



RAPID RISK ASSESSMENT

Shortage of acellular pertussis-containing vaccines and impact on immunisation programmes in the EU/EEA (first update)

2 February 2016

Main conclusions and options for response

The vaccine shortage currently affecting some EU/EEA Member States has already had direct consequences for the delivery of national vaccination programmes.

In general, the supply situation appears similar to what was previously reported, and uncertainty prevails. Some countries had to make short-term arrangements with other countries to avoid interruption of their programmes.

Since 2015, nine EU/EEA Member States have adjusted their immunisation policies. Measures included the following:

- Temporary suspension of the primary immunisation scheme
- Temporary suspension of the booster at pre-school age
- Changes to the primary immunisation schedule with regard to age at which the vaccine is given
- Modification of the vaccine formulation used as a pre-school booster
- Delayed introduction of a new antigen into the primary immunisation scheme
- Prioritisation of vaccine formulation for the primary immunisation scheme
- Use of acellular pertussis-containing vaccines not authorised in the EU

Should shortages persist at the national level, several options should be considered. These options are listed below and have been updated since the previous RRA on acellular pertussis-containing vaccines.

As much as possible, the primary immunisation schedule should be preserved in order to ensure the early and adequate protection of newborns. If alternative vaccines or other vaccine presentations are available, their use should be prioritised, in conjunction with appropriate monitoring of safety and effectiveness, rather than modifying the vaccination schedule. Preference should be given to the use of combination vaccines with the highest number of antigens.

Priority should be given in the following order:

- The infant primary immunisation series (first year of life)
- The first toddler booster (second year of life) dose
- If applicable, the first toddler booster dose should be prioritised over the school-entry booster.

In countries where vaccination during pregnancy is recommended, and if Tdap vaccine is in short supply, it is suggested that doses should be preserved for maternal immunisation, instead of adolescent or pre-school booster doses, as maternal immunisation directly benefits newborns.

More evidence on the level of protection offered by the following strategies is needed:

- Use of a low-antigen-content pertussis vaccine as pre-school booster instead of a regular-dose vaccine, and vaccination of these cohorts at a later age.
- Maternal immunisation blunting the responses to some vaccines in the infant immunisation schedule.

Source and date of request

Directorate General for Health and Food Safety (DG SANTE), 25 January 2016

Public health issue

Early in 2015, a shortage of acellular pertussis-containing combination vaccines for use in the EU/EEA immunisation programmes was brought to the attention of ECDC. This was addressed in a previous RRA published in October 2015 [1].

This RRA focuses on acellular pertussis-containing combination vaccines used in national vaccination programmes in the EU/EEA Member States (see Table 1).

Its objectives are:

- to provide an overview of the situation in the EU/EEA Member States and changes made to the routine vaccine schedules in order to overcome shortages;
- to provide updated options to be considered by EU/EEA Member States in order to adjust their national vaccination schedules to overcome supply challenges.

This rapid risk assessment is not intended:

- to propose a universal EU vaccination schedule that can completely accommodate all national situations;
- to provide an extensive evidence-based review of options on how to modify vaccination schedules;
- to discuss specifics of the various combination vaccines available on the EU market, i.e. number and types of aP vaccine components, antigen concentration of the individual vaccines or the role of combined or concomitantly administered vaccines*;
- to address vaccine procurement processes at the national level.

Consulted experts

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ECDC acknowledges the valuable contributions of all experts. The experts have submitted declarations of interests that were reviewed by ECDC and found not to be in conflict with the comments and suggestions made. The opinions expressed by individual experts do not necessarily represent the opinions of their institutions.

Abbreviations

aP: Acellular-pertussis (full-dose content)

ap: Acellular pertussis (low-dose content)

wP: Whole-cell pertussis

T: Tetanus antigen

D: Diphtheria antigen

d: Diphtheria antigen (reduced dose)

* It is understood that the use and type of vaccines should be in accordance with national vaccination policies and the summary of product characteristics of each vaccine.

DT: Diphtheria and tetanus antigens combination vaccine

DTaP-IPV: Combination vaccines that contain diphtheria (full dose), tetanus, acellular pertussis (full dose) and inactivated poliomyelitis antigens. Also referred to as 'tetraivalent' vaccine.

