Health Protection Agency

Vaccine incident guidance

Actions to take in response to vaccine errors

Vaccine Incident Guidance – Actions to take in response to vaccine errors

This document was produced by the Immunisation, Hepatitis and Blood Safety Department at the Health Protection Agency with the approval of the Health Protection Agency's Vaccine Programme Board.

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1. Background to the guidance

The credibility of an immunisation programme is highly dependent on the assurance of vaccine potency and quality. Substandard handling of vaccines may result in a loss of potency or increased reactogenicity in these vaccines. Individuals immunised with these vaccines may be at greater risk of illness or death from the diseases that the vaccines are intended to prevent. As a consequence, public confidence in immunisation programmes may be undermined, thus putting even more lives at risk.

For vaccine manufacturers, the correct handling of vaccines is a closely adhered to quality control issue. The care of vaccines beyond the point of manufacture should be awarded the same priority in clinical practice.

Despite numerous guidance documents on the storage and handling of vaccines, instances of improper vaccine storage and handling continue to be reported to the Health Protection Agency (HPA) and advice and guidance is regularly sought on the management of serious untoward vaccine incidents. Most notably, queries often arise about what to do with stocks of vaccines that have been exposed to potentially detrimental temperatures for various periods, as well as situations where incorrectly stored vaccines have been given.

Although each vaccine incident will need to be investigated on an individual basis, the management of these incidents should be consistent to avoid unnecessary confusion among both vaccine providers and the recipients of these vaccines.

For the majority of incidents involving vaccines, there is limited evidence on which to base a decision as to the impact of the error/s. The following guidance has therefore been based on a consensus of opinion from UK scientific and public health vaccine experts as well as published guidelines from Australia, New Zealand, United States and the World Health Organization.

2. Objectives of the guidance

This guidance is intended to be used by the wide range of professionals with a lead role in delivering immunisation programmes. These include amongst others: consultants in communicable disease control, health protection nurses, immunisation specialists/immunisation leads and community health service pharmacists.

The aim of the guidance is to:

- Provide a starting point from which to consider the appropriate response to vaccine incidents.
- Provide consistent advice to immunisers when incorrectly handled vaccines have been administered to patients and minimise the consequences of those errors.
- Ensure vaccines are given correctly and have the best chance of providing protection.

- Encourage vaccinators to work in an open and supportive environment in which they feel able to report vaccine incidents without fear of recrimination.

What the guidance is not:

An excuse to relax good practice!

It is never acceptable to be in the position of having to tell individuals they may not be protected by the vaccines they have received in good faith as a result of human error.

In addition to this, a considerable amount of time, money and manpower are required in having to track individuals who may have inadvertently received invalid doses of vaccine - which puts significant demands on already stretched resources.

It is accepted however, that errors will occur in even the most meticulously run organisations/clinics and it is predominantly for these errors which the guidance hopes to offer some reassurance.

Prevention of errors will always be the ideal and it is expected that immunisation providers will already be adhering to national policy recommendations for the storage, distribution and administrations of vaccines as laid out in the Department of Health's Immunisation against Infectious Disease.[1]

It is also anticipated that those storing and administering vaccines have received adequate training as recommended in the National Minimum Standards in Immunisation Training.[2]

3. How to use the guidance

The guidance is divided into the four main sections:

- Section 4 examines how to respond to errors in vaccine storage and breaches of the cold chain.

- Section 5 discusses the general principles of managing an adverse vaccine incident.

- Section 6 provides advice on how to address errors that have occurred in vaccine preparation and vaccine administration.

- Section 7 looks at the considerations that need to be taken into account when deciding whether to revaccinate individuals.

When dealing with an incident, this guidance document should be read in its entirety.
The guidance is based on the best information and evidence available at the time of publication.

4. Responding to errors in vaccine storage

4.1 The cold chain & temperature sensitivity of vaccine

The 'cold chain' is the system of transporting and storing vaccines within the temperature range of +2°C to 8°C from the place of manufacture to the point of administration. This temperature range is recommended by vaccine manufacturers and stated in the individual vaccine Summary of Product Characteristics (SPC) to ensure that a potent vaccine reaches recipients.

It is not the intention of this document to deal with how the cold chain should be maintained in any detail as this is discussed fully elsewhere.[1] It is however, expected that all staff involved in the delivery of a vaccine service have received adequate training in the care and administration of vaccines and therefore recognise the importance of reporting temperature deviances outside the recommended +2 to 8°C range to the appropriate authority.

Vaccines, in common with all biological substances, degrade over time and vaccines stored outside the +2 to 8°C range may quickly lose their potency. Exposure to extremes of heat, cold, sunlight or fluorescent light can accelerate this process further and once potency has been lost, it cannot be restored.

It is generally recommended that immunisation service providers should maintain their vaccine refrigerators as close as possible to +5°C, as this gives a safety margin of + or − 3°C.

4.2 What constitutes a significant failure in the cold chain?

There are many variations of cold chain breakdown and, as such, data is not available to cover all permutations.

For licensure purposes, vaccine manufacturers have to provide a recommended storage temperature range. For virtually all currently used vaccines, this recommended range is between +2°C and 8°C and this is stated by the vaccine manufacturer in the vaccine SPC. If vaccines are not stored between the recommended temperatures, the manufacturer can disclaim responsibility for any apparent failure of those vaccines***. It is therefore recommended that any product knowingly stored outside of the cold chain should not be used unless its stability has been verified by the manufacturer.***

Thus, when a vaccine has been stored incorrectly, it should be isolated, clearly labelled and kept in cold chain conditions until further advice has been sought from the vaccine manufacturer.

Vaccine manufacturers, when contacted following a cold chain breach, will usually say whether their vaccines can continue to be used up to their stated expiry date or whether they should be discarded. However, the manufacturers will not normally accept liability for the use of a vaccine that has been exposed to out of range temperatures and subsequently administered to individuals. ***The responsibility and liability, if these vaccines are used, therefore rests with the immunising practitioner, health service provider and/or primary care trust (PCT).***

However, when such vaccine has already been administered to individuals, an informed decision about whether revaccination should be offered needs to be made based on what is known about the

vaccine antigen and where possible, the temperature sensitivity of the final product. The stability of vaccines varies widely between different types of product but in general will depend upon the nature of the product and procedures used in its preparation.[3] Because the potency of different vaccines varies, each vaccine incident must be evaluated individually. Vaccines against the same disease but from different manufacturers may differ in their stability and must also be considered on an individual basis.

