



Public Health
England

Protecting and improving the nation's health

Vaccine Incident Guidance

Responding to errors in vaccine storage,
handling and administration

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Published January 2020
PHE publications
gateway number: GW-1062

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Executive summary

This **Vaccine Incident Guidance: Responding to errors in vaccine storage, handling and administration** is a revised and updated version of the original Vaccine Incident Guidance produced by the Health Protection Agency in 2012.

It has been developed to provide consistent guidelines, for both providers and commissioners of immunisation services, in the investigation and management of vaccine storage or administration incidents. Whilst the main focus of this guidance is where vaccine(s) has been stored outside the manufacturer's recommended temperature range (+2°C to +8°C), or where there is doubt about the effectiveness of vaccination following a storage error, it also contains advice about other commonly encountered issues such as errors in vaccine preparation and administration.

The document draws on existing guidance on vaccine storage and handling and reflects best practice procedures that should already be in place.

1. Introduction

The credibility and success of any immunisation programme is highly dependent on the administration of safe, quality vaccines. This quality is only assured through strict adherence to vaccine storage, handling and preparation procedures. Improper storage or handling of vaccines may result in a loss of product quality, effectiveness and increased reactogenicity in some vaccines.

On occasion, patients may inadvertently receive vaccine(s) that has been compromised by suboptimal handling and storage. Whilst reassurance can usually be given that no immediate harm will come to those who have received such vaccine(s), legitimate concerns may arise about the immune response and afforded protection both in the short and long term. In rare circumstances, patients may need to be recalled for repeat vaccination.

Errors in the administration, storage or handling of vaccines cause concern both for the patient/parent/carer and immuniser. They could lead to a loss of confidence in the vaccine provider or the immunisation programme as a whole. Whilst it is accepted that cold chain breaches and administration errors can occur in even the most meticulously run organisations/clinics, when they do occur, an informed decision needs to be made as to whether the vaccine has been compromised and if so, whether it presents a risk to patients. The effective management of errors is therefore essential to ensure patient safety, to maintain public confidence in immunisation programmes and to minimise vaccine wastage.

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 vaccines. The lessons learned from the incident should be shared and used to improve future practice and avoid recurrence.

2. Background to the guidance

Instances of improper vaccine storage, handling and administration are a significant concern for the national immunisation programme, with advice and guidance regularly being sought from Public Health England (PHE). Queries often arise about what to do with stocks of vaccines that have been exposed to temperatures outside the recommended range and/or how to manage patients who have received incorrectly stored vaccines.

The costs associated with loss and replacement of compromised vaccines should not be underestimated. During 2018, vaccine wastage reported through ImmForm¹ had a list price value of around £6.3 million. In terms of doses, about half of the reported vaccine wastage incidents were avoidable, but in terms of cost, these accounted for 73% (£4.6 million) of the value of reported wastage in 2018. This is likely to be under-reported and thus the true financial cost even greater. Vaccines are expensive and can be in short supply. Even when public health assurance has been given, large amounts of vaccines are being discarded as a result of perceived regulatory or licensing issues. Healthcare professionals have a responsibility to minimise financial risk and to help sustain supplies, whilst still ensuring the safety of patients and the continuing success of the national immunisation programme.

¹ ImmForm – the system used by Public Health England to provide vaccine ordering facilities and record data in relation to uptake against immunisation programmes.

3. Evidence

For the majority of vaccine-related incidents, there is limited evidence on which to base a public health decision as to the potential impact of the incident(s). The following guidance is therefore based mainly on the clinical expert opinion of UK scientific and public health vaccine experts as well as on published guidelines from the World Health Organization, Australia, New Zealand and the United States.

4. Objectives of the guidance

This guidance is intended to be used by a wide range of healthcare professionals with a role in delivering immunisation programmes. Whilst not exhaustive, these could include: General Practice staff, school immunisation providers, Screening and Immunisation Teams (SIT), Health Protection Teams (HPT) as well as by other healthcare practitioners working in other service areas where immunisations are given.

The aim of the guidance is to:

- provide a consistent approach to considering the appropriate action in response to vaccine storage and administration errors and to signpost providers to support and advice
- ensure vaccines are appropriately handled following compromised storage incidents, thus reducing vaccine wastage
- minimise the recall and unnecessary revaccination of patients by assisting providers to make an accurate assessment as to whether vaccine safety or efficacy have been compromised and to inform a proportionate response to incidents
- encourage immunisation providers to recognise the need to report vaccine errors and incidents and use the lessons learned to improve future practice

5. Good practice: guidance, training and reporting

Recommendations for the storage, distribution and administration of vaccines is detailed in PHE's 'Immunisation against infectious Disease' (Green Book)⁽¹⁾ and should be followed. All immunisation providers should have policies, protocols and procedures for the maintenance of the vaccine cold chain. These should include detailed written emergency vaccine storage and handling plans which cover the actions to take in the event of out of range temperature excursions or refrigerator break down.

As recommended in PHE National Minimum Standards and Core Curriculums for Immunisation Training^(2,3), it is expected that all staff involved in the delivery of immunisation services should have received appropriate training in the storage and administration of vaccines. Staff should therefore understand the importance of taking prompt action when vaccines are either stored outside the manufacturer's recommended temperature range (usually +2°C to +8°C) and/or where errors in vaccine administration have occurred.

It is not the intention of this document to deal with the contractual reporting obligations of vaccine incidents in detail. Providers should have local incident reporting procedures in place for informing their relevant SIT or commissioning organisation.

All incidents occurring in NHS provided immunisation programmes should be reported to NHS England using the agreed electronic reporting format and dealt with in line with the Immunisation & Screening National Delivery Framework & Local Operating Model available at: www.england.nhs.uk/commissioning/pub-hlth-res/. Serious vaccine incidents should be dealt with in line with the NHS England Serious Incidents Framework available at: <https://improvement.nhs.uk/resources/serious-incident-framework/>.

6. Principles of managing vaccine storage incidents and interruption of the cold chain

6.1 Vaccine cold chain and temperature sensitivity of vaccines

Vaccines, in common with all biological substances, degrade over time. 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⁽⁴⁾.

The 'cold chain' is a term used to describe the specific temperature conditions in which vaccines should be kept during storage and distribution to protect against loss of potency. The cold chain concept was first adopted in the 1970s by the World Health Organization (WHO) to protect the integrity and quality of vaccines in its worldwide immunisation programme. This standard practice is now universally recognised throughout the pharmaceutical industry and should be followed by everyone involved in the delivery of immunisation programmes.

For licensure purposes, vaccine manufacturers are required to recommend an optimum storage temperature range. For virtually all currently used vaccines, the recommended range is between +2°C and +8°C. The recommended temperature range is stated in the individual vaccine Summary of Product Characteristics (SPC) and forms part of the manufacturer's marketing authorisation (product license).

Maintaining vaccines within the cold chain between the recommended temperature range minimises the risk of compromising the effectiveness of the vaccine and ensures compliance with the manufacturer's product license.

6.2 What constitutes a significant breach in the cold chain?

Exposing vaccines to any temperature outside the manufacturer's recommended range is considered a breach of the cold chain and may invalidate the product license.

It is however, the length of time spent outside of the recommended cold chain conditions and the temperatures to which the vaccine(s) were exposed that may compromise the potency of a vaccine and as such, will determine the significance of the breach. While there are varying degrees of significance, each breach of the cold chain should be immediately acted upon and specialist advice should be sought in order to ascertain what action, if any, is required. Increasingly, the SPCs for some vaccines will contain information on vaccine stability outside the normal +2°C to +8°C temperature

range. Where this information is available, providers can use this to determine whether or not a single temperature excursion is likely to have affected vaccine quality.

'One off' fluctuations in fridge temperatures rising above +8°C but lasting less than 20 minutes, such as may occur when stock taking or restocking, are not likely to have breached the vaccine cold chain and as such do not require further action. The cause of the 'excursion' should be documented on the temperature recording chart, the maximum/minimum thermometer reset, and vaccines continued to be used to their expiry date. This pragmatic approach is based on studies from the U.S National Institute of Standards and Technology⁽⁵⁾ which demonstrated vaccine vials can maintain temperatures below +8°C for a minimum of 20 minutes despite the continuous influx of ambient air to the fridge. Vaccines must be stored in their original packaging to preserve this temperature stability and providers should be confident that vaccines have been stored appropriately prior to this event.

6.3 Vaccine stability following a cold chain breach

Generally, vaccines available for use in the UK are very stable and able to withstand short temperature excursions outside the recommended temperature range. Where vaccines have been stored either above or below the +2°C to +8°C range for longer periods of time, any loss of potency, although irreversible, is likely to be gradual rather than immediate or complete. Therefore, a failure to adhere to vaccine storage recommendations may not necessarily mean vaccines have been impaired to such an extent as to render them unusable. The difficulty lies in identifying the potential impact that a temperature excursion may have had on a vaccine/batch of vaccines and whether this would affect the immunological response.

6.4 Available Data

As there are so many permutations of cold chain failures, there is no single data source that is able to cover all possible scenarios. Where vaccine stability data is available, it may not provide long term evidence over the entire shelf life of the vaccine. Evidence is unlikely to be available for multiple temperature excursions and clinical evidence of vaccine efficacy for vaccine stored outside the manufacturer's recommendations is unlikely to be available. Hence it is often difficult to estimate the residual potency or life span of vaccine(s) following an excursion or reliably predict protection in clinical use.