DTaP-IPV/Hib: Combination vaccines that contain diphtheria (full dose), tetanus, acellular pertussis (full dose), inactivated poliomyelitis antigens and Hib antigen (to be reconstituted for some vaccine presentations). Also referred to as 'pentavalent' vaccine.

DTaP-IPV-Hib-HepB: Combination vaccines that contain diphtheria (full dose), tetanus, acellular pertussis (full dose) inactivated poliomyelitis antigens, Hib and Hepatitis B antigens. Also referred to as 'hexavalent' vaccine.

DTwP: Combination vaccines that contain diphtheria (full dose), tetanus and whole-cell pertussis antigens.

Tdap: Combination vaccines that contain tetanus, diphtheria (reduced dose content) and acellular pertussis (low antigen content).

Tdap-IPV: Combination vaccines that contain tetanus, diphtheria (reduced dose content), acellular pertussis (low antigen content) and inactivated poliomyelitis antigens.

Hib: *Haemophilus influenzae* type b

'2p+1' schedule: Primary immunisation schedule corresponding to two doses of primary vaccination and a booster dose, usually all given within the first 12 months of life and starting as early as at two months of life.

'3p+1' schedule: Primary immunisation schedule corresponding to three doses, given in the first year of life, starting as early as at two months of life, with a booster in the second year of life.

Background

Vaccine shortage is believed to be due to reduced production capacities for the acellular pertussis antigen that enters the final vaccine formulation of numerous combination vaccines, increased global demand for those combination vaccines that are also used throughout the EU/EEA Member States, and vaccine lots failing to meet the necessary release criteria.

This shortage forced some EU/EEA countries to adjust their childhood vaccination programmes in order to address the vaccine shortage. In some cases ad-hoc measures to procure vaccines were implemented.

Pertussis vaccines do not exist as stand-alone vaccines. Therefore, the current shortage affecting the acellular pertussis component not only negatively impacts pertussis protection but also poses the risk of reduced availability of combination vaccines containing an acellular pertussis component, in particular those that also protect against tetanus, diphtheria, polio and invasive bacterial disease caused by Hib.

These diseases are severe, and any failure to provide a high level of vaccination coverage can have dramatic consequences. For example, Ukraine reported two paralytic cases of poliomyelitis in August 2015 related to a vaccine-derived poliovirus strain in combination with low vaccination coverage [3].

Event background

In early 2015, a limited supply of combined vaccines for primary immunisation and booster series was brought to the attention of the ECDC.

Several EU/EEA Member States have requested technical assistance from ECDC, which lead to an information exchange between ECDC and EU/EEA Member States through the epidemic intelligence information services platform for vaccine-preventable diseases (EPIS-VPD) as well as during a Health Security Committee (HSC) teleconference in April 2015. Several countries reported that they had a limited stockpile of vaccines for use in their routine programmes and that it was difficult to procure specific vaccine combinations.

On 23 September 2015, the ongoing supply issues – alongside possible increased demand to vaccinate newly arrived migrants – were discussed during an HSC teleconference.

On 8 October 2015, ECDC published an RRA.

In January 2016, ECDC asked its National Focal Points for an update on the supply situation for acellular pertussis-containing combination vaccines and for information on the adjustments made to national immunisation programmes to overcome the shortage (Annex 1, Table 1).

Since 2015, nine EU/EEA Member States have adjusted their immunisation policy. Measures included the following:

- Temporary suspension of the primary immunisation scheme (e.g. Bulgaria)
- Temporary suspension of the booster at pre-school age (e.g. Bulgaria, Spain)
- Changes to the primary immunisation schedule with respect to age of vaccine administration in order to save doses (e.g. Romania)
- Modification of the vaccine formulation used as a pre-school booster with reduced diphtheria and pertussis

- antigen content vaccines (e.g. Belgium, France, Greece, Luxembourg)
- Delayed introduction of a new antigen into the primary immunisation scheme (e.g. Norway)
- Prioritisation of vaccine formulation for the primary immunisation scheme rather than for booster doses (e.g. Spain, Sweden)
- Procurement of vaccines for the primary immunisation scheme from outside the EU (e.g. Romania, Bulgaria)

ECDC threat assessment for the EU

The shortage of acellular-pertussis combination vaccines affecting the EU/EEA Member States is still ongoing and represents a public health threat to the EU. The risk lies in leaving cohorts of children temporarily unvaccinated, or vaccinated with a vaccine formulation that is not recommended for their age group to ensure full protection.

