

## Pathway to Access: Improving the Evaluation and Recommendation Process

## La voie de l'accès : Améliorer le processus d'évaluation et de recommandation

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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](http://www.biotech.ca/vaccines).

Ce document forme une partie de la série, *Les vaccins au Canada, un héritage à faire fructifier : Valeur, possibilités et défis*. Pour lire la série entière, veuillez visiter [www.biotech.ca/vaccines](http://www.biotech.ca/vaccines). (Document disponible en anglais seulement.)

## 5.1 Executive Summary / Sommaire

### 5.1.1 Executive Summary

In most developed countries, including Canada, the introduction of a new vaccine as part of a national immunization program is a complex process that goes far beyond regulatory approval. National advisory committees are typically involved to provide official recommendations based on systematic evaluation of clinical trial data, disease characteristics, and other supporting information regarding the new vaccine. These official recommendations can have a dramatic impact on vaccine demand, i.e. by directly encouraging health care and insurance providers (as well as consumers) to utilize a particular vaccine product, and/or by influencing immunization policy. Hence the development of national recommendations is considered crucial to the overall acceptance and use of new vaccines; such recommendations also play a vital role in realizing of the full value of innovation in vaccine technology.

In Canada, current evaluation and recommendation procedures that ultimately support the adoption of public vaccine programs have significant drawbacks; these mechanisms can still be characterized as lacking in harmonization and transparency, resulting in unacceptable duplication, inequities and delays. Unfortunately, such inconsistencies and delays can mean that Canadians suffer and or die needlessly due to vaccine-preventable diseases. Canada needs an efficient, predictable process for evaluating and recommending vaccines – including participation at the federal, provincial and territorial (F/P/T) levels – for both existing and new public immunization programs. This paper examines the current Canadian landscape for vaccine evaluation and recommendation, including potential solutions for future direction, and thus lays the groundwork for exploring funding issues (see Paper 6) as the next step along the continuum of implementing successful vaccination programs.

Within Canada's current national immunization system, once a vaccine has been approved by the Biologics and Genetic Therapies Directorate (BGTD), it is then subject to the scrutiny of National Advisory Committee on Immunization (NACI). Initially established in 1964, NACI is the national expert body that provides scientific recommendations for vaccine use in Canada – using evidence-based methods to assess whether the vaccine should be used, and to target groups that will most benefit from inoculation. Unlike NACI, the Canadian Immunization Committee (CIC) is a much newer committee comprised of vaccine program representatives from the federal, provincial and territorial ministries of health; its first meetings were held in 2003. While the fundamental objective in creating the CIC was to implement and meet the goals of the National Immunization Strategy (NIS, described below), the CIC was also established to develop national goals and targets for immunization programs, and for making continued, collaborative progress in promoting the harmonization of immunization schedules across Canada.

Although vaccine recommendations are made at the national level, decisions regarding the integration of new vaccines into publicly-funded immunization programs are primarily a provincial/territorial responsibility, based on the priorities and deliberations of P/T advisory committees. Ultimately, since each jurisdiction defines the list of publicly-funded vaccines and immunization schedules, Canada is presently characterized as having a fractured immunization program, often termed a “patchwork quilt”. Discrepancies exist not only in the numbers of age-related cohorts covered, but also in terms of the timing of announcements for program implementation. Overall, the multi-step process currently required for vaccine program implementation in Canada introduces undesirable disparities and delays in patient access to innovative vaccine technologies. Moreover, concerns have been expressed regarding potential overlap across the BGTD, NACI, and CIC mandates, including potential misallocation of scarce resources.

In an effort to end the inconsistencies and gaps observed in vaccine schedules across the country, the NIS was introduced in 2003 by the federal government, with an initial \$45 million in funding, followed by an additional \$300 million over three years, as announced in 2004. The NIS offered an opportunity for the federal government to demonstrate its leadership in harmonizing immunization policy, and providing a model for F/P/T cooperation towards improved health. Under NIS funding, virtually all jurisdictions successfully introduced four vaccines by 2006 (including acellular pertussis, meningococcal C conjugate, pneumococcal conjugate and varicella). Although the NIS has moved closer to its goals of improving immunization rates, reducing vaccine-preventable diseases, and ensuring equitable access (particularly to childhood and adolescent vaccines), there remain many challenges ahead.

Ultimately, the long-term success of the NIS will depend on multiple factors, including jurisdictional perspectives on NACI recommendations (and alignment with CIC recommendations) and the relevance and effectiveness of the CIC itself. The latter has been assessed as part of initial (internal) NIS evaluation by the Public Health Agency of Canada (PHAC), which has acted – since its inception in 2004 – as the lead body in overseeing immunization evaluation and recommendation processes in Canada. Notably, from a programmatic standpoint, the CIC created the first (pilot) joint working group in early 2006 to develop comprehensive operational plans specifically for human papillomavirus (HPV) vaccine programs in Canada. However, it still remains unclear whether such joint CIC-NACI working groups will also be established for other newly recommended (or future) vaccines, subsequent to NACI review.

For each vaccine approved in Canada since 1998, it has taken from 6-17 months to complete the NACI review/recommendation process to date, and it can take much longer (up to 6 years) for the adoption of a new vaccine into a publicly-funded, nationally accepted immunization program. Clearly, this is too long to wait for publicly-funded immunization programs that can prevent patient morbidity and mortality, even if the vaccine is licensed and available through the private system. Overall, from both a disease prevention and health economics perspective, there is great motivation to accelerate the NACI review process in attempt to compress the timelines required for patient access to innovative vaccine technologies.

In working towards this goal, BIOTECanada's Vaccine Industry Committee (VIC) holds the view that NACI should continue to work with manufacturers to formally define points of engagement for two-way dialogue and information sharing, i.e. to improve both the timeliness and appropriateness of NACI statements. Other avenues for enhanced NACI/industry collaborations could also include joint development of an appeal mechanism for NACI recommendations and/or full disclosure methods for NACI member affiliations (including potential conflicts of interest) – to ensure greater transparency, accountability and credibility of the scientific-based NACI review process.

At present, substantial work is urgently required to develop and implement optimal mechanism(s) for efficient review and recommendation of approved vaccines in Canada. To this end, and in the spirit of collaboration, the VIC has put forward the following recommendations for consideration by F/P/T governments and other key stakeholders.

Federal Recommendations:

1. To facilitate the timeliness 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. during clinical development, pre-licensing and pre-NACI release) for data presentation/submission to NACI as recommendations are being developed.
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.

Provincial/Territorial Recommendations:

3. 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.

Stakeholder Recommendations:

4. To discuss common critical issues in immunization, a meeting of all relevant stakeholders should be convened. Urgent matters for discussion presently encompass, but are not limited to, the following topics:
  - The current vaccine recommendation environment and its inherent inadequacies in efficiently and equitably protecting the Canadian public;
  - Potential new approaches or models for enhancing the efficiency of expert committees and vaccine recommendation procedures in Canada, including the development of cohesive (and consistently implemented) decision-making criteria, and transparent communication systems; and
  - The development of standards and best practices for vaccine recommendation procedures that match the best immunization programs of other developed nations.

### 5.1.2 Sommaire

Dans la majorité des pays développés, dont le Canada, l'intégration d'un nouveau vaccin à un programme national d'immunisation est un processus complexe, qui dépasse largement l'approbation réglementaire. On fait habituellement appel à des comités consultatifs nationaux pour formuler des recommandations officielles fondées sur une évaluation systématique de données d'essais cliniques, de caractéristiques de maladies et d'autres renseignements se rattachant au nouveau vaccin. Ces recommandations peuvent avoir une incidence considérable sur la demande en vaccins, notamment parce qu'elles incitent directement les fournisseurs de soins de santé et les assureurs (de même que les consommateurs) à utiliser un vaccin particulier et(ou) influent sur les politiques d'immunisation. L'élaboration de recommandations nationales est donc essentielle à l'acceptation et l'utilisation générales des nouveaux vaccins; elles jouent un rôle vital dans la reconnaissance de l'importance de l'innovation dans les technologies vaccinales.

Au Canada, le processus actuel d'évaluation et de recommandation menant éventuellement à l'adoption de programmes publics de vaccination présente d'importants inconvénients; on peut affirmer qu'il comporte encore 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. Des incohérences et des délais qui, malheureusement, font en sorte que des citoyens canadiens souffrent et meurent inutilement à cause de maladies évitables par la vaccination. Le Canada a besoin d'un processus efficace et prévisible d'évaluation et de recommandation – y compris une collaboration à l'échelle des gouvernements fédéral, provinciaux et territoriaux (FPT) – tant pour les programmes publics d'immunisation actuels que nouveaux. Le présent document dresse un portrait du processus actuel d'évaluation et de recommandation des vaccins au Canada, proposant notamment des solutions en matière d'orientation future, et jette ainsi les bases de l'étude de questions liées au financement (voir le document 6), prochaine étape des efforts visant à mettre en œuvre des programmes de vaccination efficaces.