Key sources of vaccine stability information include:

The WHO Temperature Sensitivity of Vaccines⁽⁴⁾. 2006. Available at: <http://apps.who.int/iris/handle/10665/69387>. This guidance provides general information on vaccine potency and the effects of adverse storage conditions for some of the vaccines used in the UK.

PATH. Summary of stability data for licensed vaccines. 2012. Available at: www.path.org/resources/summary-of-vaccine-stability-data/. This document presents data on the relative stability of licensed vaccines based on published studies and product monographs/SPCs. This does not always cover products used in the UK and there may be significant differences in manufacturer stability data between seemingly similar products. Where product specific data is unavailable however, the summary of stability data provided for each type of vaccine is very useful. http://www.path.org/publications/files/TS_vaccine_stability_table.pdf

Vaccine manufacturers. In recent years, as new vaccines are incorporated into the schedule, vaccine manufacturers have provided additional 'on label' stability data as part of the product licensure and this is detailed in the SPC or product monographs. This data is intended to guide healthcare professionals in making a clinical decision following temporary temperature excursions only. The manufacturer's medical information departments can and should be contacted for specific advice about their products when explicit incident details are provided. However, vaccines should not be disposed of until this has been discussed and agreed with the local Screening and Immunisation team.

6.5 Issues for vaccines exposed to temperatures above the manufacturer's recommended storage conditions (for example, over 8°C)

The impact of thermal damage on vaccine potency is very complex and varies for each vaccine. As a general rule, live attenuated vaccines are more sensitive to heat exposure than inactivated vaccines. However, when stored within the recommended cold chain conditions, most vaccines are very stable.

Exposing vaccine to higher than recommended temperatures does not cause an immediate loss of vaccine effectiveness but tends to lead to acceleration of the natural decline in potency.

Logically, the rate at which a vaccine loses potency speeds up as the temperature increases⁽⁴⁾. However, evidence on the thermostability of vaccines suggests such acceleration is more apparent at very high temperatures (>+37°C) than for prolonged storage at moderate temperatures (+15 to +25°C). For example, the half-life of the Gardasil HPV vaccine is estimated to be 130 months at temperatures up to +25°C, reducing to 18 months at +37°C and 3 months at 42°C⁽⁶⁾.

As high temperatures (above +25°C) are unlikely to be encountered as a result of cold chain failure in the UK, this would suggest most incidents (involving one-off exposure to moderate temperatures for a short period of time) are unlikely to significantly affect the potency of many vaccines. This is particularly true where vaccines are used early in their shelf life, and if the provider maintains good stock control (ordering what is needed

for a two to four week period) with a relatively quick turnaround of vaccines. It would therefore be anticipated that a risk assessment of such vaccines subjected to a brief ambient temperature excursion would (subject to stability data relevant to the vaccines involved) likely find the vaccines not to be significantly compromised and therefore to still be safe and effective to use.

It has been shown however, that the closer some vaccines are to their expiry date the more vulnerable they are to degradation⁽⁷⁾. Repeated short term exposure to temperatures above +8°C during storage would also be expected to have a cumulative effect on vaccine potency over time, with each exposure further contributing to the vaccine's natural decline. It would therefore be anticipated that a risk assessment of vaccines subjected to a prolonged or repeated elevated temperature excursion, subjected to substandard storage conditions that pose a significant concern (eg temperature over +25°C) or identified as nearing the end of their shelf life would be more likely to find that the vaccines have potentially been significantly compromised and should be disposed of.

Where such vaccine(s) have been inadvertently administered, consideration must be given to the possibility that individuals may have received sub-potent vaccines, and whilst they may offer protection in the short term, long term protection may be reduced.

6.6 Vaccines exposed to temperatures between 0°C and +2°C

Vaccines exposed to a minimum recorded temperature of between 0°C to +2°C are unlikely to have been affected by storage within this temperature range and where the temperature of the fridge has been verified, they can usually continue to be used up to their stated expiry date. Where vaccines stored between these temperatures have already been given, it is not usually necessary to repeat them.

6.7 Issues to consider for vaccines exposed to temperatures below 0°C

As a general rule, a vaccine's sensitivity to freezing temperatures is dependent on the vaccine preparation. Liquid formulations that contain an adjuvant, such as DTaP-containing vaccines, are more freeze sensitive than liquid formulations that do not contain adjuvant (eg pneumococcal polysaccharide vaccine, rotavirus vaccine). Most freeze-dried preparations (eg MMR, varicella vaccine) are unaffected by freezing in their lyophilised form.

Exposing some vaccines to a single episode of freezing temperatures can result in a measurable loss in vaccine potency. Where a vaccine has been subject to repeat freeze-thaw cycles, the impact on potency is likely to be even more serious.

As freezing can lead to a physical disruption of the solution and the formation of aggregates, administering vaccines that have been frozen may also increase the risk of local reactions. Frozen vials may also develop microscopic cracks 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 even potential septicaemia following administration^(1,4). For this reason, any vaccine that has been frozen or known to have been subjected to temperatures below 0°C should be disposed of. Where affected vaccine has already been inadvertently administered, a risk assessment of individual vaccine stability following potential freezing should inform whether revaccination should be considered.

6.7.1 Adjuvanted vaccines

All freeze sensitive vaccines that are known to have been stored below 0°C should be considered as potentially harmed and should not be used. Most freeze sensitive vaccines contain an aluminium adjuvant in order to elicit a strong and longer lasting immune response. Temperatures below 0°C can cause the bond between the aluminium adjuvant and the vaccine antigen to break. The adjuvant precipitates^(4,8), resulting in loss of adjuvant effect and therefore in vaccine potency.

For some adjuvanted vaccines, evidence suggests the freezing point at which damage occurs is well below zero⁽⁹⁾ and that whilst potency is reduced, the vaccine may not be totally destroyed. For example, studies of DTP vaccine demonstrated less than 15% reduction in the original potency for tetanus, diphtheria, and pertussis after a single freeze-thaw cycle. After two or more freeze-thaw cycles, potency was reduced more dramatically, by around 60%⁽¹⁰⁾.

Where adjuvanted vaccines which have been stored below 0°C have been inadvertently administered, the greatest risk of a substantially reduced immunological response is to those individuals who have received vaccines known to have been frozen or vaccines strongly suspected of being subject to repeat freeze/ thawing during storage.

6.7.2 Vaccine diluents

Lyophilised vaccines and their diluents should always be distributed and stored 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. 'Thermal shock' is damage to a vaccine that can occur when a diluent that is at too high a temperature (above +8°C) is added to a vaccine. It results in the death of some or all of the essential live organisms in the vaccine⁽¹¹⁾. It is therefore best practice to store all diluents with the

vaccine within the cold chain. This will also reduce risk that the wrong diluent is used to reconstitute a vaccine.

Diluents must not be frozen due to the risk of bacterial contamination (see section 6.7 'Issues to consider for vaccines exposed to temperatures below 0°C').

6.7.3 Visual appearance

Vaccines that are subjected to temperatures below 0°C are unlikely to show obvious physical signs that may alert the healthcare professional that the vaccine has been frozen or subjected to freezing temperatures⁽⁸⁾. The condition of the vaccine packaging may give a more easily identifiable indication as to whether a vaccine has been exposed to freezing temperatures than the vaccine itself. For example, damp, damaged, 'waxy' feeling boxes may be found in fridges where freezing has occurred.

Some vaccines that are, or have been frozen, will change in physical appearance. For this reason, it is recommended that all vaccines are inspected for obvious discrepancies from the description provided in the SPC prior to administration. Frozen vaccines may show a granular appearance or clumping in the solution once thawed. 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'⁽⁴⁾. In reality, however, it takes someone with significant experience of looking for precipitation to correctly identify a vaccine that may have been damaged by freezing.

7. Responding to a cold chain breach or compromised storage event

7.1 Discovering a cold chain breach

When a breach in the cold chain is suspected or potential problems with the storage of vaccines is identified, immediate corrective action should be taken.

Upon observing out of range fridge temperatures, it is important for healthcare providers to undertake a rapid assessment to try and establish a possible cause. Obvious causes to consider are: fridge door left ajar or open, a disruption to the electrical supply, restocking or a recent stock take, cleaning of the vaccine fridge or displacement of the thermometer probe. Wherever possible, immediate action should be taken to rectify the fault and the results of such actions documented.

Where no obvious cause can be identified and rectified, the priority must be to protect the vaccine from any further damage and/or inadvertent use until the incident has been thoroughly investigated.

7.2 The process and actions in response to a breach in the cold chain

The process or actions for response are outlined below:

1. Embargo the fridge and/or affected vaccines

Isolate potentially compromised vaccines, clearly labelling them “not for use”. These vaccines should be maintained between +2°C to +8°C. If the correct storage conditions cannot be reinstated and maintained in the current environment, consider moving the vaccines to an alternative monitored environment that is able to maintain the recommended temperature range +2°C to +8°C.

The vaccine fridge should remain switched on at the main electrical supply and all thermometers and temperatures probes should not be disturbed.

Staff within the organisation should be advised the fridge is embargoed until further notice, ensuring the vaccines are not used.

The incident should be documented according to local clinical governance guidelines.

No vaccine or vaccine storage equipment should be discarded until the incident has been discussed with the local SIT or HPT.

2. Confirm and define the incident

Providers should complete the incident checklist (Appendix B) to establish when the cold chain was last guaranteed, what time period/s are involved and what monitoring has taken place. This will help focus the investigation and identify any areas where subsequent investigation is needed.

A vaccine stocktake should be conducted to identify all vaccines stored in the fridge and the time they have been stored there, making note of where in the fridge they were stored (eg top/middle/bottom shelves) and how they were stored (eg in baskets/loose on fridge shelves).

