

Childhood vaccination and the role of the pharmacist

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Abstract

Vaccines are considered as one of the greatest advances in medical history, improving the lives of people, preventing disability and saving lives. Every year an estimated two to three million deaths are prevented through vaccination against life threatening diseases that disproportionately affect children. This article attempts to give an overview of the childhood vaccines available in South Africa, and the pharmacist's role in vaccination, with a special focus on the promotion of immunisation, safe immunisation administration, vaccine cold chain, and vaccine safety.

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Introduction

Globally, vaccination is the single most important and cost-effective public health intervention to prevent disease, disability, death and inequity, with close to three million lives saved annually.¹ The major contributor to this achievement is the Expanded Program on Immunization (EPI) of the World Health Organization (WHO) which was launched in 1974 to expand infant immunisation services and coverage, following the demonstration in the 1970s that smallpox was about to be eradicated by vaccination.² The aim of the EPI was to vaccinate all children below the age of one year against six killer diseases, namely polio, diphtheria, tuberculosis (TB), pertussis (whooping cough), measles and tetanus.²

In 2011, in response to outbreaks of vaccine-preventable diseases (VPDs) and the emerging threat of antimicrobial resistance, the WHO established the "Decade of Vaccines" to reinforce disease control and further expand vaccine coverage of new and underutilised vaccines.³ Despite the huge success of worldwide vaccination programmes, about one and a half million children still die annually from VPDs.¹ As the world moves towards Universal Health Coverage, in order to achieve the full benefits of immunisation, both high coverage and timely delivery of scheduled vaccinations are necessary to achieve Sustainable Development Goal 3.8, aimed at "access to safe, effective, quality and affordable medicines and vaccines for all" by 2030.^{1,4,5}

Since the launch of the South African EPI (EPI-SA) in 1995, its many successes include eliminating neonatal tetanus and polio, and being one of the leading African countries in introducing new vaccines into its routine immunisation schedule.⁶ The EPI-SA has set guidelines and standards on immunisation practices, with 10 antigens provided free of charge at all public sector

healthcare facilities, for vaccination against measles, polio, diphtheria, whooping cough, tetanus, hepatitis B, *Haemophilus influenzae* type b (Hib) disease, TB, pneumococcal diseases and rotavirus diarrhoea.⁷ In addition, free vaccination against cervical cancer (which is caused by the human papillomavirus) is offered to girls aged nine years and older attending grade 4 in public sector schools.⁷ Over and above vaccines against these 11 VPDs, influenza vaccination is available in public sector facilities for high risk patients, including children, during the annual influenza vaccination campaign (March to May).⁷ Vaccines against chicken pox, mumps, rubella, hepatitis A, meningococcal meningitis and influenza, and a monoclonal antibody to protect against respiratory syncytial virus (RSV) are also available for children in the private sector.⁸ Table I shows the 2018 Vaccination Schedule produced by the Paediatric Management Group (<https://www.paediatrician.co.za/>), with vaccines available in the public healthcare sector, recommended according to the EPI-SA schedule, and additional vaccines available in the private healthcare sector.⁸

Pharmacist's role in vaccination

Pharmacists have an important public health role to play in disease prevention through the provision of vaccination to the general public.⁹ Over the last number of years, vaccination services provided by pharmacists have been on the increase, with evidence of its public health benefit from various countries.¹⁰⁻¹³ The International Pharmaceutical Federation (FIP) identified the pharmacist as "a stakeholder in the immunisation neighbourhood", and has been advocating for this role of the pharmacist.^{11,12} A recent worldwide survey found that pharmacists play a role in patient education and advocacy for immunisation in 34 countries (i.e. approximately half of the world's population) and in 27 countries they play an active role as vaccinators.¹¹

Table 1. Vaccination schedule (2018) of vaccines available in the public and the private healthcare sectors in South Africa⁸

Vaccination Schedule 2018



Disease	Vaccine	Birth	6 weeks	10 weeks	14 weeks	6 months	9 months	12 months	15 months	18 months	6 years	9 years	12 years
TB	BCG	●											
Polio	bOPV	●	●										
Diphtheria, Tetanus, Polio, Pertussis	Hexaxim		●	●	●					●			
Haemophilus Influenzae, Hepatitis B	Infanrix hexa		●	●	●		●			●			
			8 weeks	12 weeks	16 weeks								
Pneumococcal	Prevenar 13 Synflorix		●	●	●		●	●	Nine and a half months				
Rotavirus	Rotarix Rotateq		●	●	●								
Measles	Measbio					●		●		12 months Measbio not required if giving MMR			
Measles Mumps Rubella	Priorix Omzyta							●	MMR at 12 months instead of Measbio		●	●	Give MMR and Varilrix separately at 6 years if not using Priorix Tetra
Chickenpox	Varilrix ONVARA							●			●		
Measles Mumps Rubella + Chickenpox	Priorix Tetra										●		
Meningococcal Conjugate	Menactra						●						For individuals 2-55 years administer 1 dose
Hepatitis A	AVAXIM 80 Havrix Junior							●	Hep A with MMR not with Measbio		●		
Tetanus, Diphtheria Pertussis, Polio	TETRA XIM Boostrix Tetra ADACEL QUADRA									Tetrixim at 6 years or Boostrix Tetra at 6 years Boostrix Tetra can be given at 12 years if not given at 6 years Adacel Quadra at 12 years	●	●	●
Tetanus, Diphtheria	Td										●		●
Human Papilloma Virus	Cervarix GARDASIL											●	●
Influenza	INFLUVAC VAXIGRIP												
Respiratory Syncytial Virus	RSV prophylaxis in high-risk infants-prevention of serious LRTI caused by RSV. Start February and end in June												
Pneumococcal	PNEUMOVAX 23 (Polysaccharide Polysaccharide Diphtheria Toxooid Conjugate Vaccine)												

● STATE EPIVACCINES These vaccines are available free from Government supplied clinics

● RECOMMENDED OPTIONAL VACCINES Some of the vaccines in this schedule are only available from private clinics

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The WHO's Health System Framework identifies equitable access to high quality, safe, efficacious and cost-effective medical products, vaccines and technologies, as one of six building blocks necessary for a well-functioning health system.¹⁴ Therefore, within South Africa's changing healthcare environment, as the country is making progress with National Health Insurance (NHI)⁵ implementation, pharmacy services will play an essential role, particularly at primary healthcare level. This is an opportunity for pharmacists to increase their public health involvement in micro-level (health promotion and disease prevention) and macro-level (policy formulation, planning and management functions) activities.¹⁵ As such, pharmacists need to plan, prepare and position themselves to be able to contribute to enhanced primary healthcare services, including vaccination services, and Universal Health Coverage.¹¹

Although vaccination services are already provided by private clinics in community pharmacies in South Africa, one of the challenges for wider implementation of these services is limited support by the healthcare system, including financial support and access to EPI vaccines, which are available free of charge at public sector facilities.¹¹ It is anticipated that with the NHI implementation and re-engineering of the healthcare system to provide Universal Health Coverage, this challenge will be addressed in future.¹¹ Internationally, reimbursement for vaccination services has been identified as instrumental in sustaining pharmacy vaccination services. A reimbursement system for vaccination services in community pharmacies, would therefore be beneficial for future advancement of pharmacy-based vaccination services.¹²

