Vaccine presentation for pneumococcal conjugate vaccines

GAVI Vaccine Presentation and Packaging Advisory Group: Interim Report for the TPP

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Glossary

**Beyond the cold chain**
This term means that the cold chain is maintained for the majority of the vaccine’s journey from the manufacturer to the recipient and is stored in facilities that have refrigeration. However, it is then transported and used beyond the cold chain so that it can be used in places where icepacks or cool water packs at +2° to +8°C are unavailable. This practice allows children to be vaccinated in remote areas where there are no refrigeration facilities.

**Intermediate store**
A store that receives vaccine from a primary store or from a higher-level intermediate store. Intermediate stores generally have vaccine refrigerators and vaccine freezers, although larger stores may have a cold room. These faculties also have the means to freeze icepacks for distribution purposes.

**Opened vial wastage**
Vaccine wastage that occurs after a vial has been opened for use. This form of wastage may arise as a result of discarding remaining doses at the end of session, not being able to draw up the number of doses indicated on the label of a vial, poor reconstitution practice, submergence of opened vials in water, suspected contamination, or patient reaction requiring the administration of more than one dose.

**Outreach**
A temporary location where vaccine is administered. Typically outreach sessions are organized from and by the service level facilities. Vaccine is generally not stored at outreach locations because refrigeration is typically not available. To maintain the cold chain, vaccine is stored in cold boxes or vaccine carriers for the duration of the immunization session.

**Outside the cold chain**
This term means that vaccine is both stored and used in a location that has no refrigeration.

**Primary store**
A principal or main vaccine store (typically the national store) that receives vaccine directly from the vaccine supplier. Primary stores generally have cold rooms and vaccine freezers or freezer rooms. They also have the means to freeze icepacks for onward distribution of vaccine to the intermediate stores. Typically they also have standby generators to ensure a reliable power supply.

**Safety box**
A container for the storage and final disposal of injection waste, including used syringes and needles. These should meet the standards defined in WHO PIS/PQS specifications.

**Secondary packaging**
The carton which contains a number of individual vaccine vials or vial pairs. Most countries store and distribute vaccines in these cartons. Also known as intermediate packaging.

**Shake test**
A means for assessing, in the field, whether an adsorbed vaccine has been frozen during storage. The test protocol is defined, *inter alia*, in Annex 2 of WHO/IVB/05.23: Guidelines on the international packaging and shipping of vaccines.

**Shipping**
The outer insulated container in which vaccine vials, contained in
container secondary packaging, is transported during international shipment. Some countries store vaccine in shipping containers at primary level. A few also use shipping containers to distribute vaccine from the primary to the intermediate stores.

Unopened vial wastage Vaccine wastage that occurs before a vial has been opened for use. This form of wastage may arise as a result of expiry, VVM indication, heat exposure, freezing, breakage, missing inventory, theft, or the discarding of unused vials returned from an outreach session.
Acronyms

°C  Degrees centigrade
AD  Auto-disable (syringe)
BCG  Bacille Calmette-Guérin (tuberculosis vaccine)
cm  Centimetres
\( \text{cm}^3 \)  Cubic centimetres
DT  Diphtheria and Tetanus toxoid (vaccine)
DTP  Diphtheria-Tetanus-Pertussis (vaccine)
EPI  Expanded Programme on Immunization
EVSM  Effective Vaccine Store Management (initiative)
EXW  Ex. Works (Incotems 2000)
FIC  Fully Immunized Child
FITG  Fully Immunized Target Group
HepB or HB  Hepatitis B vaccine
Hib  \textit{Haemophilus influenzae} type b (vaccine)
lts or l  Litres
\( \text{m}^3 \)  Cubic meters
MDVP  Multi-dose Vial Policy
MMR  Mumps-Measles-Rubella vaccine
MR  Measles-Rubella vaccine
OPV  Oral Polio Vaccine
PCV  Pneumococcal Conjugate Vaccine
PIS  WHO/UNICEF Product Information Sheets
PQS  Performance, Quality, Safety (WHO replacement for PIS system)
TT  Tetanus Toxoid (vaccine)
UNICEF  United Nations Children’s Fund
VPPAG  Vaccine Presentation and Packaging Advisory Group
VVM  Vaccine Vial Monitor
YF  Yellow Fever vaccine
WHO  World Health Organization
1. Executive summary

The Vaccine Presentation and Packaging Advisory Group (VPPAG) has undertaken a review of some of the vaccine formulation and presentation issues relating to the forthcoming Pneumococcal Conjugate Vaccines (PCV).

The group’s principal recommendations are set out in this section. The recommendations operate within the existing framework of WHO policy statements and guidelines. Specific guidance on PCV has yet to be developed.

1.1 Main conclusions and recommendations

1.1.1 Vaccine formulation

- **Formulation:** A ‘ready to use’ liquid vaccine is the preferred formulation as it facilitates delivery.
- **Preservatives:** For multi-dose vials, the vaccine should be formulated so as to enable the safe implementation of MDVP.

1.1.2 Thermostability issues

- **Heat sensitivity:** The thermostability profile of the vaccine should ideally permit the use of the VVM30 vaccine vial monitor.
- **Freezing:** If freeze-sensitive, PCV vaccines should allow the use of the ‘Shake test’ or other means (such as a vial-based freeze indicator) to assess whether freeze damage has occurred.
- **VVMs:** The WHO and UNICEF requirement that VVMs should be attached to all vaccines procured through the UN should also be maintained for PCV.

1.1.3 Vaccine presentation

- **Packed volumes:** In order to minimize impact on the cold chain, the packed volume should not exceed the maximum recommended volumes set out in Table 2 of WHO/IVB/05.23. *Guidelines on the international packaging and shipping of vaccines.* For PCV, the maxima are not stated, but based on similar vaccines the maxima should be: 3.0, 4.5, 6.0, and 12.0 cm³ for 10-, 5-, 2- and 1-dose vials, respectively. Wherever possible, manufacturers should seek to improve on these figures.
- **Number of doses per vial:** It is not possible to make a recommendation on the number of doses per vial, without further analysis on its impact on wastage. One clear conclusion is that only single-dose formulations are likely to be viable if the MDVP does not apply. If very low wastage rates can be achieved through MDVP (<6-9%), a 10-dose may be viable and has the advantage of limiting cold chain impact. It may be easier to achieve the <3-4% wastage required to make a 2-dose vial viable noting that 2% unopened vial wastage is assumed. These results are based on a preliminary analysis using the Vaccine Presentation Assessment Tool. Further work is needed to verify these preliminary conclusions and to provide additional analysis on optimal presentations.
- **Pre-filled glass syringes:** The very large volume-per-dose associated with pre-filled glass syringes makes this type of presentation generally unsuitable for use in developing countries.
• **Compact pre-filled devices:** Compact pre-filled presentations may be useful in some settings. Manufacturers of such devices should be encouraged to develop the most space-efficient method of packaging possible in order to minimize impact on the cold chain.