3. Report the incident to the local SIT

All vaccine storage incidents should be reported to the SIT in the first instance (www.nhs.uk/servicedirector/Pages/AreaTeamListing.aspx).

The SIT can provide advice regarding whether the quarantined vaccine stock can still be used and where necessary, support the provider in gathering further information/evidence to inform the risk assessment of the incident.

4. Investigate the incident

In addition to the information provided in the incident checklist (Appendix B), investigators should:

Request a refrigerator engineer to inspect/service any fridge involved in the incident and check the accuracy of thermometer(s) and data logger(s) as soon as possible (unless the cause of the breach was not related to appliance performance eg it was caused by power supply disruption).

Document the general condition of the fridge. Is it a validated vaccine fridge? Does it have an alarm? What parameters are the alarm limits set at? Did the alarm sound? Is the power supply protected from disconnection? Is it placed in a well-ventilated area? Is it used for any other purpose than vaccine storage? How old is the fridge? Have there been any maintenance issues recently?

Check the fridge service history to give some indication of when the fridge was last certified to be working properly. All validated vaccine fridges are recommended to be serviced annually and all thermometers calibrated annually. Therefore, a pre-existing

service history may give an indication of how vaccines have been managed prior to this incident.

Confirm past and current fridge temperatures and if used, examine data from a continuous data logger. Where possible, undertake continuous temperature monitoring using a data logger for a 48 hour period to establish temperature patterns of the fridge and ascertain whether the thermometer in use is measuring accurately.

Review the fridge temperature records and discuss the cold chain practice prior to this event with relevant staff. Any explanations for temperature discrepancies should be identified (eg untrained staff monitoring fridge, thermometer not reset, etc).

Collect evidence of stock management, including stock inventory records, vaccine delivery dates, and vaccine turnover. Such information can provide valuable reassurance that vaccines have not been subject to prolonged suboptimal storage.

Evidence from practice staff or a visit to the practice may be helpful in establishing whether the vaccine fridge was being stocked and running at appropriate temperatures (eg frost/ice build-up at the back of the fridge, evidence of vaccines pushed up against the back or sides of the fridge due to limited storage space, over stocking of the fridge or poor stock rotation).

5. Undertake informed risk assessment

Using available vaccine stability data, assess whether vaccine potency is likely to have been affected by the breach in the cold chain/storage conditions. Vaccines against the same disease but from different manufacturers should be considered individually.

Consider seeking further advice from the vaccine manufacturers and published vaccine stability data (see above section 6.4. Available data).

Consider seeking further specialist advice from HPT, immunisation specialists or PHE national immunisation team.

6. Outcome of risk assessment

a: Quarantined vaccines assessed as satisfactory to use

Vaccines assessed as still suitable for use should be labelled as having been involved in a cold chain incident and used as off-label stock (see section 7.3 'Using vaccines that have been temporarily stored outside the manufacturer's recommended temperature range') unless SPC states vaccine can still be used.

b: Quarantined vaccine considered compromised

Vaccines considered compromised following a cold chain incident should be destroyed as per local waste policy.

A 'Stock Incident Capture' form should be completed on ImmForm. ImmForm customers can access the Helpsheet on ImmForm titled "Fridge failures and stock incidents" for further guidance on reporting incidents leading to wastage of vaccine stocks.

c: Compromised vaccines have already been administered to patients

If patients have been administered vaccines that have been stored outside of the cold chain, the formation of an Incident Control Team (ICT) should be considered. See section 8 'Managing a vaccine incident where compromised vaccines have been administered to patients' for further guidance.

7. Documentation, reporting and evaluation

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

Healthcare professionals should report the cold chain incident via their local governance system(s) so that appropriate action can be taken, lessons can be learnt and the risk of future incidents minimised.

7.3 Using vaccines that have been temporarily stored outside the manufacturer's recommended temperature range

When applying for a vaccine license (manufacturer's marketing authorisation), manufacturers have to provide a recommended storage temperature range. This temperature range is stated in the manufacturer's vaccine SPC.

When contacted following a cold chain breach, vaccine manufacturers may be able to share in-house stability information and advise whether their vaccines can continue to be used up to their stated expiry date, or for a reduced period. This information can be used to aid clinical decisions regarding the continued use of the affected vaccines and the need to recall patients for revaccination. Unless this information is stated in the product SPC however, this additional vaccine stability information has not been assessed by the Medicines and Healthcare products Regulatory Agency (MHRA) or European Medicines Agency (EMA) who grant marketing authorisation. Use of such vaccines is therefore outside the terms of the marketing authorisation (off-label).

As the manufacturer is no longer obliged to accept full liability for the product and its continued use, the decision as to whether to use vaccines after they have been stored outside the recommended temperature range, must be made on a case by case basis following a full risk assessment. This should be undertaken by the provider service in which the cold chain breach has happened and include specialist advice from the local HPT, SIT and the vaccine manufacturer. The risk assessment should take into account the available vaccine stability data and the circumstances of the breach. Broader implications of health economics and availability of further vaccine supplies should also be considered.

Where a risk assessment finds that available data and/or advice (ie from the SIT, HPT, manufacturer or other immunisation experts), supports the conclusion that the quality, safety and efficacy of the vaccine, should not have been adversely affected by the interruption to the cold chain or storage conditions, the subsequent off-label administration of the risk-assessed temperature-breached vaccine may be considered appropriate clinical practice. Those advising on the continued use of the vaccines should inform the healthcare professionals who will be administering them that this will be an off-label use.

Where a decision has been taken to continue to use vaccines that have been stored outside the manufacturer's recommended temperature range, the prescribing practitioner/provider assumes responsibility for using the vaccine. Because of this, the advice sought, the risk assessment and its conclusions should be well-documented, to support practitioners in practice and as part of a good clinical governance process.

Providers should ensure that vaccines assessed as appropriate for administration following an incident are used up first from vaccine stock and before ordering and using new stock. Steps should also be taken to ensure that these vaccines are easily identifiable if involved in subsequent incidents.

Thresholds PHE use when recommending disposal of vaccine following a cold chain excursion tend to be conservative and risk-averse. This reflects duty of care whilst also minimising unnecessary vaccine wastage and associated costs. If PHE recommend that vaccine is discarded, this does not necessarily mean the vaccine would be ineffective; instead there may be insufficient data on which to make a recommendation to use the vaccine.

The threshold for recommending revaccination following a retrospective risk assessment may be different. A cold chain incident that leads to disposal of vaccine will not necessarily require revaccination of all individuals in receipt of affected vaccine (See section 8. Managing a vaccine incident where compromised vaccines have been administered to patients).

7.4 Supply of cold chain breached vaccine under a Patient Group Direction (PGD)

Current medicines legislation does not prevent the use of, or necessitate amendment to PGDs to deliver vaccine that has been assessed as suitable for use following a temperature excursion. However, NICE Medicines Practice Guideline (MPG2) recommendation 1.1.7⁽¹¹⁾ advises that off-label use under a PGD should be supported by best clinical practice. Whilst best practice would always be to store vaccines according to the manufacturer's instructions (eg +2°C to +8°C), providing the advice from the manufacturer and/or risk assessment indicates that continued use of the vaccine is considered to be appropriate clinical practice (see 7.3 'Using vaccines that have been temporarily stored outside the manufacturer's recommended temperature range'), supply and/or administration may continue under a PGD. Such circumstances do not necessitate a Patient Specific Direction (PSD).

8. Managing a vaccine incident where compromised vaccines have been administered to patients

8.1 Formation and role of the Incident Control Team

Where an initial investigation has established that compromised vaccines have been administered to patients and/or a large revaccination exercise is under consideration, a formal Incident Control team (ICT) should be established.

The ICT should include a lead professional or senior manager from the provider organisation, a Screening and Immunisation Lead or designated representative, a consultant in Health Protection or designated representative from the local HPT, representation from the Clinical Commissioning Group (CCG) and a representative from a relevant communications team as appropriate depending on the incident. Other relevant representatives may be asked depending on the incident. For example, a representative from the Child Health Information System may be valuable if the incident will involve the identification, recall and revaccination of large numbers of children.

An incident team meeting should be convened to review the key findings of the initial investigation. The ICT will also need to review what information is not known about the incident, whether additional information can be obtained and if not, consider how this may influence the overall decision-making process.

The ICT must decide whether the vaccine incident was sufficient to warrant informing patients of the error under the duty of candour and whether the incident may have adversely affected the potency of the vaccine(s) such that revaccination would be recommended under the duty of care (see section 10.1 Revaccination and risk assessment).

8.2 Identifying recipients of affected vaccines

Where the ICT decide that further action is required, every effort should be made to identify all patients who have received compromised vaccines

A list of those who require revaccination should be compiled using the provider's local immunisation records/database. This will give an indication of time scale involved and draw attention to those who may be at immediate risk.

The ICT should consider, if necessary, how they might trace/make contact with those who require revaccination but who have moved out of the area or have registered at another practice since the immunisation incident was identified.

The ICT should formulate guidelines for revaccination or where appropriate, recommended vaccination schedules for each recipient using the table of recommendations for revaccination (Appendix D). The vaccination schedules should take into account appropriate intervals between vaccines and the potential risk of adverse reactions.

8.3 Identifying resources/manpower required.

Before commencing a programme of revaccination, consideration needs to be given as to how, where, and in what timescale a revaccination programme will take place. There may be a need to offer special clinics in the evening or at the weekend or identify other key vaccine providers who can assist in the programme. Depending on the scale and severity of the incident, additional temporary staff may be required to counsel, advise and/or revaccinate patients.

