

# HPV Reclassification Application

For consideration by the Medicine Classification Committee

## Executive Summary

This application requests a reclassification of the Human Papillomavirus (HPV) Vaccine in New Zealand to allow pharmacists who have successfully completed an approved vaccination course to provide this vaccine without a prescription.

HPV is a very common infection that is carcinogenic.<sup>1,2</sup> A small proportion of those infected with certain strains of HPV develop cervical, anal, oropharyngeal or vulvar cancer many years later. Certain strains of HPV infection cause genital warts.

The HPV vaccine is a very well-established, effective and well-tolerated vaccine with a very important public health role – preventing infection and preventing cancer.<sup>3,4</sup> It also prevents genital warts. The World Health Organisation (WHO) states that: *“The HPV vaccine is one of the most effective vaccines ever developed.”*<sup>5</sup>

The HPV vaccine has been given to tens of millions of people worldwide,<sup>6</sup> and has been used and funded in New Zealand since 2008.<sup>7</sup> Initially the quadrivalent form (with four strains) was available in New Zealand, with a change to the 9-valent form (with nine strains) in 2017.

HPV vaccine is now funded in females and males up to the age of 26 years, and usually administered around year 8 (age approximately 12 years) in schools, or at the general practice. It works best if given before any HPV exposure, so is ideally provided before sexual debut,<sup>8</sup> although later provision can also be beneficial. WHO reports that vaccinating multiple age cohorts will shorten the time to achieve the impact of the vaccination.<sup>8</sup>

The current uptake of HPV vaccine is 67% in recent birth cohorts,<sup>9</sup> a rate that is below the 75% targeted for 2017.<sup>10</sup> This uptake rate is also around 67% in Māori, and slightly higher in Pacific and Asian populations.<sup>9</sup> The uptake has been fairly static for the last five years, despite adding a general practice recall at age 14 years. Additionally, for older cohorts of females (eg those aged 21 years or more) the numbers unvaccinated are higher, with 45% or more unvaccinated, and Māori disproportionately affected. Most eligible males are unvaccinated, given their funding and school-based programme only started in 2017.

Herd immunity is expected to occur at about 75-80%,<sup>11</sup> and a target was set in New Zealand of 75% for 2017. Improving coverage in the older cohorts of young people before they reach the age of 27 years, in males who were not part of the school-based programme, and in current cohorts is important to provide more individuals with protection from this very effective vaccine, and reduce the incidence of infection in the community. Reduction in infection will mean reduction in genital warts (as has already been seen),<sup>12</sup> as well as the cancers caused by this carcinogenic infection. Cervical cancer occurs in around 140 women per year,<sup>2</sup> and results in about 50 deaths per year.<sup>13</sup> Māori, Pasifika and Asian are over-represented in the incidence of this cancer, and under-represented in smear tests which provide an early warning of precancerous lesions.<sup>14</sup> Increasing coverage of HPV vaccine is important to minimise HPV-related cervical cancer.

Availability of HPV vaccine through pharmacists will aid access to and awareness of this vaccine, and help New Zealand to increase the rate of uptake and meet the targeted 75% coverage. It will also

help to address the lower levels of vaccination in the older eligible populations. These populations have disproportionately lower vaccination rates in Māori<sup>9</sup> and males.

Community pharmacists are very accessible health professionals. All community pharmacies must have a community pharmacist on-site at all times when open, and their hours of operation tend to be longer than that of general practice. Pharmacies are conveniently placed, being located in main shopping areas as well as local communities. No appointment is needed to see them, and there is no need for enrolment; a person can attend any community pharmacy he or she chooses to.

Vaccinations were first provided by pharmacists in New Zealand in 2010. Currently at least 450 pharmacies around New Zealand (nearly half of all community pharmacies) provide vaccinations, with more planning to do so. Further growth is expected with a positive Medicines Classification Committee recommendation for intern pharmacists to be able to vaccinate with influenza vaccine from 2020, and increasing numbers of qualified pharmacists becoming trained in vaccinations. Furthermore, the public is becoming increasingly familiar with vaccinations in pharmacy. Consumer satisfaction in vaccinations in pharmacy is high<sup>15-17</sup> with an appreciation of the convenience, and strong uptake out of hours,<sup>18</sup> particularly in working age people and adolescents. [REDACTED]

[REDACTED]

Widening vaccine access to pharmacy increases vaccine uptake,<sup>20</sup> and adding funding helps further, [REDACTED]

[REDACTED] Pharmacy also played an important role in delivering meningococcal vaccination in Northland in late 2018-early 2019 following the outbreak of meningococcal W there,<sup>21</sup> stepping up at a very busy time of year (21 December onwards).

The benefit of reclassifying HPV vaccine to allow pharmacists to administer it will be greatest and most equitable if funded also. This reclassification is the first step to help achieve that.

Consumers will benefit from this reclassification through an increase in awareness and uptake, reducing the likelihood of HPV infection and therefore providing protection against cancers caused by HPV. Consumers will benefit from easier access with no appointment and the ability to have the vaccine at a time that suits them without needing to take time off their work or study, reducing barriers to access. The vaccine can be discussed, and/or provided opportunistically when the young person is in for other reasons, such as management of minor conditions, for the measles-mumps-rubella (MMR) catch-up vaccination, or the emergency contraceptive pill.

Benefits to society and the health system will come from lower rates of infection in the community, reduced harms from the consequences of the infections, and the lower health system burden from reduced harms. Having another vaccination and applying funding would increase the number of rural and low-income pharmacies providing the vaccination service, improving equity of access.

Pharmacists can look up the full vaccination history for a person on the National Immunisation Record (NIR), and therefore can see what doses they are due for HPV. They will add the administered vaccination to the NIR also, ensuring providers are aware of doses given.

It is intended that pharmacist-administered HPV vaccination would be complementary to the school-based programme. Age-restriction would be used to ensure there is no interference with the school-based programme. It could be applied at the funding stage to allow maximum flexibility and future-proofing. Various options are provided for the age requirements.

**New Zealand is not far from the target of 75% uptake of HPV vaccine, but the current vaccination rate is static at 67% of the most recent birth cohorts. Adding pharmacy availability can help achieve the desired 75% target, and increase vaccination in the older eligible age groups by increasing the awareness and uptake of the HPV vaccine.**

## Part A

### **1. International Non-proprietary Name of the medicine.**

Human Papillomavirus Vaccine

### **2. Proprietary name(s).**

Gardasil (registered and marketed in New Zealand), Cervarix (registered but not marketed in New Zealand)

### **3. Name and contact details of the company / organisation / individual requesting a reclassification.**

This reclassification application is sponsored by the Pharmaceutical Society of New Zealand, the Pharmacy Guild of New Zealand, and Green Cross Health.

Contact details: Application prepared by Natalie Gauld Ltd [REDACTED]

[REDACTED] [natalie@nataliegauld.com](mailto:natalie@nataliegauld.com)

### **4. Dose form(s) and strength(s) for which a change is sought.**

Sterile suspension, vaccine for intramuscular injection.

There is no specific strength requirement on the reclassification sought. The strength as per the current Gardasil data sheet is as follows:

Human Papillomavirus 9-valent Vaccine, Recombinant  
1 dose (0.5 mL) contains approximately:  
Human Papillomavirus1 6 L1 Protein<sub>2,3</sub> 30 micrograms  
Human Papillomavirus1 11 L1 Protein<sub>2,3</sub> 40 micrograms  
Human Papillomavirus1 16 L1 Protein<sub>2,3</sub> 60 micrograms  
Human Papillomavirus1 18 L1 Protein<sub>2,3</sub> 40 micrograms  
Human Papillomavirus1 31 L1 Protein<sub>2,3</sub> 20 micrograms  
Human Papillomavirus1 33 L1 Protein<sub>2,3</sub> 20 micrograms  
Human Papillomavirus1 45 L1 Protein<sub>2,3</sub> 20 micrograms  
Human Papillomavirus1 52 L1 Protein<sub>2,3</sub> 20 micrograms  
Human Papillomavirus1 58 L1 Protein<sub>2,3</sub> 20 micrograms

### **5. Pack size, storage conditions and other qualifications.**

The current pack size of Gardasil is a 0.5 mL single-dose vial or pre-filled syringe. There is no need to specify a pack size on the reclassification statement.

Gardasil storage requirements are: under refrigeration at 2-8°C, protected from light. It must not be frozen.

## 6. Indications for which change is sought.

It is expected that the indications for the reclassification will be the same as in the data sheet. However, note the age options in the classification sought.

The licensed indications for Gardasil are as follows<sup>4</sup>:

“GARDASIL 9 is indicated in females aged 9 through 45 years\* for the prevention of cervical, vulvar, vaginal and anal cancer, precancerous or dysplastic lesions, genital warts, and infection caused by Human Papillomavirus (HPV) Types 6, 11, 16, 18, 31, 33, 45, 52 and 58 (which are included in the vaccine).

GARDASIL 9 is indicated in males 9 through 26 years of age for the prevention of anal cancer, precancerous or dysplastic lesions, external genital lesions and infection caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 (which are included in the vaccine).”

## 7. Present classification of the medicine.

Prescription Medicine

## 8. Classification sought.

To maximise the chances of a positive outcome at the first reclassification consideration and therefore maximise the impact on public health and preventing HPV-related cancer in New Zealanders we propose four options which vary by age of the person vaccinated.

The factors that can be considered when regarding the age for pharmacists to vaccinate HPV vaccine are as follows:

1. The current age range in the Gardasil data sheet is 9-45 years of age for females and 9-26 for males.<sup>4</sup>
2. The dosing for Gardasil changes from 2 doses to 3 doses from age 15 years. Providing the vaccine through pharmacy before age 15 years (e.g. age 13 or 14 years) is likely to increase the chances of compliance with the regimen and reduces the burden on the child and parent, and cost.
3. There is no age limit applied to general practice to allow maximum impact for the school based programme.
4. HPV vaccine is funded from 9 to 26 years.
5. The Immunisation Handbook<sup>2</sup> states: “*The optimal time for HPV administration is at age 9–13 years, as most males and females in this age group would be naïve to all HPV types.*” However, it notes that even if sexual activity has begun vaccination may be beneficial.
6. There is no physical reason why pharmacists could not vaccinate down to 9 years of age.
7. The school-based programme of administration is for persons 11 to 12 years old. Thus, pharmacy vaccinations in persons 13 year old or over should not interfere with this.
8. Pharmacists in NZ can currently vaccinate down to 13 years old based on gazette notices, for influenza and Tdap in pregnancy. A standing order was used in Northland to bring the age down to 13 years for pharmacists in the meningococcal outbreak and vaccination.
9. District Health Boards (DHBs) may have specific local needs to address, in which they may want pharmacists to be able to administer in these age groups in certain areas or certain populations.