• **Secondary packaging design:** Secondary/intermediate vaccine packaging should be designed so that vials or pre-filled devices are closely nested together with a minimum of wasted space and no superfluous packing materials.

• **Shipping containers:** Insulated containers for international shipment should conform to the norms set out in Annex 4 of WHO/IVB/05.23 – *Guidance on the international packaging and shipping of vaccines.*

### 1.1.4 Shelf life

• **Shelf life:** A minimum 36 month shelf life is preferred.
2. Discussion
This section contains a discussion of the issues that are summarized in Section 1. It is followed by five annexes:

- Annex 1 outlines the terms of reference and the methodology adopted.
- Annex 2 is a summary of the TechNet consultation exercise.
- Annex 3 sets out the assumptions made for the impact analysis.
- Annex 4 contains shows the scenarios described in Figure 1 in chart format.
- Annex 5 includes some general recommendations on country implementation. The VPPAG consider that these deserve mention but they are slightly outside the scope of the TORs.

2.1 Consultations

2.1.1 TechNet
TechNet members were asked to comment on the relationship between wastage and number of doses per vial (with and without MDVP) and to advise on the way in which cold chain and logistics costs and requirements vary as a function of storage volume per dose.

Seven responses were received but neither of these questions was directly addressed. However, a number of respondents did express a clear preference for more than one vial size (i.e. number of doses per vial) to cater for different immunization settings.

A related survey of 27 UNICEF country officers concerning expensive new vaccines showed a nearly equal preference for single-dose and 2-dose vials with a smaller number of respondents preferring larger formats. Again, over 50% of respondents wished to have a choice of two or more vial sizes. Refer to Annex 2.

2.1.2 Manufacturers’ questionnaire
A brief questionnaire was circulated to 10 vaccine manufacturers at the start of the project. Three responded. The data provided have been used to inform the assumptions outlined below, and in more detail in Annex 3.

2.2 Vaccine formulation
The assumption throughout this study is that PCVs will be manufactured in a ‘ready to use’ liquid formulation, administered by injection. However a lyophilized option is also being investigated.

2.2.1 Liquid versus lyophilized
The disadvantages of lyophilized vaccines are well known. The need for reconstitution imposes a higher workload especially when vials contain a small number of doses; mismanagement can occur during the reconstitution process; there is a need for additional storage capacity for the associated diluent; the volume of the waste stream increases, and lyophilized vaccines cannot be used under MDVP\(^1\). In the recent

\(^1\) There is at least one lyophilized vaccine whose package insert permits administration well beyond the normal 6 hour discard period. However WHO policy does not currently permit this use.
application round for new vaccines, the majority of countries have asked for a liquid pentavalent vaccine in preference to the lyophilized presentation. For these and other reasons development of a lyophilized PCV formulation is not encouraged.

2.2.2 Preservatives
The WHO Multi-dose Vial Policy (MDVP) allows re-use of unused doses in the vial in subsequent sessions, and this can reduce opened vial wastage. The MDVP requires an appropriate preservative in the formulation.

Preservatives are not needed for single-dose presentations.
Two of the three manufacturers who responded to the questionnaire have indicated that they intend to include a preservative in their PCV formulations.

2.3 Thermostability issues

2.3.1 Heat sensitivity
A high degree of thermostability is desirable to minimize the risk of heat damage and also to allow potential use beyond the cold chain. All responding manufacturers have indicated that their PCVs should be stored at +2°C to +8°C. One respondent is investigating a heat-stable formulation, although the +2°C to +8°C storage recommendation would remain the same.

As conjugate vaccines are generally relatively heat stable, a high degree of thermostability should be demanded of all PCVs. The most heat stable vaccines have a profile that allows the use of a VVM30, or 30 days (i.e., able to withstand 30 days storage at 37°C).

2.3.2 Freezing
Conjugated vaccines are generally freeze-sensitive and the questionnaire responses so far received confirm this for PCV. All respondents stated that the shake test can be used on their vaccines to identify previously frozen vaccine. One manufacturer is investigating a formulation which will give no such indication and suggests the use of a vial-based freeze indicator\(^2\) to overcome this problem.

2.3.3 Vaccine Vial Monitors (VVM)
Of the questionnaire respondents, only one stated that they do not intend to supply their vaccine with VVMs. One manufacturer confirmed that they would likely be using the VVM14 indicator.

2.4 Vaccine presentation
Vaccine presentation issues have been investigated using the draft D5 version of the Vaccine Presentation Assessment Tool (VPAT), currently under development by PATH MVI. Annex 2 sets out the assumptions made regarding volume-per-dose, schedules and wastage rates. Figure 1 summarises these in tabular form. Annex 3 shows the same data in chart form.

The data given in this report are not intended to be definitive – they simply illustrate the methodology. Establishing the ‘correct’ wastage rates to use in an individual country, and even more so across countries, is challenging. These rates are not dependent on

\(^2\) A commercial implementation of this technology does not yet exist.
average session size but rather on the integrated mix of session sizes across all settings, and as they fluctuate in time. Because PCV will be nearly two orders more expensive than the 'traditional' vaccines and will be managed differently, it is not appropriate to accept and apply existing field-derived wastage rates. This issue is further discussed in Annex A2.3 and A2.4.

The task is further complicated by the need to integrate PCV into existing low cost vaccine schedules, where control of wastage is rather less of a priority. This study highlights the requirement to obtain well-founded data on achievable wastage rates for the new category of high cost vaccines when countries implement and maintain reduced-wastage delivery regimes for high cost vaccines, without prejudicing coverage.

The wastage rates used in Figure 1 are made up as follows:

- The single antigen and pentavalent base schedules use GAVI-recommended rates\(^3\).
- To maintain consistency with the results of the vial size analysis (see section 2.3.1), the wastage rates for each of the 9 alternative PCV presentations are taken from the results of the goal-seeking algorithm at the $3-50 price point. Where the algorithm has computed a negative rate to achieve the break-even cost\(^4\), the wastage rate has been set to 1% - this is consistent with field studies for this type of device.