The ICT should consider how data will be collected to reflect invalid dose(s) and additional vaccine dose(s) administered.

8.4 Identifying training needs

Rapid training may be required for all healthcare professionals involved with the vaccine incident prior to the re-commencing of clinics and/or the arrival of a new vaccine fridge, storage equipment or vaccine stock.

Healthcare professionals involved in the revaccination clinics should be able to clearly explain both the risks and benefits of revaccination to patients and know who to contact if they are unable to answer any questions or are unsure how to proceed with re-immunisation.

The ICT should consider what supportive measures can be made available to support healthcare professionals in this role.

8.5 Communication with patients

It is important that the ICT develop a clear communication strategy before proceeding with a revaccination programme. Communication with patients and members of the public must be open, honest and transparent to avoid distress, confusion or misinterpretation.

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, for example eyesight, speech, hearing or mobility.

Generally, the best means of informing patients of a vaccine error/incident is on an individual basis, writing to patients via the GP practice or other immunisation provider (See Appendix C for sample letter). Depending on the severity of the incident, it may also be appropriate to set up a telephone helpline, especially where the incident is likely to cause a high level of anxiety, for example where newborn infants or children are involved. If a large number of patients are involved, the ICT may consider using the local media (local radio, TV or newspapers and/or adverts in local pharmacies) to communicate advice and key messages. Consideration may be given to targeted communication mediums (eg local community groups/centres, etc.) to get messages out to local ethnic, cultural and/or religious groups in the area.

8.6 Communication with the media

A lead spokesperson to liaise with the media should be identified. Both reactive and proactive press briefings should be drafted in preparation of any media interest. A 'Questions and Answers' briefing should also be drafted and agreed by all members of the ICT for use in response to media enquiries.

8.7 Re-immunise patients and record any adverse events

It is important to provide follow up advice and details of who to contact in the event of any adverse reaction for patients who have been revaccinated. Any adverse events should be documented in the patient notes and reported to the MHRA through the Yellow Card reporting system.

Any adverse events should also be documented in the final report of the incident as this information may be valuable for future management of other vaccine incidents.

8.8 Document and evaluate

The 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 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.

9. Responding to errors in vaccine preparation and administration

The following section provides guidance for those who have received sub-potent vaccine(s) as a result of an error in the preparation or administration of the vaccine. Please refer to the recommendations in revaccination schedule for further guidance (Appendix D).

9.1 Vaccines given outside of expiry date

All vaccines have an expiry date that is determined by the manufacturer and is clearly documented on the vaccine packaging. Vaccines that have been stored appropriately within the cold chain environment (and as per national recommendations) can be used up until the last day of the month indicated on the expiration date.

Vaccines that have expired should not be administered to patients. Whilst it is unlikely that a vaccine will cease to become effective on the day of expiration, given its prolonged time in storage, the potency of the vaccine is likely to have declined naturally over time. For this reason, where a vaccine has been given outside of its expiry date, the vaccine will usually need to be repeated. The vaccine should ideally be repeated on the same day or as soon as possible thereafter.

9.2 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.

It is unlikely that any data will be available on the effect mixing such vaccines would have on vaccine quality. However, it is possible that the constituents (eg 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 simply rendering the antigens ineffective.

For this reason, where vaccines have been mixed together incorrectly, vaccination will need to be repeated. The vaccine(s) should ideally be repeated on the same day or as soon as possible thereafter.

9.3 Wrong components used to reconstitute vaccine

Some vaccines require reconstitution with a diluent, or with another vaccine, prior to administration and are supplied with the diluent or vaccine that should be used.

There is little data on the effect of using a diluent other than that licensed to be mixed with the vaccine. Any adverse reactions experienced when a patient is given a vaccine mixed with the wrong diluent will depend on what has been inadvertently used as a diluent. The WHO reports that major adverse reactions have resulted from using the wrong vaccine diluent and from erroneously using other medications as diluents when these have been stored in the same fridge as the vaccines⁽¹¹⁾. Some vaccine diluents contain stabilising agents, bactericides, chemicals and/or buffers (to ensure the correct pH) 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, the vaccine will usually need to be repeated. The vaccine should ideally be repeated on the same day or as soon as possible thereafter.

In the event a healthcare professional prepares and administers only the diluent to a patient, vaccination will need to be repeated. The vaccine(s) should ideally be repeated on the same day or as soon as possible thereafter.

Where the diluent for a powdered vaccine is another vaccine (eg Infanrix Hexa or Menveo ACWY conjugate vaccine), then failure to reconstitute the vaccine correctly will mean that the recipient has not been offered protection against the antigen supplied as a powder. In this instance, the entire vaccine (liquid and powder components) should be offered again, ideally on the same day or as soon as possible thereafter.

9.4 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 as an individual cannot 'overdose' on a vaccine. However, this may lead to an increased risk of an adverse reaction.

Where vaccines are administered to patients at less than the recommended dose (eg if some vaccine spills or leaks out as vaccine is being administered), the vaccine will usually 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 or as soon as possible thereafter.

Patients who are given the wrong vaccine will require individual assessment as to whether the vaccine they have inadvertently received will provide the protection they require. In most cases, the vaccine they should have received should be given on the same day or as soon as possible thereafter. However, there will be some exceptions to this eg if the wrong DTP-containing vaccine is given, it may not be necessary to give the intended vaccine if the inadvertent vaccine provides both the required antigens and the required antigen quantity.

9.5 Vaccines given earlier than recommended age

Recommendations for the age at which vaccines should be administered are informed by the ability to respond to the vaccine, the age-specific risk for a disease, the risk of disease complications and the likelihood of achieving high coverage. If administered sooner than the recommended age, vaccines will generally not be harmful but may not evoke a good immune response or provide the desired long-term protection.

Infants

The age recommended to start an infant's first primary vaccination in the UK is eight weeks of age. Prior to this, factors such as passively transferred maternal antibodies may interfere with a good immune response. For this reason, vaccines given to infants earlier than the recommended age should usually be repeated when the individual reaches the recommended age. However, the first set of primary immunisations can be administered from six weeks of age if required in certain circumstances eg travel to an endemic country⁽¹³⁾.

If the primary immunisations are inadvertently given prior to 8 weeks of age but the infant is over 6 weeks of age, this should count as a valid dose and does not need to be repeated.

Older children and adults

Where vaccines are given more than a few months sooner than the scheduled age, consideration should be given to the likely impact this will have on longer term protection and vaccination may need to be repeated at the appropriate age. See the [Green Book Chapter 11: UK immunisation schedule](#) for specific recommendations regarding MMR vaccines and additional doses of DTaP vaccine given abroad before three years of age⁽¹³⁾.

9.6 Vaccines given later than recommended age

With the notable exceptions of rotavirus vaccine, (when the first dose should not be given above 15 weeks of age and the second dose not above 24 weeks of age) and

shingles vaccine (where the vaccine is not recommended for people aged 80 and over), it is never too late to start vaccination. Where a patient has no documented or reliable verbal history of previous immunisations, they should be assumed to be unimmunised and offered vaccines as per the UK immunisation schedule. Vaccination should be commenced using the algorithm for [Vaccination of individuals with uncertain or incomplete immunisation status](http://www.gov.uk/government/publications/vaccination-of-individuals-with-uncertain-or-incomplete-immunisation-status) (www.gov.uk/government/publications/vaccination-of-individuals-with-uncertain-or-incomplete-immunisation-status).

If rotavirus vaccine is inadvertently given beyond the recommended ages, no specific clinical action needs to be taken but the child's parents should be made aware of the symptoms of intussusception and advised to seek medical advice if concerned.

9.7 Vaccines administered at less than the recommended dosing interval

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

Inactivated vaccines with the same antigens should not usually be administered at an interval of less than four weeks. Where vaccines have been given at less than the recommended interval, the dose should be repeated once the recommended time period has elapsed and at least four weeks from the last dose given. Patients should be advised this may lead to an increased risk of local reactions. The exception is the primary schedule of DTaP-containing vaccine where a four week interval is recommended between each of the three doses but if one of these doses is given up to a week early, either inadvertently or deliberately eg for travel reasons, then this can be counted as a valid dose and does not need to be repeated. However, no more than one dose should be given early in the three-dose schedule.

Where PCV (for children born on/before 31/12/19 or in a specified risk group) and Men B have inadvertently been given at less than an eight-week interval, an additional dose should be administered 4 weeks after the inadvertent dose was given in order to provide protection at a vulnerable age without delay. As both of these vaccines were trialled and licensed as a 3-dose schedule given at least one month apart in infancy, an additional dose is acceptable and would not be expected to produce side effects beyond what may be seen following the first or second dose. In certain circumstances, for example to catch up a child who is late with the schedule, doses of PCV and MenB can be given four weeks apart if necessary to ensure the immunisation schedule is completed (eg if schedule started at 10 months of age). For more information about intervals between PCV doses, see relevant section in [Pneumococcal vaccination: guidance for HCWs on the changes to the infant schedule](#).

Live attenuated vaccines with the same antigens should not be administered at an interval of less than four weeks (unless there is a specific reason for doing so, for example repeating dose of rotavirus vaccine when infant has immediately regurgitated first dose or in the case of a vaccine error, for example where out of date vaccine has been given). Where vaccines have been given at less than the recommended interval, the second dose should be repeated at least four weeks from the first dose given. The exception is rotavirus vaccine. If a second dose of rotavirus vaccine is inadvertently given from 3 weeks after the first, no further doses are required as viral replication is likely to have occurred within this period. If the interval between the 2 doses is less than 3 weeks however, the infant should receive an additional dose of rotavirus vaccine at least 4 weeks from the first dose given and as long as the infant is still under 24 weeks of age at the time of the additional dose. The interval between the additional dose and the prematurely administered dose of rotavirus vaccine is not relevant.