10. In many countries, pharmacists are vaccinating lower age groups than 13 years old. In the United States (US), pharmacists are permitted to administer vaccinations to nine year olds in 42 of 52 states.<sup>22</sup> In Canada in 2017, nine provinces permitted pharmacist-delivered vaccines to five years of age and older.<sup>23</sup> Pharmacists in Australia can vaccinate children from 10 years of age in Tasmania,<sup>24</sup> Victoria<sup>25</sup> and Western Australia for specific vaccines,<sup>26</sup> as can pharmacists in Ireland.<sup>27</sup> In the UK, vaccinations in pharmacy tend not to have national age limits as such but depend on patient group directions used by pharmacies. Vaccinations are taking place from age 12 for HPV,<sup>28</sup> and age 2 years for meningococcal B at Boots pharmacies in the UK.<sup>29</sup> Some countries have older minimum ages, such as Switzerland (16 years in most cantons).<sup>30</sup>
11. Controlling the age limit at the funding point rather than on the reclassification provides future-proofing should the school-based programme change, or there be a local need that a DHB needs to address.

Option 1: Prescription Medicine, except when administered by a registered pharmacist or registered intern pharmacist who has successfully completed a vaccinator training course approved by the Ministry of Health and who is complying with the immunisation standards of the Ministry of Health

Option 2: Prescription Medicine, except when administered to a person 13 years of age or older by a registered pharmacist or registered intern pharmacist who has successfully completed a vaccinator training course approved by the Ministry of Health and who is complying with the immunisation standards of the Ministry of Health

Option 3: Prescription Medicine, except when administered to a person 16 years of age or older by a registered pharmacist or registered intern pharmacist who has successfully completed a vaccinator training course approved by the Ministry of Health and who is complying with the immunisation standards of the Ministry of Health

Option 4: The above options (1-3) but without the addition of registered intern pharmacist

Finally, we recommend that the committee be able to make their own decision about minimum age, should there be an alternate decided to what is proposed between 9 and 16 years.

### ***Discussion on the options***

Option 1 has no minimum age specified. This option is the most future-proofed option, as it allows pharmacists to administer to the widest range of age groups as licensed for the product, as per the data sheet.

As discussed above, there are many examples internationally of pharmacists being able to administer vaccinations to children aged 9 or 10 years old. Pharmacists would not be able to administer to ages for which the product is not licensed.

Despite pharmacists in New Zealand vaccinating earlier than Australia, NZ has fallen behind in the age groups that pharmacists can administer to. Pharmacists in Australia, while not yet able to administer the HPV vaccine, have seen a lowering of the minimum age from 16 or 18 years of age to 10 years of age in Tasmania,<sup>24</sup> Victoria<sup>25</sup> and Western Australia.<sup>26</sup>

Currently Gardasil is indicated from the age of 9 to 45 years of age in females and 9 to 26 years of age in males,<sup>4</sup> and pharmacists would need to work within the product licence. From a purely physical perspective, it is reasonable for a pharmacist to administer a vaccine to a 9 year old.

Currently in New Zealand pharmacists can administer to 13 year olds for some vaccines, and the same site is used in a 9 year old as a 13 year old (deltoid muscle in the upper arm).

With Option 1, should funding occur (as will be sought), it is expected that this funding application would include a minimum age for maximum benefit and minimum risk to the school-based programme. This could be 13 years.

Option 2 has a minimum age of 13 years which is consistent with current practices for pharmacists with influenza vaccine and Tdap in pregnancy from 13 years. It would not interfere with the school based programme (age 11-12 years), and allows the two-dose option to be given for those who are 13 and 14 years old, which is advantageous for ensuring compliance with the recommended dose, reduces the parental burden, and provides high likelihood that administration would be before sexual debut.

Option 3 has a minimum age of 16 years, well above that for the school-based programme. There is less flexibility allowable with this age should any DHBs want to use pharmacy to increase coverage for younger children without needing to do standing orders or have Medical Officer of Health authority. It also means that parents seeking a vaccine in a 13, 14 or 15 year old would need to arrange an appointment at a general practice or wait until 15 years of age to return to the pharmacy, adding an additional unnecessary barrier to access and potentially meaning that person was not vaccinated.

Option 4 allows any of the previous options 1-3 but without allowing intern pharmacists to administer the vaccine.

Intern pharmacists, i.e. pharmacists who have successfully completed their undergraduate pharmacy degree and are enrolled in the intern pharmacist (Evolve) programme are expected to be able to administer influenza vaccines from 2020 in New Zealand, based on the positive recommendation from the Medicines Classification Committee in October 2019.<sup>31</sup> The committee supported increasing the number of trained vaccinators. Thus, there is a local precedent.

In the US, student interns who have completed the Certificate Training Programme and who are operating under the supervision of a vaccinator pharmacist, are permitted to administer vaccines in 51 states and territories.<sup>22, 32</sup> The US Pediatric Pharmacy Advocacy Group in 2018 recommended pharmacists and student pharmacists being able to administer influenza, pneumococcal, meningococcal and HPV vaccines to paediatric patients.<sup>33</sup>

Intern pharmacists in New Zealand will have had the same vaccination training as nurses and other pharmacists, and will be working under supervision of a pharmacist vaccinator. This will increase the intern pharmacists' opportunities to learn within their internship with more than one vaccine type able to be provided. It also makes sense to have intern pharmacists able to discuss and administer the HPV vaccine to aid in increasing awareness and uptake in consumers.

We do not see any additional risk in having intern pharmacists provide the HPV vaccination under supervision, compared with the influenza vaccination.

### ***General comment on the options***

Every day people are dropping off the eligibility list for funded HPV vaccination by reaching 27 years of age, and the opportunity to prevent HPV-related cancer through funded administration in these people disappears. People who missed their school vaccination for HPV and could be vaccinated by pharmacists are being exposed to the virus. Pharmacists will make a difference (particularly should it

be funded) and the sooner HPV vaccine can be reclassified, the better. We have provided the options to maximise the likelihood of getting the reclassification through on the first attempt as making HPV vaccine available through pharmacists promptly will benefit people who may get less benefit should this reclassification be delayed. While we prefer Option 1 for future-proofing and flexibility, we would accept having a minimum age imposed instead if necessary. We cannot include all of the ages that might be chosen, so have instead provided a selection to allow the consultation to consider the various range of ages and comment on these or suggest others they would prefer.

Our consultation has found considerable support for Option 1 where there is no specified age and an age can be implemented should funding occur. However, a small number of people have suggested a minimum age of 15 or 16 years because of concerns about consent.

## **9. Classification status in other countries (especially Australia, UK, USA, Canada).**

The classification status in other countries is generally prescription medicine, however pharmacists are able to provide HPV vaccines under various mechanisms in multiple jurisdictions.

Appropriately qualified pharmacists can provide HPV vaccine in most states in the US.<sup>22</sup> Only two states do not allow pharmacist administration of HPV vaccine, and three allow such administration but require a prescription. In terms of age, 33 states in the US would allow pharmacists to administer HPV vaccine to a 9 year old, and 21 of these states do not require a prescription to administer HPV vaccine to this age group. A national survey of pharmacies in the US by Westrick et al in 2017<sup>34</sup> found 39% offered HPV vaccines, although patient cost is an important barrier to provision of some vaccines, and may have limited the numbers providing the HPV vaccine there.

Some Canadian provinces allow pharmacists to administer HPV vaccine without a prescription.<sup>35, 36</sup>

In the UK, the Boots pharmacy chain has pharmacists providing HPV vaccines to females and males aged 12 to 44 years with no prescription required, and a wait time in the pharmacy of five minutes after the vaccination<sup>28</sup>. This service started in Boots pharmacies in 2009 with a minimum age of 18 years, and was extended to 12 years in 2017, and has since also started in Lloyds pharmacies.<sup>37</sup>

Five European countries allow pharmacists to provide vaccinations other than influenza vaccine, in at least some cases, HPV vaccine is included.<sup>38</sup> HPV vaccines can be administered by pharmacists in Portugal, if prescribed by a medical practitioner.<sup>39</sup>

In parts of Switzerland, pharmacists can deliver the second dose of HPV vaccines, with a doctor administering the first dose.<sup>30</sup>

## **10. Extent of usage in New Zealand and elsewhere (eg, sales volumes) and dates of original consent to distribute.**

The Ministry of Health website states that over 300,000 New Zealanders have been vaccinated against HPV since 2008 when HPV vaccination first began here.<sup>7</sup> Many of these would have received three doses. Looking at birth cohorts of women who have been eligible for vaccination, the earlier birth cohorts had lower uptake, e.g. 39-56% for birth cohorts 1990-1995.<sup>9</sup> For later birth cohorts the uptake has been 60-67%, with the most recent data showing 65-67% uptake. At 67% uptake, the 2003 birth cohort has over 9000 women who missed having all scheduled doses of HPV. For earlier cohorts the number who did not get all doses is greater. Figures for males are not available,



although in the first year of availability for males through the school programme (2017), reports suggested that uptake in this programme for males was nearly as high as for females.<sup>40</sup>

Estimates in 2016 suggested 47 million women had received the full course of vaccination, and 59 million women had received at least one dose of HPV vaccine.<sup>6</sup>

HPV vaccine in New Zealand was first consented in 2006, with the currently available nine valent product (Gardasil 9) consented in 2016.

