2012 Antigen Review for the New Zealand National Immunisation Schedule: Poliovirus

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Institute of Environmental Science and Research Ltd.

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NEW ZEALAND
Te Whare Wānanga o Tāmaki Makaurau

ESR

Immunisation Advisory Centre
ĀRAINGA MATE
UNIVERSITY OF AUCKLAND

Contact details:

Helen Petousis-Harris
Immunisation Advisory Centre
Tāmaki Innovation Campus
The University of Auckland

Private Bag 92019,
Auckland 1142, New Zealand

Phone: +64 9 923 2078
Fax: +64 9 373 7030
Mobile: +64 27 471 6749
Email: h.petousis-harris@auckland.ac.nz

Executive summary

Poliomyelitis (polio) has been eradicated from most countries and 2012 saw a historic low of less than 300 cases worldwide. These were generally restricted to Nigeria, Pakistan and Afghanistan where polio is still endemic. There are still complex issues to be resolved before full eradication will be realised, including the use of oral polio vaccine which has the potential to perpetuate outbreaks of vaccine-derived polio.

The objectives for this review have been informed by the general specifications for the 2012 New Zealand (NZ) antigen review. The choice of articles reviewed is based on the purposeful selection of recent reviews and studies that may best inform policy discussions around polio vaccines for NZ.

Epidemiology

The Western Pacific was declared polio free in 2000, which further decreases the risk for polio importation into NZ. NZ has been free of the wild transmission of polio for 50 years. During this time, there have been rare cases of vaccine-associated paralytic poliomyelitis (VAPP). There were no polio cases notified in 2011. Since polio immunisation in NZ began in 1961 and 1962, a total of six polio cases have been reported. All of these cases were either laboratory-confirmed as vaccine associated (four cases) or classified as probable vaccine-associated cases (two cases).

Following the change from oral polio vaccine (OPV) to inactivated polio vaccine (IPV) in 2000, there was a rapid reduction in the proportion of children excreting polio virus and by one month after introduction of IPV no children were excreting the virus.

Safety of polio vaccines

No new safety concerns have been raised for the polio antigen containing combination vaccines. A range of DTaP-IPV combination vaccines have been demonstrated to be safe, and generally, well tolerated in preterm infants born after 24 weeks, low birth weight infants born at or greater than 820 grams, infants, toddlers and children up to seven years of age. These vaccines have been demonstrated to be safe when co-administered with routine vaccines in infants, toddlers and children.

Immunogenicity, efficacy and effectiveness

Current IPV vaccines are highly immunogenic and appear to provide herd immunity in populations where oral-oral transmission is the primary route for infection. Duration of protection following a range of schedules, including a preschool booster, appears to provide long-term protection. Global use of polio vaccines has almost eradicated polio.

Vaccine and schedule options

IPV is available as monovalent vaccines, and in tetravalent, pentavalent and hexavalent combinations with diphtheria, tetanus, acellular pertussis and hepatitis B or *Haemophilus influenza* type B (Hib) antigens. The most widely used combination vaccines are produced by sanofi-pasteur and GlaxoSmithKline. The current NZ schedule of 3+1 is in line with international policy advice for polio schedules. There are no recommendations to reduce the primary course or the booster dose, or to change the current NZ schedule. The sanofi-pasteur hexavalent vaccine may have limited use in NZ due to the inclusion of fewer pertussis antigens in the formulation. There is no new international advice to suggest any strong recommendations to change the current NZ schedule.

Implementation considerations

As of early 2013, international eradication has not yet been achieved. Importation of disease continues to be a possibility, and as there is straightforward access to combination vaccines, there is currently no reason for discontinuing the NZ IPV programme. The immunogenicity of poliovirus 3 tends to be lower than the other two, highlighting the importance of continuing travel vaccination advice to polio endemic countries.

2012 Antigen Review for the New Zealand National Immunisation Schedule: Poliovirus

Prepared as part of a Ministry of Health contract

by

Dr Helen Petousis-Harris, Immunisation Advisory Centre (PI and Lead author)

Dr Nikki Turner, Immunisation Advisory Centre

Dr Mary Nowlan, Immunisation Advisory Centre (Editor)

This review is one of a series of 18 antigen reviews presented in 15 individual reports.

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Abbreviations

ACIP	Advisory Committee on Immunisation Practices
AFP	Acute Flaccid Paralysis
AEFI	Adverse Event Following Immunisation
CDC	Centers for Disease Control and Prevention
ESR	Institute of Environmental Science and Research Ltd
GPEI	Global Polio Eradication Initiative
GBS	Guillain-Barré Syndrome
HiB	*Haemophilus influenza* type B
IPV	Inactivated polio vaccine
MMR	Measles, mumps, rubella
Polio	Poliomyelitis
NZ	New Zealand
NZPSU	NZ paediatric surveillance unit
OPV	Oral polio vaccine
SAE	Serious Adverse Event
US	United States
UK	United Kingdom
VAPP	Vaccine-Associated Paralytic Poliomyelitis
VAERS	Vaccine Adverse Events Reporting System
WHO	World Health Organization

Acknowledgements

The Immunisation Advisory Centre (IMAC) and the University of Auckland appreciates the opportunity to undertake literature reviews of the specific vaccines under consideration for, or currently in use for the NZ national immunisation programme. This work was commissioned by the Ministry of Health, to inform decision-making for changes to the schedule and to enable up-to-date clinical guidelines to be incorporated into the NZ Immunisation Handbook 2014. These documents were prepared by IMAC, in collaboration with Environmental Science and Research (ESR), under contract to the Ministry of Health, and were reviewed by members of the Prescription and Therapeutics Advisory Committee (PTAC) immunisation subcommittee 2013 to Pharmac. The authors would also like to acknowledge Val Grey, Graphic Designer, Faculty of Medical and Health Sciences, The University of Auckland, for her assistance with design and layout of these documents.

1. Background

Poliomyelitis (polio) is a highly transmissible infectious disease caused by poliovirus, a small, non-enveloped enterovirus of the family Picornaviridae. There are three serotypes of poliovirus (types 1, 2 and 3). Poliovirus infection occurs principally person-to-person via the faecal-oral route. The virus is ingested and replicates in the gut, mostly without causing symptoms, and is then excreted in faeces. Transmission can be enhanced by poor sanitation.

As most cases are asymptomatic, poliovirus can spread widely before a case of paralysis is seen. Infection is clinically inapparent in up to 95% of infections, and ranges in severity from a non-paralytic fever to viral meningitis and flaccid paralysis. Rarely, in less than 1% of cases, the virus can invade the nervous system, causing acute flaccid paralysis (AFP), usually involving the legs. Paralysis is more common in adults, occurring in up to one in 75 cases of infection.

There are several routes of poliovirus transmission. In most developing countries, the most important route is faecal-oral. Factors that affect transmission of the virus include extent of crowding, levels of hygiene, water quality, and sewage handling facilities. In areas with good sanitary conditions and uncontaminated drinking water, other routes of transmission are probably more important. Since the virus also replicates in the upper respiratory tract, polioviruses are spread through upper respiratory tract secretions as well. Past natural infection with wild poliovirus and vaccination with OPV significantly reduce the extent and duration of poliovirus shedding. Enhanced potency IPV and competing enteric infections may also reduce the extent and duration of stool shedding to a lesser degree (1).

Since the late 1950s, polio has been controlled by effective use of live oral and inactivated polio vaccines. Following eradication of polio most high income countries have switched to inactivated polio vaccines, to prevent the possibility of vaccine-associated paralytic polio, a rare consequence of OPV vaccines.

In 1988, the World Health Assembly committed to the goal of eradicating polio by ending the transmission of wild polio viruses by 2000 (2). When the programme started in 1988, there were 125 countries with endemic poliovirus and an estimated 350,000 children were paralysed each year. By 2006, there were just four countries with endemic polio – India, Nigeria, Afghanistan and Pakistan and globally, cases had dropped by 99%. Since 2000, cases have fluctuated between 2000 and 4500 a year and the goal has not to date been achieved, particularly with respect to eradicating types 1 and 3. However in 2012, case numbers came down to a historic low (222 wild polio cases and an additional 67 vaccine-associated cases) and focused on three countries still with endemic polio: Nigeria, Pakistan and Afghanistan. In May 2011, the World Health Assembly declared the persistence of polio a 'programmatic emergency for global public health'. In response, the Global Polio Eradication Initiative (GPEI) released its new Polio Global Emergency Action Plan for 2012-2013, replacing the earlier failed strategic plan (3). On the 8th February 2013, two health facilities in Nigeria were attacked, killing 11 people including health workers providing polio vaccination, further hindering progress towards eradication in that country.