To date, there is no indication on how long this shortage will last, and the situation remains of concern. The negative consequences on vaccination programmes will increase until supplies resume to normal. In the meantime, countries face the growing accumulation of susceptible cohorts and cohorts with suboptimal protection that are at risk of disease. Some countries, such as Bulgaria, are reported to have faced shortages since 2014. Some children did not receive appropriate pre-school vaccination and are in need of catch-up vaccination.

In addition to the potential impact on public health, vaccine shortages also have operational and technical consequences for the delivery and assessment of national immunisation policies and for disease surveillance systems. There are both operational and technical consequences:

Operational consequences

- Need to communicate regularly with public and healthcare professionals with regard to vaccine shortage and adaptation of vaccination schedules in order to avoid confusion.
- Need to ensure adequate documentation of individual vaccinations in order to provide supplementary immunisation to those children that were inadequately vaccinated – once supplies have reached normal levels.

Technical consequences

- Need for enhanced surveillance for selected vaccine-preventable diseases.
- Need to consider the implementation of sentinel hospital surveillance of severe pertussis in young children
- Need to consider improving diagnostic capacities.
- A periodical assessment of the level of protection through regular sero-surveys in cohorts of children who were vaccinated with modified schedules/products may be required.
- Need to enhance the monitoring of vaccine coverage of the cohorts vaccinated with a modified schedule.
- A periodical assessment of the safety profile of the vaccine products used to respond to the shortage may be required.

Options for response

The options presented in the previous RRA remain valid and have been further specified below – in particular on the use of low dose diphtheria and pertussis-combination vaccines not licensed for use in primary immunisation series [1].

The general principle remains, whenever possible, to:

- substitute the missing doses with an alternative combination/formulation vaccine rather than modifying the schedule;
- prioritise strategies that have demonstrated direct benefit towards infants (e.g. primary and maternal immunisation); vaccinating those who have close contacts with infants too young to be vaccinated provides indirect protective effects.

Options for adjusting the primary immunisation series

The priority is to preserve the primary immunisation series, with a minimum of three doses administered by the first birthday.

In case of severe shortages, the following options are suggested (in order of priority):

Interchangeability of vaccines

- If alternative vaccines or other vaccine presentations are available (see below), prioritise their use rather than modifying the schedule (e.g. rather than switching from a '3p+1' to a '2p+1' schedule with the same product) and ensure appropriate monitoring of safety and effectiveness.
- If a hexavalent vaccine (DTaP-IPV-HepB-Hib) is not available for any dose of the infant/toddler series, using the following vaccines could be considered:
 - A pentavalent vaccine (DTaP-IPV/Hib), co-administered with a HepB standalone vaccine
 - A tetravalent vaccine (DTaP-IPV), co-administered with Hib and HepB standalone vaccines
 - A trivalent vaccine (DTaP), co-administered with the recommended standalone vaccines.
- If a pentavalent vaccine (DTaP-IPV/Hib) is not available for any dose of the infant/toddler series, using the following vaccines could be considered:
 - A hexavalent vaccine according to indication (even if there is no recommendation to routinely vaccinate against HepB) as the priority remains the protection against Hib and pertussis in infants, or
 - A tetravalent vaccine (DTaP-IPV), co-administered with a Hib standalone vaccine, or
 - A trivalent vaccine (DTaP), co-administered with the recommended standalone vaccines.

Modification of the age at administration

In countries with a '3p+1' schedule, one of the primary doses in the first year of life could be temporarily suspended. The primary booster dose would then be moved up and offered at around the time of the first birthday [8]. This would correspond to the first booster dose of a '2p+1' schedule, with a two-month interval between doses. Supplementary school-entry booster vaccinations should be considered for these cohorts of children, in accordance with national vaccination policies.

Use of low dose diphtheria and pertussis-combination vaccines not licensed for use in primary immunisation series

Combination vaccines licensed in the EU/EEA Member States that contain a low-dose pertussis and diphtheria antigen (e.g. Tdap; Tdap-IPV) are not licensed for use in primary immunisation schedules. They do not contain a Hib or HepB antigen, which would have to be provided alternatively whenever needed in the schedule.

This category of vaccines has not undergone clinical trials in the age groups targeted in the primary series and, to our knowledge, there is no published information on their unlicensed usage. The earliest age at which these vaccines could be used is three years, but this may vary according to the commercial product.