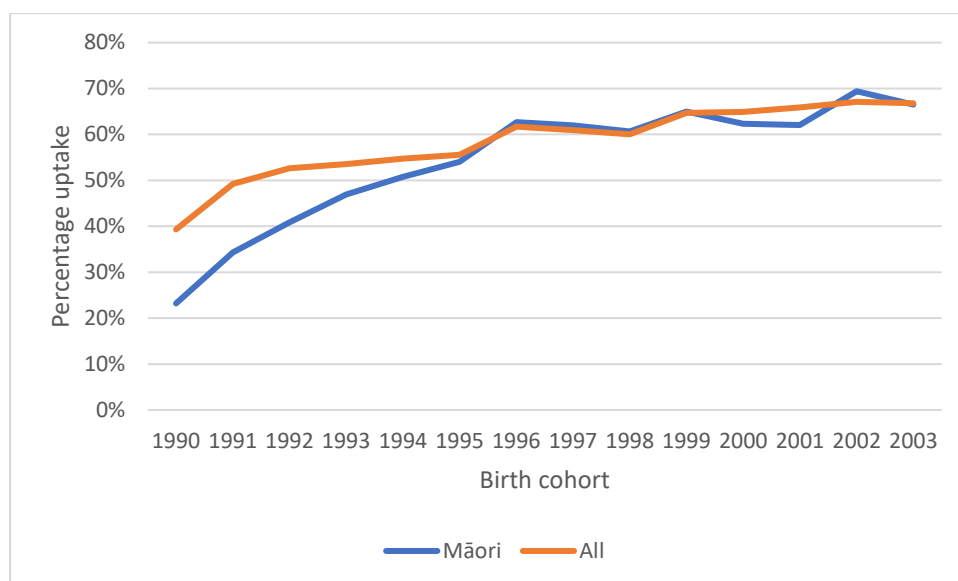
## 11. Local data or special considerations relating to New Zealand (if applicable).

### ***HPV vaccination targets and achievements***

The target for HPV vaccination was 75% coverage in NZ by December 2017, but 67% of females born in 2003 were vaccinated by then, and overall figures for males are unavailable.<sup>10</sup>

While the uptake of the HPV vaccine has been gradually increasing (Figure 1), in all eligible women and in Māori women, the latest data available shows a levelling off in the last five years for which complete data was available. This is despite a recall system being set up in general practice from 2014. Therefore, there is a need to consider other mechanisms to increase uptake.

**Figure 1 Final dose HPV vaccination coverage: girls born between 1990 and 2003**



Source: Ministry of Health, data collected to 31 December 2017.<sup>9</sup> Girls born in 2003 would have been 14 years of age as at 31 December 2017.

### ***Timeline HPV vaccine in New Zealand:***

- 1 Jan 2017: HPV vaccine funding extended in females to age 26 years
- HPV vaccine funding extended to males for the first time (up to age 26 years)
- 4-valent replaced with 9-valent
- 2 dose schedule for 14 years and under (second vaccine 6-12 months after the first)
- 3 dose schedule for 15 years and over (at 0, 2 and 6 months)
- School based program years 11 and 12
- Target for 12 year old girls to achieve 75% coverage by 31 December 2017

Sep 2008-2016 HPV vaccine is funded to females up to their 20<sup>th</sup> birthday.

Three doses are given

School-based program (initially only in general practice in Canterbury but this changed to allow school based programme from 2016)<sup>11</sup>

The initial target was 90% for three doses for all 12 year old girls, but then revised down to 70% dose 1, 65% dose 2, and 60% dose 3. From 2015, the target was gradually increased for 12 year old girls to 65% for 2015, and 70% for 2016.<sup>11</sup>

In 2014, a recall system for 14 year olds in general practice was put into place for those who had not received vaccines or not completed the course

In 2011, South Canterbury where there was no school-based system for Gardasil, but reliance on general practice was noted to have 17% uptake of Gardasil in girls born in 1997, around a third of the national average at the time.<sup>41</sup> Canterbury and South Canterbury uptake was better than this in 2014, but still lower than all other DHBs.<sup>11</sup>

### ***Cervical cancer screening and rates***

The cervical screening programme has reduced cervical cancer and deaths from this cancer by 60% since being implemented.<sup>14</sup> However, cervical cancer is higher in Māori, Pasifika and Asian women than European or other ethnicities, primarily because these women have lower rate of screening (67% for Māori, 66% for Pasifika and 61% for Asian, versus 76% for European. Additionally, there has been a downward trend in screening numbers for Pasifika. Thus, there is an inequity in the ethnic distribution of cervical cancer. However, additionally, at 71% coverage of 25-69 year olds by the National Cervical Screening Programme, we are falling short of the 80% target coverage across the board.

It is therefore unsurprising to find that most NZ women with cervical cancer have not been adequately screened.<sup>42</sup> A 2018 paper reported 133-167 confirmed cases of cervical cancer per year from the National Cancer Registry from 2008-2012. Only 13% of these women (6% of Māori and 5% of Pasifika women) had adequate screening recorded in the 84 months prior to diagnosis. Women in more deprived areas were less likely to have regular cervical screening than those in less deprived areas. Of those with a high-grade abnormal screen in the 6-84 months before diagnosis, of whom 34% were Māori, 95% received a referral for a colposcopy, and 67% had a subsequent biopsy. The authors stated: *“The failure of the system to engage women/wahine, especially Māori and those living in deprived areas, with regular cervical screening appears to be the most important modifiable risk factor associated with the diagnosis of cervical cancer in this cohort of women.”*

### ***The New Zealand Cancer Action Plan 2019-2020***

One of the key prongs of the NZ Cancer Action Plan<sup>43</sup> in their goal for New Zealanders to have fewer cancers is *“Prevent cancers related to infection”*. One of the actions under this is to *“Increase the uptake of HPV vaccinations”*.

## **12. Labelling or draft labelling for the proposed new presentation(s).**

The labelling would remain unchanged, and is not relevant to the reclassification as the product is administered in the pharmacy not by the consumer.

**13. Proposed warning statements (if applicable).**

Not relevant as the product is administered in the pharmacy and not by the consumer. A screening tool will be available for the pharmacist.

**14. Other products containing the same active ingredient(s) and which would be affected by the proposed change.**

Currently the only marketed product is Gardasil-9.

## Part B

### 1. Indications and dose

What is the medicine indicated for, and for which indication(s) is the reclassification application for?  
– What is the evidence that the proposed indication is an OTC indication ie, that the diagnosis and treatment can be understood by the consumer; that the risks of inappropriate treatment can be minimised? – What is the treatment population for the indication (age; gender etc.)? – What is the dose and dose frequency of the medicine for this indication?

#### **Indications from the datasheet:<sup>4</sup>**

GARDASIL 9 is indicated in females aged 9 through 45 years\* for the prevention of cervical, vulvar, vaginal and anal cancer, precancerous or dysplastic lesions, genital warts, and infection caused by Human Papillomavirus (HPV) Types 6, 11, 16, 18, 31, 33, 45, 52 and 58 (which are included in the vaccine).

GARDASIL 9 is indicated in males 9 through 26 years of age for the prevention of anal cancer, precancerous or dysplastic lesions, external genital lesions and infection caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 (which are included in the vaccine).

\* Evidence of vaccine efficacy is based on the core efficacy population of females 16 to 26 years of age. Immunogenicity studies have been conducted to link efficacy to younger populations (females and males 9 to 15 years of age). Currently there are no data from studies of GARDASIL 9 relating to females over 26 years of age (see Section 5.1, Immune Response to GARDASIL 9 at Month 7 Across All Clinical Studies).

The indications for the reclassification are proposed to be no different to those in the datasheet.

#### **Is the proposed indication appropriate for reclassification?**

Reclassification of Gardasil with clear indications and usage is completely in line with other reclassifications of vaccines. It will be at least as clear for the pharmacist as for general practice as to whether or not Gardasil is appropriate, particularly since the pharmacist will be using a screening tool to ensure contraindications and precautions are maintained. The consumer should usually be aware of whether or not they have had the HPV vaccine, the pharmacist will check in the National Immunisation Record (NIR). If the vaccination occurred in New Zealand it would in almost all cases be included in this record.

#### **Treatment population (see also indications and dosing and funding)**

As per the licensed indications and classification statement. It is expected that the age range will be affected by any funding initiatives through local DHBs or at a national level. Those receiving the vaccination will be those who have not been vaccinated through the school system or from general practice.

#### **Dose and dose frequency<sup>2,4</sup>**

For 9-14 year olds (age at expected completion of dosing), the dose is two vaccines with the second dose 5-13 months after the first dose (funding is for 6-12 months after the initial dose). If the second dose is provided before five months, a third dose is necessary.

For people aged 15 years and over, the dose is three vaccines, with the second dose given two months after the first dose, and the third dose given six months after the first dose. All three doses should be given within a year.

### **Funding<sup>44</sup>**

While cost is not normally a consideration for the Medicines Classification Committee, for completeness, the Pharmac funding criteria are included. Funding is for any of the following:

1. Maximum of two doses for children aged 14 years and under; or
  2. Maximum of three doses for patients meeting any of the following criteria:
    1. People aged 15 to 26 years inclusive; or
    2. Either:
      - People aged 9 to 26 years inclusive
        1. Confirmed HIV infection; or
        2. Transplant (including stem cell) patients: or
3. Maximum of four doses for people aged 9 to 26 years inclusive post chemotherapy

## **2. Presentation**

What is the proposed dose form and strength of the medicine to be reclassified? Is this the same for all indications? – What disposal considerations need to be made for the medicine? – How practical and easy to use is the proposed presentation?

### **Dose strength and form for all indications<sup>4</sup>**

Human Papillomavirus 9-valent Vaccine, Recombinant

1 dose (0.5 mL) of suspension for intramuscular injection in a single-dose pre-filled syringe contains approximately:

Human Papillomavirus<sup>1</sup> 6 L1 Protein<sup>2,3</sup> 30 micrograms  
Human Papillomavirus<sup>1</sup> 11 L1 Protein<sup>2,3</sup> 40 micrograms  
Human Papillomavirus<sup>1</sup> 16 L1 Protein<sup>2,3</sup> 60 micrograms  
Human Papillomavirus<sup>1</sup> 18 L1 Protein<sup>2,3</sup> 40 micrograms  
Human Papillomavirus<sup>1</sup> 31 L1 Protein<sup>2,3</sup> 20 micrograms  
Human Papillomavirus<sup>1</sup> 33 L1 Protein<sup>2,3</sup> 20 micrograms  
Human Papillomavirus<sup>1</sup> 45 L1 Protein<sup>2,3</sup> 20 micrograms  
Human Papillomavirus<sup>1</sup> 52 L1 Protein<sup>2,3</sup> 20 micrograms  
Human Papillomavirus<sup>1</sup> 58 L1 Protein<sup>2,3</sup> 20 micrograms

1 Human Papillomavirus = HPV.

2 L1 protein in the form of virus-like particles produced in yeast cells (*Saccharomyces cerevisiae* CANADE 3C-5 (Strain 1895)) by recombinant DNA technology.

