Appendix F

Monitoring and Management of Adverse Events Following Vaccination

For monitoring and management of adverse events following vaccination, please take reference from **Monitoring and Management of Adverse Events Following Immunisation (**Section 5**)** of the **Hong Kong Reference Framework for Preventive Care for Children in Primary Care Settings - Module on Immunisation**
https://www.healthbureau.gov.hk/pho/rfs/english/pdf_viewer.html?file=download87&title=string107&titletext=string84&htmltext=string84&resources=05_Module_on_Immunisation_Children_chapter5

Adverse event following immunisation (AEFI) is defined as any untoward medical occurrence which follows immunisation and which does not necessarily have a causal relationship with the usage of the vaccine. All vaccines, like other medicinal products, have the potential to cause an adverse event. To minimise adverse events, vaccinees should be carefully screened for precautions and contraindications before vaccine administration. Vaccinees or the carers should also be informed of the possible AEFI and the management of these events. Primary care providers should be prepared for their management if any adverse reaction occurs.

Adverse events following immunisation

Classification of AEFI

AEFI can be classified into one of the following categories:

	Description
Allergic reaction	Anaphylaxis is the severe reaction that characteristically evolves rapidly towards cardiovascular collapse requiring resuscitative therapy. Other examples of severe allergic reactions are wheezing or shortness of breath due to bronchospasm, swelling of mouth or throat, skin manifestation (e.g. hives, eczema, pruritus); or facial or generalised oedema. Allergic reactions usually occur within 24 hours of immunisation.
Local reaction	Local reactions, usually occurs within 5 days of immunisation, of concern may include abscess (sterile or infected), or other severe local reactions, such as redness and swelling that extend beyond the nearest joint or last 4 days or more.
Systemic reaction	Systemic reactions usually occur within 5 days but may occur up to 3 months after immunisation. Early onset ones of concern include toxic shock syndrome, hypotonic-hyporesponsive episode, persistent crying or screaming episodes, high fever (greater than 39°C or 102.2°F), sepsis, or rash (especially those lasts for 4 days or more or requires hospitalisation). Thrombocytopenia (with platelet $< 50{,}000/mm^3$) may have a delayed onset.
Neurological disorders	Some neurological adverse reactions may be related to vaccination. Seizures (usually generalized convulsion), encephalopathy, meningitis or encephalitis, if occurred, may have an onset within 15 days of immunisation. Brachial neuritis or Guillain-Barré Syndrome, if occurred within 3 months of immunisation, may be related to the immunisation.

- The frequency of adverse events can be classified as follows: very common (>10%), common (1-10%), uncommon (0.1-1%), rare (0.01-0.1%), very rare (<0.01%) and not previously reported.
- Most vaccines cause mild adverse events such as low-grade fever, pain or redness at the injection site and these should be anticipated.
- Anaphylaxis is a severe form of allergic reaction. It is very rare but can be fatal. The risk of an allergic reaction can be minimised by good screening prior to vaccination.

Events where evidence demonstrates no causal link or favours rejections of the causal relationship with immunisation

- Sudden infant death syndrome (SIDS) and any vaccine;
- Autism and MMR vaccine,
- Multiple sclerosis and hepatitis B vaccine
- Inflammatory bowel disease and MMR vaccine;
- Diabetes and Hib vaccine;
- Type 1 diabetes and MMR vaccine or DTaP vaccine,
- Asthma and any vaccine;
- Asthma exacerbation or reactive airway disease episodes in children and adults and inactivated influenza vaccine,
- Bell's palsy and inactivated influenza vaccine

Reporting vaccine adverse events

- Primary care providers are encouraged to report any suspected AEFI which are serious (even if the reaction is well-known), non-serious but deemed medically significant by the healthcare professional, or unexpected, to the Pharmacovigilance Unit of the Drug Office, Department of Health, to facilitate assessment process.
- Further information and Adverse Drug Reaction (ADR) report form are available on the next page or online at the following link: https://www.drugoffice.gov.hk/eps/do/en/healthcare_providers/adr_reporting/adr_report_form.html