There remain complex issues to full eradication – particularly with the continued use of the live-attenuated OPV vaccine, which has the potential to perpetuate circulating outbreaks of vaccine-derived polioviruses (2). Programmatic delivery challenges, including anti-immunisation sentiment resulting in violence to healthcare workers involved in delivering polio campaigns, also continue to be problematic (4).

2. Methodology for review

2.1 Objectives

The objectives for this review have been informed by the general specifications for the 2012 New Zealand (NZ) antigen review. These are listed below. The dates for publication are between 2009 and 2012 as per the brief. This is not a systematic review or a critique of the literature. The choice of articles reviewed is based on the purposeful selection of recent reviews and studies that may best inform policy discussions around polio vaccines for NZ.

- General specifications
  - Safety
  - Effectiveness
  - Implementation issues (practicality and possible impact on uptake)
  - The differences that need to be considered for each age group such as the variable severity of diseases and issues for vaccination
  - Different options of placement on the schedule, based on international findings and best practice
  - Different vaccine options and comparisons between the options

As polio antigen is usually included as part of multivalent vaccines that have been reviewed in more detail as priorities for NZ this review will not repeat some of the detail for the routine DTaP-containing vaccines. The reviews for both pertussis and tetanus include additional information on these vaccines.

2.2 New Zealand Epidemiology

The NZ epidemiology of polio is provided by Institute of Environmental Science and Research Ltd (ESR) and summarises the results from polio surveillance in NZ in section 3. It consists of data from notifiable disease system as well as AFP surveillance.

2.3 Literature search strategy

The general specifications have formed the focus of the literature search:

Medline search terms and strategy

MeSH term: Polio, focus, all subgroups

12287

Limit to Humans, English, 2009 – current

421

NOT Cost* Attitud* Survey

385

NOT Qualitative Interview

381

NOT Oral

Remove duplicates

223 (keep and view)

Cochrane Library search terms and strategy

Search term Polio Vaccin*

2 results (keep and view)

Scopus search terms and strategy

Polio Vaccin* Published 2011 – present

1034

Limit to: Medicine, humans, English

1031

Exclude Letter, Short survey, editorial

628

Reject Social Science, Arts and Humanities, Veterinary articles.

474

Exclude Oral poliomyelitis vaccine

338 (keep and view)

Delete duplicates

Final Endnote Library 309 Articles

2.3.1 Grey literature

Five reports and seven books were accessed

2.3.2 Additional searches

Where questions arose additional searches were undertaken to ensure there was no further available data. Where articles were missing they were accessed and added to the library. A further 267 articles were accessed.

2.3.3 Final library

The final library includes 576 references. Where systematic reviews and/or meta-analysis were available the preceding literature has been excluded from the review.

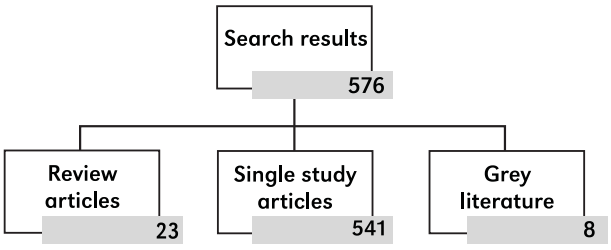

Figure 1. Flow of selection of articles for review

2.4 Participants/populations

The population for a potential universal programme are infants and children under two years of age and un- or under-immunised persons.

2.5 Interventions

The interventions included are inactivated polio vaccines, both currently used in NZ, or likely to be available and used in NZ. For childhood schedules, IPV is combined with DTaP-based combinations of which most are produced by GlaxoSmithKline and sanofi-pasteur. Many studies evaluate these combination vaccines simultaneously. Responses to poliovirus vary inconsistently and few achieve statistical significance. The information on vaccine formulation for each vaccine is derived from the product data sheet.

2.5.1 Infanrix®-hexa

Infanrix®-hexa (GlaxoSmithKline) is a subunit vaccine. Each dose contains diphtheria toxoid (≥30IU), tetanus toxoid (≥40IU), *Bordetella pertussis* antigen (pertussis toxoid 25µg, filamentous haemagglutinin 25µg, pertactin 8µg), inactivated poliovirus (type 1: Mahoney strain 40DagU, type 2: MEF-1 strain 8DagU, type 3: Saukette strain 32DagU), hepatitis B surface antigen (10µg) and *Haemophilus influenzae* type b (Hib) polysaccharide (10µg) conjugated to tetanus toxoid as a carrier protein. The diphtheria, tetanus, and pertussis components of Infanrix-hexa are the same as those in Infanrix®. The vaccine contains adjuvants of aluminium hydroxide, hydrated (0.5mg) and aluminium phosphate (0.32mg) and residuals of neomycin and polymyxin B.10. Manufacture of the vaccine includes exposure to bovine materials sourced from countries without undue risk of bovine spongiform encephalopathy (BSE). The vaccine can be administered up to the seventh birthday. The vaccine is supplied as a suspension of DTaP-IPV-HepB and a vial of lyophilised Hib powder. The Hib powder must be added to the suspension before administration.

2.5.2 Hexaxim®

Hexaxim® is a diphtheria toxoid (≥20IU), tetanus toxoid (≥40IU), *Bordetella pertussis* antigens (pertussis toxoid 25µg, filamentous haemagglutinin 25µg), inactivated poliovirus (type 1 Mahoney strain 40DagU, type 2: MEF-1 strain 8DagU, type 3: Saukette strain 32DagU) and *Haemophilus influenzae* type b (Hib) polysaccharide (10 µg) conjugated to tetanus toxoid as a carrier protein conjugated to tetanus protein vaccine. The vaccine contains adjuvants aluminium

hydroxide, hydrated (0.6 mg). The vaccine may contain traces of glutaraldehyde, formaldehyde, neomycin, streptomycin and polymyxin B which are used during the manufacturing process.

2.5.3 Adacel®-Polio

Adacel®-Polio (sanofi) is a subunit vaccine. Each dose contains pertussis toxoid 2.5µg, filamentous haemagglutinin 5µg, pertussis fimbriae types 2 and 3, 5µg, reduced diphtheria toxoid (≥2IU), tetanus toxoid (≥20IU) inactivated poliovirus (type 1: Mahoney strain 40DagU, type 2: MEF-1 strain 8DagU, type 3: Saukette strain 32DagU). The vaccine contains aluminium adjuvant (0.33mg). Manufacture of the vaccine includes exposure to bovine materials.

2.5.4 Pentacel®

Pentacel® (sanofi) is a subunit vaccine. Each dose contains diphtheria toxoid (≥30IU), tetanus toxoid (≥40IU), *Bordetella pertussis* antigen (pertussis toxoid 20µg, filamentous haemagglutinin 20µg, pertussis fimbriae types 2 and 3 5µg and pertactin 3µg), inactivated poliovirus (type 1: Mahoney strain 40DagU, type 2: MEF-1 strain 8DagU, type 3: Saukette strain 32DagU) and *Haemophilus influenzae* type b (Hib) polysaccharide (10µg) conjugated to tetanus toxoid as a carrier protein. The vaccine contains aluminium adjuvant (0.33mg) and residuals of neomycin and polymyxin B. The manufacture of this product includes exposure to bovine materials. The vaccine is supplied as a suspension of DTaP-IPV and a vial of lyophilised Hib powder.

2.5.5 Boostrix®-IPV

Boostrix®-IPV and Boostrix® Polio (GlaxoSmithKline) is a subunit vaccine. Each dose contains reduced diphtheria toxoid (≥2IU), tetanus toxoid (≥20IU), *Bordetella pertussis* antigen (pertussis toxoid 8µg, filamentous haemagglutinin 8µg, pertactin 2.5µg) and inactivated poliovirus (type 1: Mahoney strain 40DagU, type 2: MEF-1 strain 8DagU, type 3: Saukette strain 32DagU). The vaccine contains adjuvants of aluminium hydroxide, hydrated (0.3mg) and aluminium phosphate (0.2mg). Manufacture of the vaccine includes exposure to bovine materials.

