

# Reconstitution vial adapters

Comparator\* : Use without innovation (i.e. reuse prevention reconstitution needle and syringe (N&S))

## Section 1: Summary of innovation

### 1.1 Examples of innovation types:

#### Reconstitution vial adapters

**Vial adapters**  
West Pharma



Image source: <sup>a</sup>

**Mix2Vial®**  
reconstitution  
system  
West Pharma



Image  
source: <sup>b</sup>

**MixJect®** reconstitution &  
delivery system  
West Pharma



Image source: <sup>c</sup>

**EZ LINK™** Duoject



Image source: <sup>d</sup>

### 1.2. Description of innovation:

- Vial adapters facilitate the reconstitution of two vaccine components from their separate primary containers. The objective of the innovation is to eliminate the needle from the reconstitution process, making it safer.
- Vial adapters are manufactured in a variety of sizes and used to facilitate reconstitution and/or drawing up of a wide variety of pharmaceutical products including medicines and vaccines.
- A vial adapter functions by fitting over the top of a vial, while utilizing a plastic spike to puncture the rubber stopper. Most designs are compatible with Luer lock and Luer slip syringes for liquid transfer.

\* Single dose vials, rather than multi-dose vials (MDVs) were used for the comparator, because in most cases the innovation being considered is a single-dose presentation. However, when multi-dose vials are commonly used by countries for specific vaccines, a comparison against the multi-dose vial will also be conducted under Phase II for those vaccines if this innovation is prioritised.

<sup>a</sup> <https://www.westpharma.com/products/reconstitution-and-transfer-systems/vial-adapters>

<sup>b</sup> <https://www.westpharma.com/products/reconstitution-and-transfer-systems/mix2vial-and-needle-free-transfer-device>

<sup>c</sup> <https://www.westpharma.com/products/reconstitution-and-transfer-systems/mixject>

<sup>d</sup> [http://duoject.com/wp-content/uploads/2016/01/EZLink\\_InformationCard.pdf](http://duoject.com/wp-content/uploads/2016/01/EZLink_InformationCard.pdf)

Category: *Packaging and safety*

Innovation: *Reconstitution vial adapters*

Comparator: *Use without innovation (i.e. RUP needle and syringe for reconstitution)*

- Vial adapters can facilitate either (i) vial to vial reconstitution or (ii) reconstitution between a syringe prefilled with diluent and vaccine vial (table 1.1).
- In the standard process for reconstitution using a vial adapter, a vial adapter can be attached to the diluent vial, then a RUP syringe with no needle can be connected to the vial adapter via the Luer connector to draw up the diluent. The same vial adapter and syringe assembly can then be transferred to the vaccine vial, and the diluent released for mixing with the dry vaccine product. Alternatively, two vial adapters can be used (one for each vial) and only the syringe is used to transfer liquid between the two vials.
- For oral or intranasal delivery, the delivery syringe can be connected to the vial adapter to draw the dose. For parenteral vaccines, after reconstitution the vial adapter would be removed and an autodisable (AD) needle and syringe (N&S) is used to draw and inject the vaccine. An AD N&S cannot draw doses through the vial adapter, as only luer connections can interface with the vial adapter and AD syringes have fixed (permanently attached) needles. Current AD syringe standards for immunization require non-removable needles to prevent reuse.
- Other types of vial adapters can enable vial-to-vial reconstitution by directly connecting the two vials without the use of a syringe for diluent transfer (e.g. the Mix2Vial®, West Pharmaceutical Services, section 1.1).
- If the vaccine presentation includes a prefilled syringe (without a fixed needle) containing the diluent, the diluent syringe can be attached to the vaccine vial using the vial adapter as a connecting device. The diluent is then released into the vial through the vial adapter for mixing. If the presentation is single dose, it can then be reloaded back into the syringe for administration.
- This Technical Note (TN) focuses on vial adapters for the reconstitution of dry vaccines, however vial adapters can be used for non-reconstitution purposes. The following are examples of the use of vial adapters to facilitate the withdrawal of vaccines from a primary container into a delivery system for parenteral injection or for oral administration:
  - A vial adapter is necessary to withdraw vaccine doses into a disposable syringe jet injector (DSJI) needle-free syringe. This would be considered part of the DSJI system and is included in the DSJI TN.
  - A vial adapter could be used to withdraw vaccine doses into some kinds of intradermal (ID) delivery devices, like the Nanopass hollow microneedle hub technology, since the microneedles aren't long enough to pierce into a vial. This would be considered part of the ID device system and is included in that TN.
  - There are liquid oral vaccines, either in development or marketed (but not WHO prequalified) that are in glass vials and delivered orally to infants with syringes – an example is POLYVAC's Rotavin<sup>e</sup>. Use of a vial adapter for drawing the vaccine into the delivery syringe would eliminate the need for needles and reduce the risk of accidental injection of the oral vaccine, particularly if oral syringes and custom vial adapters are used (which do not enable connection with a luer needle hub.) The same needle-free approach using a vial adapter could be adopted to draw doses into a syringe for intranasal delivery.
  - Use of a vial adapter with a one-way fluid valve and air filter for drawing vaccine doses has previously been proposed to enable the extended use of preservative-free vaccines packaged in multidose vials. In this scenario, the vial adapter would be used to penetrate the