It is acknowledged that the pertussis and diphtheria concentration of the antigens are considered as insufficient to prime infants and trigger an immune response that provides clinical protection. Their use should only be considered as a last option if no alternative exists for the primary vaccination so that infants will not remain unvaccinated. In this scenario, available vaccines should be used with a pertussis toxoid (PT) antigen content as close to 25 µg as possible (as in vaccines used for primary immunisation).

A careful assessment of the situation should be conducted prior to implementation. Effectiveness should be monitored through serological and clinical surveillance. It is advised:

- to perform serological surveillance by measuring diphtheria-neutralising antibodies according to the recommended in vitro methods [9] in a reference laboratory able to measure neutralising antibodies against diphtheria. Circulating diphtheria antitoxin levels in individual serum samples above the threshold of 0.1 IU/ml are indicative of full protection against diphtheria. Diphtheria serology is suggested in the light of the absence of established immunological correlates of protection for pertussis [6];
- to ensure the documentation of individual vaccinations in order to provide supplementary immunisation when supplies have returned to normal levels. It is advised to then administer DTaP-containing vaccine before the children reach school age.

Options for possible adjustments to the pre-school, adolescent and adult immunisation series (from three years of age)

Interchangeability of vaccines

For the school-entry booster, if a tetravalent vaccine (DTaP-IPV) product is not available, the following options could be considered:

- Use of a Tdap-IPV vaccine (or Tdap and IPV vaccines co-administered) [10,11], as adopted by Belgium, France and Greece as a temporary measures (Table 1).
- Alternatively, use of a Td-IPV vaccine or the co-administration of Td and IPV vaccines. In this case, however, no vaccination against pertussis would be offered.
- Delaying the administration of the booster dose until the supply of pertussis-containing combination vaccine has returned to normal levels.

Options for vaccination during pregnancy

In countries where vaccination during pregnancy is recommended, and if a Tdap vaccine is in short supply, it is suggested that doses for maternal immunisation should be preserved over adolescent or pre-school booster doses, as maternal immunisation directly benefits newborns. Similarly, pre-school and adolescent booster doses should be prioritised over adult booster doses.

This can be schematically summarised as follows in terms of the order of preference, should severe shortages occur at the country level and prioritisation be needed. The symbol '>' suggests that the preceding population group is a preferred target for vaccination, whenever applicable:

Maternal > Pre-school booster > Adolescent booster > Adult booster

In countries where vaccination in pregnancy is not recommended, its implementation could be considered as a means to protect unvaccinated infants affected by shortages [12].

Conclusions

The vaccine shortage currently affecting some EU/EEA Member States has already had direct consequences for the delivery of national vaccination programmes. Since 2015, nine EU/EEA Member States had to adjust their immunisation policies.

In general, the supply situation appears similar to what was previously reported, and uncertainty prevails. Some countries had to make short-term arrangements with other countries to avoid interruption of their programmes.

Should shortages persist at the national level, several options should be considered. These options have been updated since the previous RRA on acellular pertussis-containing vaccines.

The primary immunisation schedule should be preserved as much as possible in order to ensure the early and adequate protection of newborns. If alternative vaccines or other vaccine presentations are available, their use should be prioritised, in conjunction with appropriate monitoring of safety and effectiveness, rather than modifying the vaccination schedule. Preference should be given to the use of combination vaccines with the highest number of antigens.

Priority should be given in the following order:

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In countries where vaccination during pregnancy is recommended, and if Tdap vaccine is in short supply, it is suggested that doses should be preserved for maternal immunisation, instead of adolescent or pre-school booster doses, as maternal immunisation directly benefits newborns.

More evidence on the level of protection offered by the following strategies is needed:

- Use of a low-antigen-content pertussis vaccine as pre-school booster instead of a regular-dose vaccine, and vaccination of these cohorts at a later age.
- Maternal immunisation blunting the responses to some vaccines in the infant immunisation schedule.