2.5.6 Infanrix® IPV

Infanrix®-IPV and Kinrix (GlaxoSmithKline) are identical subunit vaccines. Each dose contains diphtheria toxoid (≥30IU), tetanus toxoid (≥40IU), *Bordetella pertussis* antigen (pertussis toxoid 25µg, filamentous haemagglutinin 25µg, pertactin 8µg) and inactivated poliovirus (type 1: Mahoney strain 40DagU, type 2: MEF-1 strain 8DagU, type 3: Saukette strain 32DagU). The diphtheria, tetanus, and pertussis components of Infanrix-IPV are the same as those in DTaP (Infanrix®). The vaccine contains aluminium adjuvant (<0.6mg by assay) and residuals of neomycin and polymyxin B. Manufacture of the vaccine includes exposure to bovine materials.

2.5.7 Quadracel®

Quadracel® (sanofi) is a subunit vaccine. Each dose contains diphtheria toxoid (≥30IU), tetanus toxoid (≥40IU), *Bordetella pertussis* antigen (pertussis toxoid 20µg, filamentous haemagglutinin 20µg, pertussis fimbriae types 2 and 3 5µg and pertactin 3µg) and inactivated poliovirus (type 1: Mahoney strain 40DagU, type 2: MEF-1 strain 8DagU, type 3: Saukette strain 32DagU). The vaccine contains aluminium phosphate as an adjuvant (1.5mg) and residuals of neomycin and polymyxin B. The manufacture of this product includes exposure to bovine materials.

2.5.8 Revaxis®

Revaxis® (sanofi) is a subunit vaccine. Each dose contains reduced diphtheria toxoid (≥2IU), tetanus toxoid (≥20IU) and inactivated poliovirus (type 1: 40DagU, type 2: 8DagU, type 3: 32DagU). The vaccine contains aluminium hydroxide adjuvant (0.35mg).

2.5.9 Pentaxim®

The DTaP–IPV//PRP~T combined vaccine, Pentaxim®, is supplied as a freeze-dried PRP~T component that is reconstituted immediately prior to vaccination with an injectable suspension of DTaP–IPV. The PRP~T and IPV components are also licensed as monovalent vaccines under the trade names ActHib™ (sanofi pasteur) and Imovax Polio™ (sanofi pasteur), respectively, and are both WHO prequalified.

2.5.10 IPOL®

IPOL® (inactivated poliomyelitis vaccine), produced by sanofi pasteur S.A., is a suspension of three strains of inactivated poliovirus: Type 1 (Mahoney), Type 2 (MEF-I) and Type 3 (Saukett). The viruses are grown in cultures of Vero cells, then concentrated, purified and made non-infectious by inactivation with formaldehyde. Each 0.5mL dose contains: 40D antigen units Inactivated Polio virus type 1 (Mahoney), 8D antigen units Inactivated Polio virus type 2 (MEF-1), 32D antigen units Inactivated Polio virus type 3 (Saukett), and 2 – 3µl 2-phenoxyethanol, 2 – 20µg formaldehyde, up to 0.5mL Medium-199, as excipients.

2.6 Study designs

The studies included in this update are meta-analysis, systematic reviews, reviews, randomised controlled trials, and observational studies using database matching.

3. Epidemiology

3.1 Global epidemiology of polio

The Western Pacific was declared polio free in 2000, which further decreases the risk for polio importation into NZ.

3.2 New Zealand epidemiology of poliomyelitis

NZ has been free of the wild transmission of polio for 50 years (April 1962). Since this time, there have been rare laboratory confirmed cases of vaccine-associated paralytic polio myelitis (VAPP). Since the replacement of oral polio vaccine with inactivated vaccine, this is no longer a risk (5).

Polio became a notifiable disease in NZ in 1914, and data on the incidence since 1915 are available. The legal basis for notification of polio comes through the Health Act 1956. Medical Officers of Health in NZ notify poliomyelitis on suspicion. As a result of successful polio immunisation, wild-type poliovirus infection has been eliminated in NZ since the 1970s.

As part of the global polio eradication programme, NZ paediatric surveillance unit (NZPSU) was established to investigate all acute flaccid paralysis (AFP) cases. All AFP cases are required to have appropriate stool samples collected and tested in the WHO National Polio Reference Laboratory at ESR to distinguish cases caused by wild-type poliovirus from those cases associated with the use of live OPV- Sabin. The notifiable disease system and AFP surveillance forms the basis for generating polio epidemiology data in NZ.

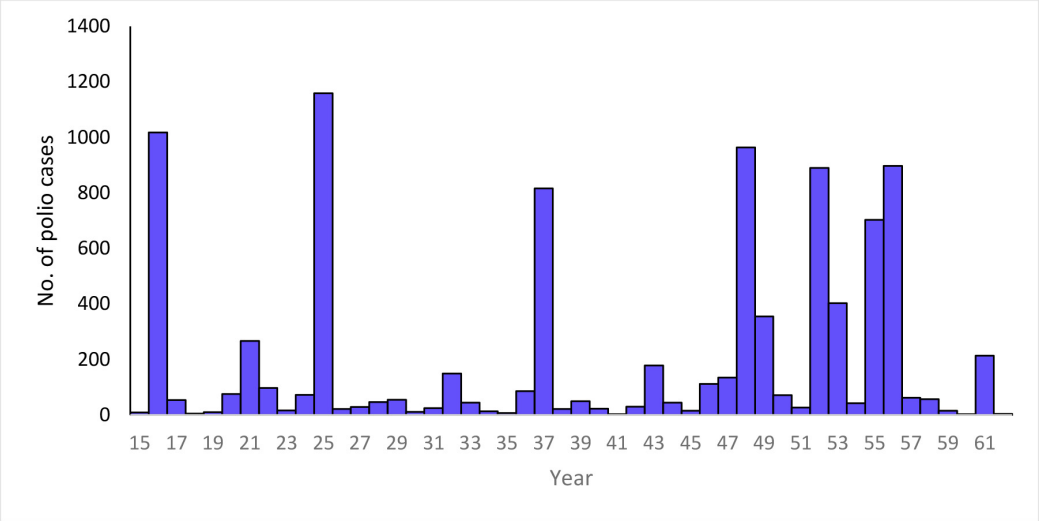

Figure 2. Poliomyelitis cases in New Zealand 1915-1962

There were no polio cases notified in 2011. Since the mass oral polio vaccine immunisation campaigns in NZ in 1961 and 1962, a total of six polio cases have been reported. All of these cases were either laboratory-confirmed as vaccine associated (four cases) or classified as probable vaccine-associated cases (two cases). Based on the limited information available, the cases in 1970 are most likely to have been vaccine-associated, one in a vaccine recipient and the other in a contact. The diagnosis of the 1977 case was poliomyelitis of unknown aetiology. The case was four years old who had completed a three-dose course of OPV at 18 months of age. No poliovirus was isolated. The 1990 case was reported to be vaccine-associated and occurred in an unimmunised adult contact of a recently vaccinated infant.

In addition to these four notified cases, there was a case of imported polio in 1976. The case was a three month old child from Tonga, who was hospitalised on arrival in NZ and diagnosed with polio. The results of any culture for poliovirus are not known. A possible case in a five year old Indian child, who had arrived in NZ a few days before the onset of paralysis, was reported in 1990. The case was finally diagnosed as Guillain-Barré syndrome (GBS).

In 1998, a case of vaccine-associated paralytic poliomyelitis (VAPP) case was notified from a four month old boy (Figure 3). The paralysis developed 14 days after the child received his second dose of oral polio vaccine. Sabin vaccine strain type 3 was isolated from his faecal specimen. In 1999, the second and probably the last case of indigenous VAPP case was notified from an unimmunised mother following her infant's first dose of the vaccine.