<sup>e</sup> PATH. Using innovation to combat diarrheal disease in Vietnam. <https://www.path.org/resources/using-innovation-combat-diarrheal-disease-vietnam/>

Category: Packaging and safety



Innovation: Reconstitution vial adapters

Comparator: Use without innovation (i.e. RUP needle and syringe for reconstitution)

septum of a vaccine vial at the point of use. Vaccine would be withdrawn using a luer syringe (without needle), and then a needle would be attached to the syringe for delivery. The valve allows vaccine to exit from the device while preventing ingress of air, moisture, bacteria or other contaminants that may be harmful to the product, patient or consumer<sup>f</sup>. However, contamination could occur when the vial adapter itself is inserted into the vial, and safe use is dependent on user compliance with steps such as alcohol swabbing the vial adapter connection before each dose. This approach is therefore **not** anticipated to be of benefit in extending the open-vial shelf life of vaccines or reducing contamination risk. In addition, luer syringes without needles do not meet current AD requirements for immunization syringes.

### 1.3 Examples of innovations and developers:

Table 1.

Product name; Image	Developer (place); website	Brief description, notes
<p><b>Vial adapters</b></p>  <p>Image source: <sup>9</sup></p> <p><b>Vented vial adapter</b></p>  <p>Image source : <sup>9</sup></p>	<p><b>West Pharmaceutical Services, Inc</b></p> <p>and</p> <p>Medimop Medical Projects Ltd</p> <p><a href="https://www.westpharma.com/products/reconstitution-and-transfer-systems/vial-adapters">https://www.westpharma.com/products/reconstitution-and-transfer-systems/vial-adapters</a></p>	<p>To facilitate transfer and reconstitution of dry vaccine product.</p> <p>These vial adapters are developed by Medimop Medical Projects Ltd, as West Pharmaceutical Services company. The devices can come in different sizes and specific design attributes, for instance there are 3 types of vial adapters<sup>h, i</sup>:</p> <ul style="list-style-type: none"> <li>• Vial adapter (simple connector between vial and syringe)</li> <li>• Vented vial adapter, has a dual-channel spike that enables large volumes to be withdrawn.</li> <li>• Swabable vial adapters, have a silicone rubber valve with a Luer-compatible connector for repeated vial access.</li> </ul>

<sup>f</sup> [http://www.medinstill.com/intact\\_valve\\_dispensing.php](http://www.medinstill.com/intact_valve_dispensing.php)

<sup>g</sup> <https://www.westpharma.com/products/reconstitution-and-transfer-systems/vial-adapters>

<sup>h</sup> <https://www.westpharma.com/products/reconstitution-and-transfer-systems/vial-adapters>




<sup>i</sup> <https://adelphi-hp.com/assets/files/MediMop/vialadaptersproductsheet.pdf>

VIPS TECHNICAL NOTE

Category: Packaging and safety

Innovation: Reconstitution vial adapters

Comparator: Use without innovation (i.e. RUP needle and syringe for reconstitution)




Product name; Image	Developer (place); website	Brief description, notes
<p><b>Swabable vial adapter</b></p>  <p>Image source: <sup>9</sup></p>		
<p><b>Mix2Vial® reconstitution system</b></p>  <p>Image source: <sup>9</sup></p>	<p><b>West Pharma</b></p> <p><a href="https://www.westpharma.com/products/reconstitution-and-transfer-systems/mix2vial-and-needle-free-transfer-device">https://www.westpharma.com/products/reconstitution-and-transfer-systems/mix2vial-and-needle-free-transfer-device</a></p>	<p>The Mix2Vial® reconstitution system is used for vial-to-vial transfer of mixing diluent with dry product after which the reconstituted product is ready for withdrawal by syringe.</p>
<p><b>MixJect® reconstitution &amp; delivery system</b></p>  <p>Image source: <sup>9</sup></p>	<p><b>West Pharma</b></p> <p><a href="https://www.westpharma.com/products/reconstitution-and-transfer-systems/mixject">https://www.westpharma.com/products/reconstitution-and-transfer-systems/mixject</a></p>	<p>The Mixject reconstitution system is a preassembled single-unit that comes with a needle attached.</p> <p>The MixJect® reconstitution and delivery system enables attachment of the prefilled syringe with diluent to the vial using an adapter that is pre-assembled with a capped needle. Following reconstitution the syringe reloads with the reconstituted product and is removed from the vial adapter with the pre-attached needle ready for immediate administration.</p> <p>The device is also able to connect to standard vials, needles, syringes and Luer lock connections with the intention of attaching a prefilled syringe with diluent to reconstitute the dry formulation (drug or vaccine) for immediate administration of the product.</p>

