Public Health England

Protecting and improving the nation's health

BUG SPECIAL
VACCINE UPDATE

Issue 300, October 2019

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300TH EDITION

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This is the 300th edition of Vaccine Update. For those of you who remember, the first online edition was number 131 in January 2007.

So 169 editions later, we are still keeping everyone up to date with vaccine supply, programme news and new resources every month and sometimes more often.

This year we launched our Value of Vaccines campaign to promote the need for everyone to get up to date with their routine vaccinations, whatever their age


Public Health England

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Issue 297, July 2019

Vaccine update

Holidaying in Europe this Summer?

Summer is here and we hope that whatever your plans, you and all your family are up to date with their routine vaccinations.

Summer is the perfect time to check the NHS website to see if any have been missed. Some parents will be able to check in their child's red book (PCHR) at weblink 16.

Please download our Value of vaccines resources to promote vaccination this summer at weblink 18.

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Revised rash in pregnancy guidance reminder

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Vaccine wastage – time to check your fridges!

Are you reporting vaccine wastage on ImmForm?

The EU Falsified Medicines Directive (FMD) and Delegated Regulation as applicable to PHE supplied vaccines for the national immunisation programme

Vaccine supply for the non routine programme

Holidaying in Europe this summer?

Check your child's Red Book

Contact your GP prior to travel if you're not up-to-date

Subscribe to Vaccine update here. Order immunisation publications here.
For centrally-supplied vaccine enquiries, email: vaccinesupply@phe.gov.uk

In the May and June editions of Vaccine update we have been celebrating the role of Vaccine heroes in delivering the vaccine programmes and this year we are delivering more vaccines than ever before with 25 million doses of flu vaccine to eligible at risk groups and to all primary school aged children, 850,000 doses of the HPV vaccine to boys as well as girls in school year 8.

Our July edition featured a celebration of the vaccine heroes on the delivery and implementation side of the workforce and we wanted to use the centenary edition as a celebration of the role that the laboratories have in monitoring surveillance and cover as well as identification of serotypes and outbreaks across the country.

When a suspected case is identified by a GP or in an hospital, a sample such as oral fluid or a dried blood spot is taken and the sample kit sent to Public Health England (PHE) in Colindale to be analysed.

The results are then reported to determine the treatment of the patient and recorded as part of the surveillance of notifiable diseases.

The service provision by these laboratory heroes is the backbone of the programmes, accurate data is essential to the maintenance of the programmes and identifying any strains or types of disease that are not vaccine preventable and in the case of those that are, confirmation of the efficacy of the vaccine prevention.

Please read on and 'Meet the teams' of our laboratory heroes and find out about 'how they do it!'.

The Vaccine Evaluation unit (VEU)

The Vaccine Evaluation Unit (VEU) is a small team within PHE specialising in the serological determination of immune responses to a number of pathogenic bacteria. We are made up of five sections: the Meningococcal Serogroups A, C, Y and W section, the Meningococcal Serogroup B section, the Multiplex section, the Serum Archives section, and the Quality section. The two Meningococcal sections – headed by Kelly Townsend-Payne and Dr. Jennifer Louth – perform Serum Bactericidal Antibody (SBA) assays and ELISAs for *Neisseria meningitidis* serogroups causing invasive disease.

Staff from the VEU MenACWY and MenB section

Selecting samples for testing

Examining a blood agar plate used in the SBA assay.

SBA assays are technically demanding tests for functional antibodies capable of killing live bacteria in the presence of human or rabbit complement. They require extra safety controls as they involve handling live cultures of pathogenic *N. meningitidis*. The Multiplex section, headed by Abigail Bell, performs assays measuring IgG antibodies against *Streptococcus pneumoniae, Haemophilus influenzae type B*, tetanus and diphtheria.

The section also performs ELISAs to measure total IgG antibodies to serogroups A, C, Y and W.

All assays are offered on a commercial basis to support clinical trials and academic studies, and as a clinical service.

Multiplexed assays allow the simultaneous measurement of multiple analytes, particularly useful in the case of *S. pneumoniae*. With twelve serotypes covered by the current pneumococcal conjugate vaccine, providing type-specific antibody levels would be extremely time consuming were a separate assay required for each.

Staff from the VEU Multiplex section

These assays are offered for research and as a clinical service, but the clinical service provides the majority of the work for this section as the response to pneumococcal vaccines can be a useful diagnostic tool for immune disorders.

The Serum Archives section, headed by Simon Tonge, manages the collections of serum samples housed by the VEU, including the PHE Sero-epidemiology Unit (SEU) archive, a collection of around 250,000 residual diagnostic samples from all age groups collected across England annually since 1986.

The SEU archive is available for use by any research group for sero-epidemiology studies of vaccine-preventable disease.

Setting up a plate of multiplex assays to measure antibodies to 12 pneumococcal serotypes simultaneously

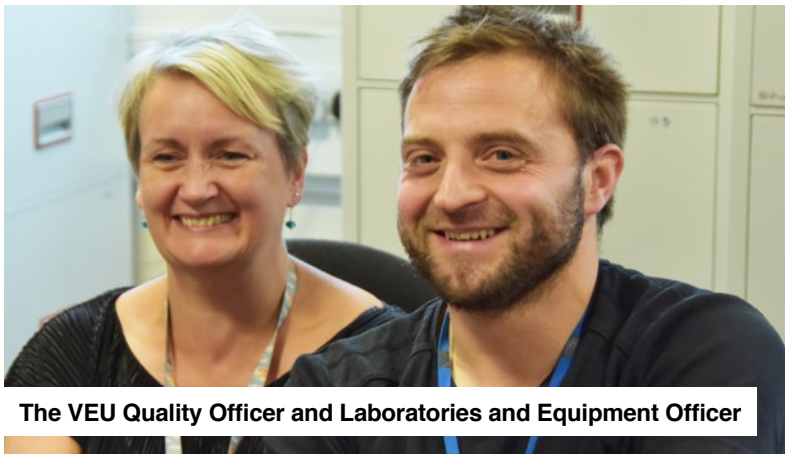
Archiving serum samples

A team of Medical Laboratory Assistants handle sample receipt for these archives, along with general duties for the whole Unit.

The Quality section, headed by Karen Telford, maintains holistic and objective oversight of all processes and underpins the work of entire Unit.

The VEU MLA team

We operate to the highest applicable standard for all our work, and we are proud of our rigorous Quality Management System.



The VEU Quality Officer and Laboratories and Equipment Officer

The VEU was created in the 1990s to assist with the accelerated development of a meningococcal serogroup C (MenC) conjugate vaccine programme in the UK. The existing MenC polysaccharide vaccine was not suitable for introduction into the national immunisation programme; it was poorly immunogenic in infants, and did not induce memory T cell production so protection was short-lived.

