NHS National Services Scotland

Vaccine Incident Guidance.

Actions to take in response to vaccine errors.

Health Protection Scotland

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This version;

- Highlights that it is always useful to check the Summary of Product Characteristics (SmPC) for additional manufacturer's stability information
- Updates the framework for the initial management of vaccine incidents and a framework for assisting Incident Management Teams in the management of cold chain incidents
- Stresses the importance of risk assessment when vaccine incidents happen, provides a framework for vaccine incident risk assessment and a vaccine incident risk assessment checklist – Appendix 1
- Updates recommendations for revaccination to reflect current revaccination programmes.

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 which 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 Health Protection Scotland (HPS) 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 Organisation.

This document supersedes Vaccine Incident Guidance – Actions to take in response to vaccine errors (September 2013) issued by HPS.

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: Immunisation coordinators, Consultants in Public Health, Health Protection Nurses, Pharmacists and Pharmacy Technicians.

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
- Encourage immunisers 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 human resource 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 may occur in even the most meticulously run organisations/clinics and it is predominantly for these errors which this guidance offers a framework within which those incidents should be managed.

Prevention of errors will always be the ideal and it is expected that immunisers will already be adhering to local NHS Board guidelines on vaccine storage and handling which are based on a national framework published by HPS. https://www.hps.scot.nhs.uk/resourcedocument.aspx?id=6330.

It is also anticipated that those storing and administering vaccines have received adequate training as recommended in the Promoting Effective Immunisation Practice e-learning programme. http://www.nes.scot.nhs.uk/education-and-training/by-theme-initiative/public-health/health-protection/immunisation.aspx.

3. How to use the Guidance

The guidance is divided into the following 4 main sections:

- Section 4 discusses the general principles of managing an adverse vaccine incident
- Section 5 describes how to respond to a cold chain breach and carry out risk assessment of the 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. Principles of managing an adverse vaccine incident

On occasions, vaccines that have been handled incorrectly or inappropriately may be administered to patients. Whilst generally, reassurance can be given that no immediate harm will come to the patient, there may be concern that the vaccines they have received may not evoke an adequate 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 and in line with Duty of Candour regulations if required.

5. Responding to errors in vaccine storage

5.1 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 (SmPC) to ensure that a potent vaccine reaches recipients. In some cases the SmPC for specific vaccines will contain additional stability information on storage above the +2 to +8°C range.

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. 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.

5.2 What constitutes a failure in the cold chain?

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

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 SmPC. 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 stored outside of the cold chain should not be used until a risk assessment has been undertaken to determine if the vaccine has been compromised.

Thus, when a vaccine has been stored incorrectly, it should be quarantined, clearly labelled and kept in cold chain conditions until a risk assessment has been undertaken.

Vaccine manufacturers, when contacted as part of a risk assessment 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 continued to be used following a risk assessment, therefore rests with the NHS Board and immuniser.

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.[1] 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.

5.3 Issues for vaccines exposed to temperatures below 0°C

5.3.1 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.[2,3]

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.[3,4] These data however are 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 compromised.

5.3.2 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[5] and therefore it is recommended the vaccines are stored between +2 to +8°C.

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

5.3.3 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 compromised.

5.3.4 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.[3]

5.3.5 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.[2] The true freezing point for most vaccines is much higher than the actual temperature at which you would expect to see evidence of freezing.[4] 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 SmPC 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'[3] but in general, it takes someone with experience of looking for precipitation to correctly identify a vaccine that may have been damaged by freezing.[6]

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 compromised and where there is any suspicion that a vaccine may have been exposed to freezing temperatures, it should be discarded.

5.4 Issues for vaccines exposed to temperatures between 0°C to +2°C

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 NHS board and immuniser, and should only be taken following a risk assessment.

5.5 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 there are is unlikely to be underpinned with clinical evidence, or looking 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.[3] 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 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 suggest that an un-sustained 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.[7] 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.