4.3 Issues for vaccines exposed to temperatures below 0°C

4.3.1 Adjuvanted vaccines

Many vaccine antigens are bound to an adjuvant in order to elicit a strong and lasting immune response. Temperatures below zero can cause the adjuvant to precipitate, resulting in loss of adjuvant effect and vaccine potency.[4,5]
All aluminium-based adjuvants are damaged by freezing and this damage is irreversible. The efficacy of a vaccine that contains aluminium-based adjuvant exposed to freezing temperatures therefore cannot be guaranteed.

For some adjuvanted vaccines, evidence suggests the freezing point is well below zero.[5, 6] This data, however, is generally laboratory-based and cannot reliably predict protection in clinical use. In the absence of information on a specific vaccine therefore the best general advice is to consider all adjuvanted vaccines exposed to temperatures less than 0˚C as potentially harmed.

4.3.2 Lyophilised vaccines

Freeze-drying has presented a solution to some of the most unstable viral vaccines with many being expected to remain very stable at low temperatures and unaffected by freezing in lyophilised form. Some live viral vaccines such as varicella, should not be refrozen once thawed[7] and therefore it is recommended the vaccines are stored between 2-8˚C.

Lyophilised conjugate vaccines would also be expected to be remain stable at low temperatures but should not be frozen.

4.3.3 Vaccine diluents

Lyophilised vaccines and their diluents should always be distributed together. Most diluents are less sensitive to storage temperatures than vaccines and sometimes do not need to be kept in the cold chain. Some diluents, however, contain adjuvant and/or stabilising agents which may be affected by fluctuations in temperature. Prior to reconstitution of a vaccine it is recommended that diluents be at the same temperature as the vaccine to avoid thermal shock to the vaccine. It is therefore best practice to store all diluents within the cold chain.

Diluents must not be frozen due to the risk of bacterial contamination (see below). The exact freezing point for most diluents is not validated. Therefore, all diluents known to have been stored below 0˚C need to be considered as potentially harmed.

4.3.4 Bacterial contamination

Frozen vials can develop hairline cracks invisible to the naked eye due to the expansion in volume when a liquid is frozen. Bacterial contamination can occur via these cracks leading to an increased risk of reactions, abscesses and potential septicaemia following administration.[1, 5]

4.3.5 Visual appearance

There is an expectation that a vaccine that is, or has been frozen, will change in physical appearance, but for most freeze sensitive vaccines this is not the case.[4] The true freezing point for most vaccines is much higher than the actual temperature at which you would expect to see evidence of freezing.[6] Some vaccines show a coagulated or granular appearance once thawed, which is why it is recommended that vaccines are inspected for obvious discrepancies from the description provided in the SPC prior to administration.

This granular matter increases the sedimentation rate of the vaccine and larger granules will not dissolve in the suspension even after vigorous shaking. This is the basis of the 'shake test'.[5] In general, it takes someone with experience of looking for precipitation to correctly identify a vaccine that may have been damaged by freezing.[8]

The condition of the vaccine packaging may actually give a more easily identifiable indication as to whether a vaccine has been exposed to ice and freezing temperatures than the vaccine itself.

All freeze-sensitive vaccines known to have been stored below 0˚C need to be considered as potentially harmed and where there is any suspicion that a vaccine may have been exposed to freezing temperatures, it should be discarded.

Vaccines exposed to a minimum recorded temperature of between 0°C to 2°C are unlikely to have been affected by such an exposure and where the temperature of the fridge has been verified, they can often continue to be used up to their stated expiry date. The decision for using vaccines that have been stored between these temperatures lies with the immuniser. Therefore, it is recommended the manufacturer should be contacted for advice and available stability data.

4.4 Issues for vaccines exposed to temperatures over 8°C

When considering the heat sensitivity of vaccines, the issues are more complex and there are limited data to validate the use of vaccines exposed to temperature above 8°C. What data exist are unlikely to be underpinned with clinical evidence, or look at the long term stability of vaccines over their shelf life following an exposure to temperatures outside the cold chain and then returned to normal storage conditions. Hence, it is difficult to estimate the residual potency or life span of the vaccine.

In general, live attenuated vaccines, even in their lyophilised form, are more sensitive to heat exposure than inactivated vaccines. Reconstituted lyophilised vaccines become even more heat-sensitive after they have been reconstituted and should be used immediately following reconstitution or within a timescale recommended by the manufacturer.

Every vaccine has a different heat sensitivity and degradation rate.[5] Logically, the rate of degradation speeds up as the temperature increases.

High ambient temperatures (up to 37°C) do not cause an immediate loss of potency but can shorten the shelf life of a vaccine.

Repeated exposure to changes in temperature (e.g. where a fridge door is regularly opened) also has a detrimental effect on vaccine potency over a period of time and as such may also shorten the shelf life of the vaccine.

Evidence on the thermostability of vaccines suggests that an unsustained increase in temperature to above 8°C for a short period of time is unlikely to significantly affect the potency of most vaccines, particularly where a vaccine provider maintains good stock control and relatively quick turnaround of vaccines. However, it has been shown that the closer some vaccines are to their expiry date the more vulnerable they are to degradation.[9] For this reason, if vaccines are identified which have been given to patients where storage problems have been prolonged, or that are near to the end of their shelf life, it may be prudent to consider recommending an additional dose of the vaccine.