Two or more different live attenuated vaccines:

Yellow Fever and MMR vaccines should be given four weeks apart as the coadministration of these two vaccines could lead to a suboptimal response to yellow fever, mumps and rubella⁽¹⁴⁾. Where these vaccines have been given at less than the four-week minimum interval, specialist advice from the SIT/HPT/NaTHNaC should be sought regarding the scheduling of revaccination.

Varicella and MMR should be administered either simultaneously or a minimum of four weeks apart. Where this interval has not been observed, evidence suggests the response to the varicella vaccine may be weakened⁽¹⁵⁾. Varicella vaccine should therefore be repeated a minimum of 4 weeks after the last dose of MMR⁽¹³⁾.

Other parenteral (injected) live attenuated vaccines, oral rotavirus and intra-nasal influenza vaccines can be administered at the same time or at any interval before or after each other.

9.8 Vaccines administered later than the recommended interval

If a vaccine is given later than the recommended interval from the last dose, as a rule (notable exceptions below), there should be no requirement to re-start a vaccination course. Responses to booster vaccinations are usually higher when there is a longer interval from primary immunisation and so protection after the completed course is expected to be equivalent to the recommended schedule. The concern where vaccines have been delayed beyond the recommended interval period is that the patient is left unprotected for a longer period of time and may have been at risk of infection between doses.

Notable exceptions:

Rotavirus vaccine: the first dose should not be given to babies older than 15 weeks of age and the second dose should not be given if the child is over 24 weeks of age.

Oral cholera vaccine: the primary course of the immunisation must be restarted if more than six weeks have elapsed between the first and second doses or if more than two years have elapsed since the last vaccination.

9.9 Potentially defective vaccines

Vaccines should be visually inspected for any foreign particulate matter and/or abnormal physical appearance prior to administration. In the event of either being observed, the vaccine should not be administered. It should be quarantined to prevent use whilst the issue is investigated and advice should be sought from the local Screening and Immunisation or Health Protection team who can seek further advice from the MHRA, manufacturer and/or PHE National Immunisation team as necessary.

Issues to consider are:

- was the product stored correctly? (to exclude incorrect storage as the cause of the suspected defect)
- if the defect is visible, was the defect identified in a new previously unopened container or had the container previously been used? (to exclude user errors such as product mix-ups)
- are there other unopened containers of the same batch available which could be checked?
- if the product requires preparation, such as addition of a diluent, was the correct procedure followed and/or correct diluent used?
- if the product is used with a medical device, could the device be the cause of the incident? (for example, a fault with the needle or syringe)

If the potential defect is identified prior to administration and an alternative unaffected vaccine is available, this can be administered in place of the affected vaccine to prevent unnecessary delay in immunising the patient.

If the vaccine has been administered prior to identifying the potential defect and the vaccine efficacy may have been compromised, the administration of a replacement dose may be considered. Seek further advice as to whether to repeat immediately or to await outcome of investigation.

Defective vaccines can be reported to the MHRA via the [Yellow Card Scheme](#) or via email to dmrc@mhra.gsi.gov.uk. Yellow Card reports of defective medicines are then

submitted to the Defective Medicines Report Centre (DMRC). The DMRC operates a 24-hour service to assist with the investigation of problems arising from medicinal products thought to be defective and to co-ordinate any necessary protective action. It provides an emergency assessment and communication system between manufacturers, distributors, regulatory authorities and users.

Where a defective medicine is considered to present a risk to public health, the company or manufacturer as appropriate, is responsible for recalling any affected batch(es) or, in extreme cases, removing all batches of the product from the market. DMRC normally supports this action by issuing a drug alert notification to healthcare professionals.

Further information about defective medicines can be found in the MHRA [Guide to Defective Medicinal Products](#).

10. Considerations and general principles for revaccination

10.1 Revaccination and risk assessment

Where a vaccine storage incident or vaccination error has been discovered, the priority is to assess the risk to patient(s) and ensure that good practices are in place to avoid any reoccurrence.

Given that revaccination is not without risk (both in terms of vaccine reactions and damage to public confidence in the immunisation programme and provider services), the decision to revaccinate should only be considered in situations where there is a high likelihood of a suboptimal response to the vaccine or where there is evidence of exceptionally poor practice overall that leads to great concern for the efficacy of vaccine(s) administered.

A decision to revaccinate patients who have been given potentially sub-potent vaccines should be based on a thorough risk assessment that balances the public health risk of receiving a sub-potent vaccine against any potential risks from revaccination (for example reactions at the injection site, fever, etc).

For most routine vaccines, repeating a dose as a replacement for the potentially affected vaccine is not likely to cause any harm. Where an incident involves multiple doses of subpotent vaccine, for example, where a full course of primary infant vaccines has been administered, repeating each dose in the course is unlikely to be needed and could increase the risk of adverse reactions. With most cold chain incidents in the UK, the reduction in potency of each dose of vaccine is likely to be modest, and so most infants would be expected to be primed. Older children who have received a full primary course of high-quality vaccines but then receive a booster of a sub-potent vaccine are still likely to have made a good response, as lower doses of antigen are able to stimulate immunological memory. For most incidents affecting vaccines given as part of a multiple-dose schedule therefore, a single replacement dose is likely to provide adequate immunity to correct for a cold chain incident.

For certain groups of patients, the threshold for revaccination may be considerably lower. For example, asplenic, immunocompromised or kidney failure patients, who may have lower responses anyway, and are more likely to benefit from additional vaccinations. These patients, and those at higher risk of exposure, should be actively encouraged to attend for revaccination in any communications.

For patients who have received vaccine in preparation for travel abroad, or following a defined exposure, the individual may no longer be at immediate risk of disease. Consideration must be given to the implications for future travel or further exposure. Ultimately the benefits of providing protection from the disease should be discussed with the individual in context of the incident and a course of action in their best interests decided on.

Given that vaccine stability is generally high, complicated individual vaccination schedules are unlikely to be necessary. In many incidents, a reasonable approach would be to offer an additional dose of affected vaccine to those who had a potentially suboptimal vaccine, suitably modified for age (eg DTaP/IPV or Td/IPV). The need for dose for dose replacement should only be considered in exceptional circumstances where there is definitive evidence that all doses received are likely to have been rendered markedly sub-potent.

Where a programme of revaccination is recommended, firm guidelines and their consistent application are essential to re-build public and provider confidence. Immunisation providers must be clear about the rationale for revaccination and equipped to manage potential issues or concern.

10.2 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 time, cost and complexity to the situation. In addition to this, the presence or absence of antibodies may not predict long term future protection and therefore it is unlikely that the results can be interpreted with any degree of certainty.

10.3 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°C to +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.

10.4 Reviewing an increase in disease notifications as an indicator of cold chain failure.

Retrospectively reviewing or looking for an increase in vaccine preventable disease notifications is not sensitive enough to indicate cold chain failure and absence of cases should not be used as reassurance that vaccination has been effective. Most cold chain incidents would only lead to mild or moderate loss of potency from vaccine and

therefore not be expected to affect short term protection, even though it could render a patient unprotected after many years. In addition to this, herd immunity would be expected to provide protection for most patients who remain in the UK.

11. General recommendations for revaccination

11.1 Live vaccines

With the exception of BCG vaccine (see Appendix D), 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 subsequently administered live vaccine viruses.

Where repeat vaccination of MMR, Varicella or Yellow Fever is required, guidance in [Chapter 11 of Immunisation against infectious disease](#) should be followed.

11.2 Inactivated vaccines

The frequency of local or systemic reactions with certain inactivated vaccines may increase with additional doses given.

Incidence of local reactions are more common in children receiving their fourth dose of an acellular pertussis (aP) vaccine: large reactions involving swelling of the whole limb or blistering at the injection site have been reported⁽¹⁶⁾. Such reactions are a recognised phenomenon and do not contraindicate further doses.

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. For advice on the immunisation of individuals with a history of severe reaction to a previous dose of vaccine, please see the relevant chapter in [Immunisation against infectious disease](#).

11.3 Combination vaccines

Vaccines containing more than one antigen in combination with others are 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 a local reaction to the additional vaccine antigen is preferable to the consequences of missing out on protection.

11.4 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.

12. Duty of candour and patient consent

12.1 Duty of candour following an incident

When a vaccine incident occurs, those involved need to decide whether patients should be informed under the duty of candour. Requirements to notify patients may vary depending on the specific circumstances of the incident, whether it resulted in potential for patient harm or distress and what may be expected of patients who receive information disclosed as part of a duty of candour.

The NMC and GMC have issued joint comprehensive guidance on the professional duty of candour which can be found at www.nmc.org.uk/standards/guidance/the-professional-duty-of-candour/. This provides useful information when considering what information to provide to patients following a vaccine incident under duty of candour.

The guidance states that, ‘Every healthcare professional must be open and honest with patients when something that goes wrong with their treatment or care causes, or has the potential to cause, harm or distress’.

In the case of vaccine incidents, the potential for harm may be an increased risk of disease in the future as a result of suboptimal immunisation. Therefore, where it is concluded that a vaccine incident may have resulted in reduced vaccine potency, there is a professional duty of candour to inform the patient that they may not be protected by the vaccine(s) they have received. Healthcare professionals should inform the patient (or patient’s advocate, carer or family) about the incident, apologise, offer an action to put matters right where appropriate (such as revaccination) and fully explain the potential short and long-term effects of what has happened.