Annex 1. Overview table

Table 1. Shortage of aP-containing vaccines in EU/EEA Member States and impact on vaccination policy, as of 28 January 2016

| Country | Situation update as of | Source | Current or anticipated shortages | Impact on vaccination policy and mitigation | | Comments | Impact (January 2016) |
|-----------------------|------------------------|--|---|--|--|--|-----------------------|
| | | | | Primary immunisation | Booster doses | | |
| Austria | 26 Jan 2016 | Communication to ECDC | Current: Shortage of dTaP-IPV combination vaccines for booster doses on the private market in 2014 and 2015. | None | Limited: In some cases, delay of booster doses for school children in the free national immunisation programme. Delay of booster doses for adolescents and adults who are vaccinated with vaccines from the private market. | The situation is expected to improve in 2016 | |
| Belgium | 26 Jan 2016 | Communication to ECDC; official statement* | Current: aP combination vaccines – DTaP-IPV | None | High: Pre-school booster affected. DTaP-IPV and temporary replacement by Tdap-IPV (same manufacturer but lower dose of diphtheria/tetanus/pertussis antigens) | | |
| Bulgaria | 26 Jan 2016 | Communication to ECDC | Current: Shortage of aP combination vaccines: hexa-, penta- and tetraivalent. No tenders for hexa- and pentavalent vaccines are opened. In January 2016, a tender procedure for tetraivalent vaccines for boosters for 2015 was initiated. | Very high: In 2015, primary immunisations were affected by penta- and hexavalent vaccine shortages. Immunisation gaps were partially closed by donation of pentavalent vaccines from Turkey in July and at the end of the year. | Very high: In 2015, the administration of the pre-school booster with tetraivalent vaccine was suspended. At the end of 2015, smaller quantities of tetraivalent vaccines could be bought, which were used primarily for booster immunisations in children who missed the pre-school vaccination in 2014. | | |
| Croatia | 25 Sep 2015 | Communication to ECDC | Current: Td vaccine used for adult booster Expected: aP combination vaccine (hexavalent, DTaP, Tdap) | Limited: Introduction of hexavalent vaccination connected to, but not dictated by, shortage in pentavalent vaccine | None | | |
| Czech Republic | 26 Jan 2016 | Communication to ECDC | Current: DTaP (used as a booster dose at 5–6 years; the proposal is to replace it with DTaP-IPV. Repeated interruptions in the supply of Tdap vaccine for adults. | None | None | | |
| Cyprus | | | | | | | |
| Denmark | 26 Jan 2016 | Communication to ECDC | Current: dTap-IPV (SSI product) for booster vaccination at five years of age. DTaP-IPV/Hib (SSI product) for primary vaccination | Limited: SSI product will be replaced by other hexavalent vaccines [†] . | None | | |

* http://www.provac.org/pdf/TETRAVAC_Repevax-FAQ_Provac_sept2015.pdf

[†] <http://www.ssi.dk/Aktuelt/Nyhedsbreve/EPI-NYT/2016/Uge%203%20-%202016.aspx>

| Country | Situation update as of | Source | Current or anticipated shortages | Impact on vaccination policy and mitigation | | Comments | Impact (January 2016) |
|----------------|------------------------|--|--|--|--|----------|-----------------------|
| | | | | Primary immunisation | Booster doses | | |
| Estonia | 26 Jan. 2016 | | No shortage but limited stocks for BCG | None | None | | |
| France | 25 Feb 2015 | Official statement* | Shortage of combination vaccine with lower pertussis antigen content (aP-combo family). Impact on pre-school booster. Decision to introduce Tdap-IPV at six years of age instead of DTaP-IPV combination vaccine | None | High: Pre-school booster affected. DTaP-IPV temporary replaced by Tdap-IPV and DTaP-IPV recommended for the booster for 11–13-year-olds of the cohort currently affected. | | |
| Finland | 26 Jan. 2016 | Communication to ECDC | No shortage but limited stocks for DTaP | None | None | | |
| Germany | 26 Jan 2016 | Communication to ECDC; official statement† | Current: aP combination vaccines – DTaP-IPV/Hib. Shortage of single products. Products can, however, be replaced by others that are still available on the market. | None | None | | |
| Greece | 26 Jan 2016 | Official statement (15 October 2015)‡ | Current: shortage of tetravalent (dTdap-IPV) and pentavalent vaccines | None | High: Temporary replacement of pentavalent second-year-of-life booster dose by hexavalent vaccine. Temporary replacement of pre-school DTaP-IPV booster by Tdap-IPV or temporary delay of administration. | | |
| Hungary | 26 Jan. 2016 | Communication to ECDC; official statement† | Current: No shortage in DTaP-IPV-Hib combined vaccine. | None From 1 April 2016, switch from a 2, 4, 6 schedule with booster dose at 21 months to a 2, 3, 4 months schedule with a booster dose at 18 months. | None | | |
| Iceland | 26 Jan 2016 | Communication to ECDC | None | None | none | | |
| Ireland | 26 Jan 2016 | Communication to ECDC | None | None | None | | |
| Italy | 26 Jan 2016 | Communication to ECDC; official statement§ | Current: Shortages in Tdap, DTaP-IPV and DTaP-IPV-Hib | None because hexavalent vaccine is used for primary immunisation | None | | |
| Latvia | 26 Jan. 2016 | Communication to ECDC | None | None | None | | |