**VIPS TECHNICAL NOTE**

Category: Packaging and safety

Innovation: Reconstitution vial adapters

Comparator: Use without innovation (i.e. RUP needle and syringe for reconstitution)

Product name; Image	Developer (place); website	Brief description, notes
<p>EZ LINK™ Duoject</p>  <p>Image source: <sup>j</sup></p>	<p><b>Duoject Medical Systems</b></p> <p><a href="http://duoject.com/realisations/ezlink/">http://duoject.com/realisations/ezlink/</a></p>	<p>A reconstitution vial with any standard luer-locked diluent prefilled syringe. The device has a protective disk that is activated following vial insertion which locks in the vial socket in place after use.</p>
<p>Serum Institute of India PVT. Ltd.</p>  <p>Image source: <sup>k</sup></p>	<p><b>Serum Institute of India PVT.LTD.</b></p> <p><a href="https://www.seruminstitute.com/product_viral_rotasiil.php">https://www.seruminstitute.com/product_viral_rotasiil.php</a></p>	<p>ROTASIIL vaccine is supplied with a vial adapter for reconstitution and drawing doses for oral delivery.</p> <p>The vaccine is a lyophilised (freeze-dried) presentation packaged in single-dose vials alongside a diluent.</p>
<p>Serum Institute of India PVT. LTD</p>  <p>Image source: <sup>l</sup></p>	<p><b>Serum Institute of India PVT. Ltd.</b></p> <p><a href="https://www.seruminstitute.com/product_influenza_vaccines.php">https://www.seruminstitute.com/product_influenza_vaccines.php</a></p> <p>Cipla Ltd.</p> <p><a href="https://www.cipla.com/en/">https://www.cipla.com/en/</a></p>	<p>Some presentations of Serum Institute’s intranasal live attenuated influenza vaccine are packaged with a vial adapter for reconstitution and drawing up doses. Cipla Ltd, markets/distributes the vaccine in India<sup>m</sup>.</p>

<sup>j</sup> <http://duoject.com/realisations/ezlink/>

<sup>k</sup> [https://www.google.com/search?q=Rotasiil+Rotavirus+Vaccine&hl=en&source=lnms&tbn=isch&sa=X&ved=0ahUKEwj-986zh-jgAhWFa1AKHbkdCucQ\\_AUIDigB&biw=1920&bih=861#imgrc=8XeGpeGcrBc7WM:&spf=1551687780860](https://www.google.com/search?q=Rotasiil+Rotavirus+Vaccine&hl=en&source=lnms&tbn=isch&sa=X&ved=0ahUKEwj-986zh-jgAhWFa1AKHbkdCucQ_AUIDigB&biw=1920&bih=861#imgrc=8XeGpeGcrBc7WM:&spf=1551687780860)

<sup>l</sup> [https://www.google.com/search?q=Rotasiil+Rotavirus+Vaccine&hl=en&source=lnms&tbn=isch&sa=X&ved=0ahUKEwj-986zh-jgAhWFa1AKHbkdCucQ\\_AUIDigB&biw=1920&bih=861#imgrc=8XeGpeGcrBc7WM:&spf=1551687780860](https://www.google.com/search?q=Rotasiil+Rotavirus+Vaccine&hl=en&source=lnms&tbn=isch&sa=X&ved=0ahUKEwj-986zh-jgAhWFa1AKHbkdCucQ_AUIDigB&biw=1920&bih=861#imgrc=8XeGpeGcrBc7WM:&spf=1551687780860)

<sup>m</sup> Cipla announces the next steps in its relationship with Serum Institute - an exclusive distribution agreement for flu vaccine ‘Nasovac-S’ for India. [https://www.cipla.com/uploads/mediakit/1443688051\\_Press-Release-Cipla-SII-agreement.pdf](https://www.cipla.com/uploads/mediakit/1443688051_Press-Release-Cipla-SII-agreement.pdf)

Category: *Packaging and safety*

Innovation: *Reconstitution vial adapters*

Comparator: *Use without innovation (i.e. RUP needle and syringe for reconstitution)*

## SECTION 2: Summary of assessment for prioritisation

### 2.1 Key benefits:

- Vial adapters are easy-to-use devices for the transfer and reconstitution of dry vaccines. Although there are multiple designs available with differing features, in general the technology is appropriate for both novice and experienced health care workers (HCWs).
- Vial adapters eliminate the needle from the reconstitution process thus providing a safer environment when reconstituting lyophilised vaccines by reducing the likelihood of needle-stick injury and reducing sharps waste (1). If the reconstituted vaccine is to be delivered orally or intranasally, vial adapters can eliminate needles entirely from the preparation and delivery process.
- This innovation can be applied to any current vial/vial or syringe/vial vaccine presentation. Vial adapters are licensed devices currently available on the market, and use of a vial adapter for reconstitution generally does not require any repackaging or regulatory process on the part of the vaccine manufacturer.