Dans le cadre du système national d'immunisation actuellement en vigueur au Canada, le vaccin est approuvé par la Direction des produits biologiques et des thérapies génétiques (DPBTG), puis fait l'objet d'un examen minutieux de la part du Comité consultatif national de l'immunisation (CCNI). Constitué en 1964, le CCNI est un comité national d'experts, chargé de formuler des recommandations scientifiques pour l'utilisation des vaccins au Canada. Il se sert de méthodes fondées sur des données probantes pour déterminer si le vaccin doit ou non être utilisé et cibler les groupes chez qui l'inoculation sera la plus profitable. Contrairement au CCNI, le Comité canadien d'immunisation (CCI) est beaucoup plus récent. Composé des représentants des ministères fédéral, provinciaux et territoriaux de la Santé chargés des programmes de vaccination, le CCI a tenu ses premières réunions en 2003. Bien que l'objet fondamental de la création du CCI fût de mettre en œuvre la Stratégie nationale d'immunisation (SNI, décrite ci-contre) et d'en réaliser les objectifs, le CCI avait également pour mandat d'établir des objectifs nationaux pour les programmes d'immunisation et de favoriser l'harmonisation des calendriers d'immunisation dans tout le pays, réalisant des progrès continus et concertés à cet égard.

Bien que les recommandations en matière de vaccins soient formulées à l'échelle nationale, les décisions concernant l'intégration de nouveaux vaccins à des programmes publics d'immunisation relèvent principalement des gouvernements provinciaux et territoriaux, et tiennent compte des priorités et délibérations des comités consultatifs provinciaux et territoriaux. En fin de compte, comme c'est chaque province et territoire qui détermine qui recevra gratuitement les vaccins et quand, le Canada se retrouve actuellement avec un programme d'immunisation raboté, souvent qualifié de « courtepointe en

patchwork ». On observe des écarts non seulement quant au nombre de groupes d'âge couverts, mais aussi quant au moment choisi pour annoncer la mise en œuvre d'un programme. En général, les nombreuses étapes que nécessite actuellement la mise en œuvre de programmes de vaccination au Canada entraînent des écarts et des retards indésirables sur le plan de l'accès des patients aux nouvelles technologies vaccinales. Le chevauchement possible des mandats de la DPBTG, du CCNI et du CCI, et une mauvaise affectation possible des ressources limitées suscitent également des préoccupations.

Afin de combler les écarts et les lacunes observés dans les calendriers de vaccination au pays, le gouvernement fédéral a mis en place la SNI en 2003, y injectant un montant initial de 45 millions de dollars, puis, comme il l'a annoncé en 2004, un montant additionnel de 300 millions de dollars sur trois ans. Le gouvernement y voyait une occasion de démontrer son leadership en harmonisant les politiques d'immunisation et en proposant un modèle de collaboration fédérale, provinciale et territoriale destinée à améliorer la santé. Grâce à l'aide financière qui leur a été allouée dans le cadre de la SNI, pratiquement toutes les provinces et tous les territoires ont pu introduire quatre vaccins en 2006 (vaccin antioquelucheux acellulaire, vaccin conjugué contre le méningocoque, vaccin conjugué contre le pneumocoque et vaccin contre la varicelle). Bien que la SNI se soit rapprochée de ses objectifs visant à accroître les taux d'immunisation, à réduire les maladies évitables par la vaccination et à assurer un accès équitable (notamment aux vaccins destinés aux enfants et aux adolescents), il reste encore de nombreux défis à surmonter.

La réussite à long terme de la SNI dépendra, en fin de compte, de nombreux facteurs, dont le point de vue des provinces et territoires vis-à-vis des recommandations du CCNI (et la conformité aux recommandations du CCI), et la pertinence et l'efficacité du CCI lui-même. Ce dernier a été évalué dans le cadre de l'évaluation initiale (et interne) de la SNI effectuée par l'Agence de la santé publique du Canada (ASPC), qui, depuis sa création en 2004, est le principal organisme de surveillance des processus d'évaluation et de recommandation des vaccins. Du point de vue des programmes, notamment, le CCI a constitué, au début de 2006, le premier groupe de travail conjoint (pilote) chargé d'élaborer des plans opérationnels complets visant notamment les programmes de vaccination contre le virus du papillome humain (VPH) au Canada. Toutefois, on ne sait pas encore avec certitude si des groupes de travail conjoints de cette nature (CCI-CCNI) seront également formés pour d'autres vaccins nouvellement recommandés (ou futurs) à la suite de l'examen du CCNI.

Pour chaque vaccin approuvé au Canada depuis 1998, il a fallu, à ce jour, de 6 à 17 mois au CCNI pour en faire l'évaluation et la recommandation, et il peut falloir encore plus de temps (jusqu'à six ans) pour intégrer le nouveau vaccin à un programme public d'immunisation accepté à l'échelle nationale. Les patients attendent manifestement trop longtemps avant d'accéder à des programmes publics d'immunisation pouvant prévenir la morbidité et la mortalité, même si le vaccin est homologué et qu'il est disponible dans le système privé. Du point de vue de la prévention des maladies et de l'économie de la santé, on observe, en général, une grande motivation à accélérer le processus d'évaluation du CCNI afin de réduire les délais d'accès aux nouvelles technologies vaccinales.

Désireux de réaliser cet objectif, le Comité de l'industrie des vaccins (CIV) de BIOTECanada est d'avis que le CCNI devrait continuer de travailler en collaboration avec les fabricants afin de trouver des moyens d'engager un dialogue bilatéral et d'échanger des renseignements, notamment pour améliorer la rapidité de la diffusion des déclarations du CCNI et leur pertinence. Afin d'accroître la collaboration entre le CCNI et l'industrie, on pourrait aussi élaborer conjointement un mécanisme d'appel des recommandations du CCNI et(ou) de divulgation complète des groupements auxquels les membres du CCNI sont affiliés (y

compris les conflits d'intérêts possibles) afin de conférer au processus d'évaluation du CCNI, reposant sur des données scientifiques éprouvées, une transparence, une responsabilisation et une crédibilité accrues.

Actuellement, il est urgent de déployer des efforts substantiels afin d'élaborer et de mettre en œuvre un mécanisme optimal garantissant l'efficacité du processus d'évaluation et de recommandation des vaccins approuvés au Canada. À cette fin et dans un esprit de collaboration, le CIV a formulé les recommandations suivantes à l'intention des gouvernements fédéral, provinciaux et territoriaux, et d'autres intervenants clés.

Recommandations à l'intention du gouvernement fédéral :

1. Afin d'accélérer l'adoption des vaccins et 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., pendant le développement clinique, avant l'homologation et avant la diffusion des recommandations du CCNI) où les parties s'engagent à présenter des données au CCNI au fur et à mesure que des recommandations sont formulées.
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 la DPGTG, du CCNI et du CCI), et à allouer des ressources humaines et financières suffisantes.

Recommandations à l'intention des gouvernements provinciaux et territoriaux :

3. 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.

Recommandations à l'intention d'autres intervenants :

4. Afin de débattre des enjeux importants liés à l'immunisation, tous les intervenants concernés doivent être conviés à une réunion. Ces enjeux comprennent, sans en exclure d'autres :
  - Le processus actuel de recommandation des vaccins et ses faiblesses quant à la protection efficace et équitable de la population canadienne;
  - Les nouvelles méthodes pouvant accroître l'efficacité des comités d'experts et du processus de recommandation des vaccins au Canada, y compris l'élaboration de critères décisionnels cohérents (et appliqués d'une manière uniforme) et de systèmes de communication transparents;
  - L'élaboration de normes et de pratiques exemplaires favorisant l'établissement d'un processus de recommandation des vaccins qui s'harmonise aux meilleurs programmes d'immunisation d'autres pays développés.

## 5.2 The Need for Predictable, Timely Evaluation/Recommendation Procedures

As described in previous papers, new vaccines are developed, licensed and commercialized based on the initiative of vaccine manufacturers. However, in most developed countries, the introduction of a new vaccine as part of a national immunization program is a complex process that goes far beyond market approval and availability. While assessment of the quality of data supporting vaccine safety and efficacy (as part of the regulatory process) constitutes an obvious starting point, official recommendations and appropriate funding are ultimately required. National advisory committees are typically involved to provide official recommendations based on systematic evaluation of available clinical data and other supporting information regarding the new vaccine. The role of such national advisory bodies is essentially to determine whether and how the new vaccine should be recommended for use in a given epidemiological, social-cultural, and economic environment.<sup>1</sup> In general, an evidence-based decision-making approach is taken, encompassing a series of elements and questions relating to disease burden, vaccine properties, relevance and feasibility of the prevention strategy, as well as its expected medical and economic impact.