5.6 Check list for responding to a cold chain breach

1. Quarantine Affected Stock

- When a cold chain breach has been identified, it is important that all the vaccines exposed to temperatures outside those recommended in their SmPC are labelled and isolated immediately and wherever possible, maintained in a functioning monitored fridge. Vaccines should not be discarded until a risk assessment of the incident has been undertaken and authorisation to do so is given by NHS Board.
- All staff within the organisation should be advised that the fridge contents have been quarantined until further notice and ensure that the vaccines are not used.
- Arrangements should be made to replenish stock if required to avoid any unnecessary service disruption.

2. Reporting the Incident

The incident should be reported and documented according to NHS Board procedures.

3. Risk assessment by NHS Board (Appendix 1 – Vaccine Incident Risk Assessment Checklist)

An initial risk assessment of the incident will be undertaken by NHS Board staff and further investigation of the incident will be carried out in line with NHS Board policy if necessary.

- Depending on the severity of the incident, a site visit may need to be carried out by an appropriately trained professional from the NHS Board.
- The refrigerator temperature records should be checked and the cold chain practice prior to this event discussed with staff:
  - What temperature monitoring has been recorded? (max/min/current temperature readings)
  - Any explanations for temperature discrepancies should be sought - e.g. stock delivery, evidence thermometer was not re-set, untrained staff monitoring fridge, etc.
  - When was the cold chain last guaranteed?
  - What time period/s are involved? (hours/days/months)
  - What is the temperature range during this period?
- The accuracy of current temperature recording devices in use should be confirmed.
- Consider confirming the current fridge temperatures where possible through continuous temperature logging using a data logger. This should be carried out for a 72 hour period to establish temperature patterns of the fridge.
- The general condition of the fridge should be documented.
  - Is it a purpose built vaccine fridge?
  - How old is the fridge? Is the fridge over 5 years old?
  - 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 historical audit data may give some indication as to when the fridge was last working properly if the incident is over an extended period of time. The audit history data may give an indication of how fridge/vaccines have been managed prior to this incident.
- Identify all vaccines stored in the fridge, the time they have been stored there, usual stock turn over and expiry dates.
- Identify which vaccines are given at the facility.
  - Does the clinic administer routine national immunisation programme 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.
- Contact vaccine manufacturers for all affected vaccines to obtain stability information based on the known particulars of the incident to determine if the vaccines have been compromised.

- Vaccines against the same disease but from different manufacturers must be considered individually.
- Check for any additional stability information contained within the SmPC

- Consider if patients have potentially received compromised vaccines as a result of the incident.

For further information regarding temperature sensitivity/stability of vaccines, the following document may be useful, in particular, Part II: Analysis of vaccine stability - vaccines commonly used in immunisation programmes. https://apps.who.int/iris/bitstream/handle/10665/69387/WHO_IVB_06.10_eng.pdf?sequence=1&isAllowed=y.

Using the above information a risk assessment will be undertaken to establish whether:

- **Vaccines have not been compromised and may continue to be administered using Patient Group Directions in line with NHS board procedures**
  - Vaccines should be labelled to indicate affected by one cold chain incident.
  - Advise to use first.
  - Advise to contact NHS Board for advice if affected vaccines are further exposed to temperatures outwith +2°C to +8°C
- **Vaccines have been compromised, however, there is no evidence that they have been administered to patients.**
  - These vaccines should now be destroyed
- **Vaccines may have been compromised and may have been or have been inadvertently administered to patients**
  - Any remaining vaccine should now be destroyed
  - An investigation summary report should be prepared for the Incident Management Team

4. Form Incident Management Team

An Incident Management Team meeting should be convened when it has been established that vaccines have been compromised by the cold chain breach and may have been or have been inadvertently administered to patients. NHS Boards may decide to form an Incident Management Team at any stage of the process if required.

The Incident Management Team should include all relevant staff – e.g. Pharmacy Lead, Clinical Governance Lead, Immunisation Lead, Communications Lead. A representative from the local Health Protection Team should also be included.

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

The team must review the key findings of this summary report and consider what information is still not known, whether it can be obtained or not and also consider how this may influence the decision making process.