4.5 Check list for responding to an adverse storage incident/cold chain breach where vaccines have been given

1. Embargo fridge

- When a cold chain breach has been identified at any level, it is important that all the vaccines exposed to temperatures outside those recommended in their SPC are labeled and isolated and, wherever possible, maintained in a functioning monitored fridge.
- Vaccines should not be discarded until directed to do so by PCT or vaccine manufacturers as they may still be useable.
- All staff within the organisation should be advised that the fridge is embargoed until further notice, ensuring the vaccines are not used.
- The incident should be reported and documented according to local PCT guidelines

2. Confirm and define the incident

- The refrigerator temperature records should be checked and the cold chain practice prior to this event discussed with staff. Any explanations for temperature discrepancies should be sought, e.g. stock delivery, evidence thermometer was not re-set, untrained staff monitoring fridge, etc.
- The accuracy of current thermometer/s in use should be confirmed with the supplier if this has not already been done prior to use.
- Depending on the severity of the incident, a site visit may need to be carried out by an appropriately trained professional (usually a community health service pharmacist).
- The general condition of the fridge should be documented. Is it a purpose-built vaccine fridge? Are there any obvious signs of freezing? Is it placed in a well-ventilated area? Is it used for any other purpose than vaccine storage?
- A check of the fridge service history may give some indication when the fridge was last working properly if the incident is over an extended period of time. No pre-existing service history may give a concerning indication of how vaccines have been managed prior to this incident.
- The current fridge temperatures should be confirmed and, where possible, continuous temperature logging using a data logger should be carried out for a 48-hour period to establish temperature patterns of the fridge.

3. Collect as much information as possible

- To include:
  - What monitoring has taken place? (max/min/current thermometer readings) and how?
  - When was the cold chain last guaranteed?
  - What time period/s are involved? (hours/days/months)
  - What is the temperature range during this period?
  - Identify all vaccines stored in the fridge, the time they have been stored there, usual stock turn over and expiry dates.
- Identify whether vaccine potency is likely to have been affected by the storage conditions identified.
- Vaccines against the same disease but from different manufacturers must be considered individually. Consider seeking further advice from vaccine manufacturers.

- Identify which vaccines are given at the facility. Does the clinic administer National Schedule vaccines, travel vaccines and/or annual influenza vaccines? This may give an indication of time scale involved and draw attention to those at immediate risk.
- How many patients are registered at the facility and what is the catchment area it serves (e.g. lots of young patients, elderly patients or travellers)? This may give an indication of the extent of the situation.

When all the information above has been collated, an incident team meeting should be convened. The incident team should include all relevant practice and PCT staff, e.g. pharmacy lead, clinical governance lead, immunisation lead and communications lead. A representative from the local Health Protection Unit should also be included.

Informed decision making by incident team

Ideally a summary of the investigation report should be drawn up and circulated for discussion prior to the meeting.

The team must review the key findings of this summary report and consider if they have enough information in order to make an informed risk assessment of the compromised vaccines. They will also need to review what information is not known, whether it can be obtained or not and consider how this may influence the decision making process.

From the evidence available, the team must make a judgement about whether the cold chain breach investigated was sufficient to consider the vaccines given to patients sub-potent and if so what action now needs to be taken (see section 7.1 Risk Assessment).

Identify recipients of affected vaccines

- Identify patients who have been given affected vaccines from facility records/vaccination database and compile a patient list for possible revaccination, identifying patients with specific risk factors, patients given vaccines as part of a course, patients given vaccines for travel.
- Consider, if necessary, how you might trace/contact those who may require revaccination but have moved on since the incident has been identified. It is important that every effort is made to identify those potentially at risk.
- Formulate revaccination schedules (if needed) for each vaccine recipient using the table of recommendations for revaccination (Table 1), taking into account appropriate intervals between vaccines and the potential risk of side effects.

Identify resources/manpower required.

- Consideration needs to be given as to how, where, and in what timescale revaccination will take place. Is there a need to offer special clinics in the evening or at the weekend or identify other key vaccine providers in the area who can help?
- Depending on the scale of the incident, additional staff may be temporarily required to counsel, advise and/or revaccinate patients.

Identify training needs

- Rapid training may be required for all staff involved with the cold chain incident prior to the recommencing of clinics and the arrival of a new vaccine fridge or vaccine stock.

- Staff involved in the revaccination clinics must be clear about the objectives and confident about the rationale for the revaccination programme prior to advising patients.
- They should be able to explain the risks and benefits to patients of being re-immunised and know who to contact (e.g. PCT immunisation lead, community paediatrician) if they are unable to answer any questions/are unsure how to proceed with re-immunisation.

Develop a communication plan and identify resources

- Communication with the public must be open and honest; the whole process should be as transparent as possible to avoid distress, confusion or misinterpretation.

- Effective means of communication should be established and maintained between all parties involved with the incident so that everyone is kept informed of the progress and developments of the incident as they occur. It is important not to forget people who may have been involved early on in discussions but who subsequently become less involved during the final stages.

- Consideration should be given to the most appropriate medium for informing the patients involved. If the incident only involves a small number of people this may be best done on an individual basis by writing to patients via the GP practice/immunisation centre. If larger numbers are involved, additional support may be needed from local radio, TV or newspapers and/or adverts in local pharmacies. Consider targeted communications mediums (i.e. local churches/temples, community groups/centres, etc.) to get messages out to local ethnic, cultural and/or religious groups in the area. It may also be beneficial to set up a telephone helpline.

- A lead spokesperson must be chosen from the PCT or SHA to liaise with the media. Both reactive and proactive press briefings should be drafted in the event of media interest. A 'Questions and Answers' briefing should be drafted and agreed by all members of the incident team for use in response to the media.

- Support needs to be in place prior to informing the individuals involved. Information resources should be identified or developed for patients, taking into consideration the language needs of the local population. Translation of this information may be essential to the community response. Accessibility needs should also be factored in, i.e. mobility, speech, hearing or eyesight.