Attempting to prolong protection by administering booster doses actually reduced the immune response. It was known that conjugate vaccines (which contain a polysaccharide antigen chemically linked to a strongly immunogenic carrier protein) could overcome these limitations, and several such vaccines were in development.

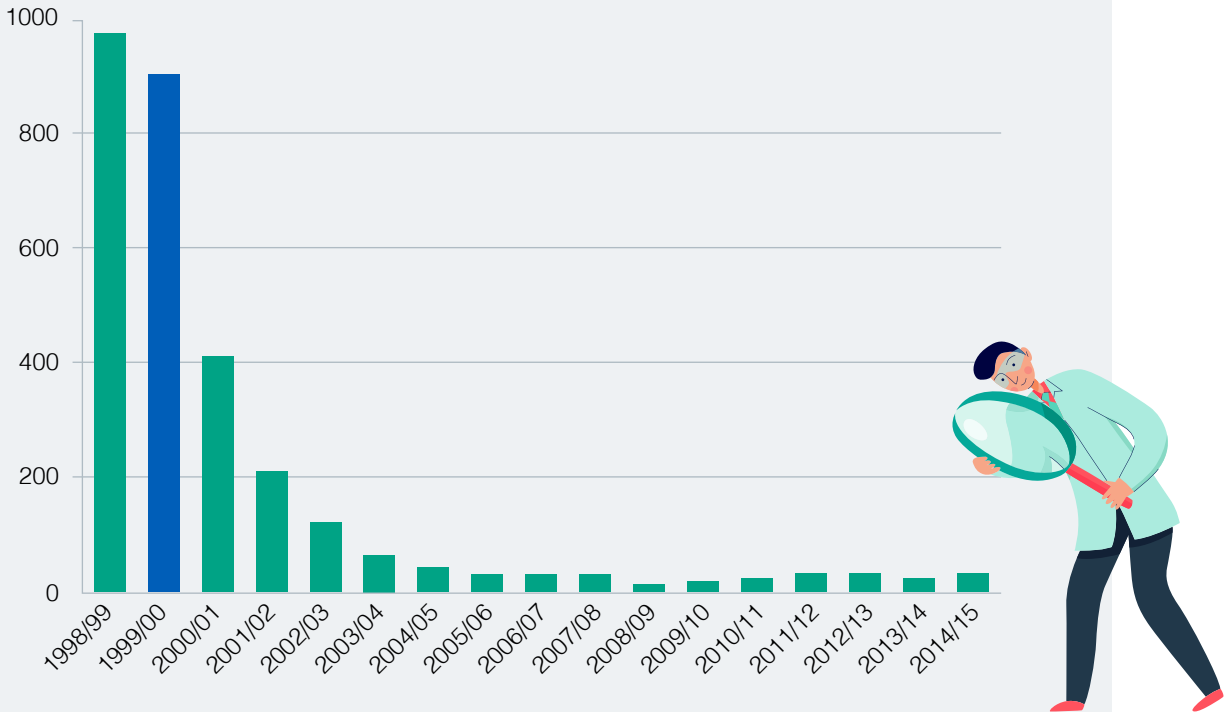
The number of cases of MenC disease reported each year was relatively low and so the traditional route to licensure, a phase 3 randomised controlled trial to demonstrate efficacy, would have been extremely time-consuming. The VEU was instrumental in performing studies to demonstrate the immunogenicity of candidate vaccines using the SBA assay as a correlate of protection against disease. Our work lead directly to the introduction of the MenC conjugate vaccine into the UK programme in 1999 and cases swiftly dropped from a peak of approximately 1000 in 1999 to a handful of cases annually by 2003. The programme has been called the biggest public health intervention of the decade.

The meningococcal conjugate vaccine programme in the UK has continued to evolve; changing from three doses at 2, 3 and 4 months of age to 3, 4 and 12 months of age in 2006, and further changing to 3 and 12 months and 13/14 years of age in 2013. These changes reflected our increased understanding of the effectiveness of the vaccine at eliminating carriage, and the importance of boosters later in life, all underpinned by research carried out by the VEU. The eventual replacement of the monovalent MenC vaccine with the quadrivalent vaccine against serogroups A, C, W and Y in 2015 was again supported by the work of the VEU.

The VEU has also carried out research to facilitate the introduction of the Bexsero meningococcal subgroup B vaccine into the UK, and our research continues to refine the UK meningococcal vaccine programmes. We have also contributed to meningococcal vaccine programmes in countries around the world – Africa, Saudi Arabia, and New Zealand amongst them. The Vaccine Preventable Bacteria Section (VPBS) in one of two Sections in the Respiratory and Vaccine Preventable Bacteria Reference Unit in the Public Health England (PHE) – National Infection Service (NIS) Laboratories, Colindale, London.

Number of cases of invasive MenC diseases in England and Wales

MenC conjugate vaccine was introduced in September 1999 (indicated by blue bar)



The Vaccine Preventable Bacteria Section (VPBS)

The Section Head is Dr Norman Fry (NIS – Immunisation and Countermeasures Division) who leads a team of 10 staff including Clinical Scientists, Biomedical Scientists and Healthcare Scientists. We provide specialist and reference laboratory testing for a number of bacteria which cause vaccine preventable diseases including *Streptococcus pneumoniae, Haemophilus influenzae, Bordetella pertussis*, and toxigenic corynebacteria. We also perform serological tests to determine immunity to diphtheria and tetanus.

Staff of the Vaccine Preventable Bacteria Section from left to right: David Litt, Norman Fry, Ginder Mann, Seyi Eletu, Alice Fuller, Samuel Rose, Alba Redin, John Duncan, Fu li, Karina Micah, Carmen Clark (Sheppard). Not in photo: **Anna Lewis** on maternity leave.

We work closely with colleagues across PHE and NIS including the Immunisation and Countermeasures Division, the Healthcare Associated Infection & Antimicrobial Resistance Division and the Tuberculosis, Acute Respiratory, Gastrointestinal, Emerging /Zoonotic Infections; and Travel Health Division and Health Protection Teams.

We are an accredited laboratory and are supported by our safety and our quality teams, and our technical lead manager Nita Doshi. We collaborate nationally and internationally, and are actively involved with several European reference laboratory networks.

The Unit and Section host two World Health Organisation Collaborating Centres (WHO CCs), the WHO CC for Streptococcal and Diphtheria Infections (Head, Prof Androulla Efstratiou) and the WHO CC for *Haemophilus influenzae* and ***Streptococcus pneumoniae*** (Heads, Dr Norman Fry and Dr David Litt). For these international activities, we work closely with UK NEQAS (External Quality Assessment Services) for Microbiology and the PHE Meningococcal Reference Unit, Manchester and provide support, expertise, training and External Quality Assurance panels.

