Pneumococcal Conjugate Vaccine (PCV) 4-dose vial presentations

Frequently Asked Questions (FAQs)
March 2017

Based on current timelines, **PCV13 4-dose vials** have become available to Gavi countries in 2017 and **PCV10 4-dose vials** are forecasted to become available in 2018. The availability of PCV10 4-dose vials is pending its prequalification by the World Health Organization, expected in late 2017, and, as the case may be, its local registration. These FAQs give an overview of the **characteristics** of these two new PCV 4-dose vial presentations, as well as the **process** of switching presentations and the **support provided by Gavi** in doing so. If you are interested in switching from your current PCV presentation to one of these new presentations, you will need to submit a request through the **Gavi country portal** during the annual reporting cycle in **May 2017**, or if urgent, through a letter to Gavi.

Note: PCV10 in a 2-dose vial presentation will no longer be available once the PCV10 4-dose presentation has been prequalified and attained local registration within your country. Countries currently supported for PCV10 2-dose vials need to submit a request to indicate to which presentation they want to switch through the Gavi country portal during the annual reporting cycle in May 2017, or if urgent through a letter to Gavi outside that date.

1. What are the characteristics of different presentations of Pneumococcal Conjugate Vaccines?

Vaccine	**PCV10**		**PCV13**	
Presentation	**2-dose vial**	**4-dose vial**	**1-dose vial**	**4-dose vial**
Commercial name	**Synflorix®**	**Synflorix®**	**Prevenar 13®**	**Prevenar 13® Multidose vial**
Pharmaceutical form	Liquid	Liquid	Liquid	Liquid
Preservative	**None**	**Yes***	**None**	**Yes***
Manufacturer	GlaxoSmithKline Biologicals (GSK)		Pfizer	
Serotypes covered	1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F**		1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F	
WHO Prequalified	Yes	No, anticipated in late 2017	Yes	Yes
Schedule	3 doses		3 doses	
Primary packaging	3 mL vial	3 mL vial	3 mL vial	3 mL vial
Storage temperature	2º-8º C	2º-8º C	2º-8º C	2º-8º C
Shelf life at 2-8ºC	48 months	36 months	36 months	24 months
Cold chain volume per dose	**4.8 cm^3**	**2.4 cm^3**	**12 cm^3**	**3.6 cm^3**
Vaccine Vial Monitor	VVM 30	VVM 30	VVM 30	VVM 30
Handling of opened multi-dose vials†	Opened vials may be kept up to 6 hours	To be confirmed. Current assumption is opened vial may be kept up to 28	N/A	Opened vial may be kept up to 28 days given certain conditions are met.

		days given certain conditions are met.		
Wastage Rate†	**10%**	**To be confirmed. Current assumption is 10%**	**5%**	**10%**
Indicative maximum price per dose (US$)	**3.05**	**3.05**	**3.30**	**3.05*** **

*2-PE: 2- phenoxyethanol

** The European Medicines Agency (EMA) has provided a positive opinion on the cross-protection of PCV10 against serotype 19A, a non-vaccine serotype.

***Future price reductions in 2018 and 2019 -2020 for PCV13 4-dose vial to respectively US$ 2.95 andUS$2.90 per dose are possible if the total volume of doses procured through the AMC for all countries reaches specific levels during 2017 and 2018-2019.

† Information provided in the table for PCV10 4-dose vial is based on assumptions and discussions with WHO. However, final open vial policies and wastage assumptions will be reviewed and revised after WHO pre-qualification. WHO policy on the use of opened multi-dose vaccine vials (2014 Revision) can be consulted at: http://www.who.int/immunization/documents/general/WHO_IVB_14.07/en/

The main differences between the 4-dose vial presentations of PCV10[1] and PCV13 and the current presentations of these vaccines are the following:

- **Number of doses in each vial.** For PCV10, there will be 4 doses in each 3 mL vial, instead of the 2 doses. For PCV13, there will be 4 doses in each 3 mL vial, instead of the 1 dose. The WHO recommended dosage is 0.5mL.
- **Addition of a preservative, 2-Phenoxyethanol (2-PE).** It is anticipated for both 4-dose presentations that with the inclusion of the preservative the opened vial can be kept up to 28 days given certain conditions are met as described in the WHO Multi-Dose Vial Policy[2].
- **Cold chain requirements.** There will be a reduction in cold chain space requirements from the current presentation to the 4-dose vial presentation for both products. Based on the current information available, the cold chain volume per dose for PCV10 will decrease from 4.8 cm^3 to 2.4 cm^3 and for PCV13 from 12 cm^3 to 3.6 cm^3.
- **Wastage.** The wastage rate for both 4-dose products is 10% assuming the discard point of an opened vial is 28 days.
- **Price.** For PCV13, the maximum price for the 4-dose presentation is US$ 3.05 per dose. For PCV10, the indicative price is US$ 3.05 per dose for the 4-dose pending supply offers from manufacturers and awards. The standard co-financing policy will be applied; for example, co-financing will remain unchanged for low income countries but will be affected for those in preparatory and accelerated transition.