Vaccine recommendations put forward by national advisory committees can have a dramatic impact on vaccine demand, i.e. by directly encouraging health care and insurance providers (as well as consumers) to utilize a particular vaccine product, and/or by influencing professional or medical societies that help shape immunization policy.<sup>2</sup> Hence the development of national recommendations for the introduction of a new vaccine into a nation's immunization program is considered crucial to the overall acceptance and use of new vaccine technologies.

In Canada, the process by which vaccines are included in immunization schedules involves a multi-step process of evaluation and recommendation, as initiated by national public health authorities. At present, this process is criticized as being fraught with undesirable delays, inequities and duplication.<sup>3</sup> There is an urgent need to revamp Canada's national immunization system, including a major overhaul of the current public health infrastructure for vaccine evaluation, recommendation, adoption, and funding. In the future, patient needs must be placed explicitly at the forefront, with a clear vision by all stakeholders in terms of providing predictable, timely access to new vaccine innovations that can prevent disease and save lives.

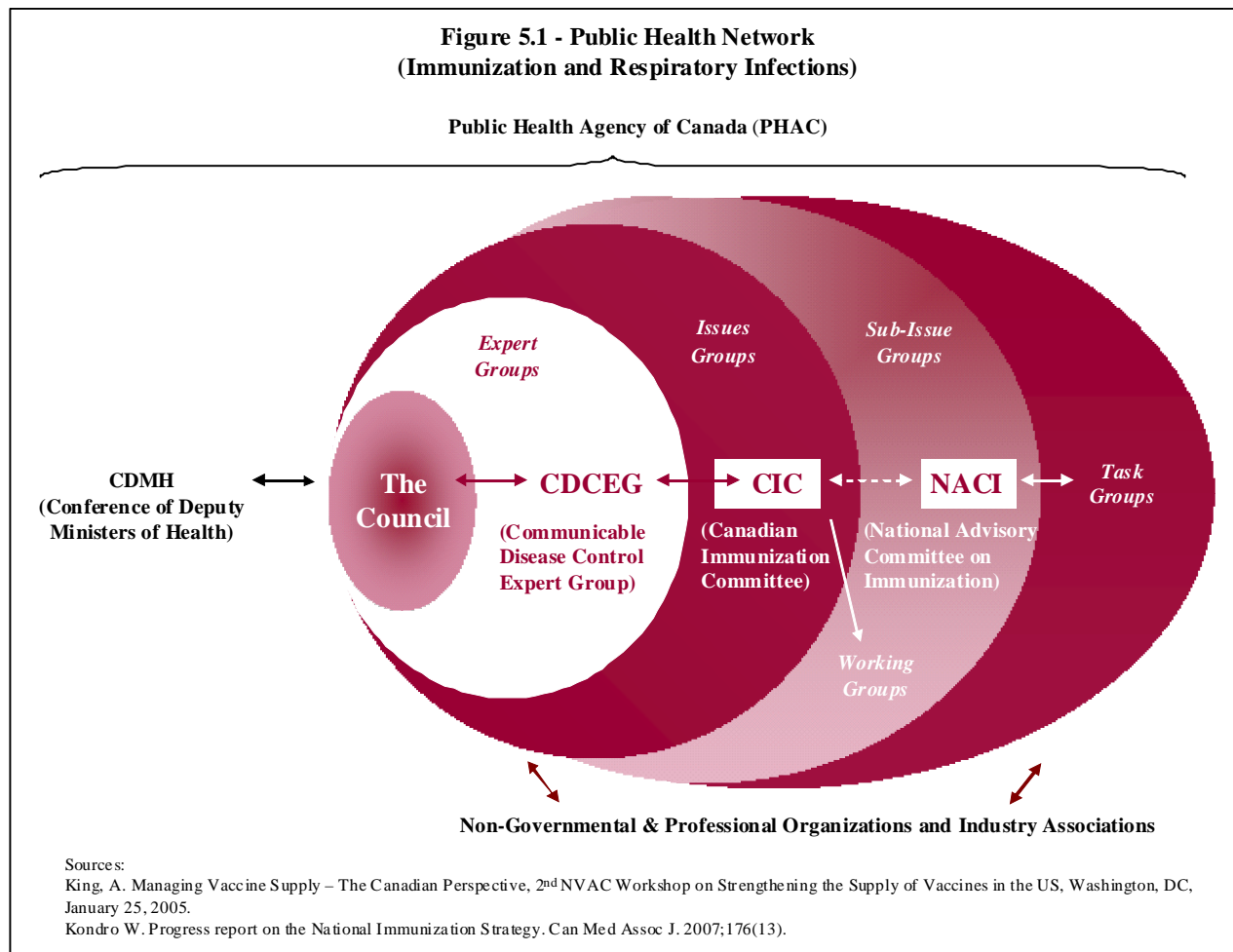
This paper examines the current Canadian landscape for vaccine evaluation and recommendation, including inherent flaws and potential solutions for future direction. This paper can be viewed as building a foundation for Paper 6 (regarding funding issues), primarily in terms of describing key elements of the current Canadian immunization infrastructure. While this paper provides a snapshot of current evaluation/recommendation processes, the next installment, Paper 6 provides further details (and historical perspective) regarding relevant federal and provincial roles in shaping current immunization mechanisms and policy, particularly where historical development sheds light on current funding procedures.

## 5.3 The Public Health Agency of Canada (PHAC)

Since its inception in 2004, the Public Health Agency of Canada (PHAC) has acted as the lead body in overseeing immunization evaluation and recommendation processes in Canada. The relevant expert groups that guide immunization procedures are collectively known as the Public Health Network, which reports to the Federal/Provincial/Territorial (F/P/T) Conference of Deputy Ministers of Health (see Figure 5.1). It is noteworthy that the national immunization bodies already in place prior to the creation of the

PHAC – including the National Advisory Committee on Immunization (NACI) and the Canadian Immunization Committee (CIC), as described in further detail below – have since been subsumed within the current PHAC reporting structure.

In essence, the Pan-Canadian PHAC was created to provide national guidance, leadership and coordination in public health in Canada, as well as to strengthen the country's abilities to respond to public health threats, outbreaks, and emergencies.<sup>4</sup> Following the SARS crisis in Canada, a key impetus for the Government of Canada in creating the PHAC was to respond to a consensus from the provinces, public health experts and concerned citizens regarding the need for federal leadership on public health issues to be consolidated within a national public agency. In September 2004, Dr. David Butler-Jones was also appointed as Canada's first-ever Chief Public Health Officer to head the agency, reporting to the federal Minister of Health.<sup>5</sup>



## 5.4 National Advisory Committee on Immunization (NACI)

### 5.4.1 NACI Role & Mandate

Within Canada's current national immunization system, once a vaccine has been approved by Health Canada's regulatory agency – the Biologics and Genetic Therapies Directorate (BGTD) – it is then subject to the scrutiny of NACI (now under the auspices of the PHAC), the national expert body that provides

scientific recommendations for vaccine use in Canada. Initially established in 1964, NACI is presently comprised of recognized experts in the fields of pediatrics, infectious diseases, immunology, medical microbiology, internal medicine and public health; the committee reports to the Chief Public Health Officer of Canada.<sup>6</sup>

Although NACI has traditionally had a strong pediatric focus, this advisory body will need to consider broadening its composition to include expertise in other medical specialties and/or disciplines as new vaccine technologies emerge. For example, NACI is already being faced with the challenge of adapting its capabilities to keep pace with newly licensed preventive vaccines, such as the zoster/shingles vaccine – which may require expertise in geriatrics, dermatology and/or ophthalmology. In addition, as many novel therapeutic vaccines are imminently expected to be approved in Canada, NACI will need to adjust its structure accordingly to provide comprehensive expertise across a wide range of indications and target populations for immunization.

NACI's current mandate is to provide the PHAC with ongoing and timely medical, scientific and public health advice relating to immunization, specifically in terms of: i) use of vaccines in humans, ii) vaccine evaluation, and iii) monitoring of vaccine associated adverse events. More broadly, NACI also advises on the need for national vaccination strategies and makes recommendations for vaccine development research. All NACI recommendations on vaccine use in Canada are published every four years in the *Canadian Immunization Guide*,<sup>7</sup> with additional updates published in the *Canada Communicable Disease Report*.<sup>8</sup>

In making national recommendations for a specific vaccine, NACI uses evidence-based methods to assess whether the vaccine should be used, and to target groups that will most benefit from inoculation. The review and recommendation process takes into account available evidence regarding both disease characteristics (e.g. epidemiology, burden of disease and high risk populations) and vaccine characteristics (including safety, immunogenicity, and efficacy or effectiveness data).<sup>9</sup> This information is generally supplied by the manufacturer that developed and tested the particular vaccine for which recommendations are being made.