Streptococcus pneumoniae identification and capsular typing

Streptococcus pneumoniae (the pneumococcus) causes a wide range of diseases from those called 'non-invasive' (e.g., ear and sinus infections and pneumonia) to 'invasive' (e.g., bacteraemia and meningitis).

The pneumococcus possesses several factors which enable it to escape human defence systems, the most important of which is a capsule (outer coat) comprised of polysaccharide (sugar) molecules. The pneumococcus is divided into >92 types (serotypes) defined by chemical differences in this capsule.

The current pneumococcal vaccines contain capsular polysaccharide antigens. Our Section monitors changes in the serotype in the circulating strains from invasive disease in both children and adults.

Karina Micah (Biomedical Scientist) setting up the Qiasymphony (Qiagen) instrument for genomic DNA extraction of Streptoccocus pneumoniae

All invasive cases are actively followed up in the childhood age groups targeted for vaccination to ascertain immunisation history and determine vaccine effectiveness. These data are pivotal in informing potential changes in national vaccine policy. Capsular typing of pneumococci can also be helpful in the investigation of instances of suspected cross-infection in hospitals or other residential institutions.

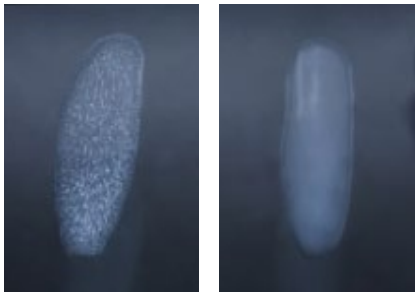
In October 2017, our laboratory replaced some of the traditional phenotypic tests used to identify and type *S. pneumoniae* isolates from invasive disease with the improved technology of whole genome sequencing (WGS). Identification and capsular type are now derived from genomic DNA sequence data using bioinformatical pipelines developed by PHE. This leap forward has revolutionised our ability to monitor strain variation and clonal expansion and has already led to some exiting new findings.

Culture-independent detection and typing of pneumococcus

We have developed an extended-specificity multiplex immunoassay for detection of *S. pneumoniae* serotype-specific antigen in urine. This assay can detect 24 of the pneumococcal vaccine serotypes/serogroups. This allows the determination of serotype data in the absence of isolates and the assay has been successfully applied to inform studies of both invasive and non-invasive pneumococcal disease and in helping to characterise outbreaks.

Haemophilus influenzae identification and capsular typing

Haemophilus influenzae can cause a number of severe illnesses including meningitis and bacteraemia. As for *S. pneumoniae* above, we characterise all *Haemophilus influenzae* isolates from invasive disease (ie blood, CSF and other normally sterile sites) in patients of all ages as part of the surveillance of invasive disease due to *H. influenzae* to determine whether the case is vaccine preventable (caused by *H. influenzae* serotype b (Hib)). This serotype historically caused the majority of serious disease, particularly in young children. Submitted isolates undergo serological serotyping and capsular genotyping. Conjugate Hib vaccine is routinely offered to all infants in the UK and capsular typing is the definitive test to determine whether the strain is a vaccine preventable serotype (i.e., Hib); a different (non-b) serotype (i.e., serotype a,c,d,e or f), or a non-capsulated strain.



Example of capsular typing of *Haemophilus influenzae* by slide agglutination. A suspension of test organism and monovalent antisera (e.g., serotype b) are mixed together. The left-hand side shows a positive result (clumping) indicating that the strain is *H. influenzae* serotype b. The right-hand side shows a suspension of the same organism mixed with saline as a control and shows no clumping.

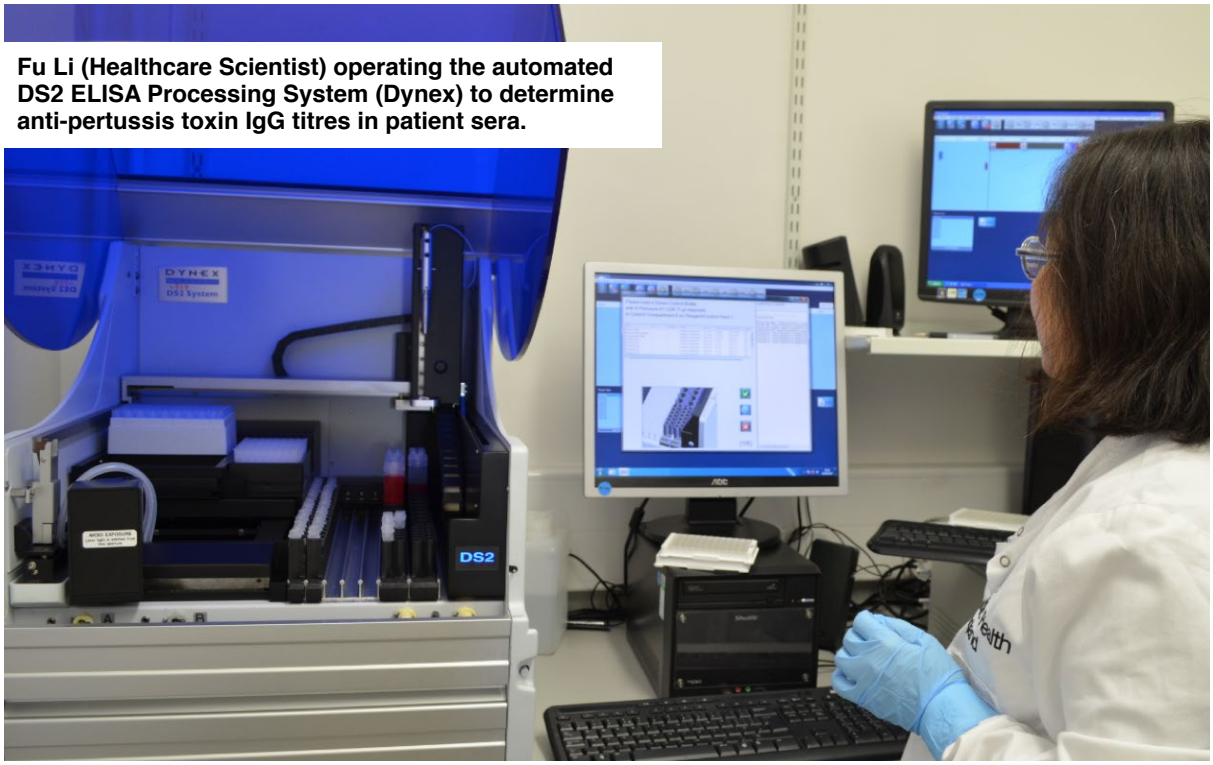
Bordetella pertussis

We offer a range of tests useful in the investigation of individual cases and outbreaks of pertussis infection (whooping cough). For patients with a history of cough (of at least 2 weeks), these include determination of significant levels of antibodies against pertussis toxin (anti-PT IgG) in sera (usually for older children and adults) and oral fluid (targeted at ages 2 to <17 years). For these tests, the timing of specimen collection is important (≥ 2 weeks after cough onset) to allow sufficient time for antibody rise.