Re-immunise patients and record any adverse events

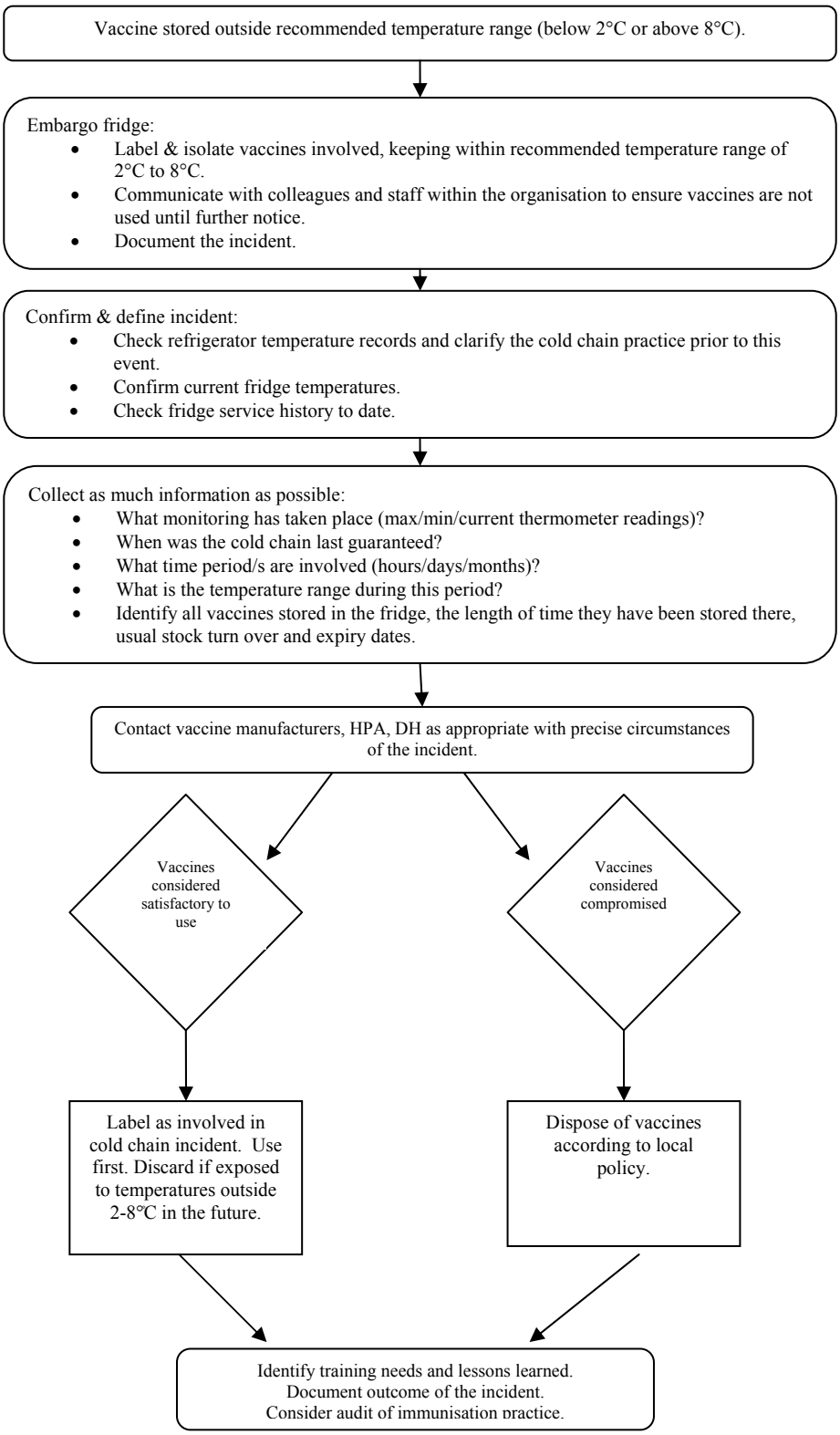
- It is important to provide follow up for patients who have been re-vaccinated. Any adverse event should be documented in the patient notes and reported to the Medicines and Healthcare products Regulatory Agency (MHRA) through the yellow card reporting system.
- Any adverse events should also be documented in the final report of the incident. This information may be valuable to future management of vaccine incidents.

Document and evaluate

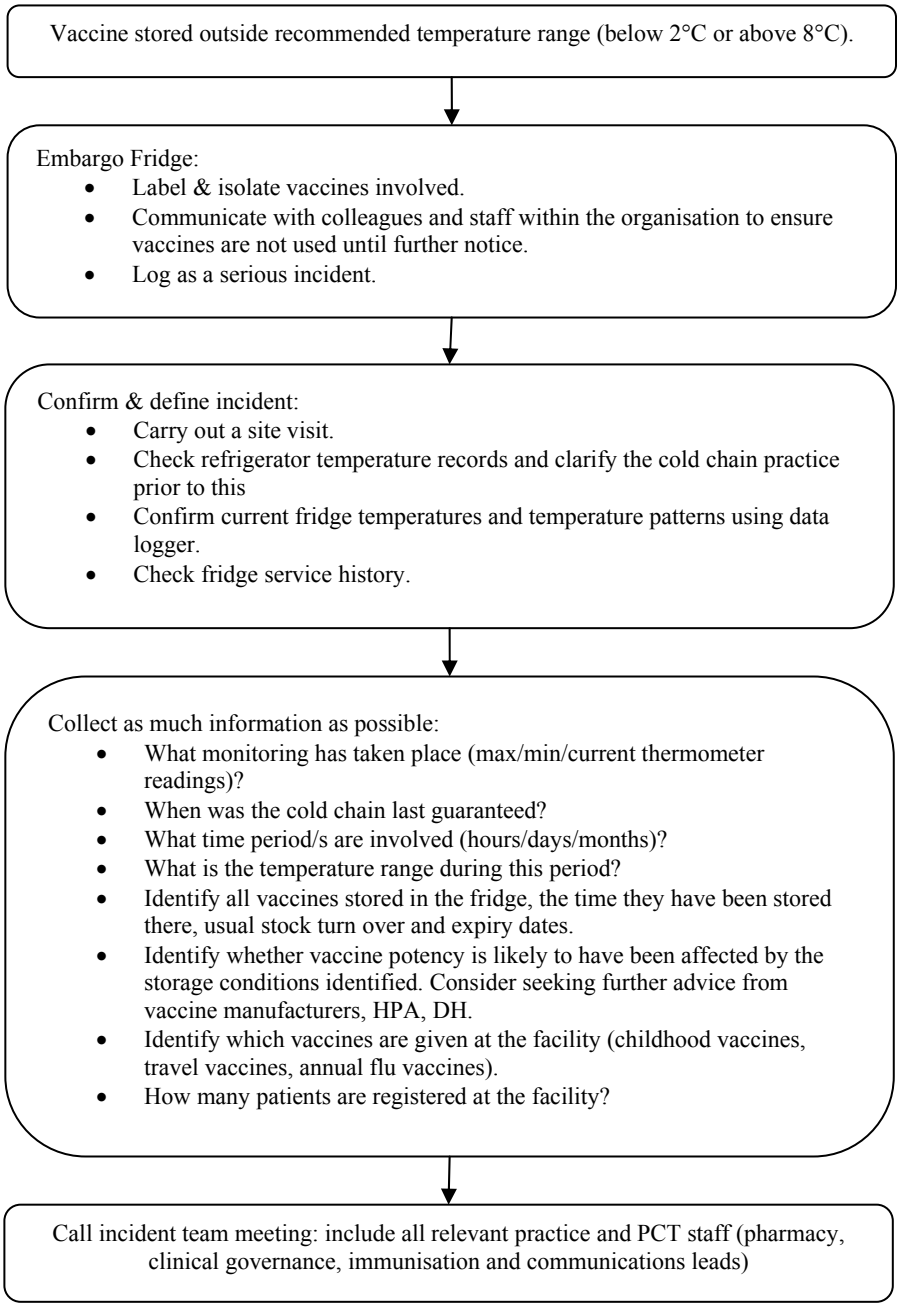
- The incident should be fully documented at every stage. This should include the cause of incident, the reason for decisions made, who advice was sought from and, where relevant, the action taken to prevent future incidents.