3 Adsorbed on amorphous aluminium hydroxyphosphate sulphate adjuvant (0.5 milligrams Al).

This is practical and easy for pharmacists to administer. No needle is provided with the prefilled syringe, but pharmacists are used to this from some other vaccines they provide and have access to variable sized needles. Pharmacists are used to disposing of used vaccine syringes and needles in sharps containers.

### 3. Consumer benefits

What is the history of this medicine's use for the proposed indication(s) ie, number of users; number of countries used in? – To what extent is this medicine used for the proposed indication(s) ie, duration of use; frequency of use? – What is the evidence that improved access is beneficial for the individual? – What is the evidence of improved consumer involvement in their health? – What are the benefits from a consumer viewpoint?

**The key benefit of access to HPV vaccine through pharmacists is increased awareness and uptake, resulting in benefits (reduced rates of HPV infection and HPV-related cancer) for the individual and the community. Pharmacy will help New Zealand reach the Ministry of Health target of 75% from the currently static 67% uptake. For consumers who missed out on the school vaccination programme with HPV, pharmacy offers a convenient choice for the vaccination.**

HPV is the most common sexually transmitted infection, and while most people do not suffer consequences or have any symptoms, for a small minority, the virus is carcinogenic or causes genital warts. The Immunisation Handbook<sup>2</sup> reports Ministry of Health data from 2015 indicating 138 new cervical cancer registrations for the year. It also reports that 97% of CIN 2/3 are HPV-positive and 88% of invasive cervical cancer is HPV-positive. In 2014, there were 282 new registrations for other HPV-related cancers, 161 in women and 121 in men. These were cancers of the vulva, oropharynx or tonsils, anus, vagina and penis. While cervical cancer is reducing in incidence (because of the national screening programme), anal and oropharyngeal cancers have been increasing. The Ministry of Health reports that about 50 women per year die from cervical cancer.<sup>13</sup> Cervical cancers usually takes 20 years to develop from the time of HPV infection.<sup>8</sup>

Genital warts arise from HPV, and are a common diagnosis in sexual health clinics. Genital warts still are often distressing, can require long treatment, and very occasionally cause hospitalisations.<sup>45</sup>

The HPV strains linked to cancer are HPV16, 18, 31, 33, 45, 52 and 58.<sup>2</sup> Genital warts arise most commonly from HPV6 or HPV11 infection. All of these strains are covered by Gardasil-9.

HPV vaccine is very effective in producing antibody responses to the HPV strains covered.<sup>2</sup> In men who have sex with men, the quadrivalent HPV vaccine prevents anal HPV infection and associated pre-cancerous lesions. In women the quadrivalent HPV vaccine has a 98% efficacy for preventing precancerous lesions related to HPV16 or HPV18. See the Immunisation Handbook for further details and references.

In New Zealand, recent data shows that high grade cervical cytology was lower in women who had received the quadrivalent HPV vaccine than in those who had not.<sup>46</sup> Patel, et al.<sup>45</sup> calculated that nearly 90% of the cervical cancer cases in Australia could potentially be prevented by the nine-valent HPV vaccine (based on 2012 data).

An authoritative text on vaccination (Plotkin's Vaccines)<sup>1</sup> states: *"High coverage of Gardasil or Cervarix is expected to eliminate, or at least significantly reduce, the incidence of precancerous and cancerous lesions associated with HPV types 16 and 18 and possibly some related types. Coverage with Gardasil-9 would further reduce lesions caused by other types."*

The prevalence of genital warts has been declining considerably, particularly in the youngest age groups in which vaccination has taken place.<sup>1, 2, 45</sup> Reductions have also been seen in heterosexual men, suggesting herd protection where men have not been vaccinated.

Juvenile-onset recurrent respiratory papillomatosis is a very rare and sometimes deadly condition in which HPV 6 or 11 is transmitted vertically from the mother to child, and Australian data suggests cases have reduced since HPV vaccination was introduced.<sup>45</sup>

### **History**

Over 300,000 New Zealanders have been vaccinated against HPV since 2008 when HPV vaccination was first funded here,<sup>7</sup> and including the current 9-valent product since January 2017. Since 2006, HPV vaccine has been used, and by 2014 was used in over 60 countries.<sup>6</sup> Estimates for the period to October 2014 suggested 59 million women had received at least one dose of HPV vaccine. In 2020, many millions more will have received a dose. It is expected that all or almost all usage would be for the licensed indication.

### **HPV vaccination is effective**

The World Health Organisation (WHO) states that: *“The HPV vaccine is one of the most effective vaccines ever developed.”*<sup>5</sup> This vaccine reduces the likelihood of developing precancerous lesions (cervical intraepithelial neoplasia or CIN 2/3 or adenocarcinoma in situ) caused by the strains of HPV that the vaccine immunises against, and therefore, this vaccine will reduce the likelihood of getting cervical cancer.<sup>2</sup>

HPV infection primarily occurs from sexual contact with an infected person, but because it is skin-to-skin contact, it can occur even with use of condoms. It can be transmitted during childbirth to a neonate.<sup>2</sup> HPV infection is extremely common, affecting about three quarters of people sometime in their lives, although for most it does not cause cancer and the virus becomes undetectable within two years. Please see chapter 9 of the Immunisation Handbook (attached) for further detail about the infection.

The 9-valent Gardasil vaccine (the only one currently on the NZ market) covers the following strains: HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58. As noted above, these are the strains linked to cancer or genital warts. The duration of protection is unknown, as is typical with new vaccines, but it is hoped to have continued protection, as the antibody levels remain very high nine years after Gardasil quadrivalent.<sup>1</sup>

### **Consumer benefits**

The consumer benefits are significant. Increased access will mean increased opportunities for discussion about the vaccine to raise awareness and increase uptake through both pharmacy and general practice.

HPV is the most common sexually transmitted infection, and while most people do not suffer consequences, for a small minority, it is carcinogenic or causes genital warts. The Immunisation Handbook<sup>2</sup> reports Ministry of Health data from 2015 indicating 138 new cervical cancer registrations. It also reports that 97% of CIN 2/3 are HPV-positive and 88% of invasive cervical cancer is HPV-positive. In 2014, there were 282 new registrations for other HPV-related cancers, 161 in women and 121 in men. These were cancers of the vulva, oropharynx or tonsils, anus, vagina and penis. The types linked to cancer are HPV16, 18, 31, 33, 45, 52 and 58. Genital warts arise most commonly from HPV6 or HPV11 infection.

As one of the most effective vaccines ever according to the World Health Organisation,<sup>5</sup> increased uptake will reduce HPV infections which cause cervical and other cancers and genital warts. Reducing cancer will save lives, save anguish, and reduce pressure on the health system. Financial

savings will accrue from reduced need for investigation and management of precancerous lesions, cancer and genital warts, and the cost to Society of early death.

This vaccine has been approved and funded in New Zealand (funded in females and males up to the age of 26 years) because of a positive benefit-risk balance. The Pharmaceutical Management Agency (Pharmac) noted that *“vaccination of schoolboys is relatively cost effective...”*.<sup>47</sup> Pharmac’s Pharmacology and Therapeutics Advisory Committee’s (PTAC) Immunisation subcommittee in 2016<sup>48</sup> noted that the evidence for Gardasil 9 was *“strong”* with *“the potential to prevent 90% of cervical cancers and 80% high grade pre-cancerous lesions”*, hence recommending HPV vaccine funding be extended to the 9-valent product, age up to 26 years and males also.<sup>12</sup> There is a positive effect on genital warts, and this was seen in New Zealanders where of all first visit clients attending four sexual health clinics the genital warts incidence changed from 15.6% in 2008 to 8.6% in 2013. This decline was most obvious in women in the eligible age group for the vaccine. At this time, no decline was seen in males in the eligible age group, however.

However, New Zealand has not met the targets it has set for HPV vaccine uptake (75% coverage by end of 2017),<sup>10</sup> which exposes many New Zealanders unnecessarily to risk of HPV infection and its consequences. This level of uptake also limits the potential for herd protection, ie protection of non-vaccinated by a large proportion of the population being vaccinated.

Benefits to consumers in brief include:

- Increased likelihood of getting an HPV vaccine and receiving protection from HPV-caused diseases including cervical cancer, anal cancer, penile cancer and oropharyngeal cancer
- Increased awareness
  - Increased numbers of health professionals able to initiate an informed conversation about HPV vaccination – so increased opportunistic contact regarding HPV
  - Increased likelihood that the consumer will see information about the HPV vaccine as information is likely to be available at schools, in general practice and in pharmacies
- Increased convenience and reduced barriers to access
  - More locations to receive the HPV vaccine
  - Availability of locations to receive the HPV vaccine that do not require enrolment, appointments or weekday visits only, providing convenience and reducing barriers to uptake
  - In some cases HPV vaccines will be available at their workplace if a pharmacy provides influenza vaccinations there, as is increasingly occurring
  - If another funded vaccine is provided through pharmacy, this will make it viable for more pharmacies to offer vaccinations to their community
- The ability to buddy onto other vaccines
  - Eligible persons could receive the HPV vaccine at the same time as they receive an influenza vaccine within the pharmacy or at workplaces
  - Eligible persons could receive their HPV vaccine at the same time as an MMR catch up vaccine within the pharmacy
  - Should another meningococcal outbreak occur where pharmacy offers the meningococcal vaccine, as in Northland recently, eligible persons could receive their HPV vaccine at the same time as meningococcal vaccine
  - If a person gets raised awareness on HPV from signage in pharmacy, they can be checked for MMR status at the same time



- An increase in the number of pharmacies providing vaccinations, particularly in low income or rural areas – becoming even more accessible and convenient for consumers
  - Currently a single funded vaccine in pharmacy is not viable for all pharmacies, so many pharmacies do not supply them. HPV vaccine available through pharmacies if funded will help ensure appropriate funding to aid with set-up and continued costs
- Benefits to consumers who are not vaccinated – reduced likelihood of becoming infected with HPV and potentially reduced risk of developing an HPV-related disease because others are immunised (herd protection) – a NZ workshop in 2014 considered that vaccination rates of approximately 75-80% would to be achieved to achieve herd immunity.<sup>11</sup>

***Evidence for increasing uptake of vaccinations through use of pharmacy providers***

Internationally, evidence shows that allowing access to vaccinations through pharmacy increases uptake, highlighted by a systematic review and meta-analysis published in 2016.<sup>20</sup> The major advantage is the accessibility and convenience, with pharmacies generally open more hours than general practice, and usually requiring no appointment. Furthermore, satisfaction with the pharmacy service is high.<sup>15, 17, 49-51</sup> A UK survey of patients receiving the influenza vaccination found 7% of recipients would not have received the vaccination without the pharmacy-based service.<sup>17</sup> A survey in four Toronto pharmacies found 28% of influenza vaccine recipients and 21% of high risk patients would not have had the influenza vaccination that season if pharmacies did not provide vaccinations.<sup>51</sup> The key reason for recipients getting the vaccine from the pharmacy was accessibility with “no waiting, no queue, no appointment, convenience and easy access”.