The oral fluid test was developed to target children who may not be willing to give blood. The specimen is taken by rubbing the swab along the gumline, for ca. 2 minutes.

When a pertussis notification is received for a patient aged between 2 and <17 years, the PHE Health Protection team will send out an oral fluid kit to the patient, which is then sent to our laboratory for testing. Both the serology and oral fluid tests are performed by ELISA (enzyme-linked immunosorbent assay) detecting the presence of specific antibodies.

We also provide confirmation of identification and further characterisation of *B. pertussis* isolates and Bordetella PCR positive specimens referred from PHE laboratories. Results of all laboratory-confirmed pertussis cases contribute to informing potential changes to vaccine policy and have been instrumental in the decision to introduce the highly effective maternal immunisation programme for pertussis in October 2012 (following the national outbreak of disease). Recently, we have supported outbreak investigation in school settings using our oral fluid assay.



Fu Li (Healthcare Scientist) operating the automated DS2 ELISA Processing System (Dynex) to determine anti-pertussis toxin IgG titres in patient sera.

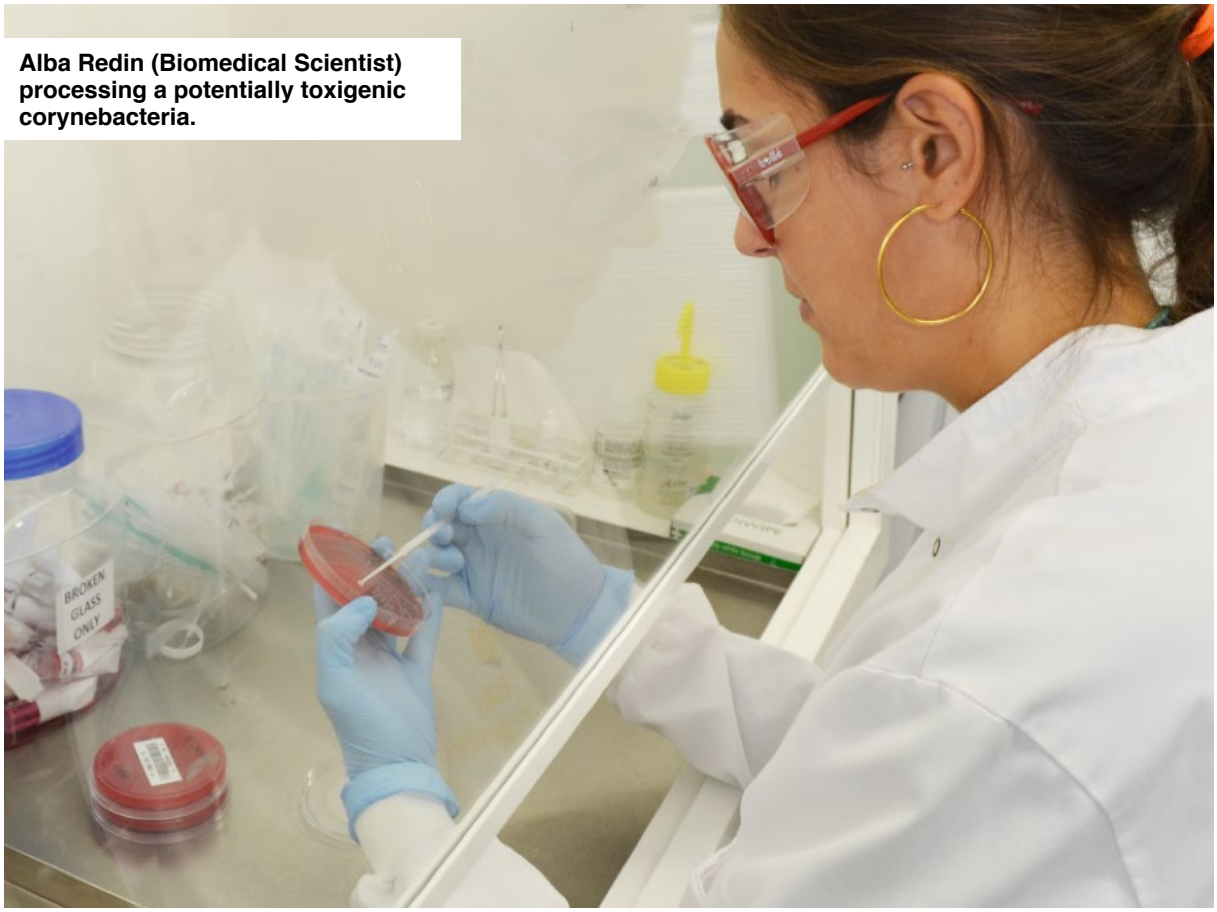
Diphtheria; identification and toxigenicity testing of potentially toxigenic corynebacteria (*Corynebacterium diphtheriae, C. ulcerans* and *C. pseudotuberculosis*)

Diphtheria is a potentially fatal toxin-mediated disease caused by *Corynebacterium diphtheriae, C. ulcerans* and rarely *C. pseudotuberculosis*. Classical respiratory diphtheria is a disease of upper respiratory tract and cutaneous diphtheria usually presents as lesions or ulcers on the skin.

Although diphtheria is now rare in the UK, it is important to identify toxigenic strains quickly as this can impact both patient care and public health action. To improve the time taken to achieve a result, since April 2014, the front-line test for putative toxigenic corynebacteria to inform public health action in England and Wales is a real-time PCR (qPCR) assay.

All isolates which are qPCR positive for the diphtheria toxin gene (*tox*) are also tested by the modified Elek test for toxin expression. As WHO CC the Section also provides confirmatory Elek testing of isolates referred by international reference laboratories.

Although diphtheria cases are rare, we have seen an increase in toxigenic *C. ulcerans* with a likely source of companion animals (eg, dogs and cats). We work closely with the PHE Emerging/Zoonotic Infections team, the Animal and Plant Health Authority and Health Protection Scotland to address these potentially complex investigations.