From the evidence available, the team must decide whether revaccination is necessary. See section 7.1

Identify recipients of affected vaccines

- Patients who have been given compromised vaccines can be identified from facility records/vaccination database. A patient list should be compiled for possible revaccination.
- Patients with specific risk factors or given vaccines as part of a course or for travel should be identified.
- 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

- 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 staffing resources 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 re-commencing 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. NHS Board Immunisation Coordinator, Community Paediatrician) if they are unable to answer any questions/are unsure how to proceed with revaccination.

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 NHS Board 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.

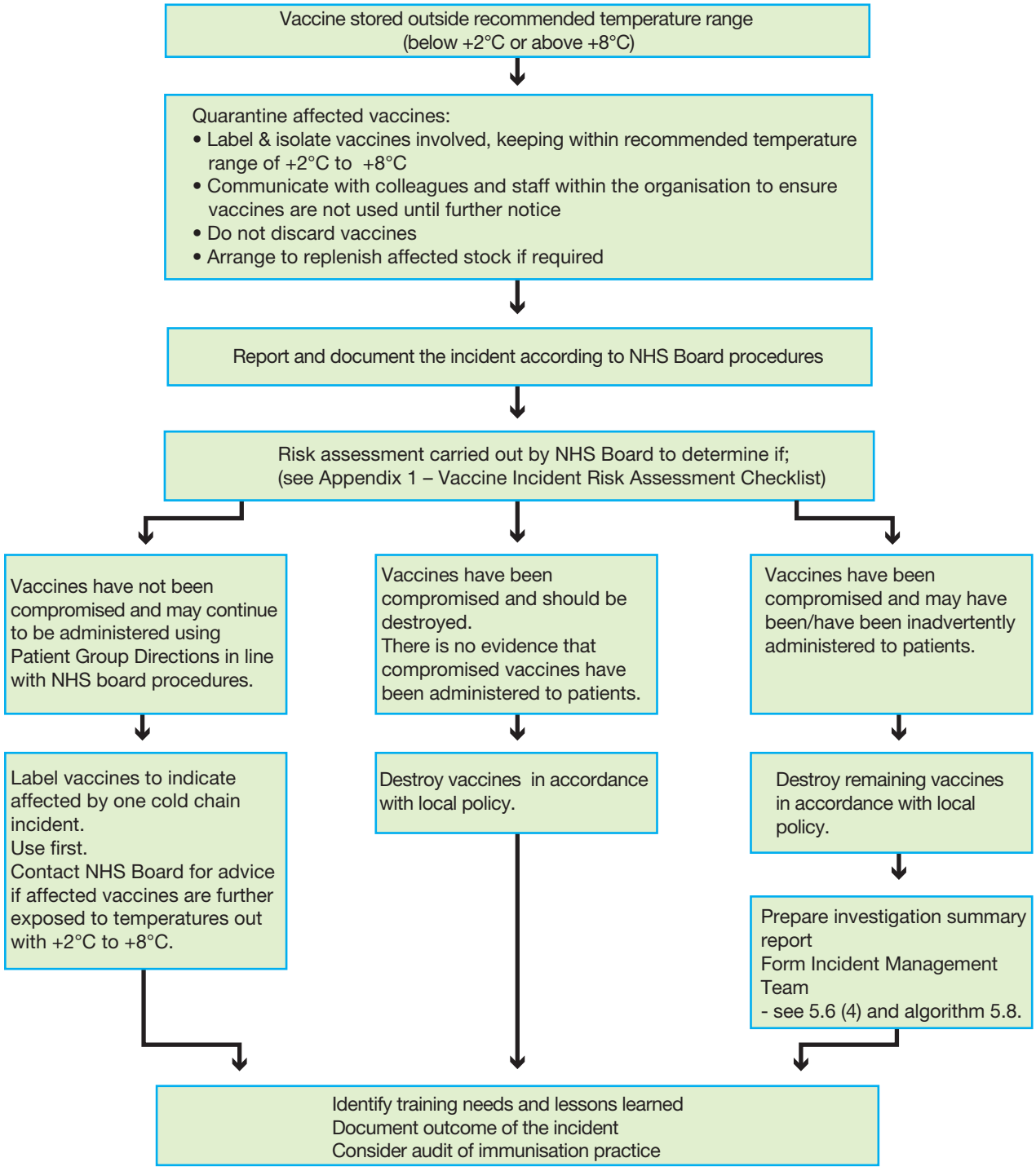
Revaccinate patients and record any adverse events