Many industry players have voiced concern that NACI review constitutes a duplicative procedure, since the vaccine clinical trial data analyzed by NACI is essentially a sub-set of the data submitted to Health Canada for product registration (market approval). While such duplicative procedures may ultimately impede patient access to vaccines, they are not unique to the adoption of immunization programs. For example, the Common Drug Review (CDR) and Joint Oncology Drug Review (JODR) processes also review safety and efficacy data for new therapeutics (or oncology drugs, respectively) subsequent to evaluation by Health Canada for product approval. However, it should also be noted that duplication of mandates not only wastes time and resources, it can also lead to contradictory recommendations. In the case of one recently approved vaccine, Menactra (sanofi pasteur's quadrivalent meningococcal polysaccharide diphtheria toxoid conjugate vaccine) was licensed and indicated by BGTD for use in 2 - 55 year olds, whereas the NACI recommendation clearly stated that Menactra should not be used in 2 - 10 year olds. Thus having recommendations from two separate national advisory bodies can also create significant confusion for the medical community and the public.

#### 5.4.2 Current NACI Recommendations

Current NACI recommendations for infants and children, adults, and travellers are publicly available (provided by the PHAC) as presented in Table 5.1 below. It should be noted that national NACI-recommended vaccine schedules differ from publicly-funded immunization schedules [e.g. for i) infants and children, including special programs and catch-up programs; ii) high risk groups; and iii) influenza vaccination]. As described in Section 5.6, publicly-funded vaccines schedules may also vary widely across the provinces and territories in Canada.<sup>10</sup>

Table 5.1	
Target group	Website
Infants & Children	<a href="http://www.phac-aspc.gc.ca/im/is-cv/index-eng.php#a">www.phac-aspc.gc.ca/im/is-cv/index-eng.php#a</a>
Adults	<a href="http://www.phac-aspc.gc.ca/im/is-cv/index-eng.php#b">www.phac-aspc.gc.ca/im/is-cv/index-eng.php#b</a>
Travellers	<a href="http://www.phac-aspc.gc.ca/im/travelvaccines-eng.php">www.phac-aspc.gc.ca/im/travelvaccines-eng.php</a>

Additional details are provided in the latest edition of the *Canadian Immunization Guide*, particularly regarding immunization guidelines for:

- Children & adults with inadequate immunization records
- Immunocompromised persons
- Infants born prematurely
- Patients in health care institutions
- Persons new to Canada
- Pregnant & breastfeeding women
- Persons with neurologic or bleeding disorders

Further updates and supplements to the *Canadian Immunization Guide* are available at: [www.naci.gc.ca](http://www.naci.gc.ca).

#### 5.4.3 International Vaccine Advisory Committees

On the global stage, the fundamental processes required to introduce new vaccines in other developed countries are roughly analogous to those in Canada, including regulatory review as the first milestone, followed by the development of national recommendations for vaccine program adoption, and subsequently, the implementation of appropriate vaccine financing and delivery mechanisms. Interestingly, this sequential set of steps was viewed as valid and applicable in the mid-20<sup>th</sup> century, when the rate of innovation was slower, and publicly-funded healthcare systems were in the early stage of development. However, this type of step-wise scheme for vaccine introduction has been deemed by many to be less appropriate in today's health care system, in which both technology and productivity have driven a faster pace of innovation, and the publicly-funded sector has been burdened with much greater financial stress.

With specific regard to establishing recommendations for national immunization programs, such recommendations for vaccine use in the United States are primarily formulated by the Centers for Disease Control and Prevention (CDC) through its Advisory Committee on Immunization Practices (ACIP).<sup>11</sup> In Australia, the Australian Technical Advisory Group on Immunisation (ATAGI) develops guidelines on

the medical administration of vaccines, working in conjunction with the Pharmaceutical Benefits Advisory Committee (PBAC) in making recommendations to the Minister for Health and Ageing regarding vaccines for the national immunization program.<sup>12</sup>

In member countries of the European Union, national or regional vaccine recommendations are based on a systematic evaluation of available clinical data, as conducted by advisory groups of experts commissioned by public health authorities. However, these recommendation processes are not standardized at the European level.<sup>13</sup> As one example, in the United Kingdom, the Joint Committee on Vaccination and Immunisation (JCVI) provides recommendations and advice to the U.K. Health Ministers on matters relating to communicable diseases (preventable and potentially preventable) through immunization.<sup>14</sup>

### 5.5 The Canadian Immunization Committee (CIC)

Unlike NACI, the Canadian Immunization Committee is a much newer committee comprised of vaccine program representatives from the federal, provincial and territorial ministries of health;<sup>15</sup> its first meetings were held in 2003.<sup>16</sup> The CIC is directly linked to NACI, both of which are part of the Public Health Network dealing with immunization issues. As shown in Figure 5.1, the CIC reports to the Communicable Disease Control Expert Group, which in turn reports to a federal/provincial body known as The Council (typically, provincial medical officers of health).

While a fundamental objective in creating the CIC was to implement and meet the goals of the National Immunization Strategy (NIS, see Section 5.7 below), the CIC was also established as a mechanism for developing national goals and targets for immunization programs in Canada, and for making continued, collaborative progress in promoting the harmonization of immunization schedules. Within the framework of the NIS, the CIC also provides a national forum to coordinate basic research, vaccine-preventable disease surveillance, and public and professional education, as well as to identify and target special-needs populations across the country.<sup>17</sup>

The CIC is supported by several working groups that assist in developing recommendations to submit to the CIC or NACI, and which also respond to questions (or requests for additional information/analyses) from these national bodies. These working groups include the Vaccine Supply Working Group (VSWG), the Vaccines Safety Expert Working Group (VSEWG), and the Professional Education Working Group (PEWG) to name a few.<sup>18</sup> The CIC also liaises with Health Canada and the U.S. Department of Health and Human Services, and convenes meetings with non-governmental organizations, professional organizations, and industry associations such as the Vaccine Industry Committee (VIC) of BIOTECanada.

In May 2006, roughly one month prior to Health Canada's approval of the human papillomavirus (HPV) vaccine, the CIC decided to create the joint CIC-NACI HPV Vaccine Expert Working Group in efforts to promote harmonization of HPV immunization programs in Canada. Hence in addition to its previously established multiple roles, the CIC began to place greater emphasis on developing programmatic plans for vaccines recommended by NACI. In essence, while NACI recommendations would determine the optimal conditions of vaccine use in the epidemiological context of Canada, CIC recommendations would focus more specifically on creating operational plans for implementing feasible immunization programs, including the identification of an acceptable (potentially narrower) range of target cohorts. From this programmatic standpoint, the CIC had thus created the first (pilot) joint working group to develop comprehensive scientific and programmatic recommendations – specifically for HPV vaccine programs in

Canada. However, as described in Section 5.9.3, it still remains unclear whether such joint CIC-NACI working groups will also be established for other newly recommended (or future) vaccines, subsequent to NACI review.

Despite recent progress in reaching consensus through NACI/CIC collaboration, the current recommendation process for public vaccine programs remains severely flawed; it continues to involve several duplicative procedures, and has no established timelines or predictability. All of these shortcomings are to the detriment of public health, particularly when the vaccine technology is already licensed for commercial use. As mentioned above, potential overlap also exists between NACI and the BGTD, which determines safety and efficacy of vaccines prior to regulatory approval. Hence at present, vaccine recommendation procedures are highly complicated, particularly since the three regulatory/advisory organizations effectively report into different bodies: the BGTD to Health Canada, NACI to the Chief Public Health Officer as head of the PHAC, and the CIC (as an F/P/T structure) to the Conference of Deputy Ministers of Health.

### **5.6 Provincial/Territorial Role in Vaccine Recommendation Process**

The NACI recommendation process and the newer CIC review procedure are often viewed as the first steps in the process by which a vaccine may become publicly funded in Canada, as described in Paper 6. It should be emphasized that although vaccine recommendations are made at the national level, decisions regarding the integration of new vaccines into publicly-funded immunization programs are primarily a provincial/territorial responsibility. This requires each jurisdiction to plan, fund and deliver vaccine programs independently – considering its own unique set of circumstances – based on the decisions of provincial/territorial advisory committees. This final step is often viewed as yet another duplicative procedure, placing further strain on scarce human and financial resources within Canada’s immunization infrastructure.

Ultimately, since each province and territory defines the list of publicly-funded vaccines and immunization schedules, Canada is presently characterized as having a fractured immunization program, often termed a “patchwork quilt”, with significant disparities across jurisdictions. Discrepancies exist not only in the numbers of age-related cohorts covered, but also in terms of the timing of announcements for program implementation. Overall, the multi-step process currently required for vaccine program implementation in Canada introduces undesirable disparities and delays in patient access to innovative vaccine technologies, thus raising ethical questions surrounding fairness and equitable access in a democratic society.