Currently there is no official required accreditation for pharmacist vaccinators in South Africa. However, according to Ethical Rule 22 of the South African Pharmacy Council, pharmacists are not permitted to perform any professional services for which they are

not adequately trained or experienced to undertake.¹⁶ In addition, comprehensive minimum standards for immunisation services are stipulated including requirements for physical facilities and equipment, procedures, documentation and record keeping, ethical aspects and training.¹⁶ Most pharmacists in South Africa have only basic theoretical training in vaccinology, as part of their undergraduate education.^{11,17} Access to additional education and specific practical training in vaccinology for pharmacists will therefore be key in expanding and further developing vaccination and vaccine-related services by pharmacists.^{11,12}

Although not all pharmacists may aspire to be vaccinators (i.e. physically administering vaccines), their role in vaccination is much more comprehensive.^{9,11,12,16} As public health advocates, pharmacists should play a crucial role in promoting the importance of vaccination in various ways, including screening of patients, patient counselling, measures to ensure safe administration of vaccines, vaccine pharmacovigilance, supply chain and cold chain management, vaccination advocacy and social mobilisation, and monitoring and evaluation.^{9,11,12,16} Figure 1 provides an overview of the comprehensive role that the pharmacist can play in vaccination.^{9,11,12,16}

Promotion of routine immunisation

Pharmacists have an important role to play in the community as they often are the first and most easily accessible point of health care and contact with the patient.^{9,16} They are therefore in a unique position to promote routine immunisation and identify those patients who are part of the target groups for certain vaccinations.¹⁶

As the world approaches the post-antibiotic era, and the pipeline of newly developed antibiotics is running dry, vaccines are increasingly becoming a key strategy in combating antimicrobial

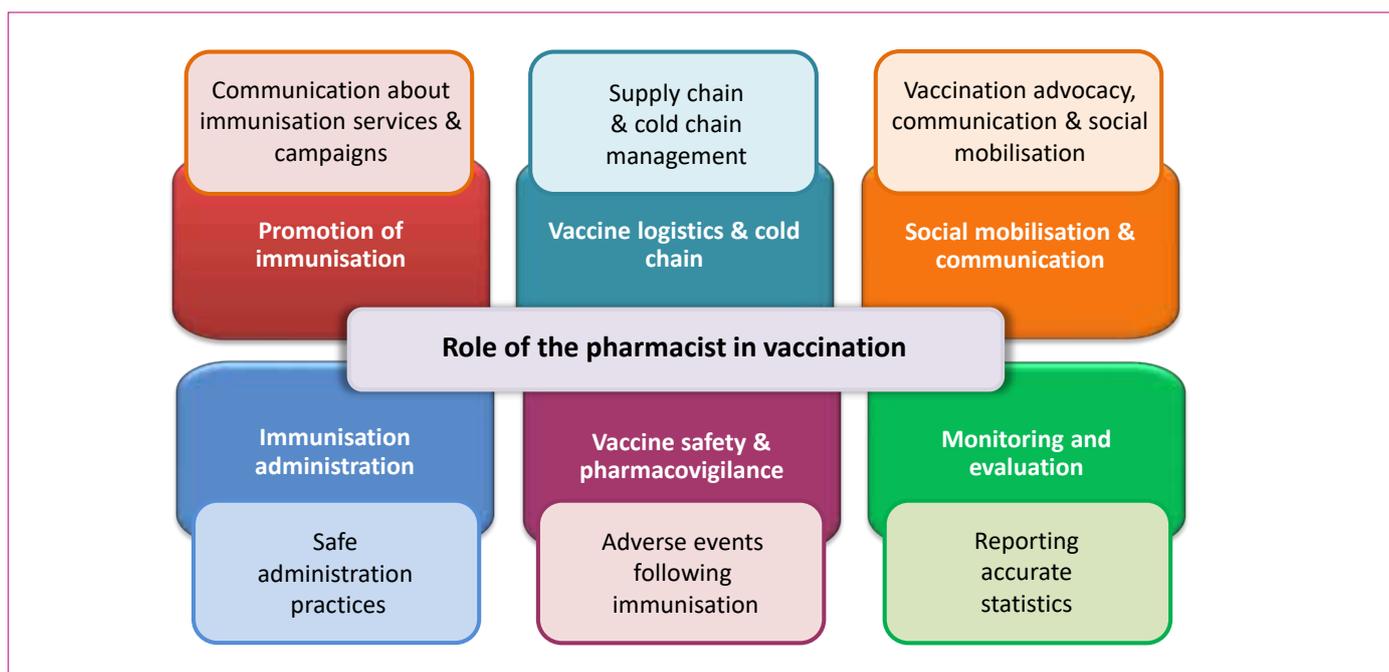


Figure 1. Role of the pharmacist in vaccination^{9,11,12,16}

Table II. Catch-up doses for the public sector vaccines, as recommended by the NDoH^{7,23}

Vaccine	Age of child	First dose	Interval for subsequent doses		
			Second dose	Third dose	Fourth dose
Bacille Calmette-Guérin (BCG)	< 1 year	Give one dose			
	≥ 1 year	Do NOT give			
Oral Polio Vaccine (bOPV)	< 6 months	Give first dose	4 weeks		
	≥ 6 months	Do NOT give			
Hexavalent (DTaP-IPV-HepB-Hib)	Up to 5 years	Give first dose	4 weeks	4 weeks	12 months (Do not give before child is 18 months old)
Pneumococcal conjugate (PCV)	< 6 months	Give first dose	4 weeks	At 9 months of age	
	6–9 months	Give first dose	4 weeks	8 weeks	
	> 9–12 months	Give first dose	4 weeks	8 weeks	
	1–6 years	Give one dose			
Rotavirus	< 20 weeks	Give first dose	4 weeks		
	20–24 weeks	Give one dose			
	> 24 weeks	Do NOT give			
Measles	< 11 months	Give first dose	At 12 months of age		
	≥ 11 months	Give first dose	4 weeks		
Tetanus-diphtheria (Td)	≥ 6 years	Give first dose	At 12 years of age		

resistance.^{18,19} Evidence has shown a high correlation between antibiotic use and resistance.¹⁹ Pharmacists can also play a very important role in antimicrobial stewardship by promoting routine immunisation.²⁰ Optimising vaccine uptake is a powerful tool to prevent VPDs, which will reduce the need to use antibiotics and subsequently prevent the development of resistance.^{19,21}

Effective vaccines do not only limit antibiotic consumption by providing direct protection against VPDs. In addition, they also provide indirect protection through 'herd immunity' by reducing transmission of pathogenic organisms to unvaccinated members of the community.^{18,22} Vaccines also prevent viral infections, and secondary bacterial infections that commonly result from VPDs, such as flu.^{18,22} While primary viral infections should not be treated with antibiotics, unfortunately, for a number of reasons, they often are.¹⁹

An opportunity to vaccinate a child should never be missed.^{7,9} Pharmacists should therefore actively screen for routine immunisation as part of providing pharmaceutical care.^{9,16} In the case where a child has missed any of his/her routine vaccinations, these vaccines should be given immediately according to the age of the child and the recommended catch-up schedule for the particular vaccine.^{7,8} A child who has not been immunised at all, should receive the full schedule of immunisations (see Table I), with the exception of OPV which should not be given beyond six months of age, rotavirus which should not be given to babies older than 24 weeks or 32 weeks, depending on the type of vaccine used, and BCG which should not be given beyond the age of one year.^{7,8} Table II provides the catch-up doses for the vaccines available in the public sector, as recommended by the National Department of Health (NDoH).^{7,23}