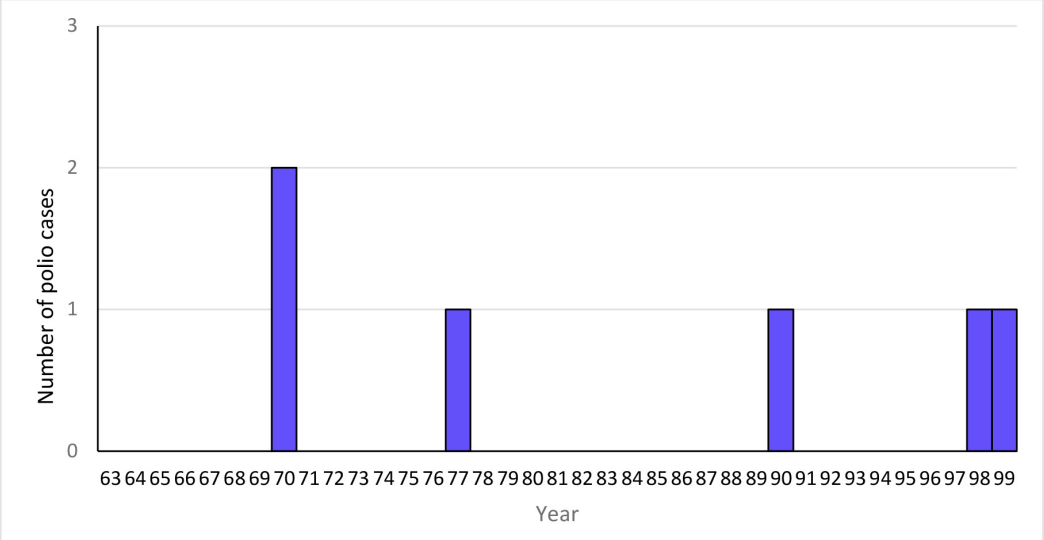

Figure 3. Poliomyelitis cases in New Zealand 1963-1999

3.3 Switch polio vaccine from OPV to IPV in New Zealand

Persistent circulation of OPV viruses increases the risks of reversion to fully neurovirulent vaccine-derived poliovirus strains in unvaccinated populations. The change from OPV to IPV in NZ provided excellent opportunity to monitor the persistence of OPV viruses excreted by the last cohorts of children immunised with OPV (6). NZ's paediatric-inpatient surveillance found that 6.9% of children excreted vaccine polioviruses before this switch, but none by one month afterwards. Acute flaccid paralysis and enterovirus surveillance detected poliovirus only once following the transition. Environmental surveillance identified polioviruses in sewage samples until May 2002 (Figure 4), after which they were detected infrequently. Intratypic differentiation and sequencing showed all polioviruses were Sabin-like. Multiple surveillance methods found OPV strains did not persist for extended periods following a vaccine switch in a developed country with a temperate climate. Sequence homology with Sabin vaccine parent strains indicated polioviruses detected more than four-months after the switch were of recent origin, consistent with importation from OPV-using countries.

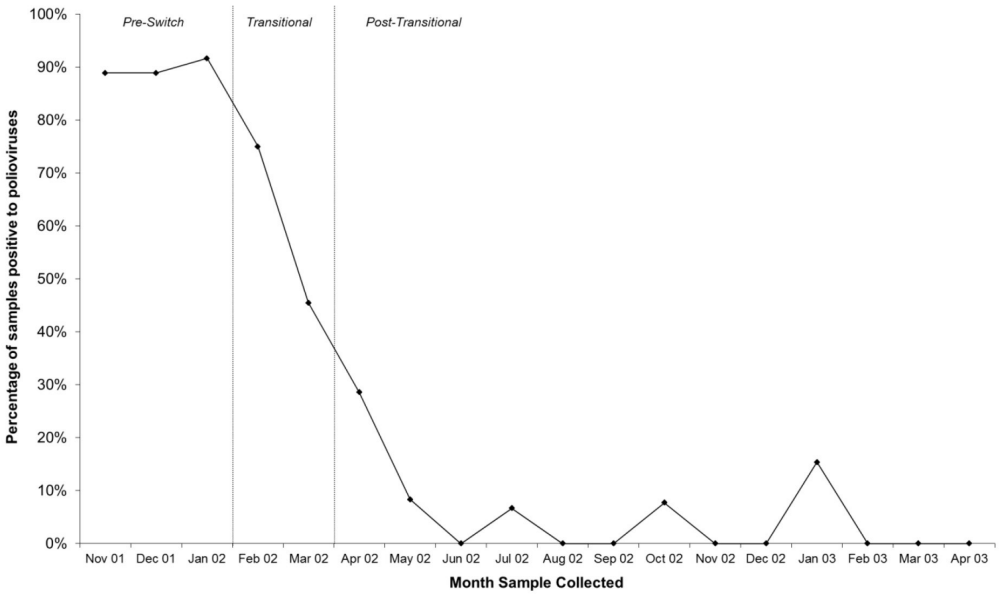

Figure 4. Poliovirus prevalence between November 2001 and April 2003 by environmental surveillance

3.4 Summary of polio epidemiology

NZ has been free of the wild transmission of polio for 50 years. During this time, there have been rare cases of vaccine-associated paralytic polio myelitis (VAPP), all of which were laboratory confirmed. There were no polio cases notified in 2011. Since polio immunisation In NZ beginning in 1961 and 1962, a total of six polio cases have been reported. All of these cases were either laboratory-confirmed as vaccine associated (4 cases) or classified as probable vaccine-associated cases (2 cases).

Following the change from OPV to inactivated polio vaccine (IPV) in 2000, there was a rapid reduction in the proportion of children excreting polio virus and by one month after introduction of IPV no children were excreting the virus.

4. Safety

4.1 Objective

The objective of this section is to review the most recent safety data for currently licenced IPV vaccines. The focus is on the new generation vaccines with some consideration for any recent updates to IPV. Only Adverse Events Following Immunisation (AEFI) that have been considered subsequent to the pivotal clinical efficacy trials are reviewed here and any major clinical differences between vaccine types.

4.2 Outcomes

Outcomes are vaccine safety including adverse events following immunisation (AEFI) and serious adverse events (SAE). Excluded is reactogenicity (injection site reactions and minor systemic reactions).

4.3 Review

Polio antigen alone has a low reactogenicity profile when compared with other antigens, and when added to multivalent vaccine, it does not increase reactogenicity. IPV-containing vaccines are used in over 100 countries with annual doses of 35-45 million infants and children receiving a course every year. Generally, the rates of adverse events are low with no clustering in any single category. Vaccine adverse events reporting system (VAERS) data for 1991-1998 were reviewed by the Centers for Disease Control and Prevention (CDC) for events attributable to IPV and no changes were observed to occur when compared with OPV data (1).

4.3.1 Combination vaccines that include polio antigen

4.3.1.1 Preterm infants

A review article, summarising more than a decade of experience with the hexavalent combination DTaP-IPV-HepB/Hib (Infanrix®-hexa) vaccine, concluded that the vaccine is generally well tolerated in pre-term (24 – 36 weeks gestation) and/or low birth weight (820 – 2020 grams) infants (7).

4.3.1.2 Infants, toddlers and children aged <seven years

A review of 11 safety studies of the hexavalent combination Infanrix®-hexa, conducted over eight years, identified the most commonly reported local reactions in all published studies have been mild and transient pain, redness and/or swelling at the injection site and fever, irritability and/or drowsiness. Across five of these studies, tolerability of Infanrix®-hexa was generally similar or superior to that of the control vaccines (separate doses of DTaP-IPV-HepB + Hib [2], DTaP-IPV-Hib + HepB [2] or DTaP + HepB + OPV + Hib [1]). Following primary vaccination doses, a low incidence (0 – 10% of doses administered) of solicited, clinically significant AEFI, which prevent normal daily activities, have been reported in the first four to eight days post-vaccination. SAE are rare (2.6% in ≥2000 infants administered) and most of which were common childhood disorders considered unrelated to vaccination, such as respiratory and urinary tract infections and gastrointestinal disorders (8).

A summary of passively reported events to the manufacturer since licensure are presented in Table 1 (8).