### 2.2 Key challenges:

- Many vial adapters for reconstitution will require use of RUP syringes without needles, however current RUP syringes are packaged with needles (either fixed or detachable).
- Purchasing and distributing multiple components (vial adapters, RUP syringes without needles) to vaccination sites may increase logistical hurdles, increase storage and disposal volumes for immunization supplies and, if not packaged together, could result in stock-outs and thus disruption to the immunization programme. If the reconstitution vial adapter is instead co-packaged with the vaccine and the diluent (refer to Table 1 for RotaSiLL and Nasovac vaccine), this would significantly increase cold chain volume.
- Vial adapters have the potential to be removed and reused, thus resulting in contamination unless the user is fully trained and compliant with aseptic standards of practice of non-reuse.

### 2.3 Additional important information

- The user will need to be trained in use of vial adapters and how to apply correct aseptic techniques to prevent contamination when reconstituting vaccine using vial adapters.
- Vial adapters, whether packaged with the vaccine or purchased separately with other immunization supplies, will result in additional costs incurred by the vaccine purchaser.



Category: Packaging and safety

Innovation: Reconstitution vial adapters

Comparator: Use without innovation (i.e. RUP needle and syringe for reconstitution)

## SECTION 3: Evaluation criteria

### 3.1 Health impact criteria

#### Indicator: Ability of the vaccine presentation to withstand heat exposure

Legend: **Green**: **Better** than the comparator: The innovation includes features that may increase heat stability; **White**: **Neutral**, no difference with the comparator; **Red**: **Worse** than the comparator: The innovation includes features that may decrease heat stability, **N/A**: the indicator measured is **not applicable** for the innovation; **Grey**: **no data** available to measure the indicator.

Table 2.

Ability of the vaccine presentation to withstand heat exposure	Parameters to measure against a comparator	Score	Assessment
	Does the innovation have features that may improve heat stability?	Neutral	The use of reconstitution vial adapters or not (comparator) will have no impact on the ability of a vaccine to withstand higher temperatures and therefore there is no difference with the comparator.

	<b><u>No difference</u></b> to the comparator
--	---

#### Indicator: Ability of the vaccine presentation to withstand freeze exposure

Legend: **Green**: **Better** than the comparator: The innovation includes features that may increase freeze resistance; **White**: **Neutral**, no difference with the comparator; **Red**: **Worse** than the comparator: The innovation includes features that may decrease freeze resistance, **N/A**: the indicator measured is **not applicable** for the innovation; **Grey**: **no data** available to measure the indicator.

Table 3.

Ability of the vaccine presentation to withstand freeze exposure	Parameters to measure against a comparator	Score	Assessment
	Does the innovation have features that may improve freeze resistance?	Neutral	The use of reconstitution vial adapters or not (comparator) will have no impact on the ability of the vaccine to withstand freeze exposure and therefore there is no difference with the comparator.

	<b><u>No difference</u></b> to the comparator
--	---

Category: Packaging and safety

Innovation: Reconstitution vial adapters

Comparator: Use without innovation (i.e. RUP needle and syringe for reconstitution)

### 3.2 Coverage and equity criteria

#### Indicator: Ease of use<sup>n</sup>

Legend: **Dark Green:** **Considerably better** than the comparator: *Better for all* applicable parameters; **Green:** **Better** than the comparator: *Better for some* of the applicable parameters **AND no difference** for the rest of the parameters; **White:** **Neutral**, no difference with the comparator; **Yellow:** **Mixed:** *Better* than the comparator *for some* of the applicable parameters **AND worse** than the comparator *for the rest* of the parameters; **Red:** **Worse** than the comparator: *Worse for some* of the applicable parameters **AND no difference for the rest** of the parameters; **Dark Red:** **Considerably worse** than the comparator: *Worse for all* applicable parameters, **N/A:** the indicator measured is **not applicable** for the innovation; **Grey:** **no data** available to measure the indicator.

Table 4.

Ease of use	Parameters to measure against a comparator	Score	Assessment
<ul style="list-style-type: none"> <li>Assessment of the potential for incorrect preparation based on usability data from field studies (or based on design of innovation if field studies not available)</li> <li>Assessment of the potential for incorrect administration based on usability data from field studies (or based on design of innovation if field studies not available)</li> </ul>	Does the innovation avoid reconstitution and is that an improvement?	Neutral	Reconstitution vial adapters are devices that substitute for needles in the reconstitution process of a dry vaccine presentation, but reconstitution is still required.
	Does the innovation require fewer vaccine product components?	Worse	The innovation would most likely require separate packages containing the vial adapter and an RUP syringe without a needle (based on expert opinion). Use of a vial adapter would then increase the number of separate vaccine product components (vaccine, delivery device, diluent, vial adapter, RUP syringe compared to vaccine, delivery device, diluent, and RUP N&S).
	<sup>o</sup> Does the innovation require additional components or equipment (such as scanners or label readers)?	NA	

<sup>n</sup> Ease of use can prevent missed opportunities resulting from the complexity of preparation and administration procedures. It could also impact the ability for lesser trained personnel to administer the vaccine (incl. self-administration). It can be assessed based on usability data from field studies (or based on design of innovation if field studies not available).