* <http://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefr=480>

† http://www.rki.de/DE/Content/Kommissionen/STIKO/Lieferengpaesse/Lieferengpaesse_node.html

‡ <http://www.hgye.hu/hirek/atmeneti-valtozas-az-oltasi-rendben/>

§ http://www.agenziafarmaco.gov.it/sites/default/files/elenco_medicinali_carenti_25.01.2016.pdf

| Country | Situation update as of | Source | Current or anticipated shortages | Impact on vaccination policy and mitigation | | Comments | Impact (January 2016) |
|----------------------|------------------------|----------------------------------|--|--|---|--|-----------------------|
| | | | | Primary immunisation | Booster doses | | |
| Lithuania | 26 Jan. 2016 | Communication to ECDC | Current: aP combination vaccines – DTaP-IPV/Hib, DTaP-IPV, Tdap Delayed delivery, reduced amount of delivered doses | None | None | | |
| Liechtenstein | | | | | | | |
| Luxembourg | 28 January 2016 | Communication to ECDC | Current: DTaP-IPV/Hib shortage (summer 2015) Temporary shortage of DTaP-IPV | Limited: Pentavalent vaccine substitution with the same vaccine initially attributed to another country | High: Pre-school booster affected. DTaP-IPV temporary replaced by Tdap-IPV | Recurring DTaP-IPV/Hib shortage. Substitution with the same vaccine from the same manufacturer initially attributed to another country – issues relating to the language of the substitution vaccine notice (not an official language in Luxembourg, additional information required). | |
| Malta | 26 Jan. 2016 | Communication to ECDC | None | None | None | | |
| Netherlands | 26 Jan. 2016 | Communication to ECDC | None | None | None | | |
| Norway | 26 Jan 2016 | Communication to ECDC | Delayed delivery/reduced volume delivered for all aP-containing combination vaccines. | None | None | Safety supplies for some of the aP-containing combination vaccines are very limited. | |
| Poland | 26 Jan 2016 | Communication to ECDC | During 2015, delayed delivery and reduced volume delivered for all aP-containing combination vaccines. No issues with DTWP vaccines currently used in the national programme. | Limited: Postponement of the implementation of dose vaccination using aP-containing combination vaccines. | High: Delayed implementation of pre-school vaccination with aP-containing combination vaccines. | | |
| Portugal | 12 Mar 15 | Technical advice request to ECDC | Shortage of combination vaccine with lower pertussis antigen content (aP-combo family). Impact on pre-school booster. ECDC provided technical advice to Portugal upon request. | - | - | | |
| Romania | 26 Jan 2016 | Communication to ECDC | Current: shortage of hexavalent, tetravalent and dT/dTap vaccines | High impact: Lack of hexavalent vaccine and substitution with the same formulation vaccine but originally licensed for countries outside of EU. | High: Shortages of vaccines used as pre-school (tetravalent vaccine) and school (dT/dTap vaccine) boosters | | |
| Slovakia | 26 Jan. 2016 | Communication to ECDC | None | None | None | | |
| Slovenia | 26 Jan 2016 | Communication to ECDC | None | None | None | | |

| Country | Situation update as of | Source | Current or anticipated shortages | Impact on vaccination policy and mitigation | | Comments | Impact (January 2016) |
|-----------------------|------------------------|-------------------------|---|--|---|---|-----------------------|
| | | | | Primary immunisation | Booster doses | | |
| Spain | 26 Jan 2016 | communication to ECDC | Current: shortage of pentavalent and dTap vaccines | Limited: Prioritisation of hexavalent vaccine for primary immunisation. Pentavalent vaccine to be prioritised for the second-year-of-life booster dose. | High: Booster at six years is delayed in a high proportion of children and immunisation for specific groups is interrupted. Prioritisation of vaccination during pregnancy in the whole country. | | |
| Sweden | 26 Jan 2016 | Communication with ECDC | Current: Possible shortage from April, 2016 for DTaP-IPV | None | None | DTaP-IPV vaccine with expiration date 31 March 2016 is currently available. | |
| United Kingdom | | | | | | | |