Safe administration of vaccines

The safe administration of vaccines starts with checking the patient's history for contraindications and precautions for the specific vaccine that is about to be administered (see Table III).^{7,23-51} Since vaccine administration is normally outside the scope of practice of pharmacists, the pharmacist's right to administer vaccines is subject to having acquired adequate skills and knowledge to do so.^{16,52} The vaccinating pharmacist is legally required to maintain good pharmacy practices at all times, with special emphasis on the importance of providing the service in a professional manner, adhering to all aspects of ensuring vaccination safety, appropriate vaccine storage and transportation, meticulous record keeping, and ensuring the confidentiality of the patient's information.^{9,16,52}

Pharmacists must ensure that they are adequately trained and familiar with the guidelines of the EPI-SA, on safe and sterile injection practices.^{16,52} Reconstitution of vaccines, if required, must be done immediately prior to their use.^{16,53,54} Different vaccines have different diluents and diluents are NOT interchangeable at all.⁵³ As such, it is of utmost importance that reconstitution of a freeze-dried vaccine must be carried out using only the specific diluent provided by the manufacturer for each type and batch of vaccine.^{7,53,54} While diluents can be stored outside of the cold chain in situations where cold chain space is limited, it is essential that they are refrigerated for 12 hours before use.^{23,53,54} This is because they must be at the same temperature as the vaccine to prevent thermal shock and loss of potency.^{23,53,54} A sterile syringe and sterile needle must be used for each immunisation, and the principle of "One Needle, One Syringe", which means that the same needle must be used for drawing up and administering the vaccine, must be adhered to.^{23,54} Hand washing before and after administering the vaccine must always be carried out.^{23,54} The use

Table III. Most common contraindications and special precautions for childhood vaccines^{7,23-51}

Vaccine	Contraindications and special precautions
Bacille Calmette-Guérin (BCG)	<ul style="list-style-type: none"> • Children with known HIV infection should not get BCG vaccination • Do not delay BCG vaccination if HIV status is unknown • Children > 12 months: Should NOT get BCG • Newborn infants: if the mother is on TB chemotherapy, the infant should be on chemoprophylaxis or treatment, and receive BCG once treatment is completed • Revaccination NOT recommended
Oral Polio Vaccine	<ul style="list-style-type: none"> • Previous anaphylaxis • Not contraindicated in HIV-infected children but should not be administered to children with primary immune deficiency, as it can result in vaccine-associated paralytic poliomyelitis (VAPP)
Hexavalent (DTaP-IPV-HepB-Hib)	<ul style="list-style-type: none"> • Known hypersensitivity to any component of the vaccine or pertussis vaccine (acellular or whole cell pertussis) • Previous encephalopathy of unknown cause within seven days after a prior dose of a pertussis-containing vaccine • Life-threatening reaction after previous administration of the vaccine or a vaccine containing the same substance • Previous Arthus reaction
Pneumococcal conjugate	<ul style="list-style-type: none"> • Previous anaphylaxis • Hypersensitivity to a previous dose or to any vaccine component including diphtheria toxoid • Whilst a mild upper respiratory tract infection is not a contraindication, postpone vaccination in patients with severe febrile illness
Rotavirus	<ul style="list-style-type: none"> • Postpone rotavirus vaccination in children with <ul style="list-style-type: none"> ◦ Diarrhoea and vomiting ◦ Acute febrile illness • Contraindications <ul style="list-style-type: none"> ◦ Hypersensitivity or anaphylaxis to rotavirus or any excipients in the formulation ◦ Hypersensitivity after previous administration of rotavirus ◦ Severe combined immunodeficiency disorder ◦ History of intussusception ◦ Uncorrected congenital malformation of the gastrointestinal tract that would predispose to intussusception • To avoid intussusception, do NOT administer <ul style="list-style-type: none"> ◦ after 24 weeks of age - monovalent vaccine ◦ after 32 weeks of age - pentavalent vaccine
Measles	<ul style="list-style-type: none"> • Contraindications <ul style="list-style-type: none"> ◦ Previous anaphylaxis ◦ Active or suspected acute respiratory infection ◦ Severe diseases of the blood system such as leukemia ◦ History of anaphylactic reactions to kanamycin or erythromycin ◦ Uncontrolled convulsions: consult with medical practitioner
Measles, mumps, rubella (MMR)	<ul style="list-style-type: none"> • Contraindications <ul style="list-style-type: none"> ◦ Previous history of severe allergic reaction to any component of the vaccine ◦ Severely immunocompromised patients, due to risk of prolonged virus replication, which may revert to virulence and result in disease ◦ Gelatin is reported to be the source of anaphylactic reactions whilst the risk of adverse reactions due to egg allergy is reported to be low ◦ Therefore, egg allergy does not constitute a contraindication to immunisation with monovalent measles or the MMR
Chickenpox (varicella)	<ul style="list-style-type: none"> • Postpone administration in patients suffering from acute severe febrile illness • Healthy subjects: presence of minor infection is NOT a contraindication • Contraindications <ul style="list-style-type: none"> ◦ Severe allergic reactions such as anaphylaxis after a previous dose ◦ Allergy to a vaccine component including neomycin; history of contact dermatitis to neomycin is NOT a contra-indication ◦ Severe immunodeficiency (e.g. patients with primary immune deficiency or severely immunocompromised HIV-positive patients) or on long-term immunosuppressive therapy
MMR plus chickenpox (varicella)	<ul style="list-style-type: none"> • Contraindications <ul style="list-style-type: none"> ◦ Hereditary problems of galactose intolerance, or glucose-galactose malabsorption ◦ Known hypersensitivity to neomycin • Higher incidence of fever observed when compared to the concomitant administration of measles-mumps-rubella and varicella vaccines at separate injection sites