Table 1. Most frequent adverse events for DTaP-IPV-HepB/Hib (Infanrix®-hexa) from launch up to 2008, spontaneously reported to the GlaxoSmithKline worldwide safety database (OCEANS)

AE	Number of AEs	Frequency per 100,000 doses
Pyrexia	1572	5.9
Injection-site erythema	570	2.1
Injection-site swelling	488	1.8
Crying	465	1.7
Injection-site reaction	294	1.1
Injection-site induration	256	1.0
Hypotonia	2218	0.8
Urticaria	210	0.8
Pallor	200	0.8
Erythema	196	0.7

AE: Adverse event; DTaP-IPV-HepB/Hib: Diphtheria, tetanus, acellular pertussis, inactivated polio vaccine, hepatitis B/*Haemophilus influenzae* type b vaccine; OCEANS: Operating Companies Event Accession and Notification System

4.3.1.2.1 Febrile events infants and toddlers less than 18 months of age

Fever is a common AEFI and a necessary causal factor for febrile seizures. A large six year study of Danish children, aged three – 18 months of age who received three doses of DTaP-IPV-Hib (Ditekipol/Act-Hib®) vaccine, assessed the relative risk of febrile seizures. The highest risk of febrile seizures during the first seven days post-vaccination was found to be on the day of the first vaccination and on the day of the second vaccination, but not on the day of the third vaccination (Table 2) (9).

Table 2. Risk of febrile seizures after DTaP-IPV-Hib vaccination (9)

	Time after vaccination (days)			
Analysis method	0	1 – 3	4 – 7	0 – 7
First vaccination				
No. of vaccinations	298,311	317,741	329,138	329,521
Children with febrile seizures	9	6	2	17
Adjusted HR[a] (CI 95%)	6.02 (2.86 – 12.65)	1.38 (0.58 – 3.31)	0.41 (0.10 – 1.81)	1.64 (0.93 – 2.88)
Second vaccination				
No. of vaccinations	339,276	339,252	339,196	339,288
Children with febrile seizures	12	14	6	32
Adjusted HR[a] (CI 95%)	3.94 (2.18 – 7.10)	1.57 (0.91 – 2.72)	0.52 (0.23 – 1.18)	1.36 (0.93 – 1.98)
Third vaccination				
No. of vaccinations	320,049	319,846	319,473	320,049
Children with febrile seizures	27	68	106	201
Adjusted HR[a] (CI 95%)	1.07 (0.73 – 1.57)	0.89 (0.70 – 1.14)	1.06 (0.86 – 1.28)	0.99 (0.86 – 1.15)

Abbreviations: DTaP-IPV-Hib - diphtheria, tetanus, acellular pertussis, inactivated polio vaccine, *H. influenzae* type b vaccine; HR - Hazard ratios; a - Adjusted for gender, multiple birth, calendar year of birth (one year interval), seasons of birth, gestational age, birth weight, parity of mother, parental history of epilepsy, maternal education, and family income at time of birth.

The relative risk of febrile seizures was increased on the day of the first two vaccination events, although the absolute risk was <4 per 100,000 doses. Compared with the unvaccinated cohort, the risk of recurrent or subsequent febrile seizures was not increased nor was the vaccine associated with an increased risk of epilepsy (9).

4.3.1.2.2 Extensive injection site reactions

With all DTaP-containing vaccines, the frequency and severity of swelling at the injection site increases with age and additional doses of vaccine. A greater incidence of local symptoms, including swelling >50mm at the injection site or extensive limb swelling, were observed after the administration of Infanrix®-hexa booster dose in the second year of life than were seen after the administration of primary doses (8).

As Infanrix®-hexa (DTaP-IPV-HepB/Hib) and Infanrix®-IPV (DTaP-IPV) contain the same tetanus, diphtheria and acellular pertussis components an increase in the incidence of injection site swelling following a booster vaccination/fourth dose using Infanrix®-IPV at four years of age would be expected (10-12).

A study of 76 healthy four to five year old Canadian children, who had previously received four doses of DTaP-IPV-Hib (Pentacel), with the last dose at 18 months of age, found that injection site redness ≥5mm following a booster vaccination with DTaP-IPV (Quadracel®) was twice as frequent in those who had pre-vaccination cell mediated immunity (defined as a mixed T_H1/T_H2 type by cytokine profile for all antigens) against diphtheria and tetanus or pertussis fimbriae types 2 and 3 compared to children without, suggesting a pre-existing immune memory is related to increased or extensive local reactions (13).

A small study of 53 Australian children aged four - six years, who had previously experienced extensive swelling at the injection site after a fourth dose of DTaP (Infanrix®) vaccine, showed an increased likelihood of an extensive site reaction after a fifth dose of DTaP administered at four - six years of age (85.2% recurrence rate) compared with 61.5% of children who received a reduced-antigen tetanus, diphtheria and acellular pertussis (Tdap; Boostrix®) vaccine (14).

4.3.2 Co-administration of IPV combination vaccines

4.3.2.1 DTaP-IPV

4.3.2.1.1 Infanrix®-IPV or Kinrix with measles, mumps, rubella and varicella vaccines

Safety and reactogenicity of co-administration of DTaP-IPV (Infanrix®-IPV) with MMR (measles, mumps, rubella, M-M-R® II) alone (n=237) or MMR and a separate varicella (Varivax®) vaccines (n=239) in four-six year old children was assessed in a US based study.

Reports of systemic and local reactogenicity at the DTaP-IPV injection site were similar between the two vaccine groups. Between 24.8% and 33.9% of participants reported any one symptom of drowsiness, loss of appetite or fever. Few participants (2.6%) reported systemic AEFI that prevented normal daily activities. Extensive swelling at the injection site was reported by 35 participants (DTaP-IPV site [n=34], MMR site [n=1]). Extensive swelling extended to an adjacent joint, maximum recorded diameter 210mm, in one participant who received DTaP-IPV and MMR. One SAE was reported, but not considered related to vaccination: croup after receipt of DTaP-IPV and MMR (15).

4.3.3 Tdap-IPV vaccines

4.3.3.1 Toddlers and children aged four to eight years

The most common AEFI were identified as pain (40 – 56%), redness (34 – 53%) and swelling (24 – 45%) at the injection site, according to unpublished data on AEFI, in four to six year olds (n=703) and six to eight year olds (n=118) following receipt of Tdap (Boostrix®) or Tdap-IPV (Boostrix®-IPV) and three published studies of Tdap (Boostrix® or Adacel®) or Tdap-IPV (Boostrix®-IPV) in four to six year olds (combined n=609) administered as a fifth dose of diphtheria, tetanus and acellular pertussis vaccine (16).

4.3.4 Tdap vaccination following a previous Td vaccination

A study in France assessed safety and reactogenicity of a Tdap-IPV (Repevax®) when administered one month following placebo or Td-IPV (Revaxis®) in 500 adults aged 18 – 40 years who had previously received five to eight doses of combination tetanus, diphtheria and polio vaccines prior to 18 years of age with their last vaccination received more than five years previously. Participants received Td-IPV followed by Tdap-IPV 21 – 46 days later (n=242) or placebo followed by Tdap-IPV 25 – 42 days later (n=242) (17).

Within 14 days of the first vaccination, 75.9% of Td-IPV recipients and 33.1% of placebo recipients reported at least one AEFI. Local reactions at the injection site were reported by 12% and 69.9% respectively. Systemic reaction was reported by 24.3% and 32.5% of participants.

Immediately after the second vaccination with Tdap-IPV, one participant who had previously received Td-IPV experienced malaise and neck rigidity within 30 minutes of Tdap-IPV injection, which resolved the same day; it was assessed to be unlikely to be vaccine related, lasting eight days. There were no immediate AEFI in participants who received Tdap-IPV after placebo.

After the second vaccination, the percentage of participants who reported pain and swelling at the injection site was lower in those who received Tdap-IPV after Td-IPV (85.1%) than in those who received Tdap-IPV after placebo (93.4%). The percentage of participants who reported redness at the injection site was similar in both groups. Participants previously given Td-IPV reported severe swelling at the injection site less frequently than those previously given placebo (1.2% vs. 7%). There were no reports of extensive swelling of the vaccinated limb or severe discomfort.