Around the world, people eligible for funded influenza vaccinations have chosen to pay to receive them without funding in a pharmacy (despite being informed they could be free from general practice) given the greater convenience and accessibility particularly.<sup>50, 52, 53</sup> As many as 6-17% of influenza vaccine recipients in the pharmacy were eligible for free vaccinations elsewhere. Funding has often been extended to pharmacy-delivered influenza vaccinations given the convenience and potential to increase uptake amongst higher risk groups.

New Zealand data also supports the improved access and convenience, and greater uptake when widening access to vaccinations to pharmacy-based services. A survey of persons receiving a pharmacist-administered influenza vaccination in 2012 found that 42% of the 213 respondents had not had the influenza vaccination the previous year, primarily because they were too busy.<sup>15</sup>



***Adolescent health needs***

A 2011 report on the Youth Health Service Review<sup>55</sup> acknowledged that New Zealand’s current health services structure and ability to meet the health needs of youth are low. This report advised having appropriate primary care services (such as school-based clinics and community-based health care services) will encourage young people to access care earlier and thus reduce the delayed

treatment which is often more costly and complex. Pharmacy would fit into such services, and should be used more for these people.

Adolescents may not attend the doctor, given most do not have chronic conditions, affecting the potential for an opportunistic mention. A study of New Zealand secondary school students in 2012<sup>56</sup> found that 19% of students had been unable to access healthcare when they needed to sometime in the last 12 months, particularly for high deprivation neighbourhoods. For 28% this was because of a lack of transport, and 46% did not want to make a fuss. Even if they do go, it will not necessarily be mentioned by a doctor given vaccination is usually delegated to practice nurses and doctors may be unfamiliar with HPV vaccination funding criteria.

With the oral contraceptive reclassification work, a common comment received during its development was that pharmacy is more youth-friendly than general practice. This is very applicable here too. There is no need for enrolment, or appointments and pharmacies are easy to get to and anonymous.

In the meningococcal C outbreak in Northland around 8 years ago, uptake of the vaccine was low in adolescents until they worked with the walk-in clinics and mobile clinics.<sup>57</sup> As a result, pharmacy was used in the recent meningococcal W outbreak in Northland to aid uptake of the vaccine in adolescents.<sup>21</sup> Most of the focus was on walk in mobile clinics which were used in all three phases. However, from phase II seven pharmacies in Northland provided funded meningococcal vaccinations, with 349 adolescents aged 13-19 vaccinated in pharmacies of whom 109 were Māori, 6 Pacific, and 234 Others. Pharmacy was willing to provide vaccinations over a particularly busy time of the year (21 Dec to 20 Jan), aiding access before schools and general practice joined the clinics and pharmacy for the final phase. Pharmacy delivered 6% of the total vaccinations given, similar to high schools (6%) and over half of that delivered by general practice (11%), despite being only seven pharmacies providing vaccinations throughout Northland. Therefore, the number of vaccinations provided per pharmacy would have been substantially higher than the number delivered by general practice. It was concluded that *“Pharmacies are a great resource to use in outbreak situations”*. With difficulties including a large proportion of teenagers being located in rural locations, challenges with transport and times of clinics, plus long wait times at the clinics, being discussed by the authors, it is logical to also quickly implement pharmacies as an additional location and resource. This is a growing area, and with more pharmacies and more pharmacists delivering vaccines and consumers becoming more familiar with pharmacy as an option, their contribution will become increasingly greater to making vaccinations as accessible and quickly as possible in another outbreak.

A systematic review found adolescent and young adult males were often unaware of HPV vaccine recommendations or had HPV misinformation which affected their likely uptake.<sup>58</sup> This is likely to be true also in New Zealand where there is no known figure for overall uptake of HPV in males, but it is expected to be very low (in single digits has been suggested) for the vast majority of males not vaccinated in the school-based system.

Please see other benefits later in this application, many of which directly or indirectly benefit the consumer.

#### ***Indirect consumer benefits of having a further vaccine funded in pharmacy***

If another vaccination is funded in pharmacy it is likely to result in the following:

- More pharmacies providing vaccinations, particularly in remote and low-income areas (see rationale below) – with consumer benefits likely

- Pharmacists thinking about vaccinations year-round, not primarily over April to June when most of the influenza vaccinations are administered, and therefore raising it more often – with consumer benefits likely
- Pharmacists becoming increasingly confident and capable in their vaccinating and public health messaging role – with consumer benefits likely
- At least some pharmacies will fund more of their pharmacist staff to do the training (which means more connection points in each pharmacy for consumers to have vaccination raised) – with consumer benefit likely in increased likelihood of opportunistic interaction, access at all hours the pharmacy is open (a minority currently may have times when no vaccinator pharmacist is available) and minimal wait time
- More locums will do the vaccinator training as it will become a core competency, so there will be better coverage when the key pharmacist/s are away, at weekends, or to bring in for an outbreak
- People will become familiar with vaccinations in pharmacy and know they can easily have a discussion about vaccination if they need it, in a drop-in fashion

[REDACTED]

For a rural pharmacy or pharmacy in a high needs area, the costs currently may not meet the costs of establishing the service with the cost of a vaccination fridge which can be \$3,000-\$10,000, costs of training and maintaining competency, developing standard operating procedures and having emergency equipment including oxygen, Ambubags and adrenaline. While this is not a funding application, reclassification is the first step to getting access through pharmacy, and without it funding is highly unlikely to happen.

**Current coverage**

New Zealand has not reached the target of 75% coverage by December 2017, (most recently getting coverage of 67% of females born in 2003, but lower numbers for earlier birth cohorts).<sup>10</sup> There are many people (particularly, but not only, males) who missed getting vaccinations in the school system. Furthermore, pharmacy has been proven effective in increasing access to vaccination in overseas research.<sup>20</sup>

[REDACTED]

There has been support elsewhere for pharmacists to provide HPV vaccines, particularly in the US. For example, in 2012-2013, the United States President’s Cancer Panel identified and considered barriers to HPV vaccine uptake, and measures to address these barriers to resolve the underuse of HPV vaccines.<sup>60</sup> Among their recommendations was the goal of maximising access to HPV vaccination services, specifying the objectives of promoting and aiding HPV vaccination outside the medical home, allowing pharmacists to administer vaccines to adolescents; and paying for vaccines through non-physician providers. The Panel stated that: “... *providing additional venue choices may*

increase the likelihood that adolescents will receive all three HPV doses.” Similarly, the National Vaccine Advisory Committee in the US in 2015 recommended pharmacy delivery of HPV vaccines.<sup>61</sup>

#### 4. Contraindications and precautions

– *What are the contraindications for the medicine and how easy are they to identify and prevent?*

From the Gardasil datasheet comes the following information<sup>4</sup>:

Hypersensitivity to the active substances of GARDASIL 9 or GARDASIL or to any of the inactive ingredients of either vaccine (Sodium chloride L-histidine Polysorbate 80 Sodium borate Water for injections). Individuals who develop symptoms indicative of hypersensitivity after receiving a dose of GARDASIL 9 or GARDASIL should not receive further doses of GARDASIL 9.

These are in line with other vaccinations provided by pharmacists and they will use a screening tool, so this is normal practice for pharmacy.

– *What are the precautions for this medicine and how easy are these to understand?*

The warnings and precautions are summarised below:

- Gardasil is not 100% effective. It is not a treatment, simply a preventer of HPV infection.
- Fainting can occur especially in adolescents and young adults with this and other vaccinations. Observe carefully for approximately 15 minutes after administration. Be prepared for rare anaphylactic reactions.
- Cervical smear tests are still needed
- A current or recent febrile illness may need a delay depending on the symptoms and cause, but a low-grade fever and mild upper respiratory infection are not generally contraindications.
- Impaired immune responsiveness e.g. due to HIV, immunosuppressive therapy, etc, may reduce the antibody response to the immunisation.
- Give with caution to people with thrombocytopenia or anticoagulation disorder because bleeding may occur following an IM injection.

Many of these are similar to other vaccinations, so familiar to pharmacists, able to be managed and have been covered in the screening tool and information the pharmacist discusses with the patient. Pharmacists undergo the same training requirements as nurses for vaccination and have to be current with the appropriate level of first aid training which includes anaphylaxis management and fainting. They have standard operating procedures in case these occur, and emergency equipment. Anaphylaxis is extremely rare at about 1-3 per 1 million but pharmacists are prepared for it. Many millions of doses of vaccines have been administered by pharmacists in community pharmacies in the US and Canada.

The IM injection instructions and bleeding disorders have been worked through in the past with IMAC and the same wording is used in this screening tool as was agreed with them previously.

Pharmacists require the person to wait in line of sight for 20 minutes after the vaccination.

– *Does the medicine have a low therapeutic index?*

No

– *What class effects need to be considered and what are the risks?*

Many effects are the same as for other vaccinations, and are listed above. Another risk is injection in the wrong place, e.g. placing the needle too high – pharmacists are trained and assessed for using the right injection site.

Pharmacists have a private area for the vaccination and a waiting area for the person to wait after the vaccination.

– *What are the risks of the medicine being used in an OTC environment?*

There are no more risks of HPV vaccine being used in a community pharmacy than anywhere else.

– *What other drug interactions need to be considered?*

– *What food and/or drink interactions need to be considered?*

Nil

– *Are there any other restrictions when taking the medicine ie, driving restrictions or operating machinery?*

Nil

– *Are there any special populations where exposure to the medicine needs to be restricted?*

HPV vaccine is not recommended to be used in pregnancy, so this will be screened for. However, no untoward effects are expected should a woman be pregnant when it is administered.<sup>1</sup>

There is nothing further than that discussed above.