Legend

■ No status update communicated to ECDC in January 2016

■ No shortage or impact on vaccination policy

■ Limited shortage and/or limited impact on vaccination policy

■ Significant shortage and/or significant impact on vaccination policy

Annex 2. Pertussis vaccination schemes in the EU

All EU/EEA Member States have introduced vaccination against diphtheria, tetanus, poliomyelitis, pertussis and *Haemophilus influenzae* type b (Hib) in their primary infant schedules, with the majority of countries also administering vaccines against invasive pneumococcal disease and hepatitis B [13]. In addition, all EU/EEA Member States recommend vaccines against measles, mumps and rubella. Vaccination against meningococcal C infection (MenC) is recommended in 18 EU/EEA Member States.

The objectives of pertussis vaccination programmes are not to eliminate the disease but to prevent severe disease and deaths among youngest infants (<6 months):

- through direct protection by vaccinating infants soon after birth;
- through immunisation of those likely to infect young infants; and
- through maternal immunisation (implemented in a few EU/EEA countries).

Six weeks of age are generally considered as the minimum age to start DTwP/DTaP vaccination, with a primary immunisation schedule offering two to three doses in the first year of life [6]. Booster doses are usually offered from 11 months of age and throughout the second year of life, depending on the national vaccination schedules.

The current vaccination schedules in EU/EEA Member States are available from the ECDC vaccine schedule platform and are summarised in Table 2 [13]. Further details are available in the previous version of the RRA [1]

Table 2. Summary of vaccination schedules in the EU, adapted from the ECDC vaccine schedule platform

| Schedule type | First year of life | | | Second year of life | Third year of life | Preschool booster | Adolescent booster | Country |
|--|--|----|-----------------------|---------------------|--------------------|---|--|--|
| '2p+1' | From 6 weeks to 6 months | | Around first birthday | | | | | |
| | P1 | P2 | B1 | | | B2 | B3 | F, IT, FI, NO, IS, SK |
| | | | | | | | | SE*, DK, RO, AT |
| '3p+1' | P1 | P2 | P3 | B1 | | B2 | B3 | BE, BG, CZ, EE, DE, GR, HU, LI, LU, |
| | | | | B1 | | B2 | | HR, CY, LV, LI, MT, NL, PL, PT, SI, ES |
| | | | | Hib-MenC combo | B1 | | | UK |
| | | | | Hib-MenC combo | | B1 | B2 | IE |
| Vaccine combination generally used in EU/EEA | <ul style="list-style-type: none">• DTaP-IPV-HepB/Hib ('hexavalent')• DTaP-IPV/Hib ('pentavalent')• DTaP-IPV ('tetavalent')• DTwP-IPV/Hib ('whole-cell pertussis combo')[†]• Hep B (used in conjunction with pentavalent) | | | | | <ul style="list-style-type: none">• DTaP-IPV• TdaP• Tdap-IPV• Tdap | <ul style="list-style-type: none">• Td• Tdap• Tdap-IPV | |

P=primary dose; B=booster dose

The various immunisation schedules in Europe for acellular pertussis -containing vaccines (full-dose content) are based on experiences with whole-cell pertussis-containing vaccines (administered at two and three months, with a third dose given at four or six months).

Infant primary immunisation scheme

The current schedules in EU/EEA Member States for vaccination below 24 months of age with acellular pertussis-containing vaccines can be divided into the following groups:

- **A so-called '2p+1' schedule** corresponding to two doses of primary vaccination and a booster dose, with the vaccines given at three, five and 12 months (in AT, FI, IT, DK, SE, ICE, NO and SK) or at two, four and 11–12 months (in FR and RO).
- **A so-called '3p+1' schedule** corresponding to three doses given in the first year of life, starting as early as two months, with a booster in the second year of life (in BE, BG, HR, CY, CZ, EE, GE, GR, HU, LV, LI, LUX, MT, NL, PL, PT, SLO and ES).

* Starting in 2016, Sweden will include an adolescent booster dose in the national immunisation programme.