Alba Redin (Biomedical Scientist) processing a potentially toxigenic corynebacteria.

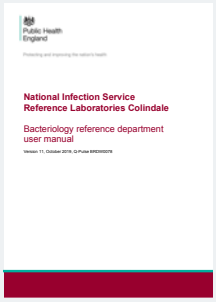
Immunity testing

We offer a specialised Vero cell tissue culture toxin neutralisation assay for serum antibodies against diphtheria toxin as a test to determine immunity status against diphtheria. Results are reported in International Units per mL and classified as susceptible, conferring some protection, protective or conferring long-term protection, according to agreed criteria. We also offer a test to measure immunity against tetanus, by detecting serum antibodies to tetanus toxoid (used in the tetanus vaccine) using a commercial ELISA kit; these results are also reported in International Units/mL. Minimum protective level is presently defined as 0.1 IU/mL.

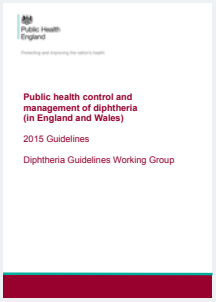
Microbiological reference services are changing and the switch to techniques such as whole genome sequencing means that we increasingly need some expertise in the analysis of these data. Our Section is fortunate to have support in Informatics/Bioinformatics from both our Unit bioinformatician, Natalie Groves and Dr Carmen Clark (Sheppard).

If you have any questions about the tests we offer or have any questions about interpretation of the results, please do get in touch. Dr Norman Fry, Section Head (norman.fry@phe.gov.uk) or Dr David Litt, Senior Scientist (david.litt@phe.gov.uk).

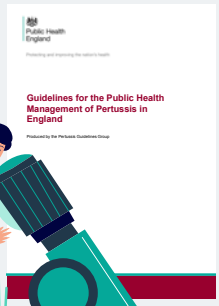
Links



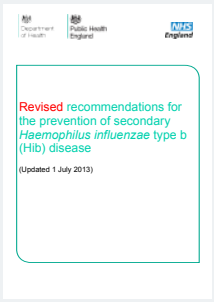
Bacteriology reference: department user manual (weblink 1)



Diphtheria: public health control and management in England and Wales (weblink 2)



Pertussis: guidelines for public health management (weblink 3)



Haemophilus influenzae type b (Hib): revised recommendations for the prevention of secondary cases (weblink 4)

Shortage of pneumococcal polysaccharide vaccine (PPV23)

Possible shortage of PPV23 during winter 2019

MSD have informed PHE and DHSC that there will be limited supplies of PPV23 vaccines until their next delivery which is expected in January 2020. This will affect both the PPV23 vials and PNEUMOVAX 23 pre-filled syringes. Practices should therefore plan to prioritise PPV23 vaccination according to the recommendations below.

Background

PPV23 continues to be recommended for:

- individuals aged from 2 years or over in clinical risk groups
- all individuals aged 65 years and over

The vaccine covers the 23 most common serotypes of Streptococcus pneumoniae (the pneumococcus) that are responsible for a range of diseases including meningitis, septicaemia and pneumonia. Pneumococcal infection occurs in the extremes of age with the highest incidence in infants and older adults. The vaccine differs from the PCV13 vaccine used for the routine childhood programme, as it covers additional 10 serotypes, and is not conjugated to a protein.

[!]

Recommendations on how to manage PPV23 immunisation (updated for winter 2019)

PPV23 provides modest protection of limited duration, especially in older adults. Booster doses are not recommended for most at-risk individuals as there is limited evidence of additional protection, but five yearly boosters are recommended for asplenic patients and those with chronic kidney disease. In contrast, PCV13 provides excellent protection to young infants and also reduces the nasopharyngeal carriage of the pneumococcus – leading to high levels of herd protection.

The remaining serotypes in PPV23, and the other serotypes not covered in any vaccine, are now responsible for the majority of residual disease.

Current arrangements

The PPV23 programme is commissioned as an enhanced service and vaccine is normally procured by general practices and reimbursed by the NHS Business Services Authority (NHS BSA). The vaccine is often delivered alongside the influenza programme, although, unlike influenza, only a single lifetime dose is recommended for most individuals.

Because of the relatively short duration of protection, and the increasing incidence with age, there are no major concerns about deferring vaccination in over 65 year olds for several months or until next year. The enhanced service payment allows for this delay.

Advice on how to manage and plan the PPV23 programme

The supply constraints affecting PPV23 vaccine will make it unlikely that practices will be able to offer the vaccine alongside influenza vaccine to all eligible patients in lower priority groups (e.g. healthy people aged 65 years and over).

Practices should therefore plan to offer PPV23 to this group throughout the year rather than aligning immunisation to take place alongside the flu programme. This will help to ensure demand for vaccine is more consistent across the year and that stock can be ordered in small quantities to cover the requirements each month, thus also reducing the risk of wastage.

1. If you are able to procure stock, the priority should be to offer vaccine to those newly diagnosed with conditions in the high priority followed by those in the moderate priority groups who have never received PPV23. When such individuals are first identified, if no vaccine is available, please ensure that their records are flagged in order to call them for a future appointment. Also ensure that other aspects of management are optimised and in place (for example antibiotic prophylaxis, or booster doses of PCV13) – as advised in relevant guidance, or by the specialist clinician caring for patient.
2. Any PPV23 dose that the surgery is able to access should be offered opportunistically to high and moderate priority groups attending an appointment at the surgery who have never received PPV23 and are due this vaccine
3. PPV23 vaccination for low priority groups (including healthy individuals aged 65 years and over) and booster doses for asplenics, those with splenic dysfunction and chronic kidney disease are less urgent and can be planned when sufficient stock is available.

Please also note that national stocks of PCV13 (Prevenar13), or separately procured PCV10 (Synflorix), should not be used in place of PPV23 because herd protection from the childhood PCV13 programme has reduced pneumococcal disease due to these serotypes across all ages, including the elderly.

PPV23 helps provide additional protection against serotypes that are not covered by PCV13 or PCV10.