- It is important to provide follow up for patients who have been revaccinated. Any adverse event should be documented in the patient notes and reported to the MHRA through the yellow card reporting system (https://yellowcard.mhra.gov.uk/).
- Any adverse events should also be documented in the final report of the incident as this information may be valuable to future management of vaccine incidents.

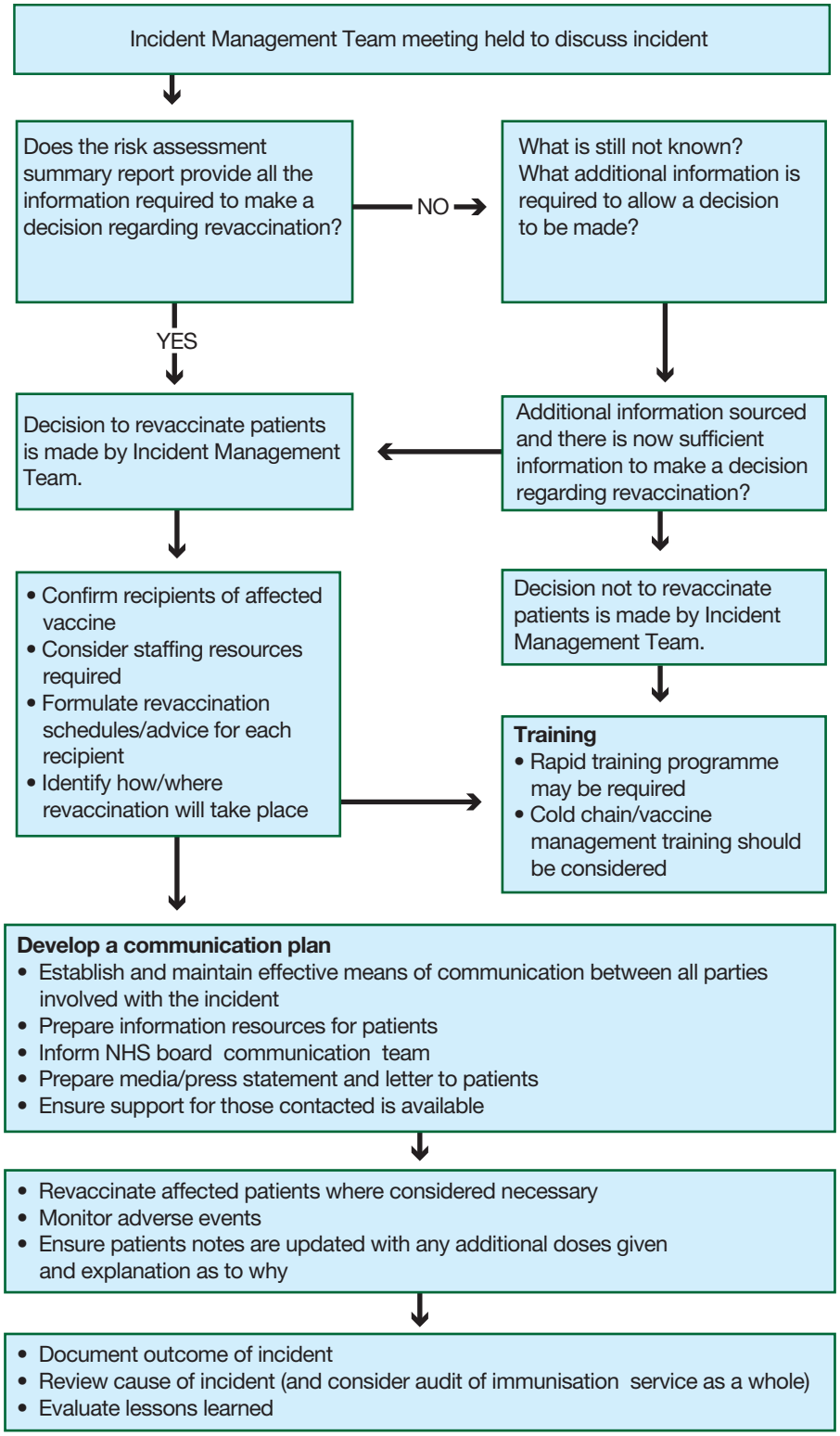
Document and evaluate

- The incident should be fully documented at every stage. This should include: the cause of incident; 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 or clinic. It is recommended 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.

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



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



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. Although it is unlikely a vaccine ceases to become effective on the day of expiry, when the degradation of vaccines over time is taken into account, vaccine stock past its expiry date has had a prolonged shelf life and thus is likely not to be as potent. Consider contacting the vaccine manufacturer to check if they have stability data for the affected vaccine beyond the expiry date.

Where a vaccine has been given outside of its expiry date and manufacturer's stability data confirms potency has been affected 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 SmPC, different vaccines must never be mixed in the same syringe prior to administration.

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

There are little data on the effect that mixing will 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 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 are 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 usually affect the overall immune response or protection afforded by the 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, the vaccine will need to be repeated, as the dose the patient received may not be sufficient to evoke a full immune response. The vaccine 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 4 weeks since 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 six-in one (DTaP/IPV/Hib/HepB + PCV vaccinations in the UK is six weeks.

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 re-start 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 revaccination should be re-scheduled 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 (8 weeks for PCV). Patients should be advised this may lead to an increase risk of local reaction.

Live vaccines should be generally given at the same time as other live vaccines or a minimum of 4 weeks apart, although there are exceptions. 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 4 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 General Considerations

The decision to revaccinate individuals who have been given potentially sub-potent vaccines is essentially a risk assessment which 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 to +8˚C range has retained at least the 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 as 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, as 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 Useful Websites and Reference documents