<sup>o</sup> This parameter is only assessed for RFID/barcodes, for all other innovations it is not applicable (N/A).



Category: *Packaging and safety*

Innovation: *Reconstitution vial adapters*

Comparator: *Use without innovation (i.e. RUP needle and syringe for reconstitution)*

Ease of use	Parameters to measure against a comparator	Score	Assessment
<ul style="list-style-type: none"> <li>Assessment of the potential for incorrect preparation based on usability data from field studies (or based on design of innovation if field studies not available)</li> <li>Assessment of the potential for incorrect administration based on usability data from field studies (or based on design of innovation if field studies not available)</li> </ul>	Does the innovation require fewer preparation steps and less complex preparation steps?	Worse	Use of the reconstitution vial adapter requires additional steps, as the vial adapter and syringe would each need to be unwrapped and individually attached to the vial. Vial adapters, due to their thick plastic spikes, also require more effort to attach and detach from a vial than a needle. The comparator RUP N&S comes preassembled with the needle and requires fewer steps to use.
	Does the innovation improve dose control?	Neutral	The use of a reconstitution vial adapter or not (comparator) has no impact on dose control.
	Does the innovation improve targeting the right route of administration?	Neutral	The use of a reconstitution vial adapter or not (comparator) has no impact on targeting the route of administration.

	<b><i>Worse</i></b> than the comparator
--	---

**Indicator: Potential to reduce stock outs based on the number of separate components necessary to deliver the vaccine or improved ability to track vaccine commodities**

Legend: **Green:** **Better** than the comparator for one of the parameters; **White:** **Neutral**, no difference with the comparator; **Red:** **Worse** than the comparator for one of the parameters, **N/A:** the indicator measured is **not applicable** for the innovation; **Grey:** **no data** available to measure the indicator.


Category: Packaging and safety

Innovation: Reconstitution vial adapters

Comparator: Use without innovation (i.e. RUP needle and syringe for reconstitution)

Table 5.

Potential to reduce stock outs based on the number of separate components necessary to deliver the vaccine or improved ability to track vaccine commodities	Parameters to measure against a comparator	Score	Assessment
<ul style="list-style-type: none"> <li>Assessment of the potential to reduce stock outs based on the innovation's features</li> </ul>	Does the innovation require fewer components?	Worse	Typically, reconstitution devices are packaged separately from the vaccine and diluent to minimize cold chain volume. This is the scenario we are evaluating for both the innovation and comparator. Use of a vial adapter would then increase the number of separate vaccine product components (vaccine, delivery device, diluent, vial adapter, RUP syringe compared to vaccine, delivery device, diluent, and RUP N&S).
	Or does the innovation include labelling that facilitates product tracking and is it better than the comparator?	Neutral	The innovation has no features that would facilitate labelling or product tracking, similar to the comparator.

 **Worse** than the comparator

**Indicator: Acceptability of the vaccine presentation and schedule to patients/caregivers**

Legend: **Dark Green**: **Considerably better** than the comparator: *Better for all* applicable parameters; **Green**: **Better** than the comparator: *Better for some* of the applicable parameters **AND no difference** for the rest of the parameters; **White**: **Neutral**, no difference with the comparator; **Yellow**: **Mixed**: *Better* than the comparator **for some** of the applicable parameters **AND worse** than the comparator **for the rest** of the parameters; **Red**: **Worse** than the comparator: *Worse for some* of the applicable parameters **AND no difference for the rest** of the parameters; **Dark Red**: **Considerably worse** than the comparator: *Worse for all* applicable parameters, **N/A**: the indicator measured is **not applicable** for the innovation; **Grey**: **no data** available to measure the indicator.

Category: Packaging and safety

Innovation: Reconstitution vial adapters

Comparator: Use without innovation (i.e. RUP needle and syringe for reconstitution)

Table 6.

Acceptability of the vaccine presentation to patients/ caregivers	Parameters to measure against a comparator	Score	Assessment
<ul style="list-style-type: none"> <li>Does the innovation include features that may improve acceptability of vaccinees and caregivers</li> </ul>	Painful or not painful	Neutral	Reconstitution vial adapters would have no impact on the vaccinees/caregivers in terms of pain or administration, which is the same as the comparator.
	Perception of ease of administration (i.e. convenience for the vaccinees/caregivers)	Neutral	
	Any other tangible benefit to improve/impact acceptability to vaccinees/caregivers	Neutral	

**No difference** to the comparator

### 3.3 Safety criteria

#### Indicator: Likelihood of contamination

Legend: **Dark Green: Considerably better** than the comparator: *Better for all applicable parameters*; **Green: Better** than the comparator: *Better for some of the applicable parameters AND no difference for the rest of the parameters*; **White: Neutral**, no difference with the comparator; **Yellow: Mixed**: *Better than the comparator for some of the applicable parameters AND worse than the comparator for the rest of the parameters*; **Red: Worse** than the comparator: *Worse for some of the applicable parameters AND no difference for the rest of the parameters*; **Dark Red: Considerably worse** than the comparator: *Worse for all applicable parameters*, **N/A**: the indicator measured is **not applicable** for the innovation; **Grey: no data** available to measure the indicator.