The overall cost implications of each vaccine presentation can also be affected by vaccine wastage. The table below provides the indicative maximum price for each presentation adjusted for wastage at different levels. The adjustment to the price accounts for the cost of

[1] Please note that these assumptions for PCV10 4-dose vial will be reviewed by WHO and may be revised during the pre-qualification process.

[2] WHO policy on the use of opened multi-dose vaccine vials (2014 Revision). http://www.who.int/immunization/documents/general/WHO_IVB_14.07/en/

wasted vaccine for each administered dose. The highlighted cells reflect the wastage rate currently assumed for each presentation, knowing that actual wastage rate will vary.

		PCV10 2-dose	PCV10 4-dose	PCV13 1-dose	PCV13 4-dose
Indicative maximum price (US$ per dose)		3.05	3.05	3.30	3.05
Price adjusted for wastage (US$ per dose)	**5% wastage**	3.21	3.21	3.47	3.21
	10% wastage	3.39	3.39	3.67	3.39
	15% wastage	3.59	3.59	3.88	3.59
	20% wastage	3.81	3.81	4.13	3.81
	25% wastage	4.07	4.07	4.40	4.07

Cells highlighted in blue are the current assumptions for wastage.

Apart from the addition of the preservative 2-PE, there will be no changes in the vaccine formulation. The immunisation schedule and intramuscular administration of the vaccine also remain the same.

2. What are the benefits of changing to a 4-dose vial?

For both vaccines, there will be a reduction in cold chain space requirements for each dose from the current presentation to the 4-dose vial presentation. See details in Question 1.

Both 4-dose vial products contain 2-PE as a preservative and the vial can be kept up to 28 days (pending WHO prequalification for PCV10 4-dose presentation). As a consequence, there will be no changes to assumed wastage rates for switch from PCV10 2-dose vial (10%) and an equivalent rate from 5% to 10% for switch from PCV13 1-dose vial will be applied.

3. What are the risks of changing to a 4-dose vial?

It is expected that there will be no implications from a vaccine safety or effectiveness perspective; however both safety and effectiveness will need to be demonstrated and approved by the WHO prequalification team for PCV10 4-dose vials.

The risks related to the introduction of the 4-dose vials are related to inappropriate use of the vaccine if health workers are not appropriately trained (e.g. suitable implementation of the multi-dose vial policy and understanding of difference in preservative for each presentation). Thus, it will be important for each country to carefully manage the switch to the new presentation and ensure sufficient training of healthcare workers and understanding of implications of the 4-dose vials.

Technical assistance will be available through the Alliance, more specifically WHO and UNICEF, in order to ensure a smooth transition to the new presentation.

4. We are interested in the 4-dose vial, when and how do we request a switch in product presentation?

In May 2017, countries will be able to formally request a switch in product presentation to the PCV 4-dose vial through the Gavi country portal as part of the annual reporting cycle (see Annex 1 for a summary of the possible product/presentation switches).

For countries currently using PCV10 2-dose vial, the portal will prepopulate a switch to PCV10 4-dose vial which the country can confirm or modify (in order to opt for PCV13 4-doses or PCV 13- 1 dose vials see Note on page 1).

If the request must be made outside of the annual reporting cycle (e.g. if the request is urgent or is made before vaccine introduction), it may be possible to do so by submitting a formal request letter to Gavi; such cases will be assessed on a country-by-country basis.

Irrespective of the formal request submission, Gavi recommends that countries **inform their Senior Country Manager as soon as possible** once they have decided to switch products or presentations, so that Gavi and its partners can ensure adequate support for a timely switch.

In order to switch presentation, the following information **must** be submitted on the portal and to the SCM:

- Desired presentation;
- Indicative desired introduction month and year for the new presentation;
- Rationale for the switch in presentation

In addition, the following supporting documents **must** be submitted on the portal and transmitted to the SCM:

- ICC (and NITAG, if applicable) endorsement and meeting minutes;
- Information on cold chain capacity and stock levels of current product at the national and regional level;
- A costed plan of activities (using the Gavi product switch budget template) – including both activities to be funded by the Gavi product switch grant **and** activities related to the switch not covered by the grant. (Refer to Question 6 for more information on the switch grant policy.)