Where, following a vaccine incident risk assessment, it is concluded that the vaccine is not likely to have been significantly compromised at the time of administration, the incident would not be anticipated to cause harm to the patient and/or continued use of the vaccine has been risk assessed and approved, any rationale for informing patients of such incidents retrospectively is less clear. The GMC/NMC guidance states “in some circumstances, patients may not need to know about an adverse incident that has not caused (and will not cause) them harm, and to speak to them about it may distress or confuse them unnecessarily”. Thus, healthcare professionals are not obliged to inform patients of incidents that do not have the potential to result in harm and which do not alter the care offered to them. If a decision is made to inform patients however, communications to them should aim to inform and apologise, outline what measures have been taken to investigate and rectify the incident and reassure that vaccines given have been assessed as being safe and potent. They need to reassure patients that the

vaccine(s) they received are not likely to have been sufficiently affected as to warrant revaccination.

12.2 Patient consent

Patients' consent needs to be obtained before the administration of any vaccine. Patients should be provided with sufficient information so as to provide valid consent and all questions should be answered fully and openly. It is at the discretion of the healthcare professional as to whether to inform patients, when obtaining consent, that a vaccine to be supplied or administered has been stored outside the terms of the marketing authorisation.

13. Information resources

UK

British Medical Association. NHS culture webpage. Section on Duty of Candour:
www.bma.org.uk/collective-voice/policy-and-research/ethics/nhs-culture

Care Quality Commission Regulation 20: Duty of candour. www.cqc.org.uk/guidance-providers/regulations-enforcement/regulation-20-duty-candour#guidance

Electronic Medicines Compendium. www.medicines.org.uk/emc/
Access vaccine SPCs and vaccine manufacturer details (last section of SPC)

General Medical Council and Nursing and Midwifery Council. Openness and honesty when things go wrong: the professional duty of candour. www.gmc-uk.org/guidance/ethical_guidance/27233.asp and www.nmc.org.uk/standards/guidance/the-professional-duty-of-candour/

ImmForm Helpsheet 18 Fridge failures.
Available at: <https://portal.immform.dh.gov.uk/Logon.aspx?returnurl=%2f> (login required)

National Travel Health Network and Centre (NaTHNaC) <https://nathnac.net/>

Public Health England. Immunisation against infectious diseases. Available at
[/www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book](http://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book)

Public Health England. Vaccines stored outside the recommended temperature range: leaflet

Public Health England. Off-label vaccine: leaflets.

International

Australia: National Vaccine Storage Guidelines - Strive for 5 - 2nd edition available at:
<https://beta.health.gov.au/resources/publications/national-vaccine-storage-guidelines-strive-for-5-2nd-edition>

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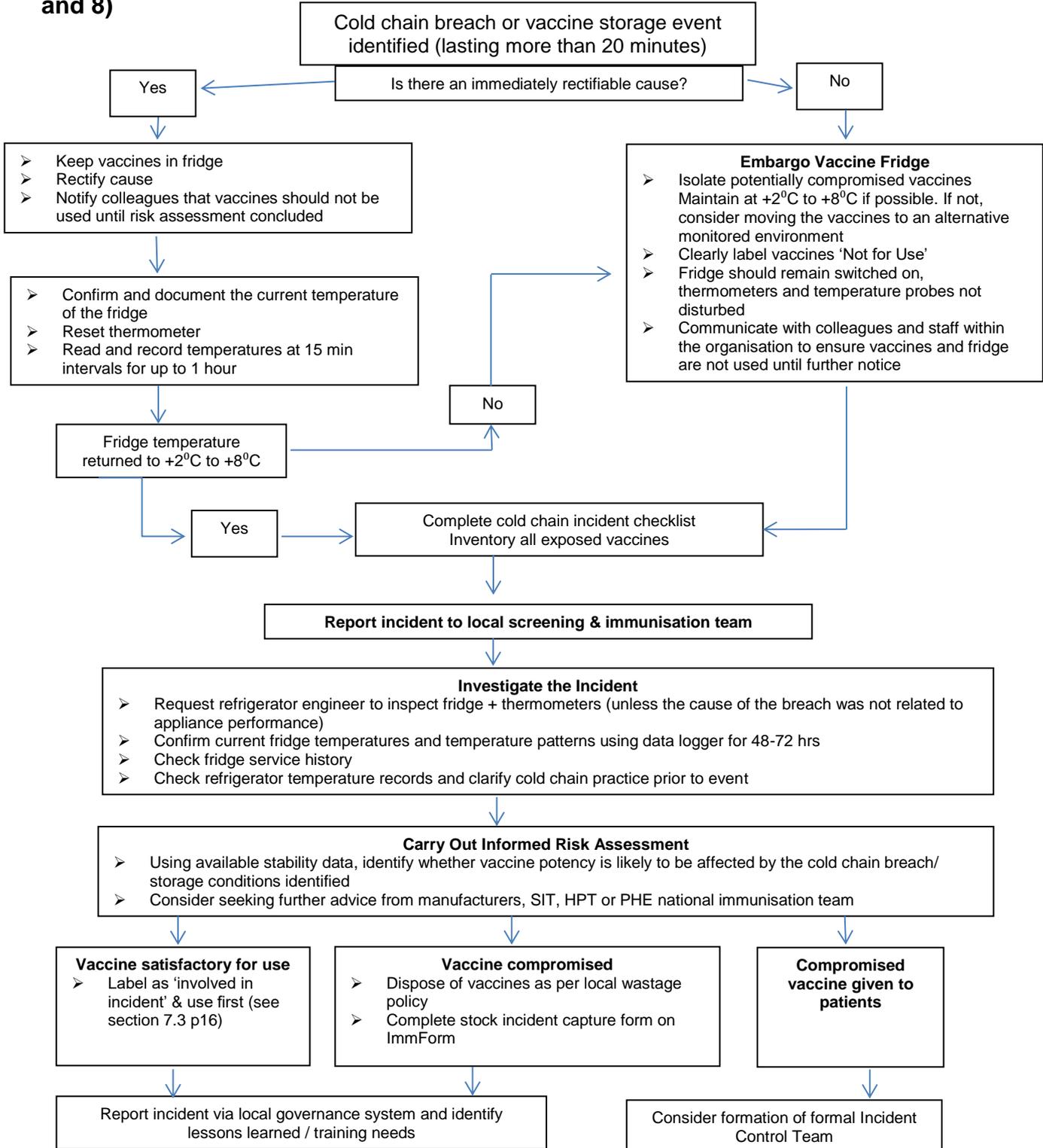
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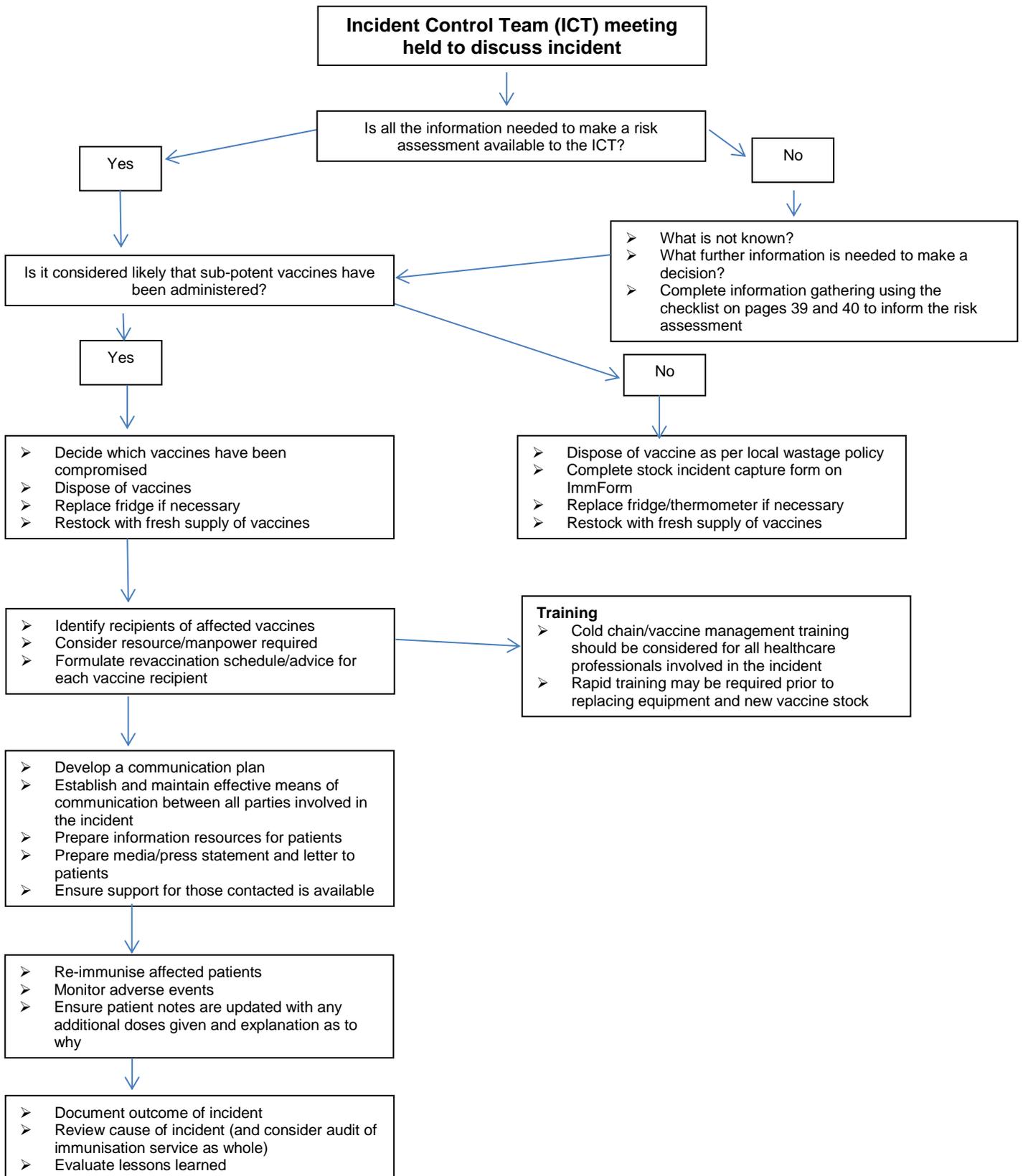
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Appendix A: Algorithms