Table 7.


Likelihood of contamination	Parameters to measure against a comparator	Score	Assessment
<ul style="list-style-type: none"> <li>Risk assessment of potential for contamination based on design of innovation and on usability data from field studies</li> </ul>	Does the innovation reduce the risk of contamination while reconstituting the dry vaccine?	Neutral	There is no difference in the risk of contamination between the innovation and the comparator while reconstituting, as this step relies on the standard aseptic practice applied by the vaccinator.

Category: Packaging and safety

Innovation: Reconstitution vial adapters

Comparator: Use without innovation (i.e. RUP needle and syringe for reconstitution)

Likelihood of contamination	Parameters to measure against a comparator	Score	Assessment
<ul style="list-style-type: none"> <li>Risk assessment of potential for contamination based on design of innovation and on usability data from field studies</li> </ul>	Does the innovation reduce the risk of contamination while filling the delivery device?	Neutral	There is no difference in the risk of contamination between the innovation and the comparator while filling the delivery device, as this step relies on the standard aseptic practice applied by the vaccinator.
	Does the innovation require fewer preparation steps and less complex preparation steps?	Worse	Use of the reconstitution vial adapter requires additional steps, as the vial adapter and syringe are packaged separately and would need to be individually attached to the vial. Vial adapters also require more effort to attach and detach from a vial compared to insertion of a needle. The comparator RUP N&S comes preassembled with the needle and requires fewer steps to use.
	Does the innovation reduce the potential risk of reuse of delivery technology?	Worse	There is a potential risk that the reconstitution vial adapter can be removed and reused, which is worse than the comparator as the reconstitution needle & syringe has an RUP feature.
	Does the innovation reduce the risk of use of nonsterile components?	Worse	The vial adapter is in sterile packaging and is intended to be used on a single vial, but could be reused which would increase risks of contamination.

 **Worse** than the comparator

**Indicator: Likelihood of needle stick injury**

Legend: **Dark Green**: **Considerably better** than the comparator: *Better for all applicable parameters*; **Green**: **Better** than the comparator: *Better for some of the applicable parameters AND no difference for the rest of the parameters*; **White**: **Neutral**, no difference with the comparator; **Yellow**: **Mixed**: *Better than the comparator for some of the applicable parameters AND worse than the comparator for the rest of the parameters*; **Red**: **Worse** than the comparator: *Worse for some of the applicable parameters AND no difference for the rest of the parameters*; **Dark Red**: **Considerably worse** than the comparator: *Worse for all applicable parameters*; **N/A**: the indicator measured is **not applicable** for the innovation; **Grey**: **no data** available to measure the indicator.

Category: *Packaging and safety*

Innovation: *Reconstitution vial adapters*

Comparator: *Use without innovation (i.e. RUP needle and syringe for reconstitution)*

Table 8.

Likelihood of needle stick injury	Parameters to measure against a comparator	Score	Assessment
<ul style="list-style-type: none"> <li>Risk assessment of the presence of sharps during the process of preparing and administering the vaccine</li> </ul>	Does the innovation contain fewer sharps?	Better	The innovation removes the use of sharps for reconstitution which is better than the comparator which uses a reconstitution N&S. If the vaccine is an injectable, a sharp for delivering the vaccine (AD N&S) would still be required.
	Does the innovation use sharps for preparing and/or administering the vaccine and is that better than the comparator?	Better	The innovation removes the use of sharps for preparing/reconstituting the vaccine which is better than the comparator which requires a reconstitution N&S. If the vaccine is an injectable, a sharp for delivering the vaccine (AD N&S) would still be required.
	Does the innovation include an auto disable feature and is that better than the comparator?	Neutral	The reconstitution vial adapter does not have an AD feature, which is similar to the RUP syringe used for reconstitution with the comparator.
	If the innovation uses sharps, does it include a sharps injury prevention feature and is that better than the comparator?	Neutral	The innovation removes the use of sharps and thus there is no requirement for a SIP feature.
	Does the innovation reduce the risk of injury after vaccine administration?	Better	As reconstitution vial adapters are less sharp than the metal needles used in standard reconstitution syringes, they are less likely to cause injury during handling and disposal.