Clearly the very low wastage rates shown for the larger multi-dose vials (e.g. 9% for 10-dose) are unlikely to be achievable in the field under current circumstances, even with strict implementation of MDVP.

**Figure 1: Summary of scenarios**

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Doses per FITG</th>
<th>Wastage rates %</th>
<th>Volumes per FITG (cm³)</th>
<th>Assembled safety box</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single antigen schedule</td>
<td>-</td>
<td>GAVI (2005)</td>
<td>Secondary container</td>
<td>50.40 368.50 930.26 1300.41</td>
</tr>
<tr>
<td>Pentavalent schedule</td>
<td>-</td>
<td>GAVI (2005)</td>
<td>Shipping container</td>
<td>59.07 322.83 783.20 1149.64</td>
</tr>
<tr>
<td>Other pre-fill</td>
<td>3</td>
<td>1.0%</td>
<td>Packed commodities</td>
<td>90.91 371.97 15.03 77.88</td>
</tr>
<tr>
<td>Pre-filled syringe</td>
<td>3</td>
<td>1.0%</td>
<td>Assembled safety box</td>
<td>166.06 830.30 60.13 311.51</td>
</tr>
<tr>
<td>Gen 1-dose vial</td>
<td>3</td>
<td>2.0%</td>
<td></td>
<td>36.73 167.91 246.32 339.24</td>
</tr>
<tr>
<td>Gen 2-dose vial</td>
<td>3</td>
<td>4.2%</td>
<td></td>
<td>18.79 96.92 246.32 339.24</td>
</tr>
<tr>
<td>Gen 3-dose vial</td>
<td>3</td>
<td>4.9%</td>
<td></td>
<td>16.56 65.14 246.32 339.24</td>
</tr>
<tr>
<td>Gen 5-dose vial</td>
<td>3</td>
<td>6.1%</td>
<td></td>
<td>14.38 39.62 246.32 339.24</td>
</tr>
<tr>
<td>Gen 10-dose vial</td>
<td>3</td>
<td>9.2%</td>
<td></td>
<td>9.91 25.11 246.32 339.24</td>
</tr>
<tr>
<td>Alt 1-dose vial</td>
<td>3</td>
<td>1.4%</td>
<td></td>
<td>45.64 273.83 68.78 339.24</td>
</tr>
<tr>
<td>Alt pre-fill</td>
<td>3</td>
<td>1.0%</td>
<td></td>
<td>183.61 918.03 68.78 339.24</td>
</tr>
</tbody>
</table>

**Notes:**

1. Data in yellow cells represent total volumes per FITG for two alternative base schedules – see Annex 2.
2. Data in white and grey cells show extra-over volumes for each of the alternative PCV presentations.
3. Doses per FITG for the two base schedules are in accordance with normal practice.

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\(^3\) GAVI (2007) recommends 5% for any liquid vaccine in single-dose vials, 10% for any lyophilised vaccines in 2-dose vials, 25% for 10-dose liquid vaccines, 50% for 10 and 20-dose lyophilized vaccines.

\(^4\) This applies specifically to the two pre-filled syringe presentations.
4) Wastage rates for PCV options are derived as described above.
5) Gen = Generic minimum vial sizes based on the assumptions presented in Annex 2.
6) Alt = Alternatives based on manufacturers’ data.

2.4.1 Number of doses per vial

Figure 3 shows the total delivered cost per dose, including cost of vaccine, syringes and safety boxes, storage, transport, doses wasted, and safe disposal of injection waste, for seven possible presentations and five single dose price points from $3-50 to $7.50 per purchased dose in $1.00 increments. The delivered cost per dose (DCD) is built up as follows:

DCD = Single dose cost per dose ± the cost differential for the presentation + syringe and safety box purchase costs + vaccine storage costs + in-country distribution costs (vaccines and commodities) + waste disposal costs.

Some of these costs vary with the wastage rate and some are independent of wastage rate.

The current version of the VPAT (D5) uses Excel’s goal-seeking function to establish a ‘break-even’ wastage rate for each presentation at each price point. The ‘break-even’ algorithm computes a wastage rate for each presentation such that all presentation options have the same total delivered cost per dose per dose, using the single-dose delivered cost as the benchmark. Figure 2 illustrates an example.

Figure 2: Example of goal-seeking module

<table>
<thead>
<tr>
<th>Purchase $/dose</th>
<th>$3.50</th>
<th>$3.56</th>
<th>$3.56</th>
<th>$3.46</th>
<th>$3.44</th>
<th>$3.40</th>
<th>$3.30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost-per-dose differentials &gt;&gt;</td>
<td>$0.000</td>
<td>$0.056</td>
<td>$0.056</td>
<td>-$0.040</td>
<td>-$0.060</td>
<td>-$0.100</td>
<td>-$0.200</td>
</tr>
<tr>
<td>Delivered dose cost</td>
<td>Single-dose</td>
<td>Compact pre-fill</td>
<td>Pre-filled syringe</td>
<td>Gen 2-dose vial</td>
<td>Gen 3-dose vial</td>
<td>Gen 5-dose vial</td>
<td>Gen 10-dose vial</td>
</tr>
<tr>
<td>Cost-per-dose at set wastage rate</td>
<td>$3.79</td>
<td>$3.79</td>
<td>$3.79</td>
<td>$3.79</td>
<td>$3.79</td>
<td>$3.79</td>
<td>$3.79</td>
</tr>
<tr>
<td>Wastage rates</td>
<td>2.0%</td>
<td>0.3%</td>
<td>-5.3%</td>
<td>4.2%</td>
<td>4.9%</td>
<td>6.1%</td>
<td>9.2%</td>
</tr>
</tbody>
</table>

Note: Negative wastage rate highlighted.

The interpretation of the ‘break-even’ wastage rates shown in Figure 2 is complex. For example, it shows that a 10-dose vial is preferred compared to a 1-dose vial, if wastage for the former is less than 9.2% and wastage for the latter is 2%.

Figure 3 is based on a wastage rate for the reference single dose vial set at a constant 2%7, for each of five price points from $3.50 to $7.50.