5. What additional activities and budgetary provisions will be required in order to prepare for and implement the product presentation switch?

Gavi has developed a budget template for countries to use to plan for a presentation switch, which can be found at http://www.gavi.org/library/gavi-documents/guidelines-and-forms/. Countries may be eligible for a product switch grant (see Question 6 below). In order to request the grant, countries need to submit the budget template through the country portal in May 2017.

In Annex 2 you will find a table containing some activity planning guidance based on the WHO New Vaccine Introduction Checklist. The list is not intended to be exhaustive, but is meant to provide some high level guidance on potential activities needed to prepare for a switch in vaccine product and/or presentation.

6. Are we eligible for additional support from Gavi if switching to the 4-dose vial presentation?

As per the current Gavi switch grant policy, countries may be entitled to a product switch grant equivalent to up to US$ 0.25 per child in the birth cohort or a lump sum of US$30,000, whichever is higher. The eligibility criteria and details of the policy can be found at: http://www.gavi.org/about/governance/programme-policies/health-system-and-immunisation-strengthening-support-framework/.

The switch grant is intended to help cover one-off costs associated with switching vaccine presentation: for example, training and printing of materials.

In order to request the product switch grant, countries must submit their budget through the country portal at the time of the product switch request, using the Product Switch Budget Template found in our website: http://www.gavi.org/library/gavi-documents/guidelines-and-forms/

7. When can we switch to a 4-dose vial?

PCV13 4-dose vial is now available, and PCV10 4-dose vial is estimated to be available in 2018. Availability of PCV10 4-dose is pending prequalification by the World Health Organization, expected by end 2017, and, as the case may be, local registration; PCV10 2-dose will remain available until PCV10 4-dose presentation has attained local registration in your country.

8. Are we obliged to switch to a 4-dose vial?

The 1-dose vial presentation of PCV13 will continue to be available to Gavi countries even now that the PCV13 4-dose vial has been prequalified; thus, such countries using PCV13 will not be obliged to switch presentations.

However, PCV10 in a 2-dose vial will no longer be available after PCV10 4-dose presentation has been prequalified and has attained local registration where required. This means that countries using PCV10 2-dose vials will be obliged to switch once PCV10 4-dose vial presentation obtains registration in country (manufacturer is assisting to obtain this local registration).

Countries currently supported for PCV10 2-dose vials need to submit a request to indicate to which presentation they want to switch through the Gavi country portal during the annual reporting cycle in May 2017, or if urgent through a letter to Gavi before that date.

9. Do you anticipate any supply constraints in the availability of the 4-dose vials of PCV?

Gavi currently does not anticipate any global supply constraints in the 4-dose vials of PCV13 nor in the 4-dose vials of PCV10. Countries are able to switch to PCV13 4-dose vials in 2017 and will to PCV10 4-dose vials as soon as it is prequalified by WHO and UNICEF is able to secure procurement (forecasted to become available in 2018). In case of a supply constrained environment, Gavi will utilise a prioritisation mechanism using relevant criteria to determine timing of switch to 4-dose vials.

10. We are planning to switch PCV products (from PCV10 to PCV13 or vice versa), should we postpone the switch until the PCV10 4-dose presentation is available?

The rationale for a switch in product needs proper justification and an affirmation that the programmatic implications related to the change in product and presentation (which are much greater than presentation alone) are fully understood and that there are plans in place to deal with them. Please refer to your WHO focal point for further technical guidance.

Counties need to present any relevant evidence to justify the product switch when requesting a switch through the country portal (e.g. surveillance data with local and regional serotype burden and distribution).

If your country is planning to switch to the PCV13 4-dose vial: You can do so already in 2017. In order to formally request a switch in product presentation to the 4-dose vial, please do so through the Gavi country portal by May 2017 (see Question 4) and inform your Senior Country Manager. In case of a supply constrained environment, Gavi will utilise a prioritisation mechanism using relevant criteria to determine timing of switch to 4-dose vials.

If your country is planning to switch to the PCV10 4-dose vial: Gavi recommends a switch of products only when the 4-dose vial becomes available (expected in 2018) to avoid creating additional burden on the health systems. Please request the switch through the Gavi country portal by May 2017 (see Question 4) and inform your Senior Country Manager. If there are delays in 4-dose vial availability, Gavi will review and approve on a country-by-country basis any requests for product switches.