	<b><i>Better</i></b> than the comparator.
--	---

Category: Packaging and safety

Innovation: Reconstitution vial adapters

Comparator: Use without innovation (i.e. RUP needle and syringe for reconstitution)


### 3.4 Economic costs criteria

#### Indicator: Total economic cost of storage and transportation of commodities per dose<sup>P</sup>

Legend: **Dark Green: Considerably better** than the comparator: *Reduces the volume per dose for applicable parameters*; **Green: Better** than the comparator: *Reduces the volume per dose for either of the applicable parameter, and there is no difference for the other*; **White: Neutral**, no difference with the comparator; **Yellow: Mixed**: *Reduces the volume for one of the parameter, and increases the volume for the other parameter compared to the comparator*; **Red: Worse** than the comparator: *Increases the volume per dose for either of the applicable parameters, and there is no difference for the other*; **Dark Red: Considerably worse** than the comparator: *Increases the volume per dose for both parameters*; **N/A**: the indicator measured is **not applicable** for the innovation; **Grey: no data** available to measure the indicator.

Table 9.

Total economic cost of storage and transportation of commodities per dose	Parameters to measure against a comparator	Score	Assessment
	Does the innovation reduce the volume per dose stored and transported in the cold chain?	Neutral	Assuming the reconstitution devices are not co-packaged with the vaccine that is kept and transported in the cold chain, the cold chain volume would be unchanged as the same vaccine vial would be used.
	Does the innovation reduce the volume per dose stored and transported out of the cold chain?	Worse	A vial adapter would have a larger volume stored and transported out of the cold chain compared to a RUP syringe used for conventional reconstitution. Volumes of RUP N&S vary by manufacturer and some prequalified 5 ml RUP N&S have volumes of 52 cm <sup>3</sup> (3) and 76 cm <sup>3</sup> (4). The West Vial Adapter and the West Mix2Vial have measured volumes of 106 cm <sup>3</sup> and 151 cm <sup>3</sup> , respectively (PATH personal communication). After reconstitution, both the innovation and the comparator would require an AD N&S for vaccine delivery.

 **Worse** than the comparator

<sup>P</sup> The assessment of the indicator is volume-related and builds upon PATH's VTIA analysis. A directional estimation is made at this stage, and a better evaluation will be done in Phase II with more antigen-specific data.



Category: Packaging and safety

Innovation: Reconstitution vial adapters


Comparator: Use without innovation (i.e. RUP needle and syringe for reconstitution)

**Indicator: Total economic cost of the time spent by staff per dose**

Legend: **Dark Green**: **Considerably better** than the comparator: *Reduces time for all applicable parameters*; **Green**: **Better** than the comparator: *Reduces time for either, and there is no difference for the other one*; **White**: **Neutral**, no difference with the comparator; **Yellow**: **Mixed**: *Reduces the time for one of the parameters, and increases the time for the other parameter*; **Red**: **Worse** than the comparator: *Increases the time for either of the applicable parameters; and there is no difference for the other one*; **Dark Red**: **Considerably worse** than the comparator: *Increases time for all applicable parameters*; **N/A**: the indicator measured is **not applicable** for the innovation; **Grey**: **no data** available to measure the indicator.

Table 11.

Total economic cost of the time spent by staff per dose	Parameters to measure against a comparator	Score	Assessment
	Does the innovation have attributes that can save time for the vaccinator in preparing and administering the vaccine?	Worse	Attaching a vial adapter followed by a RUP syringe and transferring the whole assembly to the second vial is likely to take longer than use of a RUP N&S.
	<sup>q</sup> Does the innovation have attributes that save time for staff involved in stock management?	Neutral	The innovation does not have attributes that impact the time staff spend on stock management.

 **Worse** than the comparator

**Indicator: Total economic cost of one-time/upfront purchases or investments required to introduce the vaccine presentation and of recurrent costs associated with the vaccine presentation (not otherwise accounted for)**

Legend: **White**: **Neutral**: **NO** there are no one-time/upfront or recurrent costs and this is not different than the comparator; **Red**: **Worse** than the comparator: **YES** there are one-time/upfront or recurrent costs.

<sup>q</sup> This parameter only applies to barcodes and RFID to capture the benefits for stock management processes, not based on the number of components, but the specific features of the innovation.

Category: *Packaging and safety*

Innovation: *Reconstitution vial adapters*

Comparator: *Use without innovation (i.e. RUP needle and syringe for reconstitution)*

Table 11.

Total economic cost of one-time/upfront purchases or investments required to introduce the vaccine presentation and of recurrent costs associated with the vaccine presentation (not otherwise accounted for)	Parameters to measure against a comparator	Score	Assessment
	Are there one-time upfront costs that will be incurred for use of this innovation or recurrent costs that will be incurred for use of this innovation?	Neutral	No. Reconstitution vial adapters do not have any upfront or recurrent costs. As with any innovation, vaccinators may need to be trained. However, we are not including training costs as part of the assessment in this phase.

	<b><u>No difference</u></b> to the comparator.
--	--

### 3.5 Secondary criteria on potential breadth of innovation use

Indicator: Applicability of innovation to one or several types of vaccines

Table 12.