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5 The costs of storing syringes and safety boxes at ambient temperature are not currently included in the model.
6 For lyophilized vaccines, reconstitution syringe costs vary with vial size and wastage rate.
7 This seems to be a reasonable compromise. For example, the Effective Vaccine Store Management assessment guidelines (WHO/IVB/04.16-20) allow a maximum wastage of 1% at primary store level. Additional losses can be expected further down the cold chain.
Each contour line represents a price point (e.g. $5.50 per dose) and shows the wastage rate that must be achieved for each of the 7 alternative presentations to ‘break-even’ against the reference single-dose price (at top of chart). Raising or lowering this 2% base wastage rate figure would correspondingly raise or lower the break-even wastage rates for each of the alternative combinations. Note that the two pre-filled syringe options display negative wastage rates. This is because their combination of volume and cost per dose is such that they can never achieve parity with a single-dose vial over the cost-per-dose range covered here.

2.4.2 Pre-filled presentations

Figures 1 and 2 demonstrate that both the pre-filled syringe options would have a severe impact on cold chain capacity. The largest presentation (Alt pre-fill) alone is over three times the volume of the indicative pentavalent schedule (193 cm³ compared with 59 cm³). The ‘Compact pre-fill’ option, based on the Uniject™ device, is significantly more space-efficient and it has the advantage that it would reduce the volume of the waste stream compared with standard vial presentations.

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8 The volume of the Uniject device is some 25% of the volume of a discarded 0.5ml AD syringe and needle assembly.
Currently Unijects are packaged individually in a foil pouch. This serves as a vapour barrier to prevent slow evaporation of the vaccine when the units are stored outside the cold chain (as in Indonesia). If units are to be kept in the cold chain, then it might be possible to reduce volume-per-dose by packing in multi-unit (possibly re-sealable) pouches. The device manufacturer has indicated that innovations of this sort could significantly reduce the volume-per-dose, if adopted by industry.

2.4.3 Packaging
Secondary/intermediate packaging needs to make best use of available storage space in all the types of cold chain equipment typically found in the field. This includes cold rooms, vaccine refrigerators, cold boxes and vaccine carriers. The size and format of these packs has implications for the space-efficient storage and distribution of vaccine at all levels in the cold chain.

Figure 4 is an analysis of the internal dimensions of the cold boxes and vaccine carriers currently pre-qualified by WHO. The former are used for transporting vaccines, generally in secondary packaging, down to the health facility level. The latter are largely used to transport vaccines in individual vials to outreach sessions.

The table shows the dimensions of the vaccine storage compartment for the volumetrically smallest and largest containers of each type in the current range of products.

It is extremely important to ensure that secondary/intermediate vaccine packs are designed so they fit comfortably into the types of cold boxes that are currently in the field. This reduces the number of cold boxes required and helps ensure efficient use of available transport.

2.4.4 Shelf life
VPPAG members would like to see PCV products with the longest practicable shelf-life. A period of 36 months is the desired minimum.

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9 Roderick Hausser, BD, personal communication.
Figure 4: Analysis of PIS pre-qualified cold boxes & vaccine carriers

<table>
<thead>
<tr>
<th>Type</th>
<th>Min vol dims (cm)</th>
<th>Max vol dims (cm)</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>W</td>
<td>D</td>
<td>H</td>
</tr>
<tr>
<td>Long range cold box</td>
<td>50.0</td>
<td>10.0</td>
<td>10.0</td>
</tr>
<tr>
<td>Short range cold box</td>
<td>15.9</td>
<td>6.1</td>
<td>16.5</td>
</tr>
<tr>
<td>Large vaccine carrier</td>
<td>16.0</td>
<td>9.0</td>
<td>9.0</td>
</tr>
<tr>
<td>Small vaccine carrier</td>
<td>18.0</td>
<td>4.0</td>
<td>7.0</td>
</tr>
</tbody>
</table>

Source: PIS 2000+

2.4.5 Waste management

Figures 1 and 2 and Annex 3.1 illustrate the effect of PCV introduction on the waste stream. Because the number of syringes required for the administration of a liquid vaccine is independent of vaccine wastage rates, the requirement for additional safety boxes is similar for all vaccine presentations, except for compact pre-filled devices. The VPAT spreadsheet does not specifically assess the volume of discarded vials, but this is necessarily similar to the vaccine volume per FITG shown for each of the presentation options.

A lyophilized PCV presentation would substantially increase the volume of waste because of the additional reconstitution syringes required - one per vial regardless of presentation size. In addition, the associated diluent vials or ampoules have to be disposed of safely.

2.5 Workload issues

Introduction of PCV will increase workload. This impact will be minimized if a liquid formulation is adopted in preference to lyophilized. Administration of PCV is currently intended to be aligned with the DTP/pentavalent schedule. This is likely to reduce the workload impact. There is evidence from time and motion studies that adding a vaccine to a contact has a significantly smaller effect on workload than would be the case if the vaccine were to be administered at a separate contact. The use of a pre-filled presentation would likely reduce the impact on workload still further.

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Annex 1 – TORs and methodology

A1.1 Terms of reference
The final terms of reference for the Pneumococcal and rotavirus vaccine presentation and packaging advisory group required the group to produce the following deliverables:

<table>
<thead>
<tr>
<th>The group will make recommendations for possible presentations of pneumococcal and rotavirus vaccines for procurement by developing countries through the GAVI Fund. The recommendations will cover at least the following issues. Other considerations will be addressed and included as they arise.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Vaccine formulation (liquid or other? Is this up for discussion?)</td>
</tr>
<tr>
<td>2. Multi-dose vial size (discussion to include cost and wastage considerations)</td>
</tr>
<tr>
<td>3. Single dose options including a UniJect presentation</td>
</tr>
<tr>
<td>4. Issues surrounding introduction of a mix of presentations (single dose and multi dose)</td>
</tr>
<tr>
<td>5. Matching vaccine profile to vaccination setting (clinic, schools, outreach…)</td>
</tr>
<tr>
<td>6. Inclusion of preservatives (thimerosal, 2-phenoxy ethanol, others?)</td>
</tr>
<tr>
<td>7. Applicability of multi-dose vial policy (MDVP)</td>
</tr>
<tr>
<td>8. Thermostability of the vaccine (sensitivity to heat and freezing)</td>
</tr>
<tr>
<td>9. Vaccine vial monitors</td>
</tr>
<tr>
<td>10. Packaging and how to minimize it</td>
</tr>
<tr>
<td>11. Wastage and how to minimize it</td>
</tr>
<tr>
<td>12. Cold chain requirements (volume per dose, temp monitoring)</td>
</tr>
<tr>
<td>13. Management of vaccine waste (PFS, vials, syringes)</td>
</tr>
<tr>
<td>14. Acceptability to health workers</td>
</tr>
<tr>
<td>15. WHO pre-qualification and other regulatory issues.</td>
</tr>
</tbody>
</table>

As part of the context, the group will also be mindful of the implications of any recommendation for other health systems issues related to vaccine introduction, including cost and financing, training needs for health workers (trade-off between innovation and familiarity), monitoring systems required, acceptability to the public and social mobilisation, and the whole range of issues related to introduction of any additional or new vaccine.