## **5. Undesirable effects**

– *What are the known undesirable effects and the frequencies of these? Do these vary for special populations?*

See the datasheet (attached) for full details, and the Immunisation Handbook chapter 9 (attached). The Immunisation Handbook<sup>2</sup> notes that HPV vaccine is well-tolerated, and that “*HPV vaccines have excellent safety profiles internationally*”. This is similar to the WHO position paper.<sup>8</sup>

The Gardasil datasheet<sup>4</sup> lists adverse effects from clinical trials occurring in 1% or more of those administered HPV vaccine. Most are injection site related: pain (83%), swelling (36%), erythema (31%), pruritus (4%), bruising (2%). Systemic adverse reactions: headache (13%), pyrexia (6%), nausea (3%), dizziness (2%), fatigue (2%).

The Immunisation Handbook<sup>2</sup> notes that syncope (fainting) is frequent in adolescents, as an injection reaction rather than a reaction to the vaccine. Very rare reactions such as anaphylaxis can occur, but these are similar to other vaccines, and a safety study in the US of 600,000 doses found no statistically significant increased risk of Guillain-Barre syndrome, stroke, venous thromboembolism, appendicitis, seizures, allergic reactions or anaphylaxis.<sup>1</sup> Post-marketing safety studies have found no association with conditions like autoimmune disease, or demyelinating disease.<sup>1</sup> Although Plotkin’s Vaccines<sup>1</sup>, the Gardasil datasheet<sup>4</sup> and the Immunisation Handbook<sup>2</sup> do not give a rate for anaphylaxis, the parent consent form from the Ministry of Health suggests that anaphylaxis can occur in 3 in a million people with this vaccine.

The variation with special populations has been dealt with in the contraindications and precautions.

*– What are the risks and consequences of known undesirable effects?*

Syncope risks are of falling, as for other vaccines, and the person is seated during the vaccination, and also after the vaccination if they have a history of fainting.

Anaphylaxis is serious but extremely rare and pharmacists are trained to manage it.

Other side effects are not particularly concerning or different to other vaccinations, and usually short in effect.

*– Are there any significant safety concerns for the medicine under review?*

None at all, HPV vaccines have been very well studied for safety.<sup>1</sup>

*– Have there ever been any withdrawals of the medicine or other regulatory actions taken for safety reasons (during a time period or in a specific jurisdiction)?*

HPV vaccines are very well regarded for safety.<sup>1,2</sup> In Japan, while not withdrawn, in 2013 the recommendation for HPV vaccine was suspended because of reports of complex regional pain syndrome following vaccination, although a later review found no evidence of association with HPV vaccine.<sup>1</sup>

*– Are there any withdrawal effects following cessation of use of the medicine?*

No

## **6. Overdose**

*– Is there a potential for overdose of the medicine?*

No – the pharmacist administers a single dose on each occasion.

*– What are the consequences of overdose of the medicine?*

Not applicable

*– Are there any reports of overdose of the medicine?*

Not applicable

## **7. Medication errors and abuse/misuse potential**

*– Would reclassification affect the risk of unnecessary use?*

It should not, the indications for use are clear.

*– Is the medicine be provided with necessary tools to allow correct dosing eg, liquids supplied with a measuring device?*

A needle will need to be purchased and used, this is indicated on the screening tool.

*– What are the reported medication errors post-market?*

The pharmacist is administering the medication. One potential error could be selecting the wrong vaccine, but this would be extremely unlikely and is not a specific problem with the HPV vaccine. Pharmacists have good processes to minimise the risk of selection error.

– *What are the reported cases of abuse/misuse/accidental overdose?*

Not applicable for a pharmacist-administered vaccine.

– *How would reclassification affect import considerations?*

Not applicable, it would remain prescription only with an exemption.

– *What is the addiction potential of the medicine?*

None

## **8. Communal harm and / or benefit**

– *What are the possibilities of community harm resulting from wider use of the medicine in question (eg, the development of antibiotic resistance in bacteria or increased immunisation rates)?*

There is no possibility of community harm from wider use of this vaccine; wider use will be only beneficial with the potential for herd protection

– *What are the possibilities of community benefit resulting from wider use of the medicine in question (eg, greater herd immunity as a result of improved access to a communicable disease vaccine)?*

There is the potential for greater herd immunity from increasing uptake, as discussed above. This could occur at 75-80% uptake.

## **9. Integrated benefit-risk statement**

### ***Summary of the reclassification benefits***

Availability of the HPV vaccine through pharmacy holds significant potential to increase awareness and uptake and make vaccination viable for more pharmacies and therefore extend capability and capacity. While to maximise this benefit requires funding, reclassification is the first step, and if the benefit-risk adds up, which it does, reclassification should happen as soon as possible to then allow the funding discussion to take place.

The multiple reclassification benefits include benefits to the consumer, to public health, to the health system and to pharmacy, as outlined below. These are summarised initially with justification, evidence and discussion presented below.

### **Benefits to the consumer**

- Choice of location
- Convenience – no appointment, no need to be enrolled, can go to any pharmacy providing vaccinations, little/no wait before administration
- More likely to get opportunistic mentions as many of these consumers are not going to general practice
- More pharmacies will provide vaccination
- Increased awareness
- Can ask questions of an informed and readily available health professional about the vaccine
- Increased uptake
- Reduced likelihood of HPV infection

- Reduced likelihood of HPV-caused consequences
- Assurance of safety – if it is available from the pharmacist not only the doctor it must be safe

### **Benefits to public health**

- Better utilisation of the most accessible health professional group to promote the vaccination at little or no cost, knowledgeably answer questions consumers/parents may have (providing reassurance regarding the vaccine wherever it is delivered), and provide it on the spot
- Increased uptake across the eligible population, and particularly unvaccinated males
- Increased likelihood of reaching the targets of 75% from 2017
- Reduced infection rates
- Reduced incidence of HPV-caused cancers and genital warts in those vaccinated
- Cross-recommendation – people coming for HPV to the pharmacy can be checked for childhood vaccinations including MMR and be referred to the GP or dosed as appropriate concomitantly (e.g. for MMR), and have maternal vaccine discussions for the future if appropriate
- Some protection of non-vaccinated people – the higher the rate of vaccination, the greater protection will occur for those not vaccinated.
- Increased capability and capacity of the pharmacy workforce, with benefit to uptake across other areas
- Increased pharmacy interest in their public health role and other public health initiatives

### **Benefits to the health system**

- Over 450 accessible venues where a healthcare professional can mention HPV vaccination for no additional cost to the health system. The number of such venues is likely to increase, particularly in low-income areas, with another funded vaccination
- Savings of cost and capacity in managing precancerous lesions, cancer and genital warts in those vaccinated who would not otherwise have been
- Increased vaccination capability and capacity of the health workforce
- Ability to help reduce pressure on general practice in high needs areas where there is a shortage of practice nurses
- Occasionally pharmacies have reported being able to help out with stock where a general practice has run out e.g. of influenza and that practice is awaiting a delivery
- Potential for increased uptake of other vaccinations and therefore reduction of vaccine-preventable disease and the costs and other resources involved in managing these

### **Benefits to pharmacy**

- Increased professional satisfaction from helping their community and contributing to public health goals
- For low income and rural areas where the costs for many pharmacies of setting up with vaccination service have been greater than the income, another vaccine available (and then funded) would encourage more pharmacies to offer this service to their community.
- Year-round vaccination services to keep vaccination top-of-mind for pharmacists and supporting staff members and make it worthwhile to offer the influenza vaccine for as long as possible.



An international systematic review and meta-analysis<sup>20</sup> [REDACTED] shows that pharmacy availability of vaccines aids uptake. While pharmacists mentioning vaccines can help,<sup>20</sup> it is even more helpful if the pharmacists are able to administer the vaccine as well if the person is interested in having it at the time it is raised.

The Centres for Disease Control and Prevention (CDC) in the US has been particularly positive about vaccination in pharmacy, with the Principal Deputy Director stating in a letter to pharmacists:<sup>63</sup> *“Research shows that vaccine recommendations from trusted providers are vital to increasing patients’ acceptance of needed vaccines; your practice sites provide an excellent opportunity for reinforcement of public health messages, assessment of patients’ immunization needs, strong recommendations for needed vaccines, and the provision of immunization services when indicated.”* The CDC went on to thank pharmacists for their continued efforts, and enthusiasm and innovation shown by pharmacists in addressing the needs for expanded access to vaccines.

It is logical to expect that pharmacists providing the HPV vaccine will be more informed about HPV than most pharmacists not providing this vaccine, and will also be more likely to have it top-of-mind (so remember to mention it), have promotional material available about it, and take the time to discuss it with patients.

Consumers who have had vaccinations in pharmacy have high levels of satisfaction, including in New Zealand.<sup>15, 16, 50, 52, 64</sup>

A 2018 review of HPV vaccines successes and future challenges,<sup>65</sup> reported: “Studies have illuminated how [healthcare provider] practices and communication enhance uptake and alleviate misperceptions about HPV vaccination. Strategies such as bundling vaccinations, allowing nurses to vaccinate via “standing orders,” and diversifying vaccination settings (e.g., pharmacies) may be effective steps to increase rates.” Others have also suggested using pharmacies to aid HPV vaccine uptake,<sup>61, 66-70</sup> including a President’s Cancer Panel in the US.<sup>60</sup>

An survey of an on-line panel of paediatricians and family physicians in the US conducted in 2014 with a 33% response rate found that 39% of 776 respondents would unconditionally support pharmacists administering HPV vaccinations in 13-17 year old adolescents who are past due for the vaccine.<sup>61, 71</sup> A further 25% of these respondents would support this initiative, providing the pharmacist had training in vaccination and monitoring for adverse effects. A further 15% would support this initiative if the pharmacist reported doses given to the primary care provider and referred to the primary care provider for further health care services. The same researchers asked the same questions of parents of children aged 11-17 who were in an online panel, with a 61% response rate. Unconditional support for the initiative came from 29% of parents, a further 46% would support it if the pharmacist had the appropriate training, and 6% if the pharmacist reported doses given to the primary care provider and referred to the primary care provider for further health care services. This research shows strong support for the provision that we are proposing in this application. Many parents believed doctors’ offices had more privacy (77%), but considered pharmacies more accessible, with less time for vaccinations (71%) and more convenient hours (59%).

While consumer attitudes to HPV vaccines in pharmacy have not been formally examined in New Zealand, there have been studies in the US. A 2014 US study of parents of children aged 11- 17 years<sup>69, 72</sup> found 29% of parents would be willing to get HPV vaccine at the pharmacy, with parents of children 13-17 years, or who had started the vaccination series more likely to be willing to attend the pharmacy for it. Parents who saw that this would increase the opportunity for uptake were twice as likely to be willing to get the HPV vaccine for their child at the pharmacy. The willingness to get the

vaccine at the pharmacy for their child increased if they knew their pharmacist moderately well. It is notable that many pharmacies in the US are large stores with many pharmacists. Pharmacists may be more familiar and readily accessible in New Zealand community pharmacies where the pharmacies are smaller and often owner-operated, which may help increase willingness to have the vaccine in the pharmacy.