In general, NACI recommendations represent one component used by provinces and territories to support decision-making for publicly-funded vaccine programs, and may also guide individual insurance providers in the private sector.<sup>19</sup> While CIC recommendations are also provided to assist provinces and territories in the decision-making process for implementing immunization programs, it has never been made clear exactly what role the CIC would play in augmenting the NACI mandate in determining who is at risk for vaccine-preventable disease, and who should be targeted by public programs. However, in the context of achieving public health goals, a transparent, predictable, timely mechanism for vaccine evaluation and recommendation is paramount. Taking a broader view, the successful adoption and public health impact of a vaccination program relies on how well the program is implemented, and its acceptability by the population.

## 5.7 National Immunization Strategy (NIS)

In an effort to end the inconsistencies and gaps observed in vaccine schedules across the country, NACI has worked with Health Canada to pursue a National Immunization Strategy. In February 2003, the federal government allocated \$45 million over five years to assist with NIS development, with the key objectives of achieving high coverage of publicly-funded immunization, complete coverage of all children with routine childhood vaccines, equitable access to routinely recommended vaccines, optimal vaccine safety and effectiveness, improved program coordination and efficacy, optimal cost-effectiveness, and security of vaccine supplies and national interventions as needed (e.g. in emergencies).<sup>20</sup>

The NIS was essentially introduced as an early step in healthcare reform, offering an opportunity for the federal government to demonstrate its leadership in harmonizing immunization policy, and providing a model for federal/provincial/territorial cooperation towards improved health.<sup>21</sup> To encourage collaborative, systematic decision-making using common criteria, the NIS Strategy Report of 2003<sup>22</sup> recommended that the F/P/T process for evaluating new vaccines would be based on a methodical review of an analytical framework for immunization programs in Canada, as developed by Erickson, de Wals and Farand.<sup>23</sup>

Historically, provincial funding for childhood immunization against nine diseases – including diphtheria, hepatitis B, *Haemophilus influenzae* type b, measles, mumps, pertussis (whooping cough), polio, rubella, and tetanus – was already provided through public health programs across Canada by 2003, prior to the introduction of the NIS. However, between 1998 and 2002, NACI added four vaccines to its recommended vaccine list (including adult pertussis, meningococcal C conjugate, pneumococcal conjugate, and varicella), and coverage for these vaccines was reported to be very uneven in 2003.<sup>24</sup> This heterogeneity in practice had an impact at the clinical level, where physicians reported that the costs to purchase these new vaccines privately were prohibitively expensive for many patients, and hence physicians felt uncomfortable recommending them.<sup>25</sup>

As an example for baseline reference (prior to NIS funding), 2002 immunization rates were low across most of Canada (0% - 32%) for meningococcal C conjugate, pneumococcal conjugate and varicella (chicken pox), which were not yet publicly funded in most provinces.<sup>26</sup> In contrast, 2002 immunization rates for these three vaccines were significantly higher in the Edmonton Health Region, Alberta (84% - 94%), where these vaccines were already publicly funded.<sup>27</sup> This data unambiguously demonstrated the impact of public funding of vaccination programs in terms of increasing immunization coverage rates. It also underscored the need for equitable access to routinely recommended vaccines for all Canadian children.

In a bold move to reinforce and expand the NIS, the 2004 federal budget promised an additional \$300 million over three years (through the Canadian Immunization Trust Fund) to support the introduction of all four newly recommended vaccines across all provinces and territories.<sup>28</sup> This Trust Fund was to provide financing to the provinces with some degree of flexibility regarding how they utilized the funds. While there was no mechanism for the federal government to regulate how the funds would actually be spent, the provinces/territories were aware that the public could hold them accountable if national standards were not met. Hence the creation of the Trust Fund exerted a strong political pressure to expand immunization programs to include the full complement of four new vaccines, as recommended by NACI, in all jurisdictions.<sup>29</sup>

These programs included adolescent and adult acellular pertussis vaccines, infant and adolescent conjugate meningococcal C vaccines, infant and child pneumococcal conjugate vaccines, and varicella vaccines. Under NIS funding, virtually all jurisdictions successfully introduced these four vaccines by 2006.<sup>30</sup> Indeed, preliminary estimates have suggested that twice as many Canadian children were protected against acellular pertussis, meningococcal group C infection, pneumococcal disease, and varicella in 2006 compared with 2003.<sup>31</sup> In addition, there has been a reduced burden of illness, with documented reductions in hospitalizations due to these infections.<sup>32</sup> In this regard, the NIS has been broadly hailed as a well-known success story for immunization in Canada.

It should be emphasized that it is currently premature to evaluate the full economic impact of the \$300 million NIS investment, in terms of savings within the Canadian health care system. The key underlying reasons it is still too early for such assessment include the following observations: i) the national disease surveillance system in Canada is usually 2-4 years out of date; ii) there are no standardized laboratory procedures for disease detection; and iii) there is a paucity of high quality data regarding immunization rates. Hence there is no recent, precise and conclusive evidence (with the possible exception of the pneumococcal conjugate vaccine) that the four vaccine programs introduced under the NIS have been effective in preventing disease. Consequently, it would be impossible to conduct a comprehensive cost-effectiveness analysis without this information. More broadly, since the NACI review process relies heavily on epidemiology data for vaccine-preventable diseases, the availability of current, accurate disease surveillance data is critical in supporting evaluation/recommendations procedures for new vaccines in Canada. The need for improved surveillance systems for vaccine-preventable diseases is discussed in further detail in Paper 9.

Although the NIS has moved closer to its goals of improving immunization rates, reducing vaccine-preventable diseases, and ensuring equitable access (particularly to childhood and adolescent vaccines), there remain many challenges ahead. It is widely acknowledged that the national strategy has not yet been fully developed, and key weaknesses include the need to develop: i) disease-specific goals and concrete action plans for each vaccine-preventable disease, ii) vaccine registries, iii) public education and marketing programs, and iv) formal, external NIS evaluation programs.<sup>33</sup> In addition, the initial groundwork laid by the NIS must be better leveraged to enhance existing monitoring systems to determine who is not receiving recommended vaccines, and to develop a comprehensive programmatic research agenda to determine why this is the case.<sup>34</sup>

Perhaps most importantly, a formal process has not yet been established in conjunction with the NIS to ensure sustainable federal funding for new and existing vaccines. Specifically, the \$300 million previously allocated to the NIS through Canadian Immunization Trust Fund ended in March 2007. While a “renewed” trust fund of \$300 million was announced by the federal government in 2007 – to support the introduction of the new HPV vaccine – there has been no further commitment to NIS funding in the future. Hence, there is an urgent need to establish a permanent federal financing solution to maintain the momentum presently achieved under the NIS. A longer-term funding solution will also help to permit full realization of the tremendous value of innovation in vaccine technology. Funding issues are examined in further depth in Paper 6.

Ultimately, the long-term success of the NIS will depend on multiple factors, including provincial/territorial perspectives on NACI recommendations (and alignment with CIC recommendations) and the relevance and effectiveness of the CIC itself. The latter has been the subject of recent NIS evaluation by the PHAC.<sup>35,36,37</sup> As alluded to above (and further outlined in Paper 6), the

success of the NIS will be dependent upon the availability of ongoing federal funds, and it will also be a function of jurisdictional abilities to maintain immunization programs in the absence of such longer-term federal funding. Given the importance of vaccination as a public health intervention – as well as the pressing need to enhance coordination of policies in this area – it is in the best interest of all levels of government to ensure the long-term viability of the NIS.<sup>38</sup>

Interestingly, according to the PHAC's own report,<sup>39</sup> NIS activities and federal funding have often been deemed interchangeable when discussing the impact of the NIS, thus implying that the major (and perhaps sole) consequence of the NIS to date has been the direct injection of funding within the Canadian immunization system. Other skeptics have gone so far as to criticize the NIS for creating a "massive intergovernmental vaccination bureaucracy" as its primary outcome to date.<sup>40</sup> Clearly, greater strides must be made under the NIS – including further evolution of the CIC – to achieve more incremental, tangible results in terms of minimizing duplication of effort and moving towards harmonization of immunization programs across the country. To meet this goal, however, the federal government must continue to foster coordination of the elements involved, i.e. by providing national leadership in supporting the principles established under the NIS, particularly in building an appropriate infrastructure to support efficient vaccine recommendation and funding mechanisms.

### **5.8 Status of Vaccines Approved Since 1998**

Although commendable progress has been achieved for vaccines approved since 1998 under the NIS funding umbrella, there are continuing disparities and gaps in vaccines covered by provincial/territorial immunization schedules. In addition to the current lack of uniformity in immunization programs, undesirable delays have impeded patient access to recently approved vaccines (see Table 5.2), including the four vaccines funded under the NIS as announced in Budget 2004, and other more recently recommended vaccines. Indeed, concern has been expressed by many stakeholders that current review and recommendation procedures for vaccines in Canada are still characterized by unacceptable (and potentially increasing) duplication and inefficiencies – all of which prevent timely access to innovative vaccine technologies, thus putting the population needlessly at risk of vaccine-preventable diseases.