As much as possible, discussions should be anchored in lessons learned from the field from introduction of Hib and other vaccines to maximize the feasibility of pneumococcal and rotavirus vaccine introduction and provide a range of options for both industry and countries.

This document addresses aspects of points 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 12 and 13 as they relate to pneumococcal conjugate vaccines.

A1.2 Methodology
A literature review was conducted, particularly aimed at sourcing good data on wastage rates and costs.

A brief questionnaire was circulated to 10 vaccine manufacturers at the start of the project. Three of these responded. In addition, a call was put out to TechNet members asking the following questions:

- What is the relationship between wastage and number of doses per vial (with and without MDVP)?
• How do cold chain and logistics costs/requirements vary as a function of storage volume per dose?

A summary of the consultation is attached as Annex 2.

A spreadsheet tool for assessing the impact of alternative vaccine presentations was developed. This was based on an earlier version developed for the PATH malaria vaccine study. The tool has not been fully completed at the time of writing, but it has been used in draft form to perform the analyses presented in this document.

The assumptions used were based on available evidence, supplemented by the consensus opinion of the VPPAG. Inadequate data were available on the issue of the relation between wastage, session size, and the number of doses per vial. A request to TechNet was issued, but failed to identify more than opinions.
Annex 2 – TechNet consultation
Vaccine Presentation and Packaging Advisory Group
Summary of Responses from TechNet

Background
On 13 May 2007, TechNet posted a request seeking opinion and data on this question: "For future injectable pneumococcal vaccine for infant immunization programmes, what is the preferred vial size - in terms of number of doses per vial - for supply to developing countries?"

The specific questions were:
1. What is the relationship between wastage and number of doses per vial (with and without MDVP)?
2. How do cold chain and logistics costs/requirements vary as a function of storage volume per dose?

With these assumptions:
1. The vaccine is given as 3-dose series in infancy.
   (There may also be a catch-up campaign with one dose for all up to age 5 years.)
2. Cost per dose and size of the vial stays about the same, whether it is 1-, 2-, 5-, or 10-dose vial.
   (The higher cost for a 1-dose vial is likely to be small compared to overall cost per dose.)
3. Standard cold chain requirements (2°-8°C) are needed for the new vaccines.
4. The MDVP policy may apply to some vaccines but not to others.

Responses on data
Only 7 responses were received. None of which addressed the issue of costs. Ulla Griffiths will be assessing the costs of moving to a single dose liquid DTPHepBHib (penta) in Ethiopia in September 2007, and may be able in July to obtain data on the impact of change to the 2-dose penta in Senegal.

When Rwanda switched from (?10-dose) DTP to 2-dose penta, they had to increase their delivery schedule of vaccines from quarterly to monthly which triples transport costs. Wastage was reduced, but no precise data on this.

Wastage data are available from several countries, but these do not provide a clear definition of the relationship between vial size and wastage. The data do show lower wastage with 2-dose vials. They also show that there are many other factors, especially the Multi-dose Vial Policy (MDVP) and mode of delivery (campaign versus routine) that affect wastage. Indonesia has practically zero (<0.5%) wastage with UniJect but relatively high wastage (35%) for 5-dose DTPHepB for infants compared to 20% wastage for 10-dose DT given in schools.

Opinions
The opinions expressed were:
- Need for more than one vial size to cater for different situations (several respondents)
- Consider looking at JRF data on wastage
- Key challenge will not be cold room storage, but for the vaccinator doing outreach
- UniJect has many advantages in addition to minimising wastage (because it is single dose), including reducing burden on health worker


Consider the impact if jet-injector technology that allows dose reduction – hence a 5-dose vial would become a 25-dose vial and argues for smaller vial size.

Some respondents implicitly, and one explicitly, challenged the assumption that cost per dose would remain the same, because this is not the status for current vaccines.

A survey was sent to UNICEF country officers in all GAVI-eligible except in the Americas. On preference for expensive new vaccines, of the 27 respondents, preference was for 2-dose (n=14); 1-dose (n=13); 5-dose (n=8); 2-dose (n=8). Only 10 gave a single preference, with 13 giving two, one selecting three, and one all four options. One respondent had no opinion.

Analytic work

The TechNet posting led to some analytic work from the Prof. Jacobson. See attached paper and spreadsheet. The spreadsheet has some arbitrary values that can be changed to show the impact of the cold chain costs, assuming a linear relationship between costs and vial size. However, it does not address the wastage cost, except in terms of session size. To do so, would require either data on session sizes or a simulation based on likely session sizes.

The basic relationship is that as the number of doses per vial \( x \) increases the costs for cold chain & logistics (CCL) decrease inversely, with a slope \( C/x \). The relationship for wastage has not been defined, but if linearity is assumed with a slope \( Wx \), optimal vial size to minimize costs will be the square root of \( C/W \)\textsuperscript{11}. If \( W \geq C \), optimal vial size is 1-dose; if \( C \) is about 25 times \( W \), optimal vial size is 5-dose.

Empiric data are needed to describe the relationship, and get approximate values of \( C \) and \( W \) – including establishing whether it is a linear relation or not.

Conclusion

More empiric data is needed to inform some modelling approaches to identify the optimal size for cost minimisation.

It needs to be borne in mind that factors other than cost minimisation also need to be considered, especially factors that will affect health workers in delivering the vaccine (especially in outreach). It is also important that wastage concerns do not lead to children missing out in vaccines.

\textsuperscript{11} Total cost = f(c) + f(w) \cdot Where f(c)=CC & logistics costs in relation to number of doses per vial \( x \); and f(w)= cost relationship for wastage as \( x \) changes.

\[ f(c)= A_i + C/x; \quad f(w)=A_{ii} + Wx \Rightarrow \text{Total cost} = A + C/x + Wx \]

Where \( A_i \) and \( A_{ii} \) are constants that add up to \( A \); \( C \) and \( W \) are constants if there is a purely linear relationship or more complex functions for other relations. If \( C \) and \( W \) are constants, the total cost is minimised by differentiation and simplification to \( \sqrt{C/W} \). If non-linear, the solution is more complex.
Annex 3 – Assumptions

The following basic data have been used in the scenarios considered in the body of the report and in Annex 3.