Qualitative research in a rural US area found 18 of 26 people interviewed were willing for their community pharmacist to administer the HPV vaccine or other adolescent vaccinations, despite often being unaware that pharmacists could administer vaccinations to adolescents.<sup>73</sup> The primary reason was convenience, mainly because no appointment was needed. Some thought it might reduce other providers' workload increasing convenience for the provider and the community. Some qualified this with the need for pharmacists to be appropriately qualified or following appropriate processes. Over a quarter of respondents preferred their primary care provider to do the vaccinations, usually due to a stronger relationship. Most parents believed they would still be seeing their primary care provider.

In a small US survey,<sup>74</sup> most pharmacists administering HPV vaccine reported being comfortable providing this vaccination, although noting the need for recalls and reminders. However, a pilot study in 15 pharmacies in the US in 2016 had very low uptake of HPV vaccine, with only 13 vaccine doses delivered.<sup>75</sup> The key factor behind the low uptake was the fact that HPV vaccines were not reimbursed by insurers in the pharmacy, but were reimbursed elsewhere. Gains are most likely where funding is also in place.

A pilot in the US<sup>66</sup> provided a co-ordinated model in which a single medical centre provided the first HPV dose and then gave the option of returning to the medical centre or attending a partnering pharmacy for further doses. Of the 51 patients interested in this option and referred to the pharmacy for follow-up, 23 patients got other doses at the pharmacy. All 23 patients completed the series. The others either declined or could not be reached by the pharmacy. Some people will choose to have vaccines at a pharmacy over the medical centre, and might change between them if given the option. This suggests choice is helpful, and the NIR look up can be used before doing recalls to see if the patient has gone elsewhere for the vaccination.

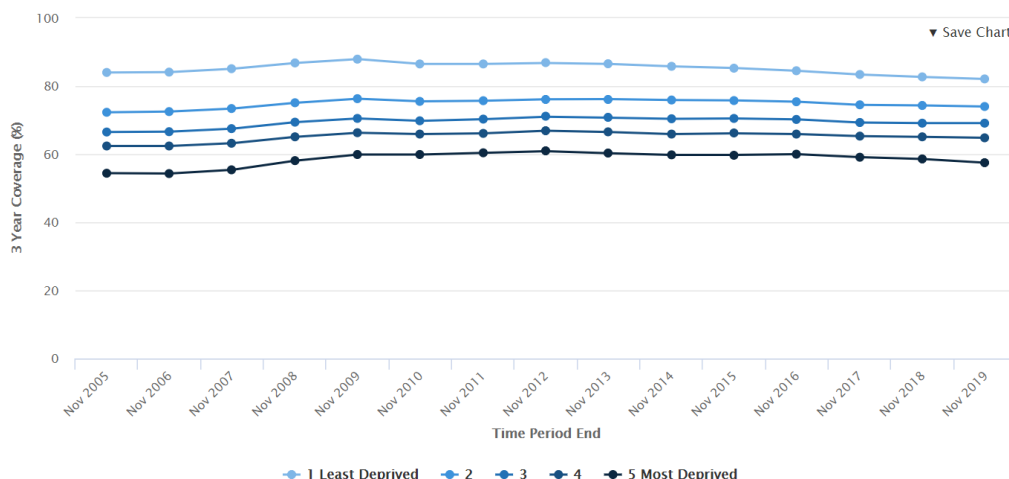
A single independent US pharmacy used pharmacists to provide education on HPV vaccinations to people filling acne or contraceptive prescriptions at the pharmacy.<sup>76</sup> In the pre-intervention year, no HPV vaccines were provided. In the post-intervention year, 21 people completed a questionnaire of which 48% had heard about HPV vaccine from the pharmacist, 24% from the doctor, and 10% saw a flyer at the pharmacy. Ten of these people were vaccinated at the time, most getting their first dose there, and most citing pharmacist recommendation as the key reason. Those choosing not to receive the vaccine usually indicated this was because of cost or lack of insurance cover.

While there are no large well-designed studies on HPV vaccine access with pharmacist recommendation and/or funding of the vaccine in pharmacy, or even small studies in New Zealand regarding HPV, it seems logical that adolescents will find pharmacy an appropriate venue for this service. The meningococcal vaccinations delivered to adolescents through pharmacies in Northland support this.<sup>21</sup> The seven pharmacies delivered 6% of the total in the outbreak, versus 11% for general practice (all of whom would provide vaccinations presumably), and 6% for schools, showing a much higher rate per pharmacy than per general practice. Healthpoint lists 45 GP practices for Northland, therefore, the per pharmacy uptake was nearly five times higher than the uptake per general practice. Pharmacy were involved in phase II and III while general practice and high schools were involved only in phase III.

### **New Zealand need and cervical cancer**

BPAC noted in 2019,<sup>10</sup> “HPV vaccination rates in New Zealand could be better; higher rates of vaccination will protect more individuals and offer more effective “herd immunity” against these conditions.” While great gains have been made in reducing cervical cancer deaths from smear tests, not all women have these, with a three-year coverage of 71% versus a target of 80%, with inequity seen for Māori, Pacific and even more so for Asian.<sup>77</sup> The least deprived group sits at 82% coverage currently, while the least deprived group is at 57% (Figure 2). Of confirmed diagnoses of cervical cancer in NZ, very few women had had screening according to NZ guidelines, with Māori, Pacific people and those living in deprived areas least likely to have done so.<sup>42</sup> Increasing HPV vaccination rates will help get to our most vulnerable directly or through herd immunity, reducing HPV infection rates in the population and the consequences of these.

**Figure 2: 3 Year Coverage in Cervical Screening by Deprivation Quintile, New Zealand, 25 to 69 Years, 15 Years to Nov 2019**



Source: National Screening Unit<sup>77</sup>

Thus, there is a need to do what we can to increase the uptake of the HPV vaccine across the whole population by reducing barriers to access, including through raising awareness, making accessible health professionals informed, proactive, and able to provide it on the spot.

### **A summary of the reclassification risk of harm**

Standard risks for vaccinations of syncope, anaphylaxis, incorrect needle placement occur in all environments including pharmacy and vaccinators are trained and equipped to manage them. Should pharmacists be able to vaccinate children under 13 years, their standard operating procedures and equipment would need to be reviewed to ensure it is appropriate for younger children.

Potential harm could arise from only providing one or two of a three dose series. This is a risk in all environments, and should be aided by accessibility and no need for an appointment. It would also be aided by allowing pharmacists to vaccinate people under 15 years as there would only be two doses required, which should equate to a greater likelihood of completion. The need to set up a recall is

included on the screening tool. This could be undertaken electronically (as for expiring repeats which many pharmacies do) should the software be adjusted as expected, or could be manual. We have collected both a phone number and an email address to give two contact points. Pharmacists will be informed by the Pharmaceutical Society, Pharmacy Guild and Green Cross Health to adjust their standard operating procedures to address recalls, if they have not already. Many pharmacies currently use reminder and recall systems for expiring repeats and to increase adherence. Telephone reminders were commonly used by US pharmacists to notify patients of upcoming doses of multiple-dose vaccines, with 89% of those providing HPV vaccine having a procedure to track the number of vaccination doses, however the survey size was small at 43 pharmacists in eight states.<sup>74</sup> Pharmacy have another two-dose vaccine, meningococcal B vaccine, which also needs a recall, and for which the target age is adolescents, so a precedent of multi-dose vaccines exists.

A possible concern for some might be that this could lead to inequities if it was not funded because the vaccine costs about \$190 per dose for the patient. However, the benefit-risk of HPV vaccine clearly is in favour of reclassification given how effective it is, and how safe it is, and that it would only be available through pharmacists who have had vaccinator training and meet the ongoing training requirements, in a pharmacy that is cold-chain accredited. Funding would be another step and will be sought to help ensure access is equitable.

Another possible concern could be an inability to do opportunistic screening in general practice or build relationships having the person come in for HPV vaccine. This reclassification would increase uptake if followed by funding, and the benefits of having more New Zealanders getting the vaccine well outweigh this. Currently we have 33% of the more recently eligible populations not getting the vaccine, and action is needed. Pharmacists refer people every day to the medical practice, for example reminding women getting the emergency contraceptive to have smear tests, or referring for ongoing contraception needs. The US physician study suggests strong support for the model we have suggested,<sup>61</sup> favouring access for those not getting it.

There are no safety disadvantages of administration in the pharmacy. The vaccine has a very good safety profile<sup>2</sup>, pharmacists have received the vaccinator training, a second person with the appropriate first aid certificate is available, they have the required emergency equipment, standard operating procedures to cover adverse events, and the screening tool for pharmacy is very thorough to ensure best practice.

There were stock shortages of the HPV vaccine in 2018, and it would not be appropriate to jeopardise the school-based programme should further shortages occur. [REDACTED]

[REDACTED] This would be of no concern for HPV vaccine without funding in place as uptake would be limited by the price. If there was funding in place it could be rolled out in a small number of DHBs first before implementing nationally to learn from this first and ensure no run on stock. There could also be a lead-in time to assist with ensuring sufficient stock. The stock situation is not a concern with the reclassification, but rather for the funding consideration.

### ***A summary of the need for the medicine at the classification proposed***

The uptake of HPV vaccine is lower than the goal (most recent figures for women are 67% and earlier cohorts were lower than this, men are unknown but likely to be under 10% for those before the school-based programme started), and lower than some other countries. Therefore, we have unnecessarily high risk in our population who are not vaccinated that could be addressed. This

particularly includes males who have not been able to get the vaccine in the school-based programme until recently. If New Zealanders miss out completely or are delayed in getting their vaccines because of access barriers, there is a disadvantage to the individual, and to public health and the health system from this. The potential to increase the uptake to achieve herd immunity means others in the population who are not vaccinated will be protected. Not all women have cervical smears and therefore reducing the amount of HPV infection in the population is helpful.