The percentage of participants who reported at least one systemic AEFI (related or unrelated to vaccine) was similar in both groups. No differences were observed for fever, headache or myalgia. Headache, approximately in one fifth of participants, was the most frequently reported systemic AEFI in both groups.

Three SAE were reported, none of which were considered related to vaccination: one case of each - severe knee sprain after placebo for dose one, severe vasovagal syncope six days after Td-IPV for dose one and severe hydrocephalus related to a colloid cyst 15 days after Tdap-IPV following placebo. Overall, reporting of at least one AEFI was lower in the group who received Tdap-IPV after Td-IPV (88.8%) than after placebo (94.6%) (17).

4.4 Summary vaccine safety

There is no recent data on monovalent IPV vaccines. No new safety concerns have been raised for the polio antigen containing combination vaccines. The frequency and severity of local reactions increases with age and additional doses of vaccine.

A range of DTaP-IPV combination vaccines have been demonstrated to be safe and generally well tolerated in preterm infants born after 24 weeks and/or low birth weight infants at least 820 grams at birth, infants, toddlers and children up to seven years of age.

DTaP-IPV combination vaccines have been demonstrated to be safe when co-administered with routine vaccines in infants, toddlers and children.

5. Immunogenicity, efficacy, effectiveness and vaccine impact

5.1 Objective

The objective of this section is to review the most recent performance data for currently licenced IPV-containing vaccines. The focus is on the new generation vaccines with some consideration for any recent updates. Consideration is given to relevant immunogenicity data, efficacy and effectiveness studies that contribute to the current understanding of the effectiveness of IPV vaccines and evidence their impact in populations.

5.2 Outcomes

The outcomes considered for this review are:

- Immunogenicity
- Efficacy of IPV
- Duration of protection
- Herd Immunity

5.3 Review

Poliovirus-neutralising antibodies are considered to be the established correlate of protection. Immune responses to IPV depend on the antigen concentration, timing and number of doses and the type of vaccine (adjuvanted etc.). Maternal antibody can interfere with early doses. Generally, the percentage of subjects with neutralising antibodies over the 1:8 threshold is considered the sero-protection rate (1).

5.3.1 Immunogenicity

The immunogenicity of Infanrix-hexa is well established. The seroprotective rates resulting from a variety of schedules with this vaccine are presented Table 3 (8).

Table 3. Representative studies showing immunogenicity of primary vaccination with Infanrix®-hexa administered according to different schedules adapted from (8).

Schedule (months)	Country (n)	% Infants achieving seroprotection 1 month after completing primary series.		
		Anti-polio ≥1:8		
		Type 1	Type 2	Type 3
2-3-4 no HBV at birth	Germany (145)	100.0	99.0	100.0
2-4-6 no HBV at birth	Spain (40)	100.0	96.9	100.0
3-4-5 no HBV at birth	Germany (416-472)	99.8	99.0	100.0
3-5-11 with no HBV at birth	Germany and Italy (177)	98.8 (100)†	95 (100)†	99.4 (100)†
6-10-14 weeks	Phillippines (320: 160 with HBV; 160 no HBV at birth)	≥94.5	≥94.5	≥94.5
† at one month after 2nd dose (3rd dose)				

5.3.1.1 Immunogenicity of Infanrix®-hexa given at 3, 5 and 11-12 months

Infant vaccines are delivered in a schedule that can be compromised because of the need to balance the local epidemiology and the need to induce protection early. Lower immunogenicity is often observed when vaccinations are given at a young age and close together.

Some countries with low infectious disease pressure and high immunisation coverage, such as Denmark, Iceland, Sweden, Finland, Italy, Norway and Austria, have adopted a 2+1 schedule with primary doses at three and five months followed by a booster at 11 or 12 months.

In order to more fully describe the immunogenicity of Infanrix-hexa, when given as a 2+1 schedule at 3, 5 and 11-12 months, a range of open label and single-blind studies were conducted in Slovakia, Germany, Italy, Finland and Sweden between 1998-2005. A total of 702 healthy infants were given Infanrix®-hexa at 3, 5 and 11-12 months of age. One month after dose two, between 96.3% and 100% of subjects had seroprotective antibodies against diphtheria, tetanus, hepatitis B and poliovirus types 1, 2 and 3; 91.7% against Hib and ≥99.0% were seropositive for each pertussis antigen. One month after booster dose, 98.9–100% of subjects were seroprotected for all vaccine antigens. Robust booster responses were observed after the third dose, as shown 6.7–52.9 fold increases in GMT for each vaccine antigen (18).

5.3.1.2 Immunogenicity of Pentaxin (Pentavac)

The immunogenicity of the sanofi pentavalent vaccine, Pentaxim®, was summarised in a 2011 expert review of the 16 years clinical experience. One month after a three-dose primary vaccination with Pentaxim, 92.2–100% of infants achieve seroprotective levels of anti-diphtheria (≥0.01 IU/ml) anti-tetanus (≥0.01 IU/ml), antipolio types 1, 2, 3 (≥1:8 1/dilution) and anti-PRP (≥0.15 µg/ml) antibodies. The seroconversion rate is 83.9–100% for pertussis antigens (anti-PT and anti-FHA). The review also found that that Pentaxim immunogenicity was not affected by co-administration with other childhood vaccines (19).

5.3.2 Efficacy of IPV

The original field trials of monovalent IPV included 400,000 children randomly assigned to vaccine or placebo and another where 200,000 children were vaccinated and observed alongside unvaccinated children. The efficacy was calculated to be 80-90% against paralytic polio and 60-70% against all from of polio. Subsequently the efficacy of the vaccine is considered over 90% (1).

5.3.3 Herd immunity

There is evidence for herd immunity as provided by IPV. In summary, when IPV was introduced in the United States (US) in 1955, the effectiveness was greater than that expected based on number of people vaccinated. More recently in the Netherlands, polio outbreaks among unvaccinated exclusive religious groups in the 1970s resulted in around 200 cases. Despite this, the large number of unvaccinated people in the general population remained unaffected. The role of herd immunity is less clear in populations where the faecal-oral route is the predominant method of transmission (1). The basic reproduction number for polio is estimated to be two-20 and the crude herd immunity threshold 50-95%. The uncertainty around these wide estimates is due to variation in hygiene standards (20).

A German study analysed serum samples in three separate years – 2001, 2005 and 2012, testing 1,632 serum samples, overall. It demonstrated relatively low levels of immunity to poliovirus-3 from 76.6% - 72.9% (95% CI 72.2 – 80.6%) compared with poliovirus-1 at 84.2% - 90.4% and poliovirus-2 at 89.8% - 91.3%. The authors concluded that immunity to poliovirus-3 was insufficient in the German population to avert the danger of polio outbreaks, particularly, with globalisation and worldwide tourism and stressed the importance of maintaining a highly effective immunisation programme (21).

5.3.4 Duration of protection

Available data indicates persistence of antibodies up to school age, whether given in a vaccination schedule as 3+1, 2+1 or 3+0. There is no data beyond that as boosters are given at this time. There is a strong anamnestic response to the pre-school booster and duration of protection following this pre-school booster is expected to be long term, possibly lifelong (1).

5.4 Summary of effectiveness

Global use of polio vaccines has almost eradicated polio. Current IPV vaccines are highly immunogenic and appear to provide herd immunity in populations where oral-oral transmission is the primary route for infection. Duration of protection following a range of schedules including a preschool booster appears to provide long-term protection.

6. Age-specific issues

6.1 Objective

The objective of this section is to consider the evidence for offering the polio vaccine to different age groups.

6.2 Review

The only concern in NZ would be from an imported case. Over half of all cases reported are in children under three years of age. As most cases are asymptomatic, poliovirus can spread widely before a case of paralysis is seen. Recent German research has supported earlier studies suggesting that immunogenicity is lower for poliovirus 3 than for the other two (21). Hence the issues for NZ remain:

- Maintaining high immunisation coverage in the infant schedule and booster ages to maintain community immunity
- Vaccination of non-immune adults
- Good travel advice and booster vaccination for those travelling to the polio-endemic countries
- Continued maintenance of the NZ acute flaccid paralysis screening to maintain surveillance for the possible re-introduction of polio viruses

7. Vaccine options

7.1 Objective

The objectives for this section are to consider the different options available to NZ in terms of available polio vaccines and schedules.