Report can be returned by fax to 2319 6319
For Follow-up report (see Guidance),
Please provide previous case Ref. No.:_____

Department of Health
Adverse Drug Reactions (ADR) Report Form

Please read the following instructions:

1. Please read the Guidance for Healthcare Professionals (http://www.drugoffice.gov.hk/adr.html); and Guidance for Pharmaceutical Industry (http://www.drugoffice.gov.hk/adr_industry.html) before completing the ADR report form.
2. ADR can be briefly described as a noxious and unintended response to a pharmaceutical product (i.e. drug or vaccine).
3. If the ADR of a newborn/child may be related to the mother, please submit a separate report for the mother.
4. Please provide information to every section.
5. **Full name and any kind of personal identifier of the patient**, such as identity card number and hospital admission number, **should not be provided** on the report form.
6. Information of individual reporter will be treated in strict confidence. Please read the Statement of Purposes overleaf in respect of the collection of your personal data.
7. As limited space is provided, please use another page for additional information if necessary.
8. For further enquiries, please contact the Undesirable Medical Advertisements and Adverse Drug Reaction Unit of Drug Office of the DH at 2319 2920.

Section (A): Patient Information

Patient initials or ref. no.: _____ **(Please read instruction 5 above)**
Sex: ❑M ❑F ❑Unknown For woman, is she pregnant? ❑No ❑Yes ❑Unknown
Weight (if known): _____kg Date of birth: (dd/mm/yyyy) ____/____/____ or age (at last birthday):_____
Ethnic group: ❑Chinese ❑Asian (Not Chinese) ❑African ❑Caucasian ❑Eurasian ❑Unknown ❑Others_____

Section (B): About the Adverse Drug Reaction

Date of onset of ADR: (dd/mm/yyyy) ____/____/____

Description of event: _____

_____

ADR category (for vaccine related ADR only):
❑Allergic reaction ❑Local reaction ❑Systemic reaction ❑Neurological disorders
Severity (can tick more than 1 box if appropriate):
❑Life threatening ❑Prolonged Hospitalization ❑Hospitalized on: (dd/mm/yyyy) ____/____/____
❑Hospitalization NOT required
Laboratory result (if applicable): _____

All Drug Therapies/Vaccines Prior to ADR (Please use trade names and, for vaccine, indicate batch number. Please circle the suspected drug.)	**Daily Dosage** (dose number for vaccines e.g. 1st DTP)	**Route**	**Date Begun**	**Date Stopped**	**Reason for Use**

Section (C): Treatment & Outcome

Treatment for ADR: ❑No ❑Yes. Details (including dosage, frequency, route, duration) _____

Laboratory result (if applicable): _____

Outcome:❑Recovered on: (dd/mm/yyyy) / / ❑Not yet recovered ❑Unknown ❑Died on: (dd/mm/yyyy) / /

Sequelae: ❑No ❑Yes: ❑Persistent disability ❑Birth defect ❑Medically significant events Details:_____

Allergies or other relevant history (including medical history, liver/kidney problems, smoking, alcohol use etc)

_____

Section (D): Reporter Details (Please read instruction 6 above)

Name of Reporter and Organization:_____ Sector of service: ❑Private ❑Public

Occupation: ❑Doctor ❑Chinese medicine practitioner ❑Dentist ❑Pharmacist ❑Nurse ❑Others_____

Correspondence Address:_____

Tel. no.: _____Fax. no.: _____ Email: _____

Also report to: ❑Manufacturer ❑Distributor/Importer ❑Others_____ Date of this report:_____

DH 2580 (12/2019)

5.2. Allergic reactions to vaccine constituents

Person may be allergic to the vaccine antigen or to a vaccine component such as animal protein, antibiotic, preservative or stabiliser. The recipient may present with skin rash as a minor form of allergic reaction. Anaphylaxis is a more severe form of allergic reaction. Typical symptoms and signs of anaphylactic reactions are generalized urticaria (hives), swelling of the mouth and throat, difficulty in breathing, wheezing, hypotension, or shock.