- A final report at the conclusion of the incident should evaluate the management of the incident, patient response and lessons learned for the future.
- Incidents such as these rarely occur in isolation and often reflect other problems in the practice. It is recommended that a full audit of the whole immunisation service where the incident has occurred is carried out to ensure that all processes and training of staff are in place and satisfactory.

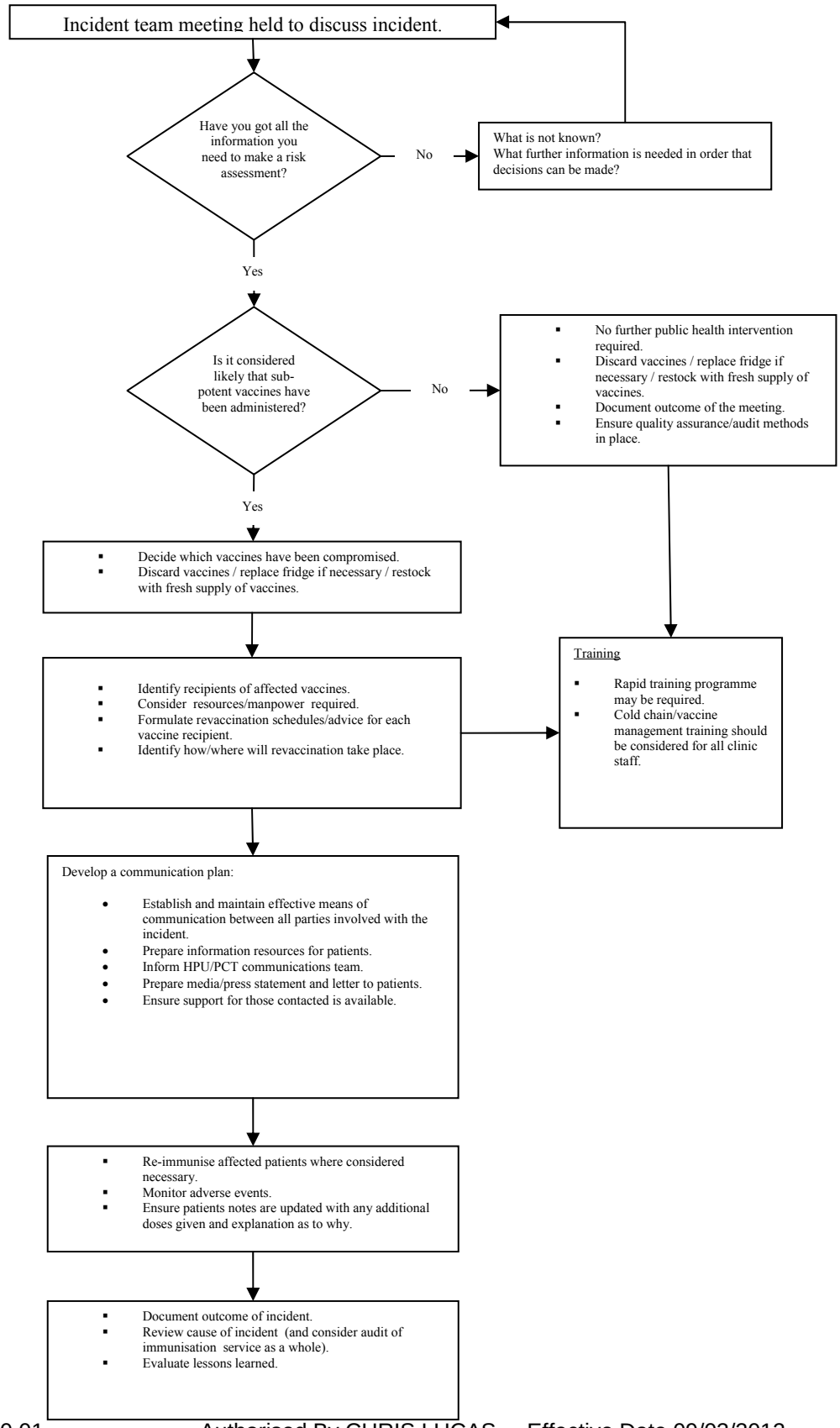
4.6 Algorithm for managing a cold chain breach where vaccines have not been administered to patients



4.7 Algorithm for managing a cold chain breach when vaccines have been administered to patients



4.8 Algorithm to assist incident team decision making - managing a cold chain incident where vaccines have been administered to patients.



5. Principles of managing an adverse vaccine incident

On occasions, vaccines may be administered to patients that have been handled incorrectly or inappropriately. Whilst generally, reassurance can be given that no immediate harm will come to the patient, there is concern that the vaccines they have received may not evoke an adequate antibody response or give sufficient long term protection.

Errors in vaccine administration can cause concern both to the patient/parent and the vaccine administrator so it is important that the situation is dealt with as efficiently and transparently as possible.