7.2 Review

IPV is a mixture of the three polioviruses, made by formalin inactivation of purified cell culture supernatants.

The current major international manufacturers of IPV antigens are based in Europe. The majority of polio vaccines are manufactured from viruses grown on the Vero cell line as shown in Table 4. The only other cell substrate currently used in IPV production is a human diploid cell line (MRC-5) (1).

Table 4. Manufacturers of IPV (bulk antigen), reproduced with permission (1)

Manufacturer	Where made	Cell substrate
sanofi pasteur	France, Canada	Vero, MRC-5
GlaxoSmithKline	Belgium	Vero
Novartis	Italy	Vero
NVI	The Netherlands	Vero
Statens Serum Institute	Denmark	Vero

IPV is available as monovalent vaccines, and in tetravalent, pentavalent and hexavalent combinations with diphtheria, tetanus, acellular pertussis, and hepatitis B or Hib antigens.

The most widely used DTaP-based combinations containing IPV are produced by sanofi-pasteur and GlaxoSmithKline (see Table 5). sanofi-pasteur markets products in Europe based on the two component pertussis $DTaP_2$ (e.g. Tetrac, Tetraxim), and elsewhere, based on the Canadian five component pertussis $DTaP_5$ (e.g. Quadracel, Pentacel, Pediacel) including in the Western Hemisphere and Asia. GlaxoSmithKline markets a full range of three component pertussis-containing vaccines under the name of Infanrix® ($DTaP_3$) worldwide, including quadrivalent, pentavalent and hexavalent combinations. In the US, a two component pertussis vaccine Hib combination ($DTaP_2$/Hib) is based on a US-Japanese product marketed for use as a fourth booster dose (1).

Table 5. Licensed IPV-Containing Combinations, reproduced with permission (1)

Manufacturer	Other valences in combination	Where licensed
sanofi pasteur	DTaP2	Europe, Latin America, Asia, Africa
	DTaP5	Canada. Latin America, Asia, Africa
	DTaP2/Hib	Europe, Latin America, Asia, Africa
	DTaP5/Hib	USA, Canada, Latin America, Asia, Africa
	DT	France
	Tdap5	USA, Canada, Asia, Africa, Europe
	Td	Europe, Asia, Africa, Latin America
GlaxoSmithKline	DT	Europe
	DTaP3	Canada, Europe, Latin America, Asia, Africa
	DTaP3/Hib	Europe, Latin America, Asia, Africa
	DTaP3/HepB	Europe, Asia, Africa, USA
	DTaP3-HepB/Hib	Europe, Latin America, Asia, Africa, Canada
	Tdap3	Europe, Canada, Latin America, Asia, Africa
Statens Serum Inst.	DTaP1	Europe
	DTaP1/Hib	Europe

One important consideration for vaccine options is that, although it does not matter which vaccine is used from a polio perspective, the hexavalent vaccine from sanofi-pasteur contains two rather than three pertussis antigens. As NZ has a significant problem with pertussis, this vaccine is unlikely to be considered.

7.3 Summary for vaccine options

The inactivated polio vaccine is a mixture of the three polioviruses, types 1, 2 and 3. The majority of IPV vaccines are manufactured from viruses from the Vero cell line, and in one vaccine the cell substrate used is a human diploid cell line MRC-5. IPV is available as monovalent vaccines, and in tetravalent, pentavalent and hexavalent combinations with diphtheria, tetanus, acellular pertussis, and hepatitis B or Hib antigens. The most widely used combination vaccines are produced by sanofi-pasteur and GlaxoSmithKline. The sanofi hexavalent vaccine may have limited use in NZ due to the inclusion of fewer pertussis antigens in the formulation.

8. Options for scheduling

8.1 Objective

This section reviews the evidence for different options for placement of polio vaccine on the childhood immunisation schedule and for special groups.

8.2 Review

The current NZ schedule of 3+1 is in line with international policy advice for polio schedules (refer section 5). There are no recommendations to reduce the primary course or the booster dose.

The current international advice is that a three dose regime is appropriate, the first two doses given preferably two months apart, although one month apart appears adequate, and the third dose six - 12 months later. The third dose can be given earlier, but antibody titres tend to be lower (1).

There is no new international advice to suggest any strong recommendations to change the current NZ schedule.

9. Implementation issues

9.1 Objective

The objective of this section is to consider any new issues around implementation.

9.2 Review

Given that polio has been eradicated in most countries throughout the world, the current rationale is to maintain polio vaccine on the childhood schedule until eradication is complete. While wild polio still circulates in the remaining countries, there is still the risk for importation and possible outbreaks in communities with very low vaccine coverage (such as religious communities) as has been observed for several diseases, including measles and polio. In 2009, transmission of vaccine-derived polio virus was reported recently in the US (Minnesota) in an under vaccinated community. The source was not determined (22).

9.2.1 Risks with importation of wild polio

The US maintains a stockpile of single-valent IPV to ensure a supply in the event of unanticipated outbreaks or vaccine shortages. The stockpile is based on the amount required for the US paediatric population for six months of routinely recommended vaccines. Monovalent polio vaccine has been previously assessed as likely to be the best option in the case of an outbreak. This stockpile is managed by rotation of products used for routine vaccination to maintain shelf life and minimise wastage. Since 2004, the doses of monovalent IPV has decreased and been replaced with combination DTaP-HepB-IPV (23).

Sustained transmission of polio virus, although unlikely, is possible. Polio vaccines offer protection from polio but incomplete protection from infection. The potential dynamics of a US polio outbreak were modelled and the potential requirements for vaccine were assessed for subpopulations with low coverage. Although the risk of poliovirus introduction was assessed as real, widespread transmission of polioviruses was considered unlikely given the high level of routine coverage. Pockets of susceptibility exist where there are un- or under-immunised children and these could potentially lead to one or more paralytic polio cases. There were several factors that were considered as risk factors for increasing vulnerability to poliovirus reintroduction:

- The shift toward combination vaccine utilisation, with limited age indications for use.
- Current trends, such as the decreasing proportion of the population with immunity induced by live polioviruses
- Aging of vaccine exemptor populations.

The authors concluded that the stockpile of polio-containing vaccine remained an important resource that would be required in the event of an outbreak of live poliovirus in a subpopulation with low vaccine coverage (23).

9.3 The role of IPV in polio eradication

The place of IPV in facilitating eradication continues to be disputed. The current WHO strategy is to stop using OPV once eradication has been certified in all areas. However, WHO advisory groups are now deliberating on the role of IPV post-eradication. The risk for countries that do not use IPV is the potential for late recognition of a return of polioviruses (1). Immunosuppressed individuals can excrete poliovirus for very long periods of time hence the ability for polioviruses to continue excretion for long periods. For NZ, clearly there would be no rush to stop the use of IPV vaccines, particularly, while they remain delivered predominantly within a combination vaccine.

9.4 Immunisation strategy in response to wild-type polio importation into New Zealand

Evidence from environmental surveillance indicates that NZ remains vulnerable to vaccine-derived or wild-type poliovirus importation. Australia reported an importation of wild poliovirus infection that occurred in Melbourne in July 2007, in a 22-year-old male university student returning to Australia from Pakistan (24). This highlighted the need for NZ to remain vigilant as the importation of wild-type polio is still possible. National Certified Committee for the Eradication of Polio and the Ministry of Health developed a National Polio Response Plan for NZ (25).

According to the response plan, the most likely scenario is similar to the one experienced by Australia in 2007. Increasingly less likely scenarios, based on the progress in global eradication, are:

- importation of vaccine-derived poliovirus following a person's travel to an area with circulating vaccine-derived polio
- importation of vaccine-associated paralytic polio, from a country using oral polio vaccine
- exposure to polio in a laboratory

The recommendations for contacts of a case are to ensure a primary course of polio vaccination has been completed, and if in doubt, offer a full primary course of IPV with at least four weeks between doses (25).