Applicability of innovation to one or several types of vaccines	Assessment
<ul style="list-style-type: none"> <li>What vaccines/antigens does the innovation apply to, based on technical feasibility?</li> </ul>	This innovation could be applied to all dry vaccine presentations that require reconstitution with a diluent, or other two-component vaccines in glass vials that require mixing.

Category: *Packaging and safety*

Innovation: *Reconstitution vial adapters*

Comparator: *Use without innovation (i.e. RUP needle and syringe for reconstitution)*

**Indicator: Ability of the technology to facilitate novel vaccine combination**

**Table 13.**

Ability of the technology to facilitate novel vaccine combination	Assessment
<ul style="list-style-type: none"> <li>Does the innovation facilitate novel combination vaccine products?</li> </ul>	<p>No.</p> <p>Reconstitution vial adapters do not have any features that facilitate novel combinations.</p>

## SECTION 4

**4.1 Robustness of data:**

**Table 14.**

Category	Assessment
<p><b>Type of study</b></p>	<p>The majority of the data used for this TN has been taken from two technical reports by PATH (5)(6), manufacturer websites/leaflets and combined with expert opinion.</p>
<p><b>Inconsistency of results</b></p>	<p>There are too few comparable studies to assess inconsistency of results.</p>
<p><b>Indirectness of comparison</b></p> <ul style="list-style-type: none"> <li>Indicate the setting in which the study was conducted (low, middle or high income setting);</li> <li>Comment if the data is on non-vaccine application of the innovation</li> </ul>	<p>All the data assessed has been for vaccine applications</p>
<p><b>Overall assessment:</b></p>	<p><i>Low to moderate</i></p>

Category: *Packaging and safety*

Innovation: *Reconstitution vial adapters*

Comparator: *Use without innovation (i.e. RUP needle and syringe for reconstitution)*

## 4.2 List of technical experts, manufacturers and/or technology developers interviewed for inputs:

**Table 15.**

Expert/type	Organisation/contact details	Notes
N/A	N/A	No interviews conducted.

## 4.3 List of technical experts, manufacturers and/or technology developers that have reviewed and provided feedback/input to the technical notes:

**Table 16.**

Reviewers	Organisation/contact details	Notes
Fatema Kazi	Gavi, the Vaccine Alliance <a href="mailto:fkazi-external-consultant@Gavi.org">fkazi-external-consultant@Gavi.org</a>	Developed TN
PATH Medical Devices and Health Technologies Team Debra Kristensen Courtney Jarrahan Mercy Mvundura Collrane Frivold	Debra Kristensen <a href="mailto:dkristensen@path.org">dkristensen@path.org</a>	Reviewed the TN
Julian Hickling	Working in Tandem Ltd <a href="mailto:julian@workingintandem.co.uk">julian@workingintandem.co.uk</a>	Reviewed TN

## 4.4 References:

1. Papania MJ, Zehrung D, Jarrahan C. 68 - Technologies to Improve Immunization. In: Plotkin SA, Orenstein WA, Offit PA, Edwards KMBT-PV (Seventh E, editors. Elsevier; 2018. p. 1320–1353.e17.
2. Chen D, Kristensen D. Opportunities and challenges of developing thermostable vaccines. *Expert Rev Vaccines*. 2009;8(5):547–57.
3. World Health Organization. Hypodermic syringes with reuse prevention feature. E013/063 [Internet]. Geneva; 2011. Available from:

*Category: Packaging and safety*

*Innovation: Reconstitution vial adapters*

*Comparator: Use without innovation (i.e. RUP needle and syringe for reconstitution)*

[https://apps.who.int/immunization\\_standards/vaccine\\_quality/pqs\\_catalogue/LinkPDF.aspx?UniqueID=77595d6d-8478-437b-94e7-9dec1897dfda&TipoDoc=DataSheet&ID=0](https://apps.who.int/immunization_standards/vaccine_quality/pqs_catalogue/LinkPDF.aspx?UniqueID=77595d6d-8478-437b-94e7-9dec1897dfda&TipoDoc=DataSheet&ID=0)

4. Hypodermic syringes with reuse prevention features. E013/106 [Internet]. Geneva; 2015. Available from:  
[https://apps.who.int/immunization\\_standards/vaccine\\_quality/pqs\\_catalogue/LinkPDF.aspx?UniqueID=e57fa1a1-b2c7-4906-bbe1-ca7afb644876&TipoDoc=DataSheet&ID=0](https://apps.who.int/immunization_standards/vaccine_quality/pqs_catalogue/LinkPDF.aspx?UniqueID=e57fa1a1-b2c7-4906-bbe1-ca7afb644876&TipoDoc=DataSheet&ID=0)
5. PATH. Multi-access vial adapters: Technical overview of commercialized multi-access, needle-free vial devices. 2007.
6. PATH. Review of multidose primary packaging and delivery systems for vaccines without preservatives. 2013;