5.1 Checklist for managing an adverse vaccine incident

-Confirm/document incident
-Define what has gone wrong/what action if any needs be taken
-Identify if revaccination is likely to be recommended for recipients
-Identify recipient/s of vaccines and plan revaccination
-Inform recipients
-Repeat vaccines/doses required
-Record any adverse events.

6. Responding to errors in vaccine preparations and administration

6.1 Vaccines given outside of expiry date

All vaccines have an expiry date determined by the manufacturer. It is unlikely that a vaccine will cease to become effective on the day of expiry. However, vaccine stock that is past its expiry date has had a prolonged shelf life, and bearing in mind the degradation of vaccine over time, the stock is likely not to be as potent.

For this reason, where a vaccine has been given outside of its expiry date, revaccination should be *considered* following the recommendations in revaccination schedule (Table 1).

6.2 Incorrect mixing of vaccines

Unless specifically recommended and stated in the vaccine SPC, different vaccines must never be mixed in the same syringe prior to administration.

Incidents have been reported to the HPA where practitioners have mixed vaccines containing different antigens in one syringe so as to prevent having to administer two separate injections.

There is little data on the effect that mixing could have on the vaccines' stability. However, it is possible that the constituents (e.g. antigens, preservatives or adjuvants) contained in one vaccine may have a detrimental effect on the other vaccine, either by reducing its potency, which results in a reduced immune response, or rendering it totally ineffective.

Where vaccines that have been incorrectly mixed have been administered, revaccination should be *considered* following the recommendations in revaccination schedule (Table 1).

6.3 Wrong diluent used to mix vaccines

Some vaccines require reconstitution with a diluent prior to administration. Vaccines that require reconstitution are supplied with the diluent that should be used.

There is little data on the effect of different diluents on vaccines, but it is unlikely that patients given vaccine mixed with the wrong diluent will experience any adverse reaction. However, occasionally, diluents contain stabilising agents specific to the vaccine they reconstitute and, as a result, using the wrong diluent could potentially affect the potency or destroy the vaccine.

Where a vaccine has been administered that has been mixed with the wrong diluent, revaccination should be *considered* following the recommendations in revaccination schedule (Table 1).

6.4 Administration of incorrect or incomplete dose of vaccine

Vaccines administered to patients that are greater than the recommended dose will not affect the antibody response or protection afforded by the vaccine because, ultimately, an individual cannot 'overdose' on a vaccine. Patients should, however, be advised this may lead to an increased risk of local reaction.

Where vaccines are administered to patients at less than the recommended dose, vaccination will need to be repeated because the doses that patients received may not be sufficient to evoke a full immune response. Vaccination should ideally be repeated on the same day.

If it is not possible to repeat the vaccine on the same day, live vaccines should be repeated following a minimum interval of four weeks since the incorrect dose. Inactivated vaccines should be repeated as soon as possible.

6.5 Vaccines given earlier than recommended age

Vaccines are generally recommended at the earliest age at which an individual would be expected to make a satisfactory response. If given sooner than the recommended age, vaccines will not be harmful but factors such as passively transferred maternal antibodies may interfere with a good immune response.

For this reason, vaccines given to individuals more than a few days earlier than the recommended age should be repeated, when the individual reaches the recommended age, and at least one month from the dose that was given too early.

The *minimum* age recommended to start infant immunisation/first primary DTaP-IPV-HIB + PCV vaccinations in the UK is six weeks.[10]

6.6 Vaccines administered later than the recommended interval

A vaccine given later than the recommended interval from the last dose will not cause any harm to the individual and, as a rule, and with exception of oral cholera and oral typhoid, there should be no requirement to restart a course of vaccines. It does, however, leave the individual unprotected for a

longer period of time and, until the recommended doses have been given, full protection might not be attained.

6.7 Vaccines administered at less than the recommended interval

Vaccines given sooner than the recommended interval from the last dose may lead to a reduced immune response and reimmunisation should be rescheduled as recommended below:

Inactivated vaccines of the same type should usually be administered following an interval of four weeks (or eight weeks for pneumococcal conjugate vaccine (PCV)). Where these vaccines have been given at less than a 21-day interval, a dose should be repeated four weeks from the last dose given (eight weeks for PCV). Patients should be advised that this may lead to an increase risk of local reaction.

Live vaccines should be given at the same time as other live vaccines or a minimum of four weeks apart. Where parenteral live vaccines have been given at less than a 28-day interval, the vaccine given second should be considered invalid and re-immunisation considered. The repeat dose should be administered at least four weeks after the invalid dose.

Oral live vaccines can be administered at the same time as parenteral vaccines or at any interval before or after each other.

Rabies post exposure and accelerated vaccine courses: Specialist advice should be sought where theses vaccines are administered at less than the recommended minimum interval.

7. Considerations when deciding whether to revaccinate

7.1 Risk Assessment

The decision to revaccinate individuals who have been given potentially sub-potent vaccines is essentially a risk assessment that must balance the risk of the individual being exposed to the vaccine preventable disease against the risk of experiencing a vaccine reaction. In addition to this, immunisers have a duty of care to ensure they have administered effective vaccine and therefore leave themselves vulnerable to accusations of negligence if the action taken in response to the error does not constitute responsible practice.

Where the balance of risk lies for individual patients will depend on the vaccine/s they have received, the number of doses given and the purpose for which they received it/them.

For those receiving routine immunisation, additional doses are not likely to cause any harm beyond the risk of a local reaction. However, where this involves more than one potentially sub-potent vaccine, for example, where a course of primary infant vaccines has been given, consideration must be given to the number of repeat doses needed in relation to how likely is it that the whole vaccine course was affected.

For patients who have received vaccine in preparation for travel abroad, the individual may no longer be at risk or at immediate risk of disease if they have already travelled, but consideration must be given to the implications for future travel if the patient believes they are protected.

For certain groups of patients, the threshold for revaccination may be considerably lower, for example, in the case of asplenic, immunocompromised and hepatitis B contact patients who have received additional vaccinations as a result of being in an identified high risk group.

Ultimately the benefit of protection from the disease versus the likelihood of local reaction should be discussed with the individual in context of the incident and a course of action in their best interests decided on.