Scotland

Health Protection Scotland, Guidance on Vaccine Storage and Handling

https://www.hps.scot.nhs.uk/resourcedocument.aspx?id=6330

Health Protection Scotland http://www.hps.scot.nhs.uk/

TRAVAX https://www.travax.nhs.uk/

United Kingdom

Immunisation against infectious disease: the green book, chapter 3 storage, distribution and disposal of vaccines https://www.gov.uk/government/publications/storage-distribution-and-disposal-of-vaccines-the-green-book-chapter-3

Electronic Medicines Compendium. https://www.medicines.org.uk/emc/

Specialist Pharmacy Service. http://www.sps.nhs.uk

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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 scarring. Specialist advice should be sought on an individual patient basis.
DTaP/IPV/Hib/ HepB	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 4th 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.[8]
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.[8]
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.[9-11] However, this has been shown not always to be the case and such additional doses are unlikely to produce an unacceptable rate of reaction.[12]
Td/IPV, DTaP/ IPV, dTaP/IPV, DTaP/IPV/Hib/ HepB	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.

Vaccine	Group	Recommendation	Rationale
Hepatitis A	Individuals who have received one or more doses for travel purposes.	Offer repeat dose/s if indicated for future travel.	Additional doses of Hepatitis A vaccine are unlikely to produce significant adverse effects. Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
	Individuals who have received one or more doses for other ongoing identified risk.	Repeat dose/s as soon as possible.	
Hepatitis B	Individuals who have received one or more doses for travel purposes.	**Repeat dose/s** as soon as possible if indicated for future travel.	Additional doses of Hepatitis B vaccine are unlikely to produce significant adverse effects. Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
	Individuals who have received one or more doses **pre-exposure** or for other ongoing identified risk.	**Repeat dose/s** as soon as possible.	
	Individuals who have received one or more doses post-exposure.	Perform blood test to ascertain infection status. At same visit, **give a repeat dose** of HepB vaccine.	
	High risk infants due a dose at birth and four weeks and a booster at 12 months.	**Repeat dose/s** as soon as possible and ensure DTaP/ IPV/Hib/HepB doses at 8 weeks, 12 weeks and 16 weeks are given on time. Ensure dose at 12 months is given and ensure testing for HBsAg is carried out at 1 year of age.	
Hib/MenC conjugate	Children under 12 months of age given as part of their primary course.	**Repeat dose/s** as soon as possible and ensure booster dose is given over 1y of age as per routine schedule.	Additional doses of Hib/ Men C conjugate vaccine are unlikely to produce significant adverse effects. Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
	Individuals over 12 months of age as part of routine schedule.	**Repeat single dose** as soon as possible.	
	Patients >2y in all high risk groups.	**Repeat dose/s given** as soon as possible.	