Responding to a cold chain breach or compromised storage event (use with sections 7 and 8)



Managing a cold chain incident where compromised vaccines have been administered to patients



Appendix B: Vaccine storage incident checklist

In the event of a cold chain breach lasting longer than twenty minutes or concerns regarding the storage of vaccines:

- ✓ Do not dispose of any vaccines or storage equipment
- ✓ Isolate potentially compromised vaccines clearly labelling “not for use”. These vaccines should be maintained between +2°C to +8°C or moved to an alternative monitored environment that is able to maintain the recommended +2°C to +8°C temperature range
- ✓ Ensure the vaccine fridge involved remains switched on at the main electrical supply and that thermometers and temperatures probes are undisturbed and all staff are aware the fridge should not be accessed.
- ✓ Complete the cold chain incident checklist questions attached.
- ✓ Inventory all exposed vaccines stored in the fridge, recording the quantity, batch number and expiry date as well as noting where they were stored in the fridge.
- ✓ Contact your **local NHS England Screening and Immunisation team** for further support and advice (www.nhs.uk/servicedirectories/Pages/AreaTeamListing.aspx).

Vaccine storage incident checklist

Date and time of incident form completion	
Fridge location/identifier	
Date and time cold chain breach identified	
What were the temperature readings when the breach was noticed?	Min: Max: Current:
Date and time of last guaranteed storage between +2°C to +8°C	
Total duration of temperature excursion (hours/minutes)	
What alerted you to the cold chain breach/storage event? <i>(eg thermometer out of range, fridge alarming, data logger)</i>	
Is there an alarm fitted on the fridge and if so: <ul style="list-style-type: none"> • what parameters are set • after how long outside of +2°C to +8°C range does the alarm sound? 	
If the alarm had gone off, would anyone have heard it?	
Type of fridge (domestic / medicine)	
How old is the fridge?	
When was the fridge last serviced?	
Has an engineer checked the fridge since the incident? What did their report say?	

How often are fridge temperatures recorded?	
What type of thermometer is in use? (<i>integral to fridge, battery operated independent thermometer, data logger</i>)	
If there is a temperature probe in the fridge, what is its position in the fridge?	
When was the thermometer last reset?	
When was the thermometer last calibrated?	
Has continuous temperature monitoring with a data logger for 48 hours been performed since incident was identified?	
Result of 48 hours continuous temperature monitoring with a data logger	
Possible reason for temperature excursion? (e.g. restocking the fridge, busy clinic, power failure)	
Are there any obvious signs of freezing (e.g. frosting on sides or back of the fridge, wet or damaged vaccine boxes)?	
Are any vaccines placed against the sides or back of the fridge (or been pushed up against the cooling plate or cold air inlet)?	
Have any of the vaccines involved in this incident previously been exposed to temperatures outside 2°C to 8°C? (i.e. involved in previous cold chain incident)	
What is the current vaccine stock in the fridge vaccine, expiry date, quantity and location in fridge?	
Has anybody been vaccinated with potentially affected vaccines?	
Has the cause of the breach been rectified and/or steps taken to prevent the problem recurring?	
Form completed by (print name and signature)	

Appendix C: Example letter to patients/carers offering revaccination

Dear (patient/carer's name)

Re: Vaccines received at (insert name of clinic/vaccination provider)

I am writing to inform you that we have recently become aware of a problem with the storage/administration (delete as appropriate) of the vaccine/vaccines you/your child (delete as appropriate) received at (clinic/vaccination provider name).

As a result of this problem you/your child may not gain full protection from this vaccination and we would therefore recommend you/your child has a repeat vaccination as soon as possible.

I understand you may have some questions regarding this incident and would ask that you call the practice/clinic on (insert telephone number) and make an appointment with (provide the name of GP or immuniser).

At this appointment we will address any questions you may have regarding the incident and you/your child may/will be (delete as appropriate) offered repeat vaccination.

I would like to apologise for any inconvenience/concern this may cause you/your family. Please be assured that this incident has been fully investigated and every step will be taken to ensure this does not happen again.

Yours sincerely

(Name of GP/Practice Manager)

Appendix D: Revaccination recommendations for people who have received compromised vaccines

Vaccine	Group	Recommendation	Rationale and relevant information
BCG	All.	Repeat vaccination is not usually recommended.	High risk of significant local reaction and keloid scarring. Specialist advice should be sought on an individual patient basis.
Cholera	Individuals who have received one or more doses for travel.	Additional or repeat dose(s) of vaccine may be indicated if still at identified risk.	Specialist advice should be sought on an individual patient basis from vaccine manufacturer or NaTHNaC regarding scheduling and possible side effects.
DTaP/IPV/Hib/HepB-containing combination vaccines	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 more common in children receiving their 4 th or booster dose of an aP vaccine. In some cases this swelling can be extensive, involving much of the upper limb. This is a benign and transient recognised phenomenon and does not contraindicate further doses ⁽¹⁶⁾ .

Vaccine	Group	Recommendation	Rationale and relevant information
			A single repeat dose may be adequate to replace multiple doses depending on age and nature of incident.
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 more common in children receiving their 4 th or booster dose of an aP vaccine. In some cases this swelling can be extensive, involving much of the upper limb. This is a benign and transient recognised phenomenon and does not contraindicate further doses ⁽¹⁶⁾ .
Td/IPV	Individuals aged ten years and over as routine adolescent booster dose , booster for travel or primary course.	Repeat dose as soon as possible.	Incidence of local reactions to Td-containing vaccines may increase in some individuals with additional doses ⁽¹⁷⁾ . Patients should be warned that they may experience more reactions at the injection site than they have to previous doses. However, this does not always occur and such additional doses are unlikely to produce an unacceptable rate of reaction.
A tetanus-containing	As part of management of a	If given to complete an incomplete course of vaccinations, or given	Although the dose(s) should still be repeated regardless of timing of incident, unless the storage/administration error is

Vaccine	Group	Recommendation	Rationale and relevant information
<p>vaccine such as: Td/IPV DTaP/IPV dTAP/IPV DTaP/IPV/Hib DTaP/IPV/Hib/HepB</p>	<p><i>tetanus prone wound.</i></p>	<p>because last dose was more than 10 years previously, repeat dose as soon as possible.</p>	<p>discovered immediately or within a few days of the vaccine having been given, it may be too late for a repeat dose to prevent tetanus in a potential exposure situation. Action would depend on time since potential exposure and whether the individual had been adequately primed or not. If exposure is still recent, it is important to repeat dose as soon as possible as delays could mean that it would be too late to provide rapid post-exposure protection. Seek expert advice.</p>
<p>dTaP-IPV</p>	<p>Given to pregnant woman for pertussis protection for infant.</p>	<p>If less than 38 weeks repeat dose as soon as possible.</p> <p>For patients 38 weeks or more offer repeat dose.</p>	<p>Incidence of local reaction to Td-containing vaccines may increase in certain individuals with additional doses⁽¹⁷⁾. Patients should be warned that they may experience more reactions at the injection site than they have to previous doses. However, this does not always occur and such additional doses are unlikely to produce an unacceptable rate of reaction.</p> <p>Immunisation after week 38 is unlikely to provide passive protection to the infant but would potentially protect the mother from pertussis infection and thereby reduce the risk of exposure for her infant.</p>

Vaccine	Group	Recommendation	Rationale and relevant information
			<p>The importance of having their infant's first primary immunisations at the scheduled time of 8 weeks should be stressed as well as the need for additional vaccination if they become pregnant in the future.</p>
<p>Hepatitis A</p>	<p>Individuals who have received one or more doses for travel purposes.</p> <p>Individuals who have received one or more doses for other ongoing identified risk.</p>	<p>Repeat dose(s) as soon as possible if indicated for future travel.</p> <p>Repeat dose(s) as soon as possible.</p>	<p>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 following routine vaccine administration.</p>
<p>Hepatitis B</p>	<p>Individuals who have received one or more doses for travel purposes.</p> <p>Individuals who have received one or more doses pre-exposure or for</p>	<p>Repeat dose(s) as soon as possible if indicated for future travel.</p> <p>Repeat dose(s) as soon as possible.</p>	<p>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 following routine vaccine administration.</p>