Meningococcal conjugate	<ul style="list-style-type: none"> • Contraindications <ul style="list-style-type: none"> ◦ Previous severe allergic or anaphylactic reaction to a vaccine component ◦ Previously diagnosed with Guillain-Barré syndrome • Immunosuppression is NOT a contraindication
Hepatitis A	<ul style="list-style-type: none"> • Postponed in the case of fever, acute disease, and chronic evolving disease • Contraindications <ul style="list-style-type: none"> ◦ Patients with known hypersensitivity to any component of the vaccine ◦ Patients with a history of anaphylaxis; vaccine contains traces of neomycin • Caution in patients with less severe manifestations of antibiotic hypersensitivity
Tetanus, diphtheria, pertussis, polio	<ul style="list-style-type: none"> • Postponed in subjects suffering from acute severe febrile illness • Presence of a minor infection is not a contraindication • Contraindications <ul style="list-style-type: none"> ◦ Known hypersensitivity after previous administration of diphtheria, tetanus, pertussis or poliomyelitis vaccines or to any component of the vaccine ◦ Known hypersensitivity to formaldehyde, neomycin, polymyxin and polysorbate 80 ◦ Previous encephalopathy of unknown aetiology, within seven days following previous vaccination with pertussis-containing vaccine; discontinue pertussis vaccination continue with diphtheria, tetanus and poliomyelitis vaccines ◦ Transient thrombocytopenia or neurological complications (for convulsions or hypotonic-hyporesponsive episodes) following an earlier immunisation against diphtheria and/or tetanus
Tetanus-diphtheria	<ul style="list-style-type: none"> • Previous anaphylaxis or hypersensitivity • Children < 6 years of age should NOT get tetanus diphtheria
Human papilloma virus	<ul style="list-style-type: none"> • Contraindications <ul style="list-style-type: none"> ◦ Previous anaphylaxis ◦ Febrile illness ($\geq 38.5^{\circ}\text{C}$) • Use with caution in moderate or severe acute illness with or without fever • Presence of a minor infection, such as a cold, should not result in the deferral of vaccination
Influenza	<ul style="list-style-type: none"> • Contraindications <ul style="list-style-type: none"> ◦ Postpone vaccination in case of febrile or acute disease ◦ Hypersensitivity to the active substances, to any of the excipients or to any component that may be present as traces such as eggs (ovalbumin, chicken proteins), formaldehyde, cetyltrimethylammonium bromide, polysorbate 80 and gentamycin ◦ Persons with a severe allergic reaction (anaphylaxis) to a vaccine component, or following a prior dose of inactivated influenza vaccine

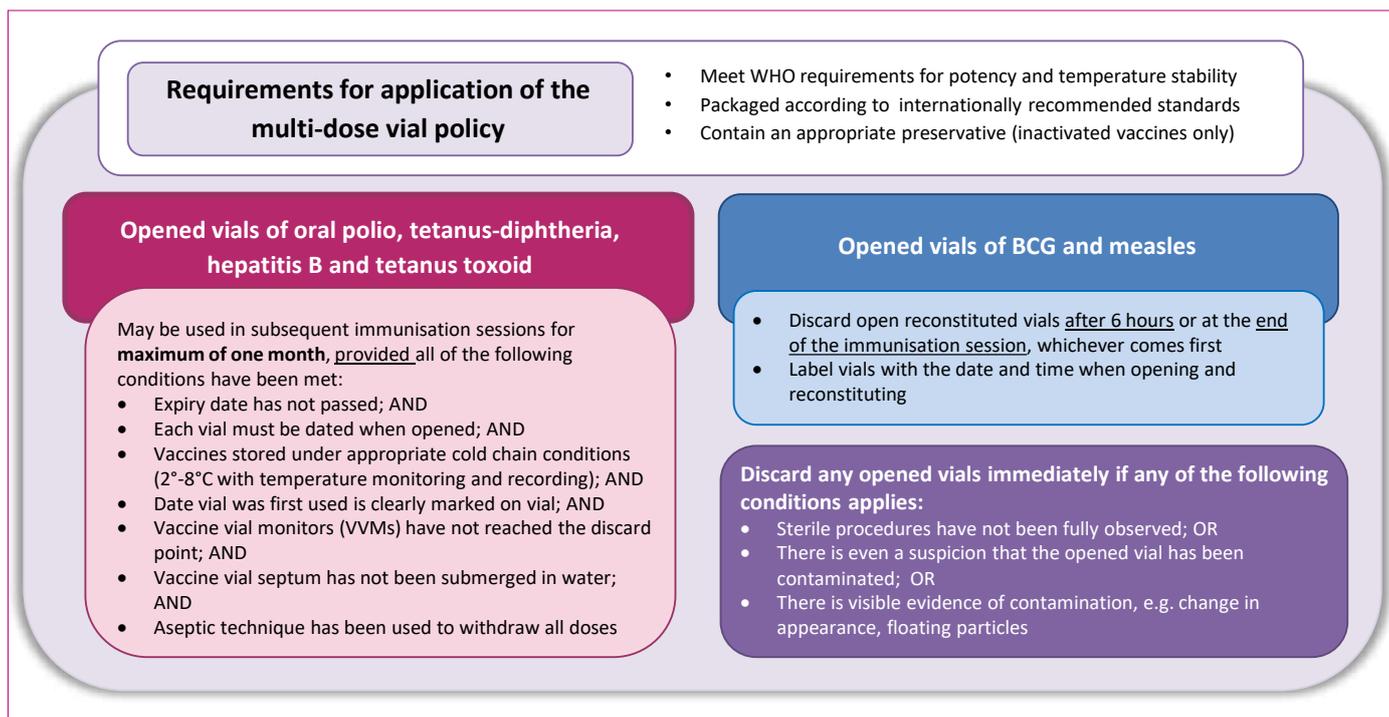


Figure 2. EPI-SA multi-dose vial policy^{7,23,55}

of alcohol swabs should be avoided as it can cause unnecessary discomfort. Instead, the skin of the vaccinee must be cleaned with cotton wool and water.²³

Vaccination safety also includes preventing needle-stick injuries, and safe disposal of vaccination equipment.^{16,23,54} Unsafe disposal of used syringes and needles endangers the health of the community and leads to pollution of the environment.^{16,23,54} It is a legal requirement to have biohazardous materials and sharps disposal container(s) available in the pharmacy.^{16,23} Pharmacists must adhere to these requirements and ensure that all used needles and syringes and empty vaccine vials are immediately disposed of into the sharps container.^{16,23}

Vaccine formulations are complex. Some vaccines are available in multi-dose vials, and will remain potent for several days after the vial has been opened, while others will not, and need to be discarded after six hours, or at the end of an immunisation session, whichever comes first.^{7,23} The EPI-SA has a multi-dose vial policy for WHO pre-qualified multi-dose vaccine vials, which should be followed to ensure vaccine safety, while minimising vaccine wastage (see Figure 2).^{7,23,55}

Pharmacists must ensure that they are familiar with the administration requirements for each individual vaccine and that the vaccine is checked for safety before administration.^{16,54} Table IV provides a summary of the recommended dose, route and site of administration for the different childhood vaccines.^{7,23,24} It is

Table IV. Dose, route and site of administration for childhood vaccines^{7,23,24}