Adolescents and young adults can find it difficult to get to the doctor in regular opening hours, and to make an appointment with the doctor. They may not be enrolled with a regular doctor. They may not have access to transport to get to their doctor. The reclassification helps overcome the barriers to access as most pharmacies are open extended hours, pharmacies can feel more youth-friendly, no appointment is needed, and they may already be in the pharmacy for another reason. Of over 6 million vaccinations administered by pharmacists at Walgreens pharmacies in the US in 12 months (2011/2012), 30% were provided outside of traditional office hours of 9-6pm weekdays.<sup>18</sup> This was particularly common in people under 18 years (51%), or 18-49 years (41%). It included 6,790 HPV vaccines administered (34% of the HPV vaccine administrations). There is no such information available in New Zealand, but it is expected that weekends and evenings would be more convenient for patients.

#### ***Precedent – how are other medicines in the same class classified?***

Some other vaccines are also reclassified to allow a trained vaccinator pharmacist the ability to administer them without a prescription – influenza vaccine (13 years and over, pharmacists and intern pharmacists who have had the training), meningococcal vaccine (16 years and over), shingles vaccine, pertussis vaccine (Tdap, 16 years and over, or 13 years and over who are pregnant). These are provided as prescription except when as is proposed here.

#### ***Other***

Note that extending HPV vaccine availability to pharmacy is another piece of the puzzle. Multi-component strategies work best.<sup>78</sup> New Zealand's rates of HPV vaccine uptake are increasing but still need incremental growth, and pharmacy is likely to provide at least some of that. An 8-10% gain on the current figures would have considerable benefit with only the additional cost of the vaccine and administration.

## **10. Risk mitigating strategies**

*– Are there any risk mitigation strategies required? If so, what risk mitigation strategies are required eg, healthcare professional education; integration of care; consumer information to be provided etc?*

Only pharmacists and intern pharmacists who have been trained as vaccinators, been assessed and have successfully completed the two-yearly update course when it is due, and are working in a pharmacy that has been cold-chain accredited can provide vaccinations in New Zealand community pharmacy.

There is a screening tool and information sheet proposed. These have been used for other reclassifications, and are a well-recognised way to aid pharmacists to systematically check for contraindications and precautions.

Pharmacists have a responsibility (as do other healthcare professionals) of ensuring they remain up-to-date and informed for the work that they do. They use IMAC resources and the Immunisation

Handbook to ensure they have the information they need on the vaccines they deliver as others do also. IMAC has a one-hour online course on HPV vaccination that pharmacists would be informed about, and the Pharmaceutical Society plays an important role in providing information in newsletters or training on new reclassifications. This additional training specific to HPV vaccine would not be mandated, but would depend on their knowledge gap analysis. The data sheet will be available for pharmacists,<sup>4</sup> as would the BPAC article from 2019.<sup>10</sup> While pharmacists will be very familiar with the Immunisation Handbook and the IMAC website, the Pharmaceutical Society (representing over 99% of practising pharmacists), the Pharmacy Guild and Green Cross Health would all inform their members of resources to use for updating themselves on HPV vaccine.

Because of a potential, if funded, that the pharmacist provision could interfere with the school-based programme, it is anticipated that a minimum age would be included at the funding stage. The proposed classification wording includes options in case it is desired that a minimum age is included at this point instead, although at \$190 per dose if not funded, there is no risk to the school-based programme if it is not funded in pharmacy, so it is logical to apply the age at the funding stage.

If there is no minimum age in the classification statement, the minimum age of 9 years as in the datasheet would apply. Pharmacists will be physically able to vaccinate down to 9 years if required (as confirmed by feedback from various parties and the overseas experience), with the only requirement being to ensure SOPs and equipment are appropriately updated for this age group. The Pharmaceutical Society, Pharmacy Guild and Green Cross Health would communicate this to their members, and pharmacy audits would ensure compliance. The lack of age in the classification statement and use of funding for managing the age would maximise future proofing of this reclassification, allowing DHBs and Pharmacs flexibility in how they used pharmacy, for example, should the school-based programme be moved earlier, e.g. year 6 or 7.

For New Zealand residents the NIR will be used to check previous vaccination of HPV and to record this administration to ensure integration with other providers, and that the person is not inadvertently provided the vaccination at incorrect dosing intervals or when it has been provided before. Pharmacists have been using the NIR for some time now, and there is a permission from the patient to put their dose on the NIR, as well as a reminder for the pharmacist to do it. This will help compliance with this requirement. There is a risk that the NIR might have a short lag or have a dose omitted from another place where a vaccination occurred, e.g. their general practice. Should there be a discrepancy, the pharmacist could check with the other provider, and if there is no evidence of it being given, provide it.

The person seeking a vaccine (and their parent if under 16 years) will be provided the information sheet before having the vaccination to help them understand the risks and benefits. This information sheet has been adapted from the school parental consent form to ensure consistency of messaging. There is a prompt on the screening tool to do this.

Parental consent will be required for patients under 16 years of age. This is on the screening form to prevent inadvertent provision without consent to a child under 16 years. From the age of 16 years, people do not need parental consent. This is very straight-forward to administer. For those under 16 years it is likely to be parent (or legal guardian) driven and arranged so parental consent should be easily obtained. In the rare case where the parent is not physically present but known to the pharmacy, verbal permission can be documented, or an email sent from the parent to the pharmacy. Currently the NIR does not have a field for recording parental consent, but it does not need to because the screening tool will have this and that will be kept as a hard or soft copy and able to be audited by Medicines Control.

Recalls will be conducted by all pharmacists providing HPV vaccinations where there are further doses required. Two forms of contact (phone and email) are collected to facilitate this process. There is a reminder on the screening tool to activate the recall if needed. Pharmacy organisations will be reminding pharmacies that they need to add recalls to their standard operating procedures for vaccines with multiple doses. The recommendation for a recall at 14 years old from general practice for HPV vaccination in those not vaccinated by then has not appeared to increase uptake at all, which could suggest that this age group might not be especially responsive to recalls wherever they come from, so multiple messages and a phone call might be needed.

The later the dosing, the greater the chance of sexual debut, and this risk is mitigated by allowing dosing for all ages and funded for 13 years and over to ensure an eligible person is not turned away.

*– What is the evidence that these proposed risk mitigation strategies would be effective?*

These strategies (mandating vaccinator training, use of screening tools, etc) have been successfully used for many years for vaccinations, and Medicines Control has indicated that vaccination screenings appear to be managed well in their audits.

Evidence suggests that the recalls are not working particularly in general practice in terms of increasing uptake. However, these are a message recommending the person attends the general practice for their HPV vaccination. It is expected that the recall in the pharmacy for follow-up doses will be more effective because they have already had a conversation with a health professional (the pharmacist) about HPV vaccination, and have already decided to have the first dose. It needs to be clear on the written information that they can get their later doses from that pharmacy, their general practice, or other pharmacies to maximise the chances they will receive further doses.

*– What post-market surveillance activities would be carried out?*

Pharmacists will be encouraged to report adverse reactions, as already occurs. The risk of side effects is not expected to be any greater through the pharmacist than in delivery through other health care professionals.

Funding is being sought for research looking at HPV vaccination uptake through pharmacy.

*– Is the proposed reclassification supported by professional bodies?*

This application is from the Pharmaceutical Society, the Pharmacy Guild and Green Cross Health. Consultation has taken place, with most providing strong support and being supportive of Option 1 in the classification possibilities, with a minimum age of 13 years being used in funding to maximise benefit and avoid interfering with the school-based programme. A small number have preferred a minimum age of 16 years. There have been no concerns raised at this point in having intern pharmacists vaccinating with HPV vaccine. Some professional bodies will be commenting directly to the committee after consultation. See also attached documents.

## Summary

HPV Vaccine 9 valent (Gardasil 9) is effective in preventing HPV infection with seven strains that are most implicated in various cancers affecting women and men, and two strains most implicated in genital warts.

The HPV vaccine has been marketed and funded in New Zealand since 2008, initially only in females and the quadrivalent form only. From 2017 the nine-valent vaccine was funded, and the funding was expanded to males, and the age was expanded to 26 years old for both genders. Ideally the vaccine

is provided before the age of 15 as most people have not reached sexual debut by then and only two doses are required instead of the three doses required from the age of 15 years. This has a lower cost for the health system and will aid compliance.

Despite a good school-based programme that is achieving similar access across various ethnicities, and a recommended recall by general practice from the age of 14 years, the uptake has fallen short of the 75% target, sitting at 67% with little growth in the last five years. Additionally, while figures for males are not known exactly, few eligible males who missed out at school are thought to have had it. Barriers to access need to be minimised to help uptake.

Pharmacy is accessible and usually requires no appointment. Widening access to pharmacy can increase uptake of vaccinations, and for HPV, this is likely to raise awareness and uptake. The benefits will be greatest with funding, and reclassification is the first step in this process. HPV vaccine has a good safety profile and qualified vaccinator pharmacists will be well able to manage this. They will be using the NIR to prevent fragmentation of care, and a recall system to help these people complete the series of vaccines (two or three doses). A screening tool and information sheet for the person and parent will be available.

There is an urgent need to increase uptake in the older groups who will be reaching 27 years old soon and losing their eligibility. Improving uptake in other groups is also a case of the sooner the better, before their exposure to the HPV vaccine strains that can cause cancer so the vaccine can be as effective as possible. Achieving a higher rate will aid herd protection and hopefully eradicate some of these HPV strains.

Pharmacists in New Zealand who have successfully completed the required vaccination and first aid courses, and have been assessed and are working in the appropriate environment can provide certain injectable vaccinations without a prescription. These vaccines are: influenza (down to age 13 years); Tdap (tetanus-diphtheria-pertussis); shingles; meningococcal and MMR vaccine. The HPV vaccine is not particularly different from a safety perspective. It is used in adolescents and young adults, primarily. The HPV vaccine requires multiple doses that are age dependent. Pharmacists already have multiple doses with meningococcal B vaccine and MMR, and this has been managed with the screening tool reminder to ensure a recall is in place. There is a school-based programme which pharmacy administration will not interfere with, through utilising a minimum age requirement either within funding arrangements (allowing future-proofing and flexibility for local or national needs), or within the classification statement.

The adverse event profile of HPV vaccine is similar to other vaccines. All vaccinations have a very rare possibility of anaphylaxis, and pharmacists are trained and equipped to manage such an event.

This application has been jointly funded by the Pharmaceutical Society of New Zealand, the Pharmacy Guild and Green Cross Health so that pharmacy can aid young New Zealanders to have easier access to an important vaccine to benefit individuals and our community.

NB Please note that the blacked out parts are unpublished data that is awaiting publication and therefore cannot be publicly available.



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