**Table 5.2 - Time Elapsed Between Vaccine Licensing and Provincial/Territorial (P/T) Program Implementation**

Vaccine	Date Licensed <sup>i</sup>	NACI Statement <sup>ii</sup>	Time Post-Licence	CIC Statement <sup>ii</sup>	Federal Funding	Program Implementation (Most P/T)	Program Implementation Post-Licence
Varicella [Varivax]	Dec 1998	May 1999	6 months	N/A	2004 (NIS) <sup>iii</sup>	2004-2006 (QC as last province, 2006)	6 years +
Adult Pertussis <sup>iv</sup> [Adacel]	May 1999	May 2000	12 months	N/A	2004 (NIS)	2004	5 years
Meningococcal C conjugate <sup>v</sup> [Menjugate]	April 2001	Oct 2001	7 months	N/A	2004 (NIS)	2004-2005	3 years +
Pneumococcol conjugate (7-valent) [Prevnar]	June 2001	Jan 2002	6 months	N/A	2004 (NIS)	2004	3 years
Human Papillomavirus, HPV (quadrivalent) [Gardasil]	July 2006	Feb 2007	7 months	Mid 2008	2007	2007 (4 provinces) 2008 (all provinces)	1 year +
Meningococcol conjugate (quadrivalent) <sup>vi</sup> [Menactra]	May 2006	May 2007	12 months	? <sup>vii</sup>	?	?	? (2 years +)
Rotavirus (pentavalent) [RotaTeq]	Aug 2006	Jan 2008	17 months	?	?	?	? (2 years +)
Rotavirus (monovalent) [Rotarix]	Oct 2007	Pending	Pending (12 months+)	?	?	?	? (1 year +)
Zoster <sup>viii</sup> [Zostavax]	Aug 2008	Pending	Pending	?	?	?	?

Adapted from: Van Exan, R., Access to New Vaccines and the Evolving Evaluation Process in Canada (draft), 2008.

<sup>i</sup> Source: Health Canada, Notice of Compliance (NOC) Database

<sup>ii</sup> Source: PHAC, NACI

<sup>iii</sup> The four vaccines funded under the NIS Trust Fund (announced in 2004) are shaded in light grey.

<sup>iv</sup> Currently delivered as Adacel or Boostrix (licensed in 2008), both of which are combination vaccines that provide protection against diphtheria, pertussis, and tetanus, for adolescents and adults.

<sup>v</sup> Two other meningococcal C vaccines were subsequently licensed in Canada: NeisVac-C in 2002; and Meningitec in 2004.

<sup>vi</sup> Publicly funded immunization programs are not vaccine specific, but rather, disease-state specific. In all 13 jurisdictions in Canada, there are publicly funded programs for meningococcal C vaccine in infants and adolescents. As a quadrivalent vaccine, Menactra offers additional protection, i.e. to disease-causing serotypes A, C, Y and W-135.

<sup>vii</sup> Question mark (?) denotes processes not clearly defined at present.

<sup>viii</sup> Market availability expected in 2009.

## 5.9 Current NACI and CIC Recommendation Procedures

### 5.9.1 Delays in NACI Recommendations

Unnecessary and undesirable delays between Health Canada approval and NACI recommendations have recently generated significant concern among vaccine manufacturers, including VIC members. For example, for vaccines approved in 2006, NACI decisions followed Notice of Compliance (NOC) announcements by seven months for Gardasil (Merck's quadrivalent vaccine that targets HPV) and 12 months for Menactra. The NACI recommendation for RotaTeq (Merck's oral pentavalent rotavirus vaccine to prevent rotavirus gastroenteritis in infants) was issued 17 months subsequent to its approval. A second oral rotavirus vaccine, Rotarix (GlaxoSmithKline's live monovalent human rotavirus), was approved by Health Canada in October 2007, and is still awaiting the announcement of NACI recommendations. Most recently, Zostavax (Merck's zoster vaccine live) was granted NOC status in August 2008 and is currently undergoing NACI review.

In general, while it can take up to 17 months to complete the NACI review and recommendation process, it can take much longer for the adoption of a new vaccine into a publicly-funded, nationally accepted immunization program (e.g. up to six years). Clearly, this is too long for the public to wait to have access to new immunization programs that can prevent morbidity and mortality due to vaccine-preventable disease. During this waiting period, the population is needlessly at risk, even if the vaccine technology is licensed and available through the private system (i.e. for those who are aware of the new vaccine and can cover the costs, either firsthand or through third party insurance). Hence patient access during this period is extremely limited and inequitable, particularly since the cost of (or insurance coverage for) the new vaccine may not be affordable to all Canadians. In addition, while awaiting NACI review, health care professionals are left in the awkward position of having to make recommendations to patients regarding the use of a new vaccine without adequate advice.

As one poignant example of the serious problems associated with the delays in access to public vaccination programs, the six year delay between Health Canada approval and implementing publicly-funded programs for varicella resulted in seven documented pediatric deaths that potentially could have been prevented by the varicella vaccine.<sup>41</sup> Although one of the seven deaths occurred in 2005, this four-year-old boy could have been immunized three years previously (in 2002), had a national varicella immunization program been in place. Unfortunately however, provinces did not necessarily run catch-up programs when publicly-funded varicella immunization programs were initially introduced. While delays in patient access can lead to potentially disastrous public health outcomes, such delays are also counterproductive from a health economics standpoint – in terms of potential cost-savings lost. Conversely, the faster new vaccine technologies are made available to the public, the lower the costs for the health care system to treat vaccine-preventable diseases.

### 5.9.2 Update on Joint CIC-NACI Working Committee on HPV

Of the vaccines licensed in Canada since 2006, Gardasil was the first and only vaccine to undergo CIC review subsequent to receiving NACI recommendations, i.e. after the CIC was ushered in as a new body (with additional review procedures) under the auspices of the NIS introduced in 2003. As such, Gardasil was widely considered as a test case for collaborative program planning, coordinated by NACI and CIC. In this specific case, the CIC created a multidisciplinary joint CIC-NACI HPV Vaccine Expert Working Group in May 2006 to develop comprehensive scientific and programmatic recommendations for HPV vaccine programs in Canada. The joint working committee included members from the CIC and NACI, as well as representatives from public health, vaccinology, sexual health, gynecology, cancer, aboriginal health, nursing and family medicine to ensure that multiple perspectives were discussed and that the group's mandate was met.<sup>42</sup>

The joint CIC-NACI committee based its recommendations for HPV vaccine programs on the analytical framework for immunization programs in Canada, as developed by Erickson, de Wals and Farand.<sup>43</sup> This framework includes 58 criteria classified into 13 categories, broadly including burden of disease, vaccine characteristics, alternate immunization strategies, social and economic costs and benefits of vaccination, feasibility and acceptability of vaccination, the ability to evaluate vaccination programs, and research questions and considerations for the Canadian healthcare system. While certain elements of the framework have been used by NACI in proposing recommendations for the use of the HPV vaccine in Canada,<sup>44</sup> the joint CIC-NACI HPV Working Group focused specifically on the epidemiology of HPV, vaccine characteristics, Canadian disease modeling and economic analyses, as well as on the feasibility and acceptability of HPV immunization programs.<sup>45</sup> The resulting analyses and recommendations were forwarded to the CIC for consideration in the development of CIC recommendations on the HPV vaccine program and options.

Although CIC recommendations were intended to help implement a harmonized approach towards the introduction of the HPV vaccine in Canada, there was considerable confusion regarding the actual role of the joint CIC-NACI committee in achieving this goal. For example, there had never been any clear confirmation that the joint working group would provide specific guidance or advice regarding funding issues. In fact, skepticism was voiced by many that the joint committee would only create further duplication within the system.

Indeed, it was not until July 2008 that the CIC Statement with recommendations on HPV vaccination programs (based on joint CIC-NACI analyses) was publicly issued, a full two years after Health Canada had approved Gardasil. During this lengthy deliberation process, the joint CIC-NACI working group was criticized by some provincial public health stakeholders and medical authorities as lacking adequate transparency and leadership, and even worse – the ability to make timely decisions on behalf of the Canadian public.