Vaccine	Form	Dose	Route	Site of administration
Bacille Calmette-Guérin (BCG)	Freeze-dried powder with diluent for reconstitution	0.05 ml	Intradermal	Right upper arm, at the insertion of the deltoid muscle, in the upper layer of the skin
Oral Polio Vaccine	Suspension	0.1 ml (2 drops)	Oral Do NOT inject	<ul style="list-style-type: none"> • Directly into the mouth • If immediately spat out or vomited, repeat • Not affected by feeding (breast or other)
Hexavalent (DTaP-IPV-HepB-Hib)	Suspension	0.5 ml	Intramuscular	<ul style="list-style-type: none"> • < 1 year of age: Anterolateral aspect of the upper left thigh • > 1 year of age: Deltoid muscle of left arm
Pneumococcal conjugate	Clear solution	0.5 ml	Intramuscular	<ul style="list-style-type: none"> • < 1 year of age: Anterolateral aspect of right thigh • > 1 year of age: Upper arm in the deltoid muscle • Can be administered with the hexavalent vaccine, but at a different site
Rotavirus (monovalent)	Suspension: Clear colourless liquid	1.5 ml	Oral Do NOT inject	<ul style="list-style-type: none"> • Child should be seated in a reclining position • Squeeze the entire contents of the tube in the inner cheek • There are no restrictions on the infant's consumption of food or liquid, including breast milk, either before or after vaccination
Rotavirus (pentavalent)	Suspension: Pale yellow clear liquid (may have pink tint)	2 ml		
Measles	Freeze-dried powder with diluent for reconstitution	0.5 ml	Subcutaneous	<ul style="list-style-type: none"> • < 1 year of age: Mid lateral aspect of left thigh • ≥ 1 year of age: Right upper arm
Measles, mumps, rubella (MMR)	Freeze-dried powder with diluent for reconstitution	0.5 ml	Intramuscular	<ul style="list-style-type: none"> • ≤ 12 months of age: Intramuscular in anterolateral aspect of the thigh • > 12 months of age: Intramuscular in deltoid muscle
Chickenpox (varicella)	Freeze-dried powder with diluent for reconstitution	0.5 ml	Subcutaneous	Outer aspect of the upper arm (deltoid area)
MMR plus chickenpox	Freeze-dried powder with diluent for reconstitution	0.5 ml	Subcutaneous or intramuscular	<ul style="list-style-type: none"> • Subcutaneously: Outer aspect of upper arm • Young children: Intramuscular in lateral aspect of the left thigh • Older children: Intramuscular in left upper arm
Meningococcal conjugate	Solution	0.5 ml	Intramuscular	Depending on the child's age and muscle mass: <ul style="list-style-type: none"> • Anterolateral right thigh OR • Deltoid region
Hepatitis A	Suspension	0.5 ml	Intramuscular	<ul style="list-style-type: none"> • Young children: Anterolateral part of the right thigh • Older children: Lateral aspect of the right arm at the deltoid muscle
Tetanus, diphtheria, pertussis, polio	Suspension	0.5 ml	Intramuscular	Deltoid muscle of right arm
Tetanus-diphtheria	Suspension	0.5 ml	Intramuscular	Deltoid muscle of the left arm
Human papilloma virus	Suspension	0.5 ml	Intramuscular	<ul style="list-style-type: none"> • Deltoid region of the non-dominant arm OR • Higher anterolateral area of the thigh
Influenza	Suspension	> 6 months to < 3 years: 0.25 ml > 3 to < 9 years: 0.5 ml	Intra-muscular or deep subcutaneous	<ul style="list-style-type: none"> • < 1 year of age: Anterolateral aspect of the thigh • > 1 year of age: Upper arm in the deltoid muscle

important to note that the monovalent measles vaccine is the only vaccine within the EPI-SA that cannot be administered together with any other vaccine.³⁴ This particular measles vaccine has not been subjected to clinical testing for simultaneous administration with other vaccines, which means that it cannot be licensed for administration with other vaccines. In the event where a child requires the measles vaccine and other vaccines at the same time, the measles vaccine must be given immediately and a visit to receive the remaining vaccines must be scheduled one month later.³⁴

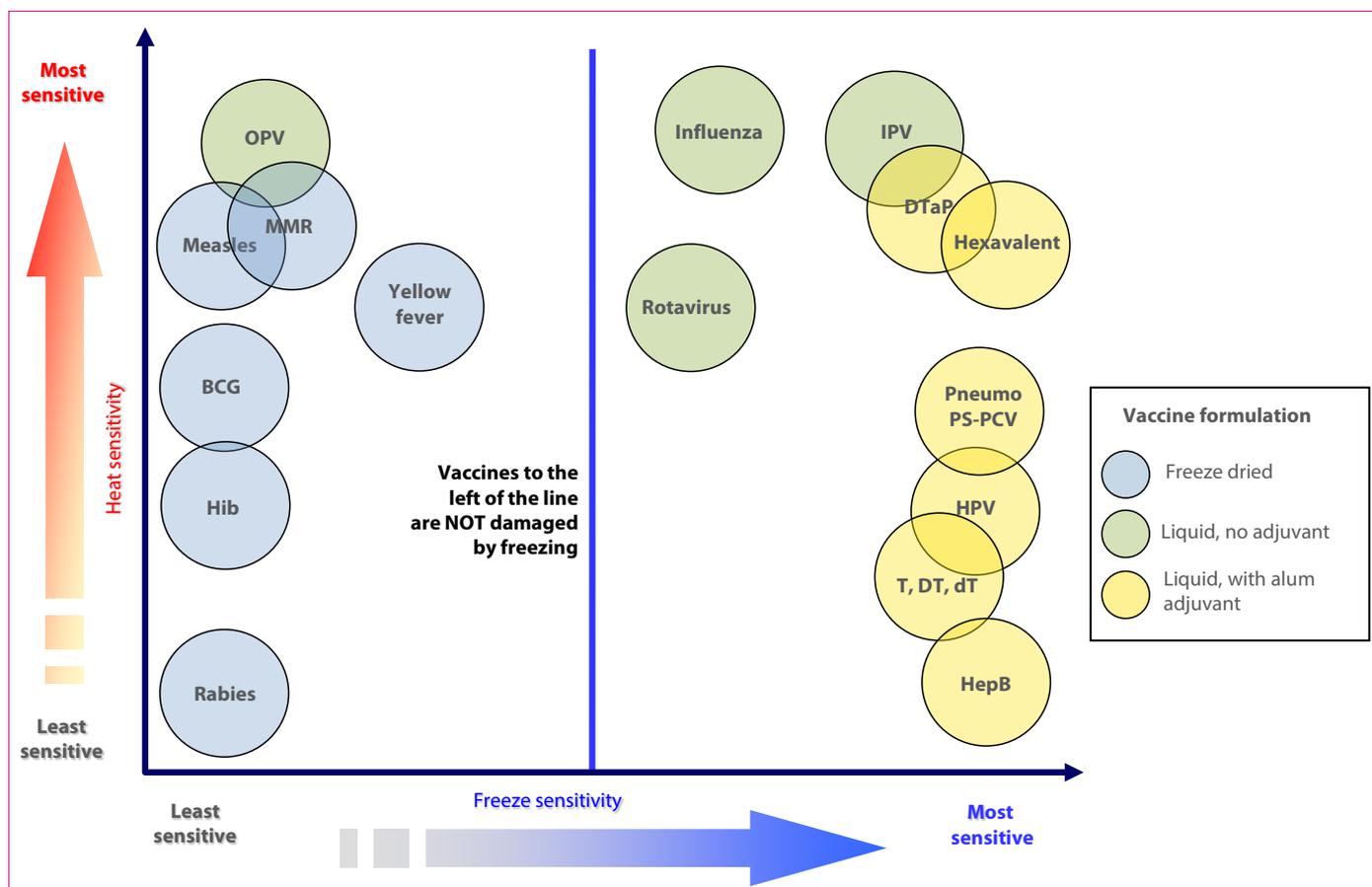
An anaphylactic reaction (i.e. serious allergic reaction that can be fatal if not treated immediately) following administration of a vaccine is a risk factor for all vaccines, although rare.²³ Pharmacy legislation stipulates training for the vaccinating pharmacist in cardio-pulmonary resuscitation techniques and the necessary support to be able to manage adverse effects following immunisation (AEFI).¹⁶ A fully equipped emergency tray must be available at the immunisation point, including adrenaline 1:1000 solution, antihistamine (e.g. promethazine) injection, hydrocortisone injection and equipment (e.g. plaster, gauze, cotton wool, sterile wound dressings), in case of a rare unexpected anaphylactic reaction.¹⁶