Annex 1: Summary of product/presentation switch possibilities

From current product/ presentation	To desired product/ presentation	Availability of desired product/ presentation	How to request a switch	Requirements
PCV10 2-dose	**PCV10 4-dose**	As soon as it attains prequalification by WHO (expected end 2017) and UNICEF is able to secure procurement. PCV10 2-dose will remain available until PCV10 4-dose has attained local registration in your country.	The switch to PCV10 4-dose will be pre-populated in the Country Portal. Please confirm the switch dates and related amounts by May 2017 as part of the annual reporting cycle. If the request is urgent, submit a formal letter to Gavi; these cases will be assessed on a country by country basis. Please inform your SCM as soon as possible regardless of the formal request.	Mandatory information: - Desired presentation - Desired switch month/year - Rationale for the switch Mandatory documents: - ICC and NITAG endorsement - Cold chain capacity and stock levels - Costed plan of activities, using the Gavi budget template
PCV13 1-dose	**PCV10 4-dose**	As soon as it attains prequalification by WHO (expected end 2017) and UNICEF is able to secure procurement.	Formally request a switch as part of the annual reporting cycle in the Country Portal by May 2017. If the request is urgent, submit a formal letter to Gavi; these cases will be assessed on a country by country basis. Please inform your SCM as soon as possible regardless of the formal request.	
PCV13 4-dose	**PCV10 4-dose**			
PCV10 2-dose	**PCV13 4-dose**	Currently available		
PCV13 1-dose	**PCV13 4-dose**			
PCV10 2-dose	**PCV13 1-dose**			
PCV13 1-dose	**PCV13 1-dose**			

Annex 2: Product/Presentation switch activity planning guidance

Below is a table containing some activity planning guidance based on the WHO New Vaccine Introduction Checklist[3]. The list not intended to be exhaustive, but is meant to provide some high level guidance on potential activities needed to prepare for a switch in vaccine product and/or presentation.

Theme	Activity
Decision-Making and Switch Request	Evaluate suitability of new product and/or presentation with support from advisory bodies (e.g. NITAG) and Alliance partners
	Approval of switch by decision-making bodies (e.g. Minister of Health, ICC, etc.)
	Develop a plan for the product/presentation switch, including activities, budget and timeline
	Submit request through the Gavi Country Portal, including application for Gavi Product Switch Grant
Planning and Funding	Establish Working Group to coordinate switch in the country (or mobilise an existing working group/ICC to take responsibility for the switch)
	Develop risk communication plan / risk management strategy for AEFI, if applicable for new presentation (e.g. transition from single dose to multi-dose vial)
	Secure funding for activities not covered by the Gavi Product Switch Grant or partners
Vaccine Procurement and Distribution	Carry out inventory of existing product/presentation
	Produce schedule for consumption of old product/presentation before introduction of new product and ensure that this is followed
	If not already licenced, complete licensure of new vaccine product/presentation
	Take action to ensure customs regulations do not prevent or delay vaccine shipment
	Confirm shipment plan for new product/presentation and distribution of vaccines to sub-national levels ahead of stock-out of existing presentation

[3] Principles and considerations for adding a vaccine to a national immunization programme. http://www.who.int/immunization/programmes_systems/policies_strategies/vaccine_intro_resources/nvi_guidelines/en/

Human Resources and Training	Identify training needs in relation to the product switch, e.g. train master trainers or train health care workers (all levels) in requirements of new vaccine product/presentation and use of existing presentation ahead of switch
Document production and distribution	Update and print training and other materials for health workers to include specific requirements and attributes of new vaccine product/presentation (e.g. guidelines, handbook for health workers, FAQs, fact sheets, video, posters, pre- and post-knowledge tests, allowing provision to adapt them to local language(s))
	Revise and distribute any recording and reporting tools (e.g. vaccination logs, tools for wastage calculation) that refer to old vaccine presentation
Cold chain, logistics and vaccine management	Update stock management tools to include the new product/presentation (central and intermediary levels)
	If new product requires more cold chain or dry storage space, ensure this has been organised
Surveillance and monitoring	Ensure adequate monitoring of vaccine wastage of new product/presentation
	Ensure National AEFI Expert Review Committee is able to provide technical guidance on causality assessment of AEFIs potentially related to new product/presentation
	Develop risk communication plan / risk management strategy for AEFI associated with the new presentation
	Make provisions for enhanced supervision following the switch to ensure good vaccine management
Evaluation	Conduct visits to local facilities to confirm switch and correct use of new product/presentation
	Gather lessons on successes and challenges of product/presentation switch to inform future switches