As described in Paper 6, rather than waiting for a consensus or recommendation achieved through this protracted and uncertain joint decision-making process, several provinces decided to implement HPV programs prior to such a CIC-NACI announcement. For these jurisdictions, the decision to implement publicly-funded HPV programs was based on deliberations by provincial/territorial advisory committees and the availability of federal funding to support school-based HPV immunization programs. Overall, while the joint CIC-NACI working group for HPV vaccination may have been considered a disappointment by some, others (including several immunization specialist and public health officials)

have deemed it a dismal failure. Unfortunately, although it was initially hoped that the introduction of CIC evaluation might assist in accelerating and harmonizing the incorporation of new vaccines into publicly-funded programs, this new “second step” (involving joint CIC-NACI review) appears to have further complicated the process by introducing potential new misunderstandings, barriers or delays that may hinder patient access to new vaccines.

### 5.9.3 Implications for Other Recently Recommended Vaccines

Apart from Gardasil, four other newly approved vaccines have entered the Canadian market since 2006. As described in Section 5.9.1, NACI statements have been issued for Menactra and RotaTeq, but not yet for Rotarix and Zostavax. Within Canada's current immunization infrastructure, these vaccines will all be subject to the ‘new’ recommendation procedures, including both NACI and CIC review. It is believed that these recently licensed vaccines will follow a review/recommendation process roughly analogous to that for Gardasil, although there is uncertainty whether joint CIC-NACI working groups will be formally established for each of these vaccines subsequent to initial NACI review. In this context, it is noteworthy that since the joint CIC-NACI HPV committee represented the first working group of its kind, it was essentially viewed as a pilot program structure that may or may not be pursued for other new vaccines. If joint CIC-NACI working groups are indeed to become a permanent part of the immunization system in Canada, first, for program development, their role and relevance must be clearly established. Second, major changes must be made to ensure transparency and predictability are maintained in the evaluation and recommendation process. At present, substantial work is still required to define and implement optimal mechanism(s) for efficient review and recommendation of approved vaccines in Canada.

It should also be emphasized that – with the exception of Menactra, which is funded in certain provinces<sup>46</sup> – the four vaccines approved since Gardasil in 2006 are generally not yet part of publicly-funded vaccine programs in Canada. Current coverage of these vaccines relies primarily upon private insurance providers and out-of-pocket payments by the general public, with significant inequities in access across the country. In addition, based on the significant time elapsed between licensing and national program implementation for many vaccines to date, manufacturers have voiced concerns that inherent delays in national recommendation procedures are likely to impede incorporation of these newer vaccines into national immunization schedules, ultimately delaying wider patient access to these novel vaccine technologies.

#### 5.9.4 Enhancing NACI/Industry Collaboration

In the context of increasing the efficiency of the NACI review process, one key issue that has been recently debated is the optimal timing of data submission by vaccine manufacturers for NACI review. Currently, NACI reviews relevant components of the data package (dossier) that a manufacturer submits for regulatory review by Health Canada, known as a New Drug Submission (NDS). In particular, NACI focuses on data from clinical trials as the key element for vaccine evaluation. However, the NACI review process is not based on a formal mechanism to engage vaccine manufacturers, and is conducted behind closed doors. At present, NACI rarely requests manufacturers to present information on new vaccines, and is generally not in the practice of holding open dialogue with manufacturers regarding these new technologies. Occasionally, NACI has put forward very weak or conservative scientific recommendations for certain vaccines – including Adacel and Menactra – due to a lack of sufficient data to answer all of its scientific questions. Thus improvement is required in NACI/industry collaborations to facilitate timely, thorough and appropriate decision-making in the NACI evaluation and recommendation process.

In the case of Adacel, the initial NACI statement issued in 2000 (one year after licensure by Health Canada) was very conservative; it stated: “There are no data available at the moment on which to base a recommendation for universal routine use” [of Adacel].<sup>47</sup> However, in September 2003, NACI published revised recommendations to “update the previous pertussis control strategy, in particular coverage of adolescents and adults, to reflect results of the National Consensus Conference on Pertussis<sup>48</sup> that took place in May 2002.” In the end, it took over five years for Adacel to be introduced universally into the immunization programs of all provinces and territories. It has been suggested that this delay was the result of insufficient epidemiologic data available to NACI and the lack of initial consensus on the appropriate goals of the national pertussis control strategy.<sup>49</sup> In this specific case, a strong NACI recommendation was not forthcoming until a broad national consensus was reached on the need for this intervention, and it was only after the revised NACI statement was issued – and federal funding was made available under the NIS for vaccine purchase – that immunization programs were implemented in all parts of the country. Overall, the Adacel case demonstrated that the elapsed time between Health Canada approval and the second NACI statement had an adverse impact on patient access, and unnecessary cases of pertussis (e.g. in adolescents) were reported during this undesirable delay.<sup>50</sup>

For Menactra, the initial NACI statement was issued in early 2007 (a year after Health Canada approval), and this statement did not make any recommendation for routine public health use of the vaccine.<sup>51</sup> This left physicians with little guidance on whether to offer this vaccine to patients. However, with new scientific information provided by the manufacturer during 2008, the NACI statement is being reviewed and is expected to be re-issued in January 2009 – almost three years following initial vaccine licensure. Once again, these circumstances have led to an unfortunate delay in patient access to a newly approved vaccine. Indeed, for both Adacel and Metactra, undesirable delays could probably have been circumvented, given the opportunity for timely industry input.

Overall, from both a disease prevention and health economics perspective, there is great motivation to accelerate the NACI review process in attempt to compress the timelines required for patient access to innovative vaccine technologies. In order to realize this goal, the process for interaction between NACI and manufacturers needs to be formalized, including regular meetings with each manufacturer and ongoing two-way dialogue as NACI recommendations are being developed. Enhanced information sharing between NACI and industry would facilitate the flow of scientific data in a more efficient, timely

manner; this type of collaborative approach would also increase the likelihood that the scientific review is adequately comprehensive and favourable.

A staged information sharing approach<sup>52</sup> is likely to be most effective, and the VIC holds the view that NACI should continue to work with manufacturers to define appropriate points of engagement (e.g. during clinical development, pre-NOC, and pre-NACI release) to improve the timeliness of NACI statements. To support this mutually beneficial information exchange, manufacturers would need to assemble an appropriate cross-functional medical/scientific/policy team(s) to adequately address NACI questions and engage in scientific and policy dialogue. All meetings and shared data should be held under strict confidence to allow manufacturers to share proprietary information.

1. *Clinical Development:* For products in clinical testing, manufacturers could update NACI (potentially on an annual basis) through oral presentations/meetings regarding vaccine technologies in the company pipeline, including scientific descriptions and proposed timelines for clinical development. This approach would permit early feedback from NACI, particularly with regard to potential gaps in the data package that could be addressed by the manufacturer prior to submitting a full NDS. During late-stage clinical trials, NACI could also initiate relevant literature reviews and begin to analyze Canadian epidemiologic data (e.g. burden of disease) prior to the submission of the NDS to Health Canada. Such a proactive approach would help to ensure that adequate epidemiologic data is available to complete NACI recommendations in a timely manner. This data could also be shared with the manufacturer, thus facilitating evaluation of the potential impact of the new vaccine in Canada.
2. *Pre-NOC:* For products that have been submitted to BGTD for regulatory review, manufacturers should present or submit summary clinical data to NACI well in advance of the anticipated NOC. At this pre-NOC stage, manufacturers could also provide a draft product monograph, as well as other published/unpublished information that becomes available during the BGTD review process (e.g. regarding duration of protection, vaccine stability, additional target age groups or indications, and/or unusual rare adverse events). This approach would not be intended to duplicate BGTD procedures, but rather to provide NACI with early access to information needed to make a timely recommendation on vaccine use in Canada. If any concerns were to arise during this intermediate period of information exchange, manufacturers should work jointly with NACI to resolve them. Similarly, NACI should be required to formally engage the manufacturer if the committee has any outstanding questions or requirements, to ensure the issues can be addressed in a timely manner.
3. *Pre-NACI Release:* During the post-NOC period, but prior to the release of NACI recommendations, manufacturers should provide NACI with the final approved monograph. Assuming that the majority of the review has been completed prior to the NOC stage as described above, the VIC believes it should only take an additional 90 days to review the information provided in the final monograph, such that NACI recommendations could be released 90 days post-NOC. Finally, since scientific information is likely continue to become available after a recommendation for a specific vaccine is made, NACI should also consider providing a mechanism for ongoing scientific review within the first year or two following the initial NACI statement.

It should be emphasized that the staged information sharing approach represents a joint series of activities between the manufacturer and NACI which requires ongoing discussion with a common objective – to ensure timely and appropriate access to new vaccines in Canada by developing timely, scientific-based

recommendations. Moreover, this approach should help to ward off potential criticism that NACI is responsible for introducing undue delays in its recommendation process, particularly when compared with other international advisory bodies. In this context, concerns have also been raised that NACI needs significantly more resources to support its work, and may need more than three annual meetings for its deliberations. A greater time commitment may be required from its members; this could be offset by shorter work-terms. Travel funding and research support for full-time staff will also need to be increased.