Allergic reactions to vaccine components

1. MMR vaccine
- Measles and mumps vaccine viruses are both grown in chick embryo fibroblasts tissue culture. However, persons with a severe egg allergy can receive measles- or mumps-containg vaccines in the usual manner because the content of these proteins is extremely low.
- Many MMR reactions are attributable to gelatine allergy.

2. Yellow fever vaccine
- Grown on egg embryos and do contain residual egg protein.
- For egg-sensitive persons, a scratch test or intradermal test can be perfomed before administering the vaccine to check for reactivity.

3. Influenza vaccine
- Most inactivated influenza vaccines and live attenuated influenza vaccine are grown on egg embryos and do contain residual egg protein.
- Recombinant influenza vaccine is a vaccine that is created synthetically by recombinant technology and it does not require egg during the production process.
- Individuals with a history of anaphylaxis to egg should have seasonal influenza vaccine administered by health care professionals in appropriate medical facilities with capacity to recognise and manage severe allergic reactions. Recombinant influenza vaccine contains no egg protein.

4. Varicella, MMR, MMRV and zoster vaccines
- These vaccines contain gelatine and persons with history of an anaphylactic reaction to gelatine or gelatin-containing products should be evaluated by an allergist prior to receiving gelatin-containing vaccines.

5. Hepatitis B vaccine
- Allergy to yeast or allergy to latex has been suggested as a possible cause of vaccine reactions.

As the above list is not exhaustive, primary care providers should consult package inserts of individual vaccines for the list of vaccine constituents before vaccination.

Antibiotic-induced allergic reaction

1. IPV, MMR, varicella and zoster vaccines contain neomycin.
2. In additional to neomycin, IPV also contains streptomycin and polymyxin B.
- Person with history of anaphylactic reactions to the above antibiotics should not receive these vaccines.
- More often, neomycin allergy present as contact dermatitis (delayed-type cell-mediated immune response) rather than anaphylaxis, which is not a contraindication for administration of vaccines containing neomycin.

Management

Vaccinees should remain under observation for a short interval to ensure that they do not experience an immediate adverse event. It is recommended that the recipients remain in the vicinity of the place of vaccination for at least 15 minutes. Severe anaphylactic reactions usually happen rapidly within 15 minutes of vaccination, but can occur within hours.

Management of local and systemic adverse reactions

- Treatment of local adverse reaction such as pain and swelling at the injection site can be alleviated by applying a cold compress to the injection site.
- Paracetamol can be prescribed for pain or fever if necessary.
- The most common immediate adverse event in adults and older children is a vasovagal episode either immediate or soon after vaccination. Anyone who complains of giddiness or light-headedness before or after vaccination should be advised to lie down until free of symptoms.
- Specialist medical care is needed for management of the rare but more severe AEFI such as Guillain-Barré syndrome, encephalitis and idiopathic thrombocytopenic purpura.

Management of anaphylaxis (See Figure 2)

- All primary care providers providing vaccinations should be familiar with the practice emergency plan and resuscitation procedures. Emergency equipments and medications should be checked regularly and readily available for immediate use.
- Early recognition of anaphylaxis is important. Primary care providers should distinguish anaphylaxis from other conditions such as vasovagal episode. (see Table 21)
- Seek help and call ambulance immediately if anaphylaxis is suspected.
- Assess airway, breathing, circulation and level of consciousness of patient. Perform cardiopulmonary resuscitation (CPR) if necessary.
- Administer adrenaline intramuscularly in case of anaphylaxis. (See Table 22).
- If oxygen is available, administer by facemask at a high flow rate.
- Record all vital signs, medications administered to the patient, including the time, dosage, response, and the name of the medical personnel who administered the medication, and other relevant clinical information.
- Because of the possibility of delayed reactions, individuals who have had an anaphylactic reaction should be sent to hospital, even though they may appear to have made a full recovery.
- Report the adverse event.