Vaccine	Group	Recommendation	Rationale
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 adverse effects. Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
Influenza (inactivated)	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 adverse effects. Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
Influenza (Live)	All individuals given the vaccine.	Revaccination **only** recommended if during influenza season. **Repeat dose/s** a minimum of 4 weeks since last dose.	Additional doses of flu vaccine are unlikely to produce significant adverse effects. Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
Japanese Encephalitis	Individuals who have received one or more doses for travel.	Offer additional dose/doses of vaccine if still at identified risk.	Specialist advice should be sought on an individual patient basis from vaccine manufacturer or TRAVAX regarding scheduling and possible adverse effects.
Meningococcal group B 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.	**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.	Additional doses of MenB vaccine are unlikely to produce significant adverse effects.
Meningococcal group ACWY Conjugate vaccine	Adolescents receiving a dose at around age 14 years. 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.	**Repeat dose given** as soon as possible. **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 adverse effects. Adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.

Vaccine	Group	Recommendation	Rationale
MMR	Patients given one or more doses.	**Repeat dose/s** a minimum of 4 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 (PCV).	Children under 12 months of age given as part of their primary course.	**Repeat dose/s** allowing a minimum of two months between dose if more than one dose is required. Ensure booster dose is given over 1y of age as per routine schedule.	Additional doses of PCV vaccine are unlikely to produce significant adverse effects. Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
	Individuals over 12 months of age.	**Repeat single dose** (unless in one of the high risk groups for whom two doses over 1y of age is recommended, in which case more than one dose may be required depending on vaccine incident).	
Pneumococcal polysaccharide vaccine (PPV).	Patients >2y in all high risk groups.	**Flag patient notes** to ensure they receive a booster after 3 years instead of 5.	The safety and effectiveness of reimmunisation with pneumococcal polysaccharide vaccine at intervals of less than 3y is not known. Revaccination is associated with increased risk of local reaction and may induce immunological hyporesponsiveness.[13]
	Given routinely as patient is >65 years.	Revaccination **not** recommended.	The balance of risk and benefit does not favour giving repeat doses of PPV unless in an identified high risk group.

Vaccine	Group	Recommendation	Rationale
Rabies	Individuals who have received one or more dose for identified occupational risk.	Check antibody levels and boost if levels <0.5IU/ml.	Frequency of local reaction may increase with additional doses given. Adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
	Individuals who have received one or more doses for travel.	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.	Risk of rabies outweighs any possible adverse effects.
	Individuals who have received one or more doses for **post exposure prophylaxis.**	Repeat any affected doses.	
Rotavirus	All individuals given the vaccine.	**Repeat dose/s** a minimum of 4 weeks since last dose provided child <24 weeks old. After discounted dose an additional dose should not be given if the additional dose is first dose and infant is > 15 weeks old.	Additional doses of rotavirus vaccine are unlikely to produce significant adverse effects. Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
Shingles (herpes zoster)	All individuals given the vaccine.	**Repeat dose** a minimum of 4 weeks since last dose.	Additional doses of shingles vaccine are unlikely to produce significant adverse effects. Any adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
Tick-borne encephalitis vaccine	Individuals who have received one or more doses for identified occupational risk.	Offer additional dose/doses of vaccine if still at identified risk.	Adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration.
	Individuals who have received one or more doses for **travel.**	Offer additional dose/doses of vaccine if indicated for future travel.	Specialist advice should be sought from vaccine manufacturer or TRAVAX regarding scheduling and possible side effects.