Interestingly, Canada's Common Drug Review process now initiates the review of data for certain drugs (e.g. that treat life-threatening disease or offer significant cost-savings) prior to NOC assessment; this is known as the pre-NOC CDR submission process.<sup>53</sup> In addition, some large drug manufacturers in the United Kingdom have recently begun to interact with the U.K. National Institute for Health and Clinical Excellence (NICE) to share data early-on from Phase II and III trials, i.e. to help expedite eventual drug reimbursement and patient access to novel therapies. At present, these interactions focus primarily on traditional pharmaceuticals (rather than vaccines), yet this type of strategy could serve to inform future models in public health and intergovernmental cooperation for introducing immunization programs in Canada. The key point illustrated by these examples is that national agencies involved with evaluation and recommendations that help support reimbursement decisions need to be involved as early as possible in reviewing clinical or other relevant data (ideally during the pre-licensing stage) in order to minimize potential delays in public access to new medicines.

In addition to the issues outlined above – regarding the need for enhanced NACI/industry interactions in accelerating NACI review times – there are other aspects of NACI/industry collaborations that will also require improvement in the future. For example, there is no appeal mechanism in place for stakeholders subsequent to NACI review. However, to maintain and improve upon the credibility the NACI review process, the VIC believes that a formal appeal mechanism should be implemented in the event that manufacturers and/or stakeholders do not agree with NACI recommendations. This is especially true in cases where Expert Opinion (Level 3 evidence) is relied upon, and manufacturers are not currently informed of whether the opinion is unanimous or whether the recommendation is scientifically debatable. In this context, the VIC recommends that NACI continues to document the levels of scientific evidence used to support recommendations, and to disclose the source of the evidence and selection method as part of a transparent review process.

It is noteworthy that in the U.S., the ACIP (as introduced in Section 5.4.3) is subject to the U.S. federal Open Meetings Act and therefore holds its meetings in public. This lies in stark contrast to the situation for both Canada's NACI and the U.K.'s JCVI.<sup>54</sup> The open U.S. system is perceived as promoting public trust; it avoids portraying the image of hiding information. At present, it appears unlikely that NACI meetings will be held as public forums in the foreseeable future, yet there are certain measures which could be implemented in the nearer-term to achieve greater public trust. For example, the VIC believes that selection criteria and affiliations for NACI representatives should be fully disclosed, including potential conflicts of interest. These efforts could serve to ensure greater transparency and accountability – while also building public confidence – in the NACI review process.

Finally, there is no process currently in place to guarantee that a manufacturer will have access to an embargoed copy of a NACI statement before it is publicly released. Yet for NACI statements pertaining to vaccines with a single manufacturer, the VIC believes that NACI should provide that manufacturer with an embargoed copy of its recommendations before they are published. Most importantly, gaining access to an embargoed copy of the relevant NACI statement would permit the manufacturer to work with

NACI to ensure that accurate information is effectively and efficiently communicated to the public; joint efforts of this nature would help to further enhance industry collaboration with NACI. In addition, receiving an embargoed copy of NACI recommendations would allow the manufacturer to prepare for its own communications and public relations activities surrounding national recommendations for an emerging vaccine technology and/or immunization program.

Overall, there is significant room for improvement in terms of achieving optimal NACI/industry relations, and the VIC is firmly committed to building strong partnerships with NACI for this purpose. The VIC was pleased to participate as a non-governmental organization (NGO) with observer status at a NACI meeting in June 2008, and has recommended that a VIC staff member(s) be regularly included as an NGO observer at NACI meetings in the near-term future. In general, the VIC is dedicated to working jointly with NACI by engaging in open dialogue regarding all relevant immunization issues. The over-arching goals for these collaborative initiatives will be to promote consistency and timeliness of NACI recommendations, and to achieve greater levels of transparency and accountability in the review process – for the collective benefit of all stakeholders across Canada.

## 5.10 Recommendations

At present, evaluation and recommendation procedures that ultimately support the adoption of public vaccine programs in Canada remain severely flawed; these mechanisms can still be characterized as lacking in harmonization and transparency, resulting in unacceptable duplication, inequities and delays. Unfortunately, such inconsistencies and delays can mean that Canadians suffer and or die needlessly due to vaccine-preventable diseases. Canada needs an efficient, predictable process for evaluating and recommending vaccines – including participation at the federal, provincial and territorial levels – for both existing and new public immunization programs.<sup>55</sup> Achieving predictable recommendation procedures with established timelines will represent a key cornerstone in realizing equitable access to vaccines across the country, primarily by facilitating well-informed, timely funding decisions. To this end, and in the spirit of collaboration, the VIC has put forward the following recommendations for consideration by federal, provincial and territorial governments and other key stakeholders.

### Federal Recommendations:

1. To facilitate the timeliness 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 two-way dialogue, and formal definition of points of engagement (e.g. during clinical development, pre-NOC and pre-NACI release) for data presentation/submission to NACI as recommendations are being developed.
  - Compressing current timelines for the NACI recommendation processes will play a critical role in enabling the funding of newly recommended vaccines by provincial/territorial public health programs within six months of Health Canada approval (see Paper 6 Recommendations), ultimately accelerating patient access to innovative vaccine technologies.
  - 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.
  - Achieving improved efficiencies in the NACI recommendation process should be tied to continued investment in (and future expansion of) NIS goals, i.e. to ensure that Canadians continue to benefit from domestic and global vaccine innovations in a timely, equitable manner.
2. To minimize duplicative, bureaucratic efforts in evaluating and recommending new vaccines, the federal government should aim for increased efficiencies, including the provision of adequate financial and human resources.
  - The federal government should consider mechanisms to streamline decision-making by NACI the CIC. At present, these bodies contribute independently to the decision-making processes for the incorporation of new vaccines into jurisdictional immunization schedules in Canada. Their distinct (and/or shared) roles and responsibilities in the recommendation process must be made considerably more transparent, and clearly communicated. These bodies also need to function in a more synchronized manner, with less complexity and minimal redundancy (including minimal overlap with BGTD approval procedures), and with involvement by all relevant stakeholders, (including manufacturers, the medical community and the general public).

- Given that the treatment and control of infectious disease has been acknowledged as a national priority (and the PHAC has been established to lead public health initiatives in Canada), the federal government should be well positioned as a central coordinating function to promote greater efficiency in vaccine adoption, i.e. via investing greater effort to minimize current overlaps (and consequent delays) in recommendation procedures.

Provincial/Territorial Recommendations:

3. 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.
  - Jointly, provincial/territorial governments must work together cooperatively with the federal government and other stakeholders (including manufacturers) to make consistent, standardized recommendations to improve the harmonization of vaccine schedules.
  - Provincial/territorial governments should aim to minimize potential regional differences or disagreements to jointly transcend any obstacles in providing equitable, timely access to new vaccines for the benefit of all Canadians.

Stakeholder Recommendations:

4. To discuss common critical issues in immunization, a meeting of all relevant stakeholders should be convened. Stakeholder involvement should include vaccine manufacturers; federal and provincial/territorial government representatives; Health Canada officials; public health and public policy officials (e.g. representing the PHAC, NACI and CIC); medical professionals; the scientific and research community; and patients, parents or the general public. Urgent matters for discussion presently encompass, but are not limited to, the following topics:
  - The current vaccine recommendation environment and its inherent inadequacies in efficiently and equitably protecting the Canadian public
  - Potential new approaches or models for enhancing the efficiency of expert committees and vaccine recommendation procedures in Canada, including the development of cohesive (and consistently implemented) decision-making criteria, and transparent communication systems
  - The development of standards and best practices for vaccine recommendation procedures that match the best immunization programs of other developed nations, potentially including mechanisms by which evaluation meetings are held in public and/or funding decisions are closely aligned with national vaccine recommendations (see U.S. examples in Paper 6, Section 6.7.1).

In continuing to build upon incremental successes achieved under Canada's NIS to date, and in working to further improve recommendation procedures to support national immunization programs, stakeholders at all levels must intensify efforts and initiatives to enhance the existing decision-making infrastructure. Specifically, greater energy must be directed towards increasing the predictability and timeliness of recommendation decisions for new vaccines, primarily by avoiding unnecessary bureaucracy and duplication in allocating scarce resources at the federal and provincial/territorial levels. Canada still faces the urgent need for a predictable vaccine recommendation process – one that also works towards creation of a uniform national immunization schedule that best serves all citizens from coast to coast. In addressing this important call to action, our collective, concerted efforts will be required to ensure that when the next breakthrough vaccine arrives in Canada, patient access will not be impeded by unacceptable disparities or delays that originate from (or attenuate decision-making downstream to) the vaccine recommendation process. A proactive strategy of this nature would also be valid and advisable from the public health and health economic perspectives.

## 5.11 References

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