Fainting (syncope) is possible after and even before any vaccination, especially amongst older children, as a psychogenic response to the needle injection. Precautionary measures should therefore be in place to avoid injury from fainting.^{23,56}

Vaccine logistics and cold chain

An important responsibility of the pharmacist is to ensure that vaccines are available and that they are transported and stored correctly. Minimum standards for the procurement, storage and distribution of thermolabile pharmaceutical products, including vaccines, are stipulated by the Rules relating to Good Pharmacy Practice¹⁶ in terms of the Pharmacy Act (Act 53 of 1974).^{52,57} Pharmacists have a professional responsibility to ensure that vaccines and their diluents maintain their appropriate stability and potency by storing them in a dedicated vaccine fridge, which is correctly packed to allow for cold air circulation with the temperature maintained between 2 °C and 8 °C, monitored daily, and twice daily recorded on a temperature monitoring chart.^{16,23,53,57-59}

Vaccines are delicate biological substances that can become less effective or destroyed if they are exposed to either too high (> 8 °C) or too cold (< 2 °C) temperatures, and/or are exposed to direct sunlight or fluorescent light.^{53,58,59} Hence, while vaccines are heat sensitive, some vaccines are also destroyed by freezing and any loss of potency due to either heat or light is cumulative, permanent and irreversible.²⁵ A very useful 'tip' to remember which vaccines should not be frozen, is to look for the 'T' in the name of these vaccines, which also applies to the vaccine 'diluent'. Figure 3 illustrates the temperature sensitivity of vaccines.^{53,60}



Adapted from WHO/PATH Temperature Sensitivity of Vaccines presentation (WHO/PATH)

Figure 3. Temperature sensitivity of vaccines^{53,60}

Vaccine vial monitors

Vaccine vial monitors (VVMs) consist of heat sensitive chemicals that are applied to the label of the vial, to monitor the cumulative heat exposure of an individual vial from the time when it leaves the manufacturing plant.^{23,53} For vaccines in multidose vials containing a preservative allowing them to be used in a subsequent vaccination session, the VVM appears on the label. In the case of vaccines with no preservative, which must be discarded six hours after opening, the VVM appears on the cap. Figure 4 shows how the VVM should be interpreted.^{23,53}

Symbol	Explanation	Stage
	The inner square is lighter than the outer circle. If the expiry date has not Passed, USE the vaccine.	I
	As time passes the inner square is still lighter than the outer circle. If the expiry date has not passed, USE the vaccine	II
	Discard point: The colour of the inner square matches that of the outer circle. DO NOT USE the vaccine	III
	Beyond the discard point: Inner square is darker than the outer circle. DO NOT USE the vaccine	IV

Figure 4. Interpretation of the vaccine vial monitor^{23,53}

VVMs can help to indicate problems with the cold chain, which has a major effect on vaccine potency; however, they do not directly measure the potency of the vaccine. It is important to note that the VVM does NOT measure exposure to freezing temperatures. For freeze-sensitive vaccines, it is essential to verify that they have not been frozen before using them, by inspecting the freeze tag. Should there be any concern that a vaccine has been frozen, the 'shake test' must be performed.^{23,53,58}

The shake test

A vaccine that has been frozen is no longer a uniform cloudy liquid, but tends to form granules or flakes which gradually settle to the bottom (i.e. form a sediment) after the vial has been shaken. To check using the shake test, a vial from the same batch as the vaccine under suspicion is frozen until solid and then left to thaw. Both vials are held together in the same hand and shaken vigorously for 10–15 seconds, observed for signs of granular particles or flakes, and then left to rest. Between five and 30 minutes later, both vials are observed for signs of granular particles or flakes, and their sedimentation rates are compared. If the sedimentation rate in the suspect vial is much slower than that of the deliberately frozen control vial, the suspect vial may be used. If the sedimentation rate in the suspect vial is the same as that of the deliberately frozen control vial, the vial fails the test and should NOT be used (see Figure 5).^{23,53,58}

Vaccine safety and pharmacovigilance

Ensuring the safety of vaccines, starting from manufacturing to the time they are administered, is of paramount importance to health authorities globally.⁶¹ All vaccines used in South Africa are approved and licensed by the South African Health Products Regulatory Authority (SAHPRA).⁶² In addition, for quality assurance, each vaccine batch that arrives in the country is first tested for safety by the National Control Laboratory (NCL) in Bloemfontein. Only once certified as safe by the NCL, are they released by SAHPRA for distribution into the market.^{62,63}

Vaccines are generally very safe, but as with any other medicine, there are risks associated with vaccination.⁶⁴ The benefits of vaccination however far outweigh the risks.⁶⁴ Unfortunately there