† Only in Poland

The only exceptions to these schedules are the UK and Ireland that – after primary vaccination at two, three and four months of age (UK) or at two, four and six months (IRE) – do not include a pertussis booster dose in the second year of life but rather between three and five years after primary immunisation.

All EU/EEA countries have shifted to acellular pertussis-containing vaccines except Poland, which still uses whole-cell pertussis-containing combination vaccines for primary immunisation and the first booster dose.

Vaccination policies for older age groups

School-age children and adolescents

The objective of the pre-school and adolescent booster is: i) to offer direct protection of those vaccinated by ensuring adequate circulating antibodies at protective levels in order to reduce the risk of infection due to waning immunity, ii) to limit the risk of infections of younger unprotected siblings in a household.

School entry

To date, all countries offer a booster dose around the time of school entry (so-called 'pre-school booster'). This booster dose is to account for reduced vaccine effectiveness observed among pre-school and school-age children [8]. The mechanisms involved are not entirely clear but there is a body of evidence in the EU, particularly in Italy and Sweden [14,15]. In Sweden, a two-dose priming schedule at three and five months of age, with a booster dose at 12 months, was adopted for primary immunisation. Findings from the long-term enhanced pertussis surveillance scheme indicated that waning immunity in the first DTaP-vaccinated cohorts lead to pertussis among 7- to 8-year-olds and demonstrated waning of vaccine-induced protection from pertussis. These findings led to the addition of a pre-school booster dose of acellular pertussis vaccine starting in 2007 [14,16].

During adolescence (11 to 18 years)

Seventeen EU/EEA Member State recommend booster doses during adolescence (11 to 18 years).

The objective of a dose given at this age is to extend protection until late adolescence and until childbearing age. There is little evidence of the impact on severe pertussis in infants but these strategies may have an impact on the targeted population and may decrease the circulation of the bacterium in the population at large. The indirect effect on infants is not well established [6].

Adults

Vaccination of adults can occur for different reasons:

- **As part of the regular booster policy:** Adults can be offered boosters of aP vaccine in combination with tetanus toxoid and reduced-dose diphtheria vaccine (Tdap) either once in their lifetime or every 10–20 years depending on the country (AT, BE, CZ, FR, DE, GR, IE, LI). Although these programmes (other than vaccination of pregnant women) have an impact on the directly targeted populations, there is as yet no substantial evidence that they have had a significant impact on severe pertussis in infants [6].
- **As part of the 'cocooning strategy':** Infants who are too young to be vaccinated are protected by vaccinating close contacts who could otherwise potentially become a source of infection. The cocooning strategy is recommended in some EU/EEA Member States (BE, FR, DE, LI). This strategy may have an impact on disease prevention in some settings if high vaccination coverage can be achieved in a timely manner. The overall impact and cost-effectiveness are likely to be substantially lower compared to maternal immunisation, which requires only one dose, whereas cocooning requires, as a minimum, multiple doses for parents and family members.
- **Maternal vaccination (during pregnancy):** A limited number of countries in the EU (Belgium, the UK, Ireland and Spain) have introduced maternal Tdap vaccination during pregnancy to help prevent mortality due to severe pertussis infection in infants too young to be vaccinated. A Tdap vaccine is used for vaccination during pregnancy.

Recent evidence consistently indicates that maternal immunisation with aP-containing vaccine during the third trimester of pregnancy is safe and highly effective in protecting infants from pertussis and that it may have a high positive impact on morbidity and mortality in infants too young to have been vaccinated. Experience in the UK with the vaccination of pregnant women indicates high impact on infant pertussis-related mortality. This outcome is probably primarily due to the direct protection conferred by the transfer of maternal antibodies, with some contribution from reduced risk of transmission through reduced likelihood of peripartum pertussis in the mother.

The point estimate for the vaccine effectiveness of maternal vaccination > 7 days before birth was 91% (95% CI: 84%–95%) using the screening method, with adjusted vaccine effectiveness estimated at 93% (95% CI: 81%–97%) in an associated case-control study [12,17,18]. However, a recent study in the UK showed that maternal immunisation can blunt the subsequent responses to some vaccines in the infant immunisation schedule. This phenomenon needs to be further monitored and could be possibly prevented by giving a booster dose of DTaP, Hib, MCC, and PCV-13 in the second year of life [19,20].

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