Table: Priority groups for Pneumococcal polysaccharide 23-valent vaccine (PPV23)

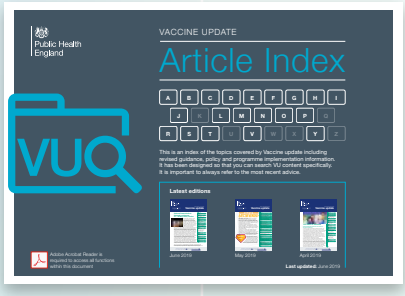
Clinical risk group	Examples (decision based on clinical judgement)
High priority	
Asplenia or dysfunction of the spleen	This also includes conditions such as homozygous sickle cell disease and coeliac syndrome that may lead to splenic dysfunction.
Immunosuppression	Due to disease or treatment, including patients undergoing chemotherapy leading to immunosuppression, bone marrow transplant, asplenia or splenic dysfunction, HIV infection at all stages, multiple myeloma or genetic disorders affecting the immune system (e.g. IRAK-4, NEMO, complement deficiency) Individuals on or likely to be on systemic steroids for more than a month at a dose equivalent to prednisolone at 20mg or more per day (any age), or for children under 20kg, a dose of 1mg or more per kg per day.
Individuals with cerebrospinal fluid leaks	*It is important that immunisation does not delay the cochlear implantation.*
Moderate priority	
Chronic respiratory disease	This includes chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema; and such conditions as bronchiectasis, cystic fibrosis, interstitial lung fibrosis, pneumoconiosis and bronchopulmonary dysplasia (BPD). Children with respiratory conditions caused by aspiration, or a neurological disease (e.g. cerebral palsy) with a risk of aspiration. Asthma is not an indication, unless so severe as to require continuous or frequently repeated use of systemic steroids (as defined in Immunosuppression below).
Chronic heart disease	This includes those requiring regular medication and/or follow-up for ischaemic heart disease, congenital heart disease, hypertension with cardiac complications, and chronic heart failure.
Chronic kidney disease	Nephrotic syndrome, chronic kidney disease at stages 4 and 5 and those on kidney dialysis or with kidney transplantation.
Chronic liver disease	This includes cirrhosis, biliary atresia and chronic hepatitis.
Diabetes	Diabetes mellitus requiring insulin or oral hypoglycaemic drugs. This does not include diabetes that is diet controlled.
Low priority	
Healthy over 65s	

New resources

Vaccine update Index has now been published

Vaccine update is a rich source of information. Following requests from subscribers, we have now created a new searchable index (weblink 5) so that you can find information about vaccine guidance, policy and programme implementation which was published in previous issues of Vaccine update more easily.

You can also find a link to the index on the Vaccine update home page at weblink 6.

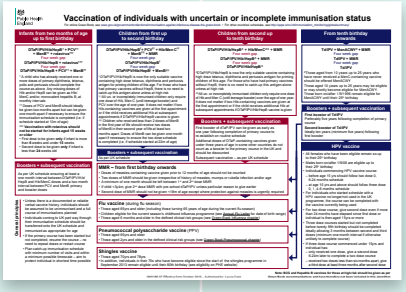


Vaccination of individuals with uncertain or incomplete immunisation status

This chart helps health professionals work out which vaccines are advised for people who are incompletely immunised with all the vaccines recommended for their age.

The wording for eligibility in the HPV section has recently been revised so please ensure you always use the most up to date version (Download at weblink 17).

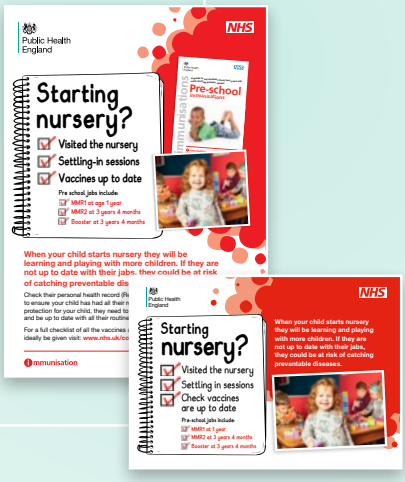
An equivalent screening algorithm is available at weblink 8.



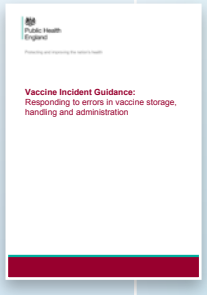
Starting nursery post card and poster

This poster and postcard are aimed at parents and carers to remind them to check that their child is up to date with their vaccinations. It features the MMR vaccine and the pre-school booster.

They are suitable for all GP practices, schools and nursery settings and are available to order. Primary and secondary school versions of the poster and postcard are also available at weblink 7.



Vaccine incident guidance: responding to vaccine errors in vaccine storage, handling and administration

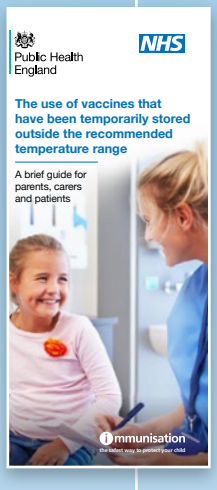


This document has recently been substantially revised and has been republished at weblink 10. Its purpose is to provide consistent guidelines for both providers and commissioners of immunisation services in the investigation and management of vaccine storage or administration incidents. In addition to providing advice about incidents where vaccines have been stored outside the recommended temperature range, it also contains advice about errors in vaccine preparation and administration.

Off-label vaccine: revised leaflets

Information for parents and healthcare professionals about off-label vaccines. Children and adults are sometimes offered off-label vaccines (vaccines authorised for use but being used in a way that is slightly different from the terms laid down in their license). These documents, one for parents and one for health professionals, describe the circumstances that can lead to vaccines being used 'off-label' and why this may be recommended. They are not currently available to order in print copies but can be downloaded at weblink 11.

Vaccines stored outside the recommended temperature range



A revised leaflet for parents is available at weblink 12 which explains what happens when vaccines have inadvertently been stored outside of the recommended storage temperature range. Not all vaccines that have fallen outside the recommended storage temperature need be destroyed – some vaccines can still be used. However, if they are used, they are described as being 'off-label' vaccines. This leaflet provides information on why vaccines are kept under controlled temperature conditions and what 'off-label' vaccines are. It is intended for parents, carers and patients.

Green Book chapter 21 – Measles

The Measles chapter has been extensively revised, please take a look and familiarise yourself with the newly formatted and updated chapter. See weblink 16.

The revisions include:

- update of the epidemiology to 2018
- in the 'normal immunoglobulin' section hyperlink to PHE guidance inserted
- 'Administration with other vaccines' section updated and table 21.1: 'recommended intervals between MMR and other live vaccines' added
- 'Pregnancy and breastfeeding' section – wording updated and link to 'MMR vaccine: advice for pregnant women' inserted
- 'Rare and serious events' section – wording updated
- 'Other conditions reported after vaccines containing measles, mumps and rubella' section – wording updated
- link to 'viral rash in pregnancy' guidance added to 'Management of cases, contacts and outbreaks' section
- 'Dosage of normal immunoglobulin' section removed and replaced by a link to the 'measles prophylaxis' page
- 'Supplies' section updated
- references in the Bibliography updated

Flu vaccination for children under 18 years leaflet

Children under 18 who are at risk from flu will be offered either the nasal spray or the injected vaccine which both offer protection against 4 strains of flu virus.