A3.1 Vial sizes

During the video conference on 26th July it was agreed that the following presentations should be investigated: Compact pre-filled devices based on Uniject™ data; pre-filled syringe; single-dose; 2-dose; 5-dose and 10-dose. For the sake of completeness, 3-dose has also been added to the list.

Some manufacturers have provided volume-per-dose information. These data are incorporated in Figure A2.1.

Figure A2.1 – Vial sizes and volume-per-dose data

<table>
<thead>
<tr>
<th>Vial or pre-fill</th>
<th>Diameter (cm)</th>
<th>Height (cm)</th>
<th>Vol/dose (cm³)</th>
<th>Mfr A</th>
<th>Vol/dose (cm³)</th>
<th>Mfr B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uniject</td>
<td>24.55</td>
<td>no data</td>
<td>Vol/dose (cm³)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-fill</td>
<td>54.8</td>
<td>60.59</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-dose</td>
<td>1.65</td>
<td>3.6</td>
<td>10.97</td>
<td>15.0</td>
<td></td>
<td>no data</td>
</tr>
<tr>
<td>2-dose</td>
<td>1.65</td>
<td>4.1</td>
<td>6.19</td>
<td>n/a</td>
<td>no data</td>
<td></td>
</tr>
<tr>
<td>3-dose</td>
<td>1.65</td>
<td>4.1</td>
<td>4.13</td>
<td>n/a</td>
<td>no data</td>
<td></td>
</tr>
<tr>
<td>5-dose</td>
<td>1.65</td>
<td>4.1</td>
<td>2.48</td>
<td>n/a</td>
<td>no data</td>
<td></td>
</tr>
<tr>
<td>10-dose</td>
<td>1.65</td>
<td>5.1</td>
<td>1.52</td>
<td>n/a</td>
<td>no data</td>
<td></td>
</tr>
</tbody>
</table>

Notes:

a) Vial-based presentations based on generic vial sizes in 50 vial secondary packaging.

The Manufacturer B figure for pre-filled syringes is based on a current arrangement with 2 trays of 5 pre-filled syringes per box.

The ‘generic’ column is based on standard vial sizes and assumes that PCV will be presented as a single vial liquid at 0.5ml per dose. The volume-per-dose figures in this column assume 50 vial packs based on the typical industry arrangement with vials arrayed as Figure A2.2. The calculation assumes carton material 1.5mm thick with a hinged lid.

Figure A2.2 – 50 vial pack
A secondary carton containing 125 TT-Unijects with 25mm needles measures 16.5 x 15.5 x 12.0cm which gives a volume-per-dose figure of 24.55 cm$^3$.\textsuperscript{12}

It was agreed during the video conference on 26\textsuperscript{th} July that the pre-filled syringe presentations should be based on a standard 0.5ml AD syringe. The figure assumed in the ‘generic’ column is based on the 95\textsuperscript{th} percentile volume for currently pre-qualified AD syringes (range 29.17 to 56.67 cm$^3$ each). This gives a conservative figure which should allow for the likely lower packing density of pre-filled devices.

The bulking factor for shipping containers is assumed generally to be 5.0, except in the one case (Alt 1-dose) where specific data was provided (BF=6.0).

\section*{A3.2 Wastage rates – field data}

Wastage rate recommendations in GAVI (2007)\textsuperscript{13} are: 5\% for any liquid vaccine in single-dose vials, 10\% for any lyophilised vaccines in 2-dose vials, 25\% for 10-dose liquid vaccines, 50\% for 10 and 20-dose lyophilized vaccines.

There is some field evidence for Uniject wastage rates. Sutanto \textit{et al}\textsuperscript{14} report a 2\% wastage rate in Indonesia, whilst Levin \textit{et al} report a rate of less than 1\% for Hepatitis B-Uniject in the same setting\textsuperscript{15}. PATH similarly report less than 1\% for TT-Uniject in Ghana\textsuperscript{16}. Based on these data, a 2\% to 3\% figure would seem to be a conservative figure to adopt because some degree of unopened vial wastage must be allowed for in countries with imperfect cold chains\textsuperscript{17}. It seems reasonable to adopt the same figure for other pre-filled devices.

Reliable evidence for wastage rates in single-dose vials has been hard to find, but it is likely to be somewhat higher than for pre-filled because of the additional preparation steps involved in opening a vial and filling a syringe.

For larger format vials, Figure A2.3 shows consolidated mean wastage rate data for Ghana for the years 2002 to 2004, Niger, 2003 and 2004, Senegal, 2003, and Togo, 2003 and 2004. Although the mean wastage rates are mostly lower than the standard GAVI-endorsed figures\textsuperscript{18}, a notable feature of the two tables is the apparently huge monthly variation for some of the antigens. Some of the lower rates may reflect campaign activities, but the very high rates (e.g. 97\% for TT) are rather difficult to explain. This degree of variation would be totally unacceptable for an expensive vaccine such as PCV – such a vaccine will only be economically viable in settings where wastage is rigidly controlled and is both low and consistent.

\textsuperscript{12} PATH. \textit{Introducing TT-Uniject: A guide for program planners.} December 2003, p 21.

\textsuperscript{13} GAVI. \textit{Guidelines on country proposals for support to immunization services, new and under-used vaccines and injection safety.} 2007.


\textsuperscript{17} For example, the Effective Vaccine Store Management assessment guidelines (WHO/IVB/04.16-20) allow a maximum wastage of 1\% at primary store level. Additional losses can be expected further down the cold chain.