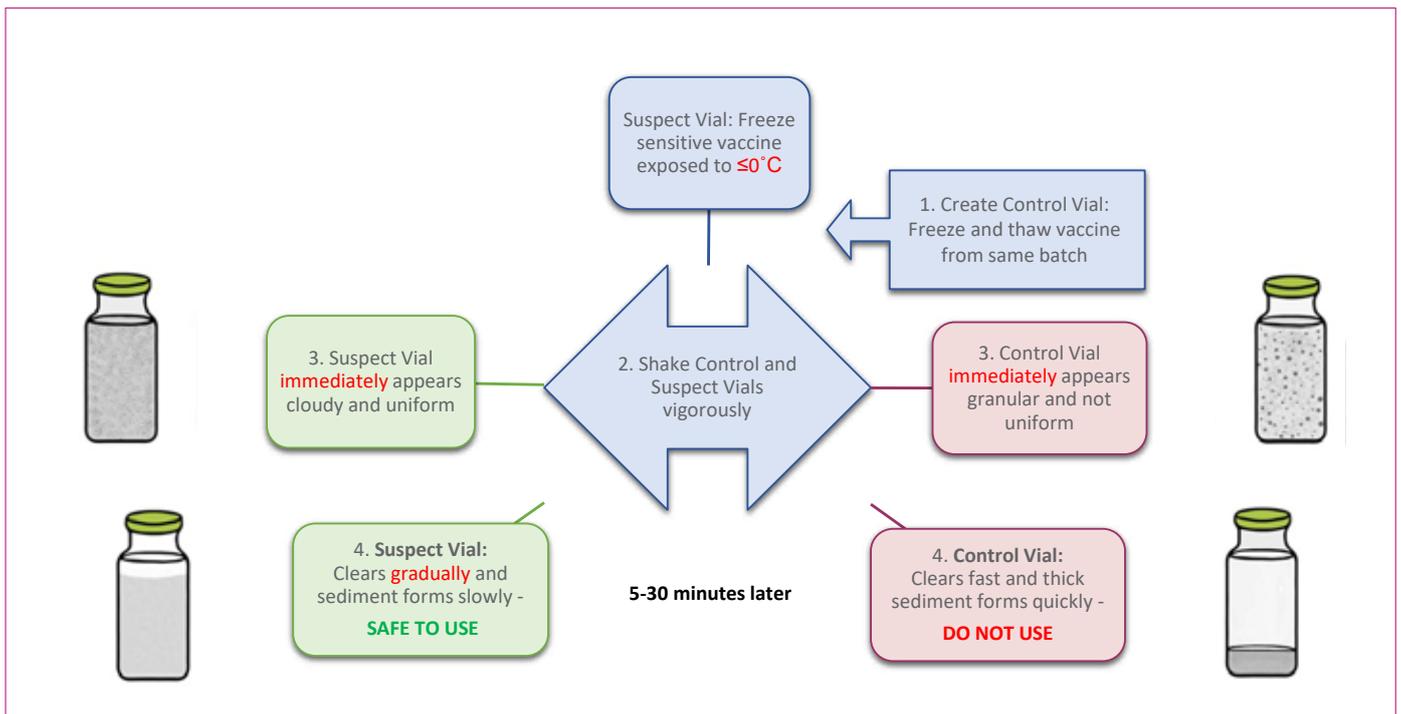


Figure 5. Interpretation of the shake test^{23,53,58}

are many misconceptions about vaccines, which often result in misleading and disturbing publications about vaccine safety.^{65,66} As a result parents become vaccine hesitant, delay vaccination or refuse vaccination.⁶⁶ In response to these misleading publications, the WHO initiated the Vaccine Safety Net (VSN) project, which is a global network of websites evaluated by WHO, that provide reliable information on vaccine safety.⁶⁷

Surveillance on AEFI and monitoring of immunisation safety increase the credibility of the immunisation programme, and public confidence in vaccines.^{56,65,68} The EPI-SA has an AEFI surveillance system, which requires that all suspected AEFI cases are reported within 24 hours, by health professionals at all levels, and are investigated within 48 hours following the AEFI.^{23,68} AEFI surveillance is however passive and relies mainly on reports from patients visiting the health facilities, and reports from health professionals on cases they believe are linked to immunisation (either the vaccine itself or immunisation practices).^{23,56,68}

At patient level, the pharmacist should screen for contraindications and precautions before vaccinating, ensure appropriate vaccine dosing and safe administration, intervene if an AEFI occurs and document any AEFI.^{9,16} Table V gives a summary of the AEFIs for the childhood vaccines used in South Africa.^{7,23-51,64} For more detailed information, always consult the product information and post-marketing information, which is compiled from active and passive surveillance data.

Advocacy, communication and social mobilisation

Pharmacists can engage in a number of advocacy and communication activities to promote vaccination, increase access to vaccines and instil confidence in the immunisation programme.^{23,66} During the 2017 Pharmacy Month in South Africa, which was dedicated towards campaigning for vaccination under the theme *"Protect yourself, protect your family, protect your community"*, pharmacists played an important role in education and advocacy for vaccines.^{12,69}

Misinformation leading to distrust in vaccines can compromise the health of individual patients, their families and the public at large.¹² Many misconceptions about vaccines exist, with an increasing amount of misinformation on vaccines and vaccination being available on the internet and other social media platforms.^{70,71} Pharmacists and other healthcare workers can be instrumental in providing patients with relevant and correct information about the benefits of vaccination for their children as well as themselves, and build trust in the immunisation programme.^{66,70} Through building a trusting relationship, they can ease the fears of many patients. Providing accurate information and facts about the significant risks associated with not being vaccinated, can help to debunk common misconceptions.⁷⁰ Healthcare workers, including pharmacists, should however equip themselves, to ensure they

Table V. Possible adverse events for childhood vaccines^{7,23-51,64}

Vaccine	Possible adverse events
Bacille Calmette-Guérin (BCG)	<ul style="list-style-type: none"> • Initial reaction to intradermal vaccination: Papule formation lasting maximum 4–6 weeks • Papule heals by itself and develops into a scar, which is normal (visible in 40% of infants). Do not squeeze or put anything on the papule • Usual reaction and no cause for alarm: Oozing, ulceration and lymphadenopathy in 1–10% of cases • Lymphadenopathy < 1.5 cm: Not clinically significant • Occasionally the papule becomes a pustule. Complete AEFI notification and refer all cases with significant lymphadenopathy or a draining sinus
Oral Polio Vaccine	<ul style="list-style-type: none"> • May be associated with a flu-like illness and gastroenteritis • Mild fever • Very rare adverse reactions <ul style="list-style-type: none"> ◦ Vaccine-associated paralytic poliomyelitis (VAPP)
Hexavalent (DTaP-IPV-HepB-Hib)	<ul style="list-style-type: none"> • Pain, redness and swelling at the site of injection within 24–48 hours after administration of vaccine • Irritability • Fever $\geq 38^{\circ}\text{C}$ and acute illness • Persistent nodule may develop • Headache • Anorexia, vomiting and diarrhoea • Rare adverse reactions <ul style="list-style-type: none"> ◦ Anaphylaxis or severe allergic reactions ◦ Hypotonic-hyporesponsive episode (HHE) ◦ Seizures ◦ Arthus reaction, i.e. local inflammatory reaction with necrosis; more likely to occur after four or five previous doses of vaccines containing tetanus, diphtheria and pertussis components
Pneumococcal conjugate	<ul style="list-style-type: none"> • Redness, swelling and pain at the site of injection • Mild fever • Uncommon adverse reactions <ul style="list-style-type: none"> ◦ Crying ◦ Seizures (including febrile seizures) • Rare adverse reactions <ul style="list-style-type: none"> ◦ Hypersensitivity reactions such as dyspnoea and facial oedema

<p>Rotavirus</p>	<ul style="list-style-type: none"> • Mild fever • Irritability • Abdominal pain, vomiting, diarrhoea and flatulence • Very rare adverse reactions <ul style="list-style-type: none"> ◦ Intussusception, i.e. when a part of the intestine folds in on itself (like a telescope), resulting in severe abdominal pain, persistent vomiting, bloody stools, abdominal bloating and/or high fever. Intussusception can be fatal without medical intervention
<p>Measles</p>	<ul style="list-style-type: none"> • Burning or stinging at the injection site • Transient morbilliform rash (looks like measles) • Mild fever up to 30 days after vaccination • Very rare adverse reactions <ul style="list-style-type: none"> ◦ Anaphylaxis or severe allergic reactions ◦ Seizures and immune thrombocytopaenia purpura (ITP) have been reported
<p>Measles, mumps, rubella (MMR)</p>	<ul style="list-style-type: none"> • Mild adverse reactions <ul style="list-style-type: none"> ◦ Reaction at the injection site ◦ Transient rash and fever that may occur 6–11 days after vaccination • Serious adverse reactions which are rare <ul style="list-style-type: none"> ◦ Thrombocytopaenia ◦ Encephalopathy and seizures due to the measles component ◦ Orchitis and aseptic meningitis and deafness due to the mumps component ◦ Arthritis due to the rubella component ◦ Anaphylaxis or severe allergic reactions
<p>Chickenpox (varicella)</p>	<ul style="list-style-type: none"> • Pain, redness and swelling at the injection site • Fever (Oral $\geq 37.5^{\circ}\text{C}$) • Uncommon adverse reactions <ul style="list-style-type: none"> ◦ Fever (Oral $> 39.0^{\circ}\text{C}$) ◦ Fatigue and malaise • Higher incidence of pain, redness and swelling after the second dose was observed as compared to after the first dose
<p>MMR plus chickenpox (varicella)</p>	<ul style="list-style-type: none"> • Irritability • Rash • Pain, redness and swelling at the injection site • Fever (Oral $\geq 37.5^{\circ}\text{C}$) • Uncommon adverse reactions <ul style="list-style-type: none"> ◦ Fever (Oral $> 39.0^{\circ}\text{C}$) ◦ Lethargy, fatigue and malaise • Rare adverse reactions <ul style="list-style-type: none"> ◦ Anaphylaxis or severe allergic reactions
<p>Meningococcal conjugate</p>	<ul style="list-style-type: none"> • Mild local and systemic reactions reported within seven days after vaccination; mean duration of two days for the local reactions and less than five days for the systemic reactions • Headache • Redness and soreness at the injection site • Fever • Fainting
<p>Hepatitis A</p>	<ul style="list-style-type: none"> • Local reaction at the site of injection <ul style="list-style-type: none"> ◦ Injection site pain, erythema or swelling • Mild systemic complaints <ul style="list-style-type: none"> ◦ Malaise, fatigue and low-grade fever ◦ Decreased appetite ◦ Irritability and insomnia ◦ Headache ◦ Abdominal pain, diarrhoea, nausea and vomiting • Arthralgia and myalgia
<p>Tetanus, diphtheria, pertussis, polio</p>	<ul style="list-style-type: none"> • Anorexia, nausea, vomiting and diarrhoea • Headache • Fatigue, fever $> 37.5^{\circ}\text{C}$, irritability • Pain, redness and swelling at the site of injection • Erythema • Rare adverse reactions <ul style="list-style-type: none"> ◦ Lymphadenopathy ◦ Myalgia, arthralgia ◦ Arthus reaction