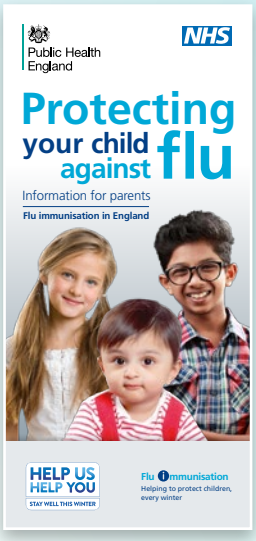
This leaflet is to explain to parents of children who are eligible for a flu vaccine why they may need to reschedule their appointment with their GP when the right flu vaccine is available. See weblink 15.

Copies can be ordered using product code: 2016059CH

Flu vaccination for people aged 65 and under

Adults aged under 65 will be offered an injected quadrivalent influenza vaccine (QIV) which offers protection against 4 strains of flu virus.

This leaflet at weblink 9 is to explain to people who are eligible for a flu vaccine why they may need to reschedule their appointment with their GP when the QIV flu vaccine is available.



Protecting your child against flu leaflet

This leaflet explains which children are eligible for flu vaccination, as well as describing the disease and the vaccine. Printed copies can be ordered using product code: 2902552C.

There are translated versions of this leaflet available to download in Arabic, Bengali, Simplified Chinese, French, Italian, German, Gujarati, Hindi, Polish, Portuguese, Romani, Romanian, Somali, Turkish, Tagalog, Tamil, and Urdu. The translated versions are download only at weblink 15.

There are versions of this leaflet as an audio file and a version in Braille is available to order from the HealthPublications website.See weblink 18.

Vaccine Supply – centrally supplied

Vaccine supply for the 2019 to 2020 Flu programme

Children's flu vaccine availability for 2019 to 2020

As in previous years, PHE is centrally suppling flu vaccine for children included in this year's flu programme, including those aged from six months to less than 18 years old in clinical risk groups. It remains the responsibility of GPs and other providers to order sufficient flu vaccine directly from manufacturers for older eligible patients of the flu programme in 2019 to 2020.

The following vaccines are now available to providers of the children's flu programme in England via the ImmForm website.

Please refer to guidance from your respective health departments for arrangements in Scotland, Wales and Northern Ireland.

Vaccine	Manufacturer
Fluenz Tetra®	AstraZeneca
Quadrivalent Influenza Vaccine (split virion, inactivated) (QIVe)	Sanofi Pasteur

Fluenz Tetra ordering information

As in previous years, order controls will be in place on ImmForm for 2 purposes:

- to ensure demand is mapped against available supply at any point in time, and
- to reduce the amount of Fluenz Tetra® ordered across England but ultimately not administered to children

Please refer to the ImmForm website for the most up to date information on ordering for 2019 to 2020.

Information for General Practice on editing Fluenz Tetra orders

Due to the anticipated large volume of orders for Fluenz Tetra® in the first few weeks of ordering, orders for this product will be assembled as soon as they are placed. **Please do not edit your Fluenz Tetra® order after you have clicked 'confirm order' as any changes will not be reflected in your delivery.** If you need to make an adjustment to your order after it has been placed, please contact the ImmForm helpdesk.

Inactivated flu vaccine ordering information

PHE supplies an inactivated vaccine that is suitable for all children from 6 months to less than 18 years old. It should be used for eligible children who are contraindicated for Fluenz Tetra (or otherwise unsuitable) **and** are in a clinical risk group. This vaccine is Quadrivalent Influenza Vaccine (split virion, inactivated), and will have an order cap of 20 doses per week.

All influenza vaccines for the 2019 to 2020 season

Information on all influenza vaccines that have been marketed in the UK for the 2019 to 2020 season are available via weblink 14. Please refer to the flu letter for information on which vaccines are eligible for reimbursement in the 2019 to 2020 season.

Centrally supplied vaccines can be used for the purposes defined in chapter 3 of the Green Book, and in the 'Vaccines available on ImmForm' helpsheet.

Ordering additional Gardasil for the universal HPV immunisation programme

Since 1 September 2019, the human papillomavirus (HPV) vaccine has been offered to boys, in addition to girls, as part of the routine school aged immunisation schedule. Customers can order the additional required volumes of Gardasil through ImmForm alongside vaccine used for the girls' programme.

Update to Bexsero Patient Information Leaflet

Every pack of Bexsero (Meningitis B vaccine; 10 doses) is supplied with a pad of ten Patient Information Leaflets (PILs), as well as there being a single PIL inside each Bexsero pack. Since late-September 2019, an updated version of the PIL pad has been distributed with Bexsero orders. As you start to receive PIL pads that do not match the PIL within the pack, please dispose of the single PIL from inside the pack, as it will be out-of-date.

MMR vaccine ordering

There are currently two different vaccines available to order for the MMR programme, MMRvaxPRO® and Priorix®. Orders for Priorix® are capped at 20 packs per order per week for accounts in England and Wales. Controls are also in place for Scottish customers. This is needed to rebalance central supplies.

The alternative MMR vaccine, MMRvaxPRO®, remains available to order without restriction. If you specifically require additional Priorix® stock, for example because you serve communities that do not accept vaccines that contain porcine gelatine then please contact the ImmForm Helpdesk for assistance at helpdesk@immform.org.uk or 0844 376 0040.

The EU Falsified Medicines Directive (FMD) and Delegated Regulation as applicable to PHE supplied vaccines for the national immunisation programme

Full information on FMD as it applies to centrally supplied vaccines for the National Immunisation Programme can be found in the April 2019 edition of Vaccine update. ImmForm vaccines in FMD-compliant packs (i.e. subject to the requirements of the Delegated Regulation) are being distributed for the majority of centrally-supplied products. The last products to be issued in FMD-compliant packs will go live towards the end of 2019 and into 2020. The exact start dates will be different for different products (the month is indicated in the table below for each product).

We will continue to update this information as forecasts become more accurate so please check for updates via the ImmForm news pages regularly. We would encourage all of our customers to visit the GOV.UK page on FMD and spend some time becoming familiar with the content and links to various other guidance documents on the implementation of the legislation.

Please note that both vaccines supplied by PHE for the 2019 to 2020 children's flu programme will be issued in FMD-compliant packs and will be subject to the requirements of the Delegated Regulation.