\textsuperscript{18} TT in the three francophone countries is an exception at 35\% against GAVI’s 25\%.
Figure A2.3: Wastage rates for four West African countries

Ghana

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Vial size</th>
<th>Monthly over 3 years</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG</td>
<td>20</td>
<td>41%</td>
<td>27%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Pentavalent</td>
<td>2</td>
<td>6%</td>
<td>1%</td>
<td>19%</td>
<td></td>
</tr>
<tr>
<td>OPV</td>
<td>10</td>
<td>14%</td>
<td>1%</td>
<td>28%</td>
<td></td>
</tr>
<tr>
<td>Measles</td>
<td>10</td>
<td>29%</td>
<td>10%</td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>TT</td>
<td>10</td>
<td>23%</td>
<td>2%</td>
<td>43%</td>
<td></td>
</tr>
<tr>
<td>YF</td>
<td>10</td>
<td>38%</td>
<td>23%</td>
<td>53%</td>
<td></td>
</tr>
</tbody>
</table>

Niger, Senegal, Togo

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Vial size</th>
<th>Monthly over 2 years</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG</td>
<td>20</td>
<td>37%</td>
<td>23%</td>
<td>72%</td>
<td></td>
</tr>
<tr>
<td>DTP</td>
<td>10</td>
<td>16%</td>
<td>1%</td>
<td>65%</td>
<td></td>
</tr>
<tr>
<td>OPV</td>
<td>10</td>
<td>20%</td>
<td>7%</td>
<td>49%</td>
<td></td>
</tr>
<tr>
<td>Measles</td>
<td>10</td>
<td>37%</td>
<td>21%</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>TT</td>
<td>10</td>
<td>35%</td>
<td>10%</td>
<td>97%</td>
<td></td>
</tr>
<tr>
<td>YF</td>
<td>10</td>
<td>30%</td>
<td>13%</td>
<td>44%</td>
<td></td>
</tr>
</tbody>
</table>

Notes

a) Senegal data for 1 year only
b) Source: EPI monthly reports

In addition, figures over a four month period from a sentinel site in Malawi in 2004 showed wastage rates of around 30% for BCG, 5% for pentavalent, 10-15% for OPV and 20% for measles.

It appears from these data that the GAVI guideline figures are achievable in an African setting, and may be unduly pessimistic. Note that achieving a low wastage rate for 10 or 20 dose liquid vaccines requires the adoption of the Multi-dose Vial Policy (MDVP). For multi-dose lyophilized vaccines, low wastage rates can only be achieved in settings where session frequency is planned so as to reduce wastage. We believe, for example, that EPI Malawi has limited vaccination sessions to specific days each week in order to increase session size with this end in view. This practice may lead to reduced coverage due to an increase in ‘missed opportunities for vaccination’, but has been adopted increasingly by developing countries that pay for their own vaccines and wish to economize by reducing wastage.

For the sake of the analysis, it has been agreed that the GAVI-recommended figures should be used for the base schedule.

A3.3 Wastage rates for PCV

Following discussions with VPPAG members, the goal-seeking approach described in the main report has been used to establish break-even wastage rates for the various presentation options at each of the agreed price points. This allows the earlier discussions regarding appropriate wastage rates with and without MDVP to be put aside.

Vial sizes are assumed – these are the most commonly used.
A3.4 Base schedule

The spreadsheet tool uses a base schedule as a means for assessing the overall volumetric effect of a new vaccine introduction. The two schedules in Figure A2.4 have been adopted for this purpose. The former is representative of those African countries that have adopted pentavalent DTP-HepB+Hib\(^{20}\). The later is representative of those that continue to use the ‘traditional’ schedule, with the addition of HepB or Hib\(^{21}\). Approximately 24 sub-Saharan countries have, or will shortly have, a pentavalent schedule — some without Yellow Fever. A further 9 countries have the ‘traditional’ schedule, plus Hepatitis B or Hib. Only 6 countries still retain the ‘traditional schedule’. A further 5 countries, including Nigeria and South Africa, have non-standard schedules\(^{22}\).

Figure A2.4: Base schedules

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Doses/vial</th>
<th>Dose per FIC</th>
<th>Wastage (GAVI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG</td>
<td>20</td>
<td>1</td>
<td>50%</td>
</tr>
<tr>
<td>OPV</td>
<td>10</td>
<td>3</td>
<td>25%</td>
</tr>
<tr>
<td>DTP-HepB+Hib</td>
<td>2</td>
<td>3</td>
<td>10%</td>
</tr>
<tr>
<td>Measles</td>
<td>10</td>
<td>1</td>
<td>50%</td>
</tr>
<tr>
<td>Yellow Fever</td>
<td>10</td>
<td>1</td>
<td>50%</td>
</tr>
<tr>
<td>TT (for CBAW)</td>
<td>10</td>
<td>2</td>
<td>25%</td>
</tr>
</tbody>
</table>

For the sake of the analysis, it has been agreed that the GAVI-recommended maximum wastage figures should be used for the base schedules.

A3.5 Price points

The cost analysis is based on a vaccine cost-per-dose ranging from $3.50 up to $7.50 in steps of $1.00. The cost differential between single and 10-dose vials is set at $-0.20 in accordance with information received from one of the responding manufacturers. In the absence of better data, the cost differential for compact pre-filled devices and pre-filled

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\(^{20}\) A 2-vial lyophilized presentation with a DTP-HepB diluent and lyophilized Hib.

\(^{21}\) 10 dose HepB and Hib vaccines have a similar volume per dose.

\(^{22}\) See [http://www.who.int/immunization_monitoring/en/globalsummary/ScheduleResult.cfm](http://www.who.int/immunization_monitoring/en/globalsummary/ScheduleResult.cfm) This site does not indicate the vial sizes used in each country. The most common sizes are assumed.
syringes is set at +$0.054 in accordance with BD’s stated policy of filling the Uniject device at the single-dose cost plus the cost of an AD syringe$^{23}$.  

$^{23}$ Roderick Hausser, BD, personal communication.
Annex 4 – Scenarios

A4.1 FITG charts

Primary and high level intermediate storage: +2 to +8 deg C

- Base
- Base + Other pre-fill
- Base + Pre-filled syringe
- Base + Gen 1-dose vial
- Base + Gen 2-dose vial
- Base + Gen 3-dose vial
- Base + Gen 5-dose vial
- Base + Gen 10-dose vial

Low level intermediate store: all vaccines at +2 to 8C

- Base
- Base + Other pre-fill
- Base + Pre-filled syringe
- Base + Gen 1-dose vial
- Base + Gen 2-dose vial
- Base + Gen 3-dose vial
- Base + Gen 5-dose vial
- Base + Gen 10-dose vial
- Base + Alt 1-dose vial
Commodities (SB = safety box)

Assembled safety boxes

Schedule
Annex 5 – Increasing the effective capacity of the cold chain

The new generation of high cost vaccines, such as PCV, will typically be supplied in vials containing fewer doses than traditional vaccines. In order to accommodate the substantial additional vaccine volumes, countries will need to:

- Improve vaccine logistics.
- Focus on reducing unopened and opened vial wastage (a single-dose presentation is one way to minimize opened vial wastage).
- Accelerate the preparation of comprehensive and accurate cold chain equipment inventories that include accurate storage capacity data and functional status.
- Put in place the management resources to maintain these inventories.
- Plan and grow cold chain capacity.