Tetanus-diphtheria	<ul style="list-style-type: none"> • Common reactions which may occur 48 hours post vaccination <ul style="list-style-type: none"> ◦ Mild fever ◦ Pain, redness and swelling at site of injection occasionally • Rare adverse reactions <ul style="list-style-type: none"> ◦ Arthus reaction
Human papilloma virus	<ul style="list-style-type: none"> • Injection site pain and swelling in the arm are common • Itching, rash, redness and urticaria • Nausea, diarrhoea, abdominal pain, headache, myalgia, fever (38 °C) are not uncommon • Syncope, dizziness, lymphadenopathy and anaphylaxis have been reported
Influenza	<ul style="list-style-type: none"> • Local reactions: Soreness, erythema and induration at the site of injection • Nonspecific systemic symptoms: fever, chills, malaise and myalgia • Rare adverse reactions <ul style="list-style-type: none"> ◦ Immediate hypersensitivity (possible allergic) reactions e.g. hives, angioedema, allergic asthma or systemic anaphylaxis ◦ Severe allergic and anaphylactic reactions in response to a number of vaccine components

have sufficient knowledge about vaccine misinformation, have good communication skills and dedicate sufficient time towards listening and responding to parents' concerns.⁷⁰

As part of the multi-disciplinary healthcare team, pharmacists have the opportunity to engage with multiple stakeholders (private sector, public sector, non-governmental organisations, universities, media, communities) to work towards social mobilisation for high vaccination coverage.⁷² These activities should however be tailored to the needs and characteristics of the particular community or target population e.g. level of literacy and education, access to healthcare services, socio-economic status, prior knowledge, culture.²³ One of the biggest challenges in social mobilisation is to reach children who do not have access to routine immunisation services, making outreach programmes critical.¹¹ Sporadic measles and diphtheria outbreaks over the last two years in South Africa, point to sub-optimal childhood vaccination coverage.^{73,74} Pharmacists can therefore play an important role as part of the multi-disciplinary healthcare team during catch-up campaigns. Private-public partnerships can also benefit these outreach programmes, as was evident from a 2017 catch-up campaign in the Tshwane District, during which nearly 1 000 children were vaccinated.⁶⁹

With the re-engineering of primary healthcare in South Africa, emphasis is placed on a public health approach with promotional and preventive elements.¹⁵ Pharmacists, especially those in community pharmacies, have multiple opportunities to embrace and advance public health through immunisation advocacy.⁹ An important public health role of the pharmacist in performing micro-level activities is to be actively involved in educating the public and other healthcare professionals about immunisation, to advocate for paediatric immunisation, and to advocate for the public health benefits of increased vaccination coverage.^{11,16} This is underpinned by the global evidence of the value of vaccines in disease prevention, and the necessity to ensure increased vaccination uptake.¹¹ For pharmacists to contextualise their role in vaccination services, and play an active role in advocacy and social mobilisation, a comprehensive understanding of the risks and benefits of vaccines, the goals of the EPI-SA, vaccination coverage

rates and the epidemiology of VPDs would be beneficial.⁹ Targeted education and training in vaccinology and good communication skills would be key.¹¹

Monitoring and evaluation

Surveillance plays a crucial role in the control, elimination and eradication strategies for VPDs.⁶⁸ Public health intervention programmes, like the EPI, are assessed partially through surveillance.⁶⁸ For this purpose, health professionals working in the community, including pharmacists, are essential in the detection of acute flaccid paralysis (AFP), neonatal tetanus (NNT), measles and AEFIs.⁶⁸ All healthcare workers should therefore be trained and knowledgeable on simple case definitions of AFP, NNT, measles and AEFIs to ensure detection and referral of these cases to district public health authorities for active surveillance.⁶⁸

For monitoring purposes, the NDoH supplies every infant with a 'Road-to-Health' booklet (RtHB).^{11,23} This includes the child's immunisation record, which must be updated at every vaccination session.^{11,16,23} Also, a record of all immunisations must be kept in the pharmacy for a period of at least five years.¹⁶ Information on immunisations can be shared with physicians and local clinics upon request. It can also be used to remind patients when their vaccinations are due and to generate reminder letters for booster doses.^{11,16,23} Moreover, immunisation statistics must be provided to the local District Health Co-ordinator for epidemiological purposes and for stock control, if EPI vaccines are supplied to the pharmacy by the local authority.^{11,23} Providing statistics for vaccines purchased through the private sector, is currently not a requirement.

Monitoring, using good quality indicators, is an important tool to measure the performance of the entire immunisation programme, and to ultimately guide policies.⁷⁵ Official vaccine administrative coverage figures for South Africa are generated by the District Health Information System (DHIS) in the public sector and are published annually by the Health Systems Trust in the District Health Barometer.⁷⁶ Immunisation coverage is a basic health indicator, and is used to assess the functioning of the health system. Statistical data on vaccination services is therefore a

critical element for performance monitoring and evaluation of the EPI-SA, emphasising the importance of having accurate statistics available.⁷⁶ Currently, South Africa does not have any electronic patient-level data or electronic data integrated across the private and public sectors, on the supply chain for medicines and vaccines. Development of such an integrated data management system would be essential for programme management, and for monitoring and evaluation of the NHI implementation.^{77,78}

Conclusion

The purpose of the EPI-SA is to prevent death and reduce suffering from diseases of childhood that can be prevented by immunisation. Vaccination is still considered one of the greatest and most cost-effective public health interventions against infectious diseases to date. Vaccination is therefore a key strategy in the fight against antimicrobial resistance, which is now regarded as a global public health crisis. Pharmacists involved in providing vaccinations are in a privileged position to ensure this protection. Pharmacists should relentlessly take up the role of providing this very essential service in the communities they serve, and ensure that they have the necessary knowledge and skills to do this.

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