Product	Brand name	Month FMD-compliant packs will be issued which require verification and decommissioning
Pneumococcal conjugate vaccine (PCV)	Prevenar13	Live
DTaP/IPV vaccine for pregnant women	Boostrix-IPV	Live
Meningococcal Group ACWY vaccine	Nimenrix	Live
Measles-Mumps-Rubella (MMR) vaccine	MMR VaxPRO	Live
DTaP/IPV/Hib/HepB vaccine	Infanrix Hexa	Live
Tuberculosis vaccine (BCG)	BCG Vaccine AJV	Live
Meningococcal Group B vaccine	Bexsero	Live
Shingles (Herpes zoster) vaccine	Zostavax	Live
Hib/MenC vaccine	Menitorix	Live
Measles-Mumps-Rubella (MMR) vaccine	Priorix	Live
Rotavirus vaccine	Rotarix	October 2019
Human papillomavirus (HPV) vaccine	Gardasil	October 2019
DTaP/IPV vaccine for infants	Repevax	December 2019
Td/IPV vaccine	Revaxis	January 2020
Purified protein derivative (Mantoux test)	Tuberculin PPD-2TU	All stock will be in non-FMD packs (as it is unlicensed in UK)

PHE have also issued, and continue to issue, many products in FMD-barcoded packs that were manufactured before the legislation came into force. These packs are not required to be verified and decommissioned, but this can be done optionally.

If you have identified yourself to PHE as being exempt from decommissioning under Article 23 of the Delegated Regulation and this has been agreed, then you will be supplied with decommissioned vaccine.

Please see our guidance for more information on the roles and responsibilities in relation to FMD and the Delegated Regulation, regarding vaccines and other medicines centrally supplied by PHE to the NHS and other customers. This document is accessible via GOV.UK with weblink 13.

Vaccine supply for the non-routine programme

HEPATITIS A VACCINE

Adult

- **GSK**: Havrix Adult PFS singles and packs of 10 are available
- **Sanofi Pasteur**: Avaxim is available
- **MSD**: VAQTA Adult is available

Paediatric

- **GSK**: Havrix Paedatric PFS singles and packs of 10 are available
- **MSD**: VAQTA Paediatric is available

HEPATITIS B VACCINE

Adult

- **GSK**: Engerix B PFS singles and packs of 10 are available
- **GSK**: Engerix B vials singles are available
- **GSK**: Engerix B vial packs of 10 are unavailable
- **GSK**: Fendrix is available
- **MSD**: HBVAXPRO 10 µg is unavailable until further notice
- **MSD**: HBVAXPRO 40 µg is unavailable until further notice

Paediatric

- **GSK**: Engerix B Paediatric singles are available
- **MSD**: HBVAXPRO 5µg are available

COMBINED HEPATITIS A & B VACCINE

- **GSK**: Twinrix Adult singles and packs of 10 are available
- **GSK**: Twinrix Paediatric is available
- **GSK**: Ambirix is available

COMBINED HEPATITIS A & TYPHOID VACCINE

- **Sanofi Pasteur**: Viatim is available

TYPHOID VACCINE

- **Sanofi Pasteur**: Typhim is available
- **PaxVax**: Vivotif is available

RABIES VACCINE

- **GSK**: Limited supply of Rabipur is currently available. Supply issues resulting from manufacturing constraints have now resolved, however, GSK do not expect the situation to fully normalise until late 2019
- **Sanofi Pasteur**: Rabies BP is currently out of stock. An alternative vaccine is available, please contact Sanofi Pasteur directly for more information

Pneumococcal Polysaccharide Vaccine (PPV)

- **MSD**: Limited supplies of Pneumococcal Polysaccharide Vaccine vials are available
- **MSD**: Limited supplies of PNEUMOVAX 23 PFS are currently available

Pneumococcal polysaccharide conjugate Vaccine (PCV)

- **Pfizer**: Prevenar 13 is available

VARICELLA ZOSTER VACCINE

- **GSK**: VARILRIX is currently available
- **MSD**: VARIVAX is currently available
- **MSD**: Limited supplies of ZOSTAVAX is currently available. Resupply is expected Q1 2020

DIPHTHERIA, TETANUS AND POLIOMYELITIS (inactivated) VACCINE

- **Sanofi Pasteur**: Revaxis is available

MMR

- **MSD**: MMRvaxPro is currently unavailable. Resupply expected February 2020
- **GSK**: Supplies of Priorix are available

MENINGITIS ACWY VACCINE

- **GSK**: Limited supply of Menveo is available
- **Pfizer**: Nimenrix is currently available

YELLOW FEVER

- **Sanofi Pasteur**: Stamaril is available

HUMAN PAPILLOMAVIRUS VACCINE

- **MSD**: GARDASIL is currently unavailable resupply expected Q4 2019
- **MSD**: Gardasil 9 is currently available
- **GSK**: Cervarix is currently available

Weblinks

Weblink 1	https://www.gov.uk/government/publications/bacteriology-reference-department-brd-user-manual
Weblink 2	https://www.gov.uk/government/publications/diphtheria-public-health-control-and-management-in-england-and-wales
Weblink 3	https://www.gov.uk/government/publications/pertussis-guidelines-for-public-health-management
Weblink 4	https://www.gov.uk/government/publications/haemophilus-influenzae-type-b-hib-revised-recommendations-for-the-prevention-of-secondary-cases
Weblink 5	https://www.healthpublications.gov.uk/ViewArticle.html?sp=Svaccineupdateindex
Weblink 6	https://www.gov.uk/government/collections/vaccine-update
Weblink 7	https://www.gov.uk/government/publications/immunisations-resources-for-schools
Weblink 8	https://www.gov.uk/government/publications/screening-of-individuals-with-uncertain-or-incomplete-screening-status
Weblink 9	https://www.gov.uk/government/publications/flu-vaccination-for-people-aged-65-and-under
Weblink 10	https://www.gov.uk/government/publications/vaccine-incident-guidance-responding-to-vaccine-errors
Weblink 11	https://www.gov.uk/government/publications/off-label-vaccine-leaflets
Weblink 12	https://www.gov.uk/government/publications/vaccines-stored-outside-the-recommended-temperature-range-leaflet
Weblink 13	https://www.gov.uk/government/publications/fmd-guidance-for-recipients-of-phe-supplied-vaccines
Weblink 14	https://www.gov.uk/government/publications/influenza-vaccine-ovalbumin-content
Weblink 15	https://www.gov.uk/government/publications/flu-vaccination-leaflets-and-posters
Weblink 16	https://www.gov.uk/government/publications/measles-the-green-book-chapter-21
Weblink 17	https://www.gov.uk/government/publications/vaccination-of-individuals-with-uncertain-or-incomplete-immunisation-status
Weblink 18	https://www.healthpublications.gov.uk/Home.html