9.5 Summary for implementation issues

Unvaccinated adults and adolescents continue to need a three dose regime, preferably at zero, two and six months. International eradication has not yet been achieved, as importation continues to be a possibility, and as there is straightforward access to combination vaccines, there is currently no reason for discontinuing the NZ IPV programme. The immunogenicity of poliovirus 3 tends to be lower than the other two, highlighting the importance of continuing travel vaccination advice to polio endemic countries.

10. International policy and practice

10.1 Objective

The objective to this section is to summarise international practice with regard to the use of IPV vaccines. The use of OPV vaccination schedules has not been included.

10.2 Review

IPV- containing vaccines are well established in the immunisation schedules of developed countries. The ideal schedule is accepted as a primary course of two or three doses during the first six months of life, followed by a booster in the second year of life, and possibly another booster before school entry as summarised in Table 6 summarises.

Table 6. Schedules of IPV Administration for Primary Immunization in Infant/Toddlers/Children in Countries Recommending IPV-only schedules in 2012, reproduced with permission (1)

Schedule	Timing	Countries
2 + 1 + 1	2, 4, and 18 months, 4-6 years[1]	United States
	3, 5, and 11-12 months, 5-6 years	Sweden, Slovakia, Italy, Norway, Denmark, Finland
	3, 5, and 12 months, 14 years	Iceland
	2, 4, and 6-18 months, 4-6 years	Greece
3 + 1 + 0	2, 4, 6, and 18 months	Spain
	2, 3, 5, and 18 months	Malaysia
3 + 0 + 1	2, 4, and 6 months, 4 years	Australia, Ireland, Portugal, Korea
	2, 3, and 4 months, 4-6 years	United Kingdom
	2, 4, and 6 months, 4-6 years*	United States
3 + 1 + 1	2, 4, 6, and 18 months, 4-6 years	Switzerland, Austria, Canada, Croatia, Israel, Romania
	2, 3, 4, and 11-18 months, 5-7 years	Hungary, Belgium, France, Luxembourg
	2, 3, 4, and 11-14 months, 9 years	Germany
	3, 4, 5, and 18 months, 10 years	Czech Republic
	3, 4, 5, and 12 months, 4 years	Netherland
	3, 4.5, 6, and 18-24 months, 6-7 years	Estonia, Latvia, Lithuania

[1] The current US recommendations call for a 2 + 1 + 1 or a 3 + 0 + 1 schedule as the third dose can be given any time between 6 and 18 months of age.

10.3 Summary of international policy and practice

IPV-containing vaccines are well established in the immunisation schedules of all developed countries. Schedules vary, but are usually as a primary course of two to three doses during the first six months of life, followed by a booster in the second year of life, and possibly another booster before school entry.

With respect to polio, the NZ immunisation schedule is in line with current international policy and practice.

References

1. Vidor E, Plotkin SA. Poliovirus vaccine—inactivated. In: Plotkin SA, Orenstein WA, Offit PA, editors. Vaccines. 6th ed.: Elsevier; 2013. p. 573-97.
2. Thompson KM. The role of risk analysis in polio eradication: modeling possibilities, probabilities and outcomes to inform choices. Expert Rev Vaccines. 2012;11(1):5-7.
3. Roberts L. Polio campaign. The polio emergency. Science. 2012;337(6094):514-6.
4. Roberts L. Polio campaign. Closing a deadly refuge. Science. 2012;337(6094):520-1.
5. Wilson N, Baker MG. Celebrating 50 years of polio elimination in New Zealand: but inadequate progress in eliminating other vaccine-preventable diseases. The New Zealand medical journal. 2012;125(1365):67-74.
6. Huang QS, Greening G, Baker MG, Grimwood K, Hewitt J, Hulston D, et al. Persistence of oral polio vaccine virus after its removal from the immunisation schedule in New Zealand. Lancet. 2005;366(9483):394-6.
7. Lyseng-Williamson KA, Dhillon S. DTPa-HBV-IPV/Hib vaccine (Infanrix hexa): a guide to its use in infants. Paediatric drugs. 2012;14(5):337-43.
8. Zepp F, Schmitt HJ, Cleerbout J, Verstraeten T, Schuerman L, Jacquet JM. Review of 8 years of experience with Infanrix hexa (DTPa-HBV-IPV/Hib hexavalent vaccine). Expert Rev Vaccines. 2009;8(6):663-78.
9. Sun Y, Christensen J, Hviid A, Li J, Vedsted P, Olsen J, et al. Risk of febrile seizures and epilepsy after vaccination with diphtheria, tetanus, acellular pertussis, inactivated poliovirus, and Haemophilus influenzae type B. JAMA : the journal of the American Medical Association. 2012;307(8):823-31.
10. Medsafe. Datasheet: Infanrix-hexa [Internet] [Internet]. Wellington: New Zealand Medicines and Medical Devices Safety Authority; 2011. Available from: http://www.medsafe.govt.nz/profs/Datasheet/I/Infanrixhexainj.pdf
11. Medsafe. Datasheet: Infanrix-IPV [Internet] [Internet]. Wellington: New Zealand Medicines and Medical Devices Safety Authority; 2011. Available from: http://www.medsafe.govt.nz/profs/Datasheet/i/InfanrixIPVinj.pdf
12. U.S. Food and Drug Administration. Package insert: Infanrix [Internet] [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; 2012. Available from: http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM124514.pdf
13. Scheifele DW, Ochnio JJ, Halperin SA. Cellular immunity as a potential cause of local reactions to booster vaccination with diphtheria and tetanus toxoids and acellular pertussis antigens. Pediatr Infect Dis J. 2009;28(11):985-9.
14. Quinn P, Gold M, Royle J, Buttery J, Richmond P, McIntyre P, et al. Recurrence of extensive injection site reactions following DTPa or dTpa vaccine in children 4-6 years old. Vaccine. 2011;29(25):4230-7.
15. Klein NP, Weston WM, Kuriyakose S, Kolhe D, Howe B, Friedland LR, et al. An open-label, randomized, multi-center study of the immunogenicity and safety of DTaP-IPV (Kinrix) co-administered with MMR vaccine with or without varicella vaccine in healthy pre-school age children. Vaccine. 2012;30(3):668-74.
16. Centers for Disease C, Prevention. Updated recommendations for use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine from the Advisory Committee on Immunization Practices, 2010. MMWR Morb Mortal Wkly Rep. 2011;60(1):13-5.
17. Beytout J, Launay O, Guiso N, Fiquet A, Baudin M, Richard P, et al. Safety of Tdap-IPV given one month after Td-IPV booster in healthy young adults: a placebo-controlled trial. Hum Vaccin. 2009;5(5):315-21.
18. Van Der Meeren O, Kuriyakose S, Kolhe D, Hardt K. Immunogenicity of Infanrix hexa administered at 3, 5 and 11 months of age. Vaccine. 2012;30(17):2710-4.
19. Plotkin SA, Liese J, Madhi SA, Ortiz E. A DTaP-IPV//PRP approximately T vaccine (Pentaxim): a review of 16 years' clinical experience. Expert Rev Vaccines. 2011;10(7):981-1005.
20. Fine PEM, Mulholland K. Community immunity. In: Plotkin SA, Orenstein WA, Offit PA, editors. Vaccines. 6th ed.: Elsevier; 2013. p. 1395-412.

21. Reinheimer C, Friedrichs I, Rabenau HF, Doerr HW. Deficiency of immunity to poliovirus type 3: a lurking danger? BMC Infect Dis. 2012;12:24.
22. Alexander JP, Ehresmann K, Seward J, Wax G, Harriman K, Fuller S, et al. Transmission of imported vaccine-derived poliovirus in an undervaccinated community in Minnesota. The Journal of infectious diseases. 2009;199(3):391-7.
23. Thompson KM, Wallace GS, Tebbens RJ, Smith PJ, Barskey AE, Pallansch MA, et al. Trends in the risk of U.S. polio outbreaks and poliovirus vaccine availability for response. Public Health Rep. 2012;127(1):23-37.
24. Carnie JA, Lester R, Moran R, Brown L, Meagher J, Roberts JA, et al. Public health response to imported case of poliomyelitis, Australia, 2007. Emerging infectious diseases. 2009;15(11):1733-7.
25. Ministry of Health. National Poliomyelitis Response Plan for New Zealand. Wellington, New Zealand: Ministry of Health; 2009.

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