In relation to the last point, there are a number of ways to increase the effective capacity of the cold chain. Some of these relate purely to vaccine management; others involve the purchase of new cold chain equipment. Figure 5 sets out the principal options and summarises their advantages and disadvantages.

**Figure 5: Strategies for increasing the effective capacity of the cold chain**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Programme-wide strategies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1 <em>Existing vaccines:</em> Substitute a multi-valent vaccine for existing single-antigen vaccines</td>
<td>• Reduction in patient injection load and health worker workload.</td>
<td>• The formulation and/or presentation of the replacement may take more space. • Most programmes have already made this change.</td>
</tr>
<tr>
<td>1.2 <em>New vaccine:</em> Investigate implications of alternative presentations.</td>
<td>• Vial size can be tailored to suit known session size.</td>
<td>Only possible if a choice of presentations is offered.</td>
</tr>
<tr>
<td>1.3 Reduce wastage rates by better monitoring and session planning.</td>
<td>• Reduced vaccine costs.</td>
<td>Sessions planned solely in order to reduce wastage often lead to ‘lost opportunities’. This is not recommended.</td>
</tr>
<tr>
<td>1.4 Reduce vaccine wastage by adopting MDVP.</td>
<td>• Reduced vaccine costs. • More space-efficient multi-dose vial sizes possible. • Potentially fewer ‘lost opportunities’.</td>
<td>Only applicable to liquid vaccines. Many programmes have already adopted this policy.</td>
</tr>
</tbody>
</table>

<p>| <strong>2. Primary store level strategies</strong> | | |
| 2.1 Increase the number of deliveries per year from the vaccine manufacturer. | • Large reductions in peak storage volumes are possible. • Reduction in losses arising from cold chain failure because, per event, less vaccine is at risk. | Increased shipping costs and additional management. • Probably not practical to have more than 4 deliveries per year in most settings. • Greater risk of stock-outs if deliveries are unreliable and/or stock control is not robust. |</p>
<table>
<thead>
<tr>
<th>Strategy</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.2 Reduce safety stock levels (as measured in weeks/months)</td>
<td>• Can be considered in association with 2.1.</td>
<td>• Greater risk of stock-outs if deliveries are unreliable and/or stock control is not robust.</td>
</tr>
<tr>
<td>2.3 Move all lyophilized vaccines to -20°C storage.</td>
<td>• Current WHO advice only requires OPV to be stored at -20°C, but freezer room capacity may have been calculated for earlier recommendations. • Lyophilized vaccines are not harmed by storage at -20°C.</td>
<td>• Many programmes continue to store BCG and measles at -20°C, so this ‘win’ may not be available.</td>
</tr>
<tr>
<td>2.4 Convert existing freezer room(s) to cold room(s) and purchase chest freezers for OPV.</td>
<td>• Only OPV need be stored at -20°C. • OPV is a very compact vaccine. If current WHO guidelines are followed, freezer rooms may be under-utilized.</td>
<td>• Cost of substitute chest freezers or freezer rooms.</td>
</tr>
<tr>
<td>2.5 Purchase additional/larger cold room(s)</td>
<td>• Costs can be minimized if coordinated with the normal equipment replacement cycle.</td>
<td>• Significant cost implications. • Space may not be available at the primary store site and/or the electricity supply and/or stand-by generator may not be sufficient.</td>
</tr>
</tbody>
</table>

### 3. Intermediate store level strategies

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 Increase delivery frequency from primary store.</td>
<td>• Reductions in peak storage volumes at intermediate store are possible. • Reduces risks arising from cold chain failure because less vaccine will be lost per event.</td>
<td>• Increased transport costs. Increased stock management. • May not be possible in countries with seasonal access restrictions.</td>
</tr>
<tr>
<td>3.2 Reduce safety stock levels (as measured in weeks/months).</td>
<td>• Can be considered in association with 3.1.</td>
<td>• Greater risk of stock-outs if deliveries are unreliable and/or stock control is not robust.</td>
</tr>
<tr>
<td>3.3 Move all lyophilized vaccines to -20°C storage.</td>
<td>• As 2.3.</td>
<td>• Only applicable in larger intermediate stores (typically regional level) with -20°C storage.</td>
</tr>
<tr>
<td>3.4 Purchase additional or larger</td>
<td>• Costs can be minimized if</td>
<td>• Significant cost implications.</td>
</tr>
</tbody>
</table>

---

24 Depending on the type of freezer room, it is possible simply to change the thermostat. If the refrigeration units need to be replaced, the cost of new units is a substantial percentage of the overall cost of a new room, so may not be worthwhile. Source: Soren Spanner, UNICEF, personal communication.

25 A 264 litre freezer (PIS E3/98-M) costs around USD 600, EXW.

26 Approximate cold room prices ex. UNICEF-SD, 2007: 40m³ USD 19,000; 30m³ USD 17,000; 10m³ USD 12,600.
<table>
<thead>
<tr>
<th>Strategy</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>capacity cold chain equipment for existing stores.</td>
<td>coordinated with the normal equipment replacement cycle.</td>
<td>• Space may not be available at the store site. • The electricity supply may not be sufficient.</td>
</tr>
<tr>
<td>3.5 Establish additional intermediate stores</td>
<td>• Improved vaccine distribution may be possible with careful location planning.</td>
<td>• Cost and additional staffing requirements.</td>
</tr>
</tbody>
</table>

### 4. Health facility store level strategies

| 4.1 Increased delivery frequency from intermediate store as 3.2. | • As 3.1. | • At the periphery transport availability and reliability is typically a major constraint. • Staff may not be available to collect or deliver vaccine more frequently. |
| 4.2 Purchase additional refrigerators, and/or substitute larger capacity units. | • If an additional unit is required where only one was previously needed, this provides backup in the event of unit failure. | • Cost. • If an additional unit is needed, this increases the vaccine management workload. |

A notable feature of this table is that the number of available management options decreases progressively from the centre to the periphery. Unless health facility refrigerators have been over-sized, there is a strong probability that additional or larger equipment will have to be purchased for PCV introduction in many settings.
References

General material


Time and motion studies


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**Tools**


Vaccine Presentation Assessment Tool. Version D5 (under development)