Vaccine	Group	Recommendation	Rationale and relevant information
	<p>other ongoing identified risk.</p> <p>Individuals who have received one or more doses post-exposure.</p>	<p>Perform blood test to ascertain infection status. At same visit, give a repeat dose of HepB vaccine.</p> <p>If infant <12m, repeat affected dose/s and ensure testing for HBsAg is carried out at 1 year of age. Ascertain whether monovalent HepB vaccine or Infanrix hexa required.</p>	<p>Additional testing for infection at appropriate interval from exposure may be required.</p>
<p>Hib/MenC conjugate</p>	<p>Individuals over 12 months of age as part of routine schedule.</p> <p>Patients >2y in high risk groups.</p>	<p>Repeat single dose as soon as possible.</p> <p>Repeat single dose as soon as possible.</p>	<p>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 routine vaccine administration.</p>
<p>Human Papillomavirus (HPV)</p>	<p>Patients given one or more doses.</p>	<p>Repeat dose(s) as soon as possible.</p>	<p>Additional doses of HPV are unlikely to produce significant side effects. Any adverse events following revaccination</p>

Vaccine	Group	Recommendation	Rationale and relevant information
		If more than one dose to be repeated, observe the minimum recommended interval between doses according to age as per Green Book chapter 18a.	would be expected to be similar to those reported with routine 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 side effects. Any adverse events following revaccination would be expected to be similar to those reported with routine vaccine administration.
Influenza (live)	All children given the vaccine.	Revaccination only recommended if during influenza season. Repeat single dose as soon as possible.	No additional risk of adverse events from giving additional doses of live influenza vaccine would be expected. Any pre-existing antibodies should neutralise the attenuated vaccine viruses.
Japanese encephalitis	Individuals who have received one or more doses for travel.	Additional or repeat dose(s) of vaccine may be indicated if still at identified risk.	Specialist advice should be sought on an individual patient basis from vaccine manufacturer or NaTHNaC regarding scheduling and possible side effects.
Meningococcal ACWY conjugate vaccine	Individuals over ten years of age as part of routine schedule.	Repeat single dose as soon as possible.	Additional doses of MenACWY conjugate vaccine are unlikely to produce significant side effects. Any adverse events following revaccination would be expected to be

Vaccine	Group	Recommendation	Rationale and relevant information
	<p>Individuals in high risk groups for whom the vaccine is recommended.</p> <p>Individuals who have received the vaccine for travel (including Hajj).</p>	<p>Repeat dose given as soon as possible.</p> <p>Offer additional dose of vaccine as soon as possible if not yet travelled or if indicated for future travel.</p>	<p>similar to those reported with routine vaccine administration.</p>
<p>Meningococcal B</p>	<p>Children under 12 months of age given as part of their primary course.</p> <p>Individuals over 12 months of age as</p>	<p>Repeat dose(s) as soon as possible allowing a minimum of two months before any subsequent dose(s) is given if one is indicated/scheduled. Ensure the routine booster dose is given after the first birthday, leaving at least a 2-month interval since the last MenB dose.</p> <p>Repeat dose(s) as soon as possible.</p>	<p>Infants who require revaccination with Men B at the same time as other routine primary immunisations should be given prophylactic paracetamol as is normally recommended for the 8 week and 16 week primary immunisations⁽¹⁸⁾.</p> <p>The vaccine was trialled and licensed as a 3 dose schedule in infancy, therefore any adverse events following revaccination would be expected to be similar to those reported with routine vaccine administration.</p>

Vaccine	Group	Recommendation	Rationale and relevant information
	<p>part of routine schedule (up to second birthday).</p> <p>Patients >2y in specified high risk groups.</p>	<p>Repeat dose(s) given as soon as possible allowing one-month interval between doses if more than one required.</p>	
<p>Meningococcal C conjugate vaccine (if given to patients in a cold chain incident going back several years when this vaccine was still used)</p>	<p>Children given the vaccine under 12 months of age as part of their primary course.</p> <p>Patients >2y in all high-risk groups.</p>	<p>No need to repeat. Ensure single potent dose of Hib/MenC has been given over 1y of age as per routine schedule.</p> <p>Repeat as combined Hib/MenC single dose as soon as possible unless patient has since received a potent dose of MenACWY conjugate vaccine.</p>	<p>MenC vaccine is no longer recommended in infancy. Additional doses of MenC conjugate vaccine are unlikely to produce significant side effects. Prior to Sept 2006 the vaccine was given as a 3 dose schedule.</p> <p>Any adverse events following revaccination would be expected to be similar to those reported with routine vaccine administration.</p>
<p>MMR</p>	<p>Patients given one or more doses.</p>	<p>Repeat dose(s) allowing a minimum of 4 weeks between doses if more than one dose is required.</p>	<p>There is no additional risk of adverse events from giving further doses of MMR vaccine. Any pre-existing antibodies should neutralise the attenuated vaccine viruses in subsequent doses.</p>

Vaccine	Group	Recommendation	Rationale and relevant information
<p>Pneumococcal conjugate vaccine (PCV)</p>	<p>Children under 12 months of age given as part of their primary course.</p> <p>Individuals over 12 months of age as part of routine schedule (up to second birthday).</p> <p>Patients >2y in specified high risk groups (severely immunocompromised including bone marrow transplant patients, patients with acute and chronic leukaemia, multiple myeloma</p>	<p>Repeat dose(s) as soon as possible allowing eight weeks before any subsequent primary dose is given if one is indicated/scheduled. Ensure the routine booster dose is given after the first birthday, leaving a minimum four week interval since the last PCV dose.</p> <p>Repeat single dose as soon as possible.</p> <p>Repeat single dose as soon as possible.</p>	<p>Additional doses of PCV vaccine are unlikely to produce significant side effects. The vaccine was trialled and licensed as a 3 dose infant schedule. Therefore any adverse events following revaccination would be expected to be similar to those reported with routine vaccine administration.</p>

Vaccine	Group	Recommendation	Rationale and relevant information
	<p>or genetic disorders affecting the immune system)</p>		
<p>Pneumococcal polysaccharide vaccine (PPV)</p>	<p>Patients >2y in all high-risk groups and given routinely as patient is ≥65 years.</p>	<p>Flag patient notes to ensure they receive a replacement dose after 3 years Risk groups eligible for 5 yearly boosters should continue to receive these after this replacement dose</p>	<p>The safety and effectiveness of reimmunisation with pneumococcal polysaccharide vaccine at intervals of less than 3 years is not known. Revaccination is associated with increased risk of local reaction and may induce immunological hyporesponsiveness.¹⁹</p>
<p>Rabies</p>	<p>Individuals who have received one or more doses for identified occupational risk.</p> <p>Individuals who have received one or more doses for travel.</p>	<p>Repeat any affected doses.</p> <p>Repeat affected doses if sufficient time before travel. If insufficient time to complete all affected doses before travel, warn patient to seek prompt advice and treatment in event of exposure.</p>	<p>Adverse events following revaccination would be expected to be similar to those reported with normal vaccine administration and the risk of rabies outweighs the risk of possible side effects.</p>

Vaccine	Group	Recommendation	Rationale and relevant information
	<p>Individuals who have received one or more doses for post exposure prophylaxis.</p>	<p>Repeat any doses not given before travel on patient's return if rabies vaccination needed for future travel.</p> <p>Repeat any affected doses as soon as possible and according to recommended schedule.</p>	<p>Specialist rabies advice is available from Public Health England's Rabies and Immunoglobulin Service (RIgS). Telephone 020 8327 6204</p>
<p>Rotavirus</p>	<p>Infants who have received one or more doses as part of their primary course.</p>	<p>Repeat 1st dose only if infant is less than 15 weeks old.</p> <p>Repeat 2nd dose only if infant is less than 24 weeks old.</p>	<p>Vaccination should not be initiated for infants after 15 weeks of age (i.e. 14 weeks and 6 days). Second vaccination should not be given to children over 24 weeks of age.</p> <p>Additional doses of rotavirus vaccine are unlikely to produce significant side effects. Any pre-existing antibodies should neutralise the attenuated vaccine viruses in subsequent doses. Adverse events following revaccination would be expected to be similar to those reported with routine vaccine administration.</p>

Vaccine	Group	Recommendation	Rationale and relevant information
Shingles (herpes zoster)	All individuals given the vaccine.	Repeat dose given.	No additional risk of adverse events from giving additional doses of shingles vaccine would be expected. Any pre-existing antibodies should neutralise the attenuated vaccine viruses. Check whether any contraindications (such as commencement of immunosuppressant medication) have arisen since previous dose before giving a repeat dose.
Tick-borne encephalitis	Individuals who have received one or more doses for identified occupational risk. Individuals who have received one or more doses for travel.	Additional or repeat dose(s) of vaccine may be indicated if still at identified risk. Additional or repeat dose(s) of vaccine may be offered if indicated for future travel.	Specialist advice should be sought from vaccine manufacturer or NaTHNaC regarding scheduling and possible side effects.
Typhoid (Vi and Ty21a)	Individuals who have received the vaccine for travel.	Additional or repeat dose(s) of vaccine may be offered if indicated for future travel.	Additional doses of typhoid vaccine are unlikely to produce significant side effects.
Varicella	Individuals aged over 1 year who	Repeat dose(s)	No additional risk of adverse events from giving additional doses of varicella

Vaccine	Group	Recommendation	Rationale and relevant information
	<p>have received one or more doses.</p>	<p>allowing a minimum of four weeks between doses if more than one dose is required.</p>	<p>vaccine would be expected. Any pre-existing antibodies should neutralise the attenuated vaccine viruses in subsequent doses.</p>
<p>Yellow Fever</p>	<p>Individuals who have received the vaccine for travel.</p>	<p>Repeat dose may be indicated if still at identified risk (eg if required for future travel).</p>	<p>Specialist advice should be sought from vaccine manufacturer or NaTHNaC regarding scheduling. 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 in subsequent doses.</p>