Vaccine	Group	Recommendation	Rationale
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.
Ty21a	Individuals who have received the vaccine for travel.	Offer additional dose of vaccine if indicated for future travel.	Please note for oral Typhoid - Doses five-fold higher than the recommended doses do not produce significant side effects but can increase the possibility of shedding the *S.* typhi Ty21a organisms in the faeces.[14]
Varicella	Individuals who have received one or more doses.	Repeat dose/s a minimum of 4 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 4 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.

Appendix 1 Vaccine Incident Risk Assessment Checklist

Vaccine Incident Risk Assessor

Name and designation	
Department/NHS Board	
Incident reference no.	
Incident Address	
Incident Contact Name	
Incident Contact telephone no.	
Incident Contact email address	
Date of incident	

Vaccine Incident Risk Assessment	Comments
An initial risk assessment of the cold chain incident has been undertaken by NHS Board staff and	(a) (b)
(a) A site visit is not necessary (b) Due to the severity of the incident further investigation is required and a site visit will be carried out by an appropriately trained professional from the NHS Board.	
The refrigerator temperature records have been checked and the cold chain practice prior to this event discussed with staff: • What temperature monitoring has been recorded? (max/min/current temperature readings) • Any explanations for temperature discrepancies should be sought e.g. stock delivery, evidence thermometer was not re-set, untrained staff monitoring fridge, etc. • When was the cold chain last guaranteed? • What time period/s are involved? (hours/days/months) • What is the temperature range during this period? • There is evidence that the thermometer has been reset after each reading	

The accuracy of current temperature recording devices in use has been confirmed.	Yes/No
Confirm the current fridge temperatures where possible through continuous temperature logging using a data logger. This should be carried out for a **72 hour** period to establish temperature patterns of the fridge.	
The general condition of the fridge should be documented. • The fridge is a purpose built vaccine fridge? • How old is the fridge? • Approximate age if over 5 years old. • Are there any obvious signs of freezing? • Is the fridge placed in a well ventilated area? • Is the fridge used for any other purpose than vaccine storage?	Make: ..... Model: ..... Serial No. ..... Age: .....
Check the fridge audit history. This may give some indication as to when the fridge was last working properly if the incident is over an extended period of time. No pre-existing audit history may give a concerning indication of how vaccines have been managed prior to this incident.	
Identify all vaccines stored in the fridge, the time they have been stored there, usual stock turn over and expiry dates.	

Identify which vaccines are given at the facility. Does the clinic administer; • Routine national immunisation programme vaccines • Travel vaccines • Annual influenza vaccines	Yes/No Yes/No Yes/No
This may give an indication of time scale involved and draw attention to those at immediate risk.	
Contact vaccine manufacturers for all affected vaccines to obtain stability information based on the known particulars of the incident to determine if the vaccines have been compromised. Vaccines against the same disease but from different manufacturers must be considered individually.	Prepare report for Incident Management Team.
Consider if patients have potentially received compromised vaccines as a result of the incident.	

Outcome of vaccine incident risk assessment.

The vaccine incident risk assessment is now complete.
Select one of the following statements only;

	Tick one box only	What to do next
Vaccines have not been compromised and may continue to be administered using Patient Group Directions in line with NHS board procedures.	☐	• Label vaccines to indicate affected by one cold chain incident. • Advise to use first. • Advise to contact NHS Board for advice if affected vaccines are further exposed to temperatures out with +2°C to +8°C.
Vaccines have been compromised, however, there is no evidence that they have been administered to patients. These vaccines should now be destroyed.	☐	• Arrange for vaccines to be destroyed in accordance with local policy.
Vaccines have been compromised and may have or have been inadvertently administered to patients.	☐	• Destroy remaining vaccines in accordance with local policy. • Prepare investigation summary report for Incident Management Team. • Form Incident Management Team.

Record of affected vaccines

Manufacturer	Vaccine Name	Batch Number/s	Quantity	Expiry Date/s