7.2 Antibody testing

Antibody testing is generally not straightforward or useful for many of the vaccines provided in the UK and should not be undertaken without a definitive goal. Taking blood from patients, especially children, is often traumatic and adds cost and complexity to the situation. In addition to this, the presence or absence of antibodies may not predict future protection and therefore the results can often be difficult to interpret with any degree of certainty.

7.3 Vaccine testing

There is no simple and inexpensive method that can be used to assess whether a vaccine exposed to temperatures outside the recommended 2-8˚C range has retained at least minimum required potency. It can take several months to determine whether a particular batch of vaccine is potent and this is therefore generally impractical in managing local incidents.

8. General principles for revaccination

8.1 Live vaccines

With the exception of BCG vaccine (see Table 1), there is no additional risk of adverse events from giving additional doses of live vaccine. The frequency of adverse events following a live vaccine usually falls with the number of doses given because any pre-existing antibodies will neutralise subsequent vaccine viruses.

8.2 Inactivated vaccines

The frequency of local or systemic reactions with certain inactivated vaccines may increase with additional doses given.
Individuals who have concerns regarding previous local or systemic reactions should be assessed on an individual basis, balancing the risk of disease against the risk of an adverse reaction.

8.3 Combination vaccines

Vaccines containing more than one antigen in combination are now often the only means of immunising individuals against certain diseases in the UK. Occasionally, individuals may not require revaccination with all antigens contained in the vaccine but the required antigen is not available in a single vaccine. Under these circumstances, additional doses of the combination vaccine should be given because the risk of local reaction to additional vaccine antigen is preferable to the consequences of missing out on a needed dose.

8.4 Routine schedule doses

Where revaccination is indicated, the repeat dose of vaccine should usually be given in addition to routine scheduled doses. Ensure a minimum interval of one month is left between the additional dose and routine doses of same vaccine type.

9. Information resources

9.1 Vaccine manufacturer customer contact details

Baxter Healthcare Limited
Customer Care line - Tel 0163 520 6140
e-mail - ukmedical@baxter.com

Crucell UK Ltd
Medical Information - Tel 0844 800 3908
E-mail - http://www.crucell.co.uk

GlaxoSmithKline UK
Customer Contact Centre -Tel 0800 221 4411
E-mail - customercontactuk@GSK.com

Novartis Vaccines
Medical Information – Tel 08457 451 500
Medical Information e-mail: serviceuk@novartis.com

Pfizer
Medical Information - Tel 01737 331111
E-mail - MedInfoUK@Pfizer.com

Sanofi Pasteur MSD
Medical Information - Tel 01628 587693
E-mail - medinfo@spmsd.com

9.2 Useful websites and reference documents

UK

Department of Health Immunisation page
http://www.dh.gov.uk/en/Publichealth/Immunisation/index.htm
(includes Local Co-ordinators Toolkit Vaccine Supply, Distribution and Storage information
http://www.dh.gov.uk/en/Publichealth/Immunisation/Localcoordinatorstoolkit/DH_110311)

Electronic Medicines Compendium
http://www.medicines.org.uk/emc.aspx

Health Protection Agency
http://www.hpa.org.uk/

National Travel Health Network and Centre (NaTHNaC)
http://www.nathnac.org

UK Medicines Information (UKMi)
http://www.ukmi.nhs.uk/

International

Australia: Proceedings of the National Vaccine Storage Workshop
http://www.health.gov.au/internet/immunise/publishing.nsf/Content/providers

New Zealand: What to do when things go wrong
http://www.immune.org.nz/site_resources/Professionals/latest%20resources/2005/What_to_do_when_things_go_wrong_0405.pdf

US: CDC Vaccine Storage and Handling Toolkit
http://www2a.cdc.gov/vaccines/ed/shtoolkit/

World Health Organisation (WHO): Temperature sensitivity of vaccines
http://www.who.int/vaccines-documents/DocsPDF06/847.pdf

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Table 1: Revaccination recommendations for people who have received sub-potent vaccines.

Vaccine	Group	Recommendation	Rationale
BCG	All	Repeat vaccination not usually recommended	High risk of significant local reaction and keloid scaring. Specialist advice should be sought on an individual patient basis.
DTaP/IPV/Hib	Children who have received ***one or more doses*** as part of their primary course.	**Repeat dose/s** as soon as possible	**Incidence of local reaction to DTaP containing vaccines may increase with additional doses** Parents should be advised that local reactions are increasingly more common in children receiving their fourth dose of an aP vaccine – occasionally these have been very large reactions and involve swelling of the whole limb or blistering at the injection site. This is a recognised phenomenon and does not contraindicate further doses.[11]
DTaP/IPV and dTaP/IPV	Children who have received a ***single booster dose following primary course.***	**Repeat dose** as soon as possible	**Incidence of local reaction to DTaP containing vaccines may increase with additional doses** Parents should be advised that local reactions are increasingly more common in children receiving their 4th and subsequent doses of an aP vaccine – occasionally these have been very large reactions and involve swelling of the whole limb or blistering at the injection site. This is a recognised phenomenon and does not contraindicate further doses.[11]
Td/IPV	Individuals 10 years and over who have received either routine adolescent ***booster dose***, booster doses for travel purposes or primary course.	**Repeat dose/s** as soon as possible	Incidence of local reaction to Td containing vaccines may increase in certain individuals with additional doses.[12-14] However, this has been shown not always to be the case and such additional doses are unlikely to produce an unacceptable rate of reaction [15]
Td/IPV, DTaP/IPV, dTaP/IPV, DTaP/IPV/Hib	As part of management of ***a tetanus prone wound***	If given to complete an **uncompleted course** of vaccinations, repeat dose as soon as possible	Tetanus vaccine given as part of wound management for someone who is fully immunised will only be effective at preventing tetanus at the longer half of the range of incubation periods. Unless a problem is discovered with the vaccine within the high-risk period, it is likely to be too late for a repeat dose to be helpful. If the wound is high risk then immunoglobulin should have been administered.
Hepatitis A	Individuals who have received one or more doses for travel purposes. Individuals who have received one or more doses for other ongoing identified risk.	Offer **repeat dose/s** if indicated for future travel. **Repeat dose/s** as soon as possible	Additional doses of hepatitis A vaccine are unlikely to produce significant side effects. Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.