Table 21. Clinical features which may assist differentiation between a vasovagal episode and anaphylaxis.[1,3]

	Vasovagal episode	Anaphylaxis
Onset	• Immediate, usually within minutes of or during vaccine administration	• Usually within 15 minutes, but can occur within hours, of vaccine administration
	Symptoms / Signs	
Skin	• Generalised pallor • Cool, clammy skin	• Skin itchiness • Generalised skin erythema • Urticaria • Angioedema
Respiratory	• Normal respiration; may be shallow, but not laboured	• Cough • Wheeze • Hoarseness • Stridor • Signs of respiratory distress (tachypnoea, cyanosis, rib recession) • Upper airway swelling (e.g. lip, tongue, throat, uvula, larynx)
Cardiovascular	• Bradycardia • Weak/absent peripheral pulse • Strong carotid pulse • Hypotension – usually transient and corrects in supine position • Loss of consciousness – improves once supine or in head-down position	• Tachycardia • Weak/absent carotid pulse • Sustained hypotension and no improvement without specific treatment. • Limpness and pallor may suggest hypotension in infants and young children • Loss of consciousness – no improvement once supine or in head-down position
Gastrointestinal	• Nausea or vomiting	• Abdominal cramps • Diarrhoea • Nausea or vomiting
Neurological	• Feels faint or light-headed	• Sense of severe anxiety and distress

Figure 2. Anaphylactic reactions: treatment algorithm for healthcare providers (Modified from anaphylaxis algorithm of Resuscitation Council UK[4])

- Call for help, never leave patient alone
- Lie patient supine in "head down and feet up" position if conscious (unless this results in breathing difficulties)
- Lie patient on left side and position to keep airway clear if unconscious
- Cardiopulmonary resuscitation if necessary

↓

Adrenaline 1:1000 - 0.01ml/kg/dose intramuscularly
Repeat after 5 minutes if no better
(see Table 22 for quick dosage reference)

↓

When skill and equipment available:

- Establish airway
- High flow oxygen
- IV fluid challenge
- Monitor: - Pulse oximetry
  - Blood pressure
  - ECG

↓

Documentation
Transfer to hospital
Report adverse events

Table 22. Quick reference for dosage of adrenaline (The recommended dose for adrenaline is 0.01mg/kg body weight) (Adopted from Immunization Action Coalition[2])

	Age group	Range of weight (kg)*	Range of weight (lb)	Adrenaline dose 1mg/ml injectable (1:1000 dilution) IM
Infants and Children	1-6 months	4-8.5 kg	9-19 lb	0.05 ml (or mg)
	7-36 months	9-14.5 kg	20-32 lb	0.1 ml (or mg)
	37-59 months	15-17.5 kg	33-39 lb	0.15 ml (or mg)
	5-7 years	18-25.5 kg	40-56 lb	0.2-0.25 ml (or mg)
	8-10 years	26-34.5 kg	57-76 lb	0.25-0.3 ml (or mg)†
Teens	11-12 years	35-45 kg	77-99 lb	0.35-0.4 ml (or mg)
	≥ 13 years	46+ kg	100+ lb	0.5 ml (or mg)‡

Note: If body weight is known, then dosing by weight is preferred. If weight is not known or not readily available, dosing by age is appropriate.
*Rounded weight at the 50th percentile for each age range
†Maximum dose for children
‡Maxim20or teens

(Source: Section 5 of the Hong Kong Reference Framework for Preventive Care for Children in Primary Care Settings - Module on Immunisation https://www.healthbureau.gov.hk/pho/rfs/english/pdf_viewer.html?rfs=PreventiveCareForChildren&file=ModuleOnImmunisation_Chapter5)