs and the broader capabilities of the vaccine industry, and will also help to secure a reliable, robust vaccine supply.

Given that immunization is a crucial, shared responsibility across F/P/T government and public health officials, manufacturers, the medical/scientific and investment communities, as well as the general public, the VIC recommends that meetings should be convened for all relevant immunization stakeholders on a consistent, ongoing basis (potentially by the PHAC, in conjunction with the VIC),¹³⁹ i.e. to promote frequent, transparent dialogue regarding vaccine governance and financing issues, as well as to continue the evaluation of best practices for vaccine program development as implemented in other higher income countries. Overall, substantial collaborative work lies ahead to achieve the ambitious goal of streamlining the process for making high-value vaccines available to patients as ultimate end-users. Specifically, considerable concerted efforts will be required to ensure that when the next breakthrough vaccine arrives, patient access will not be impeded by unacceptable discrepancies or delays in vaccine program adoption.¹⁴⁰ In building upon Canada's current immunization foundation – and working towards a new, more efficient and coordinated paradigm in vaccination program oversight – it remains incumbent upon each stakeholder group to do its part (in open consultation with other participants) in advancing the Canadian vaccine enterprise to the next level of success.

10.6 Recommendations

The first decade of the 21st century has been deemed as the most productive in the history of vaccine development, with the arrival of a broad range of lifesaving vaccines to protect against a host of infectious diseases.¹⁴¹ On the global horizon, many new “high-performance” (safer, more effective) vaccines and delivery technologies – as well as next-generation therapeutic vaccines to treat diseases that today seem unconquerable – are also anticipated to emerge from an exceptionally rich pipeline. Indeed, there is every reason to believe that immunization will continue far into the future as a vital mainstay of public health. As key contributors to the dynamic vaccine development landscape, Canada's scientists and companies continue to lead efforts to improve health worldwide, through commercialization of cutting-edge vaccine technologies. Yet the accelerated growth and bright prospects of the Canadian vaccine sector have been accompanied by a new set of complex challenges, particularly in terms of adapting to rapid change, and in developing optimal strategies for vaccine program development and delivery within the public sector.

Despite recent successes in decreasing the incidence of vaccine-preventable diseases, Canada's current immunization system is still considered fragile (with undesirable duplication of efforts, inequities, and delays); major reform is urgently needed to safeguard its tremendous value and potential public health impact in the near- and longer-term future. In essence, realizing the full promise of vaccination will demand significant attention to developing alternative future models for efficient immunization governance (including predictable recommendation procedures), permanent/sustainable funding and procurement mechanisms, and ultimately, timely patient access to innovative vaccines. Furthermore, to facilitate vaccine program adoption, renewed investment and bold leadership will be required to ensure that enhanced policy frameworks instill effective oversight, consensus-building, and sharper focus on accountability.

Collectively, in building on past achievements in improving Canada's vaccination system, stakeholders at all levels will be required to develop innovative collaborative approaches to strengthen the existing immunization infrastructure – with the goal of securing the quality, harmonization and sustainability of national vaccination programs as critical cost-effective solutions in protecting public health. In the spirit of such collaboration, and under the broader VIC mandate to work with key immunization partners in creating an enabling vaccine environment in which Canadians are ensured full, timely access to existing and breakthrough vaccines, the VIC has put forward the following recommendations for consideration by F/P/T governments and other stakeholders (see further details presented in Papers 3, 5, 6, 7 and 9).

Federal/Provincial/Territorial (F/P/T) Recommendations

1. Policy approaches to developing an efficient vaccine marketplace should encourage long-term investment in R&D in the vaccine sector. These initiatives should assist in sustaining and enhancing vaccine research in Canada, thus driving future innovation in the development of next-generation preventive and therapeutic vaccine technologies.
2. To minimize duplicative, bureaucratic efforts in evaluating and recommending new vaccines, the federal government should aim for increased efficiencies (and minimal redundancy across BGTD/NACI/CIC mandates), including the provision of adequate financial and human resources. Canadian immunization authorities (including NACI/CIC officials) should also endeavour to leverage the substantial financial/human resources currently in place in other developed countries, e.g. through more frequent, formal collaboration with the U.S. Advisory Committee on Immunization Practices (ACIP) and/or other national vaccine advisory bodies.

3. To facilitate the timeliness and predictability of vaccine adoption and patient access to new immunization programs, NACI should issue recommendations on the use of new vaccines within 90 days of Health Canada approval. This will require enhanced NACI/industry collaboration, including ongoing dialogue, and formal definition of points of engagement (e.g. pre- and post-licensure) for data presentation/submission to NACI as recommendations are being developed.
 - Enhanced NACI/industry collaborations in other areas, e.g. in jointly creating an appeal mechanism for NACI recommendations and in developing full disclosure methods for NACI member affiliations (including potential conflicts of interest), should help to build public trust, while ensuring greater transparency, accountability and credibility of the scientific-based NACI review process.
4. To build on the success of the National Immunization Strategy (NIS), a sustainable federal funding mechanism should be established for immunization programs (potentially in the form of a permanent trust fund of \$100 million per year minimum) to ensure new vaccine technologies can be incorporated into public vaccine programs.
5. The federal government should work with the provinces/territories to establish a standardized, sustainable funding mechanism to ensure adoption of new, recommended vaccines in public health programs within approximately six months of their approval by Health Canada.
6. To minimize disparities and gaps in Canada's immunization programs, the provinces and territories should aim to work towards a national immunization schedule that is followed across the country.
7. With the imminent launch of therapeutic vaccine technologies in Canada, Health Canada should work in a transparent manner with manufacturers and other relevant stakeholders (including members of NACI, and those affiliated with CDR and JODR/pCODR procedures) to determine the most appropriate route(s) of evaluation and financing for therapeutic vaccines.
8. In working towards an optimal, modern, fair and transparent vaccine procurement system, revisions should be made to specific terms/conditions in improving current PWGSC/VSWG contract flexibility (e.g. to increase vaccine delivery lead times and decrease vaccine waste) – to help build long-term manufacturing capacity to ensure the stability of the domestic vaccine supply.
 - Implementation of more favourable pricing structures is required, i.e. to reflect the full intrinsic value of vaccines as both high-technology products and effective primary prevention tools.
9. To support timely, accurate, and comprehensive vaccine program-related research and evaluation, F/P/T governments should allocate significant additional funds/resources to strengthen Canada's multi-faceted (but currently fragmented) disease surveillance and post-marketing safety surveillance infrastructure(s).

Stakeholder Recommendations

10. To discuss common critical issues in immunization, meetings of all relevant stakeholders (including F/P/T government and public health officials, regulators, policy makers, medical professionals, vaccine manufacturers/developers and researchers, investors, payers, and the general public) should be convened on a regular basis – potentially by the PHAC, in conjunction with the VIC. Urgent matters that require transparent dialogue encompass, but are not limited to, the following topics:
- Potential new governance/funding models to encourage predictable recommendation procedures and sustained financing mechanisms, i.e. to support timely, equitable access to recommended vaccines by all Canadians. (Alternative models for vaccine program development and implementation should be viewed as opportunities to attain the optimal medical, societal and economic value of immunization, while promoting stable investment to support future innovation in vaccine technologies.)
 - Continued identification of best practices for vaccine program development and delivery in other higher income nations that merit consideration in the context of the Canadian vaccine landscape.

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