Hepatitis B	Individuals who have received one or more doses for travel purposes Individuals who have received one or more doses **pre-exposure** or for other ongoing identified risk. Individuals who have received one or more doses post-exposure	**Repeat dose/s** as soon as possible if indicated for future travel. **Repeat dose/s** as soon as possible Perform blood test to ascertain infection status. At same visit, **give a repeat dose** of HepB vaccine. If infant <12m, repeat affected dose/s and ensure testing for HBsAg is carried out at one year of age.	Additional doses of hepatitis B vaccine are unlikely to produce significant side effects. Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
Hib/MenC conjugate	Children under 12 months of age given as part of their primary course Individuals over 12 months of age as part of routine schedule Patients >2y in all high risk groups	**Repeat dose/s** as soon as possible and ensure booster dose is given over 1y of age as per routine schedule **Repeat single dose** as soon as possible **Repeat dose/s given** as soon as possible	Additional doses of Hib/ Men C conjugate vaccine are unlikely to produce significant side effects. Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
Human Papillomavirus (HPV)	Patients given ***one or more*** doses	**Repeat dose/s** as soon as possible	Additional doses of HPV are unlikely to produce significant side effects. Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
Influenza	All individuals given the vaccine	Revaccination **only** recommended if during influenza season. **Repeat single dose** as soon as possible	Additional doses of flu vaccine are unlikely to produce significant side effects. Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
Japanese	Individuals who have received one or more	Offer additional dose/doses of vaccine if still at	Specialist advice should be sought on an individual patient basis from vaccine

Encephalitis	doses for travel	identified risk	manufacturer or NaTHNaC regarding scheduling and possible side effects.
MeningitisC conjugate vaccine	Children under 12 months of age given as part of their primary course Individuals over 12 months of age as part of routine schedule Patients >2y in all high risk groups	**Repeat dose/s** as soon as possible and ensure booster dose is given over 1y of age as per routine schedule **Repeat single dose** as soon as possible **Repeat dose/s given** as soon as possible	Additional doses of Men C conjugate vaccine are unlikely to produce significant side effects. Prior to Sept 2006, the vaccine was given as a three-dose schedule. Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
Meningitis ACWY Conjugate vaccine	Individuals who have received the vaccine for travel purposes ** In particular, pilgrims who have received the vaccines for Hajj.* Individuals who have received one or more doses for other ongoing identified risk.	**Offer additional dose** of vaccine if indicated for future travel. **Repeat dose given** as soon as possible	Additional doses of Men ACWY conjugate vaccine are unlikely to produce significant side effects. Adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
Meningitis ACWY polysaccharide vaccine	Individuals who have received the vaccine for travel purposes ** In particular, pilgrims who have received the vaccines for Hajj.* Individuals who have received one or more doses for other ongoing identified risk.	**Offer vaccination with Men ACWY conjugated vaccine** if indicated for future travel. **Repeat dose given** as soon as possible	Revaccination with polysaccharide may induce immunological hyporesponsiveness to further doses of polysaccharide C or to meningococcal group C conjugate vaccine.[16]
MMR	Patients given ***one or more*** doses	**Repeat dose/s** a minimum of four weeks since last dose	There is no additional risk of adverse events from giving additional doses of MMR vaccine. Any pre-existing antibodies should neutralise the attenuated vaccine viruses in subsequent doses.
Pneumococcal conjugate vaccine	Children under 12 months of age given as part of their primary course.	**Repeat dose/s** allowing a minimum of two months between doses if more than one dose is required. Ensure	Additional doses of PCV vaccine are unlikely to produce significant side effects.

(PCV)	Individuals over 12 months of age	booster dose is given over one year of age as per routine schedule **Repeat single dose** (unless in one of the high risk groups for whom two doses over one year of age is recommended, in which case more than one dose may be required depending on vaccine incident).	Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
Pneumococcal polysaccharide vaccine (PPV)	Patients >2y in all high risk groups Given routinely as patient is >65 years	**Flag patient notes** to ensure they receive a booster after 3 years instead of 5. Revaccination **not** recommended	The safety and effectiveness of reimmunisation with pneumococcal polysaccharide vaccine at intervals of less than three years is not known. Revaccination is associated with increased risk of local reaction and may induce immunological hyporesponsiveness.[17] The balance of risk and benefit does not favour giving repeat doses of PPV unless in an identified high risk group.
Rabies **Rabies continued**	Individuals who have received one or more dose for identified occupational risk. Individuals who have received one or more doses for **travel.** Individuals who have received one or more doses for **post exposure prophylaxis.**	Check antibody levels and boost if levels <0.5IU/ml. If sufficient time prior to travel, check antibody levels and boost if <0.5IU/ml. If insufficient time to check antibody levels, repeat affected doses. If travel complete but vaccine indicated for future travel check antibody or repeat any affected doses. Repeat any affected doses	Frequency of local reaction may increases with additional doses given. Adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration. Risk of rabies outweighs any possible side effects.
Tick-borne encephalitis vaccine	Individuals who have received one or more doses for identified occupational risk. Individuals who have received one or more doses for **travel.**	Offer additional dose/doses of vaccine if still at identified risk. Offer additional dose/doses of vaccine if indicated for future travel.	Adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration. Specialist advice should be sought from vaccine manufacturer or NaTHNaC regarding scheduling and possible side effects
Typhoid Vi	Individuals who have received the vaccine for travel.	Offer additional dose of vaccine if indicated for future travel.	Adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration. Please note for oral typhoid, doses five-fold higher than the recommended doses do

Ty21a	Individuals who have received the vaccine for travel.	Offer additional dose of vaccine if indicated for future travel.	not produce significant side effects but can increase the possibility of shedding the *S. typhi* Ty21a organisms in the faeces. [18]
Varicella	Individuals who have received one or more doses.	Repeat dose/s a minimum of four weeks since last dose.	No additional risk of adverse events from giving additional doses of varicella vaccine would be expected. Any pre-existing antibodies should neutralise the attenuated vaccine viruses.
Yellow Fever	Individuals who have received the vaccine for travel.	Offer repeat dose (if still indicated for future travel) a minimum of four weeks since last dose.	No additional risk of adverse events from giving additional doses of yellow fever vaccine would be expected. Any pre-existing antibodies should neutralise the attenuated vaccine viruses.

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