Disposable-syringe jet injectors (DSJIs)

Comparators[a]:

- **SC/IM DSJI subtype is compared with autodisable (AD) needle & syringe (N&S);**
- **ID DSJI subtype is compared with Bacille Calmette-Guerin (BCG) AD N&S**

Note to VIPS Steering Committee (SC): In the November 2018 VIPS SC meeting, in an effort to reduce the number of innovations reviewed in Phase 1, the SC recommended to remove intradermal (ID) DSJIs from the list as WHO had recently purchased a stockpile of devices (enough for 5 million injections) and further market incentives may not be needed. However, only one device has been WHO prequalified and it has been only used for one vaccine. The two countries that have been willing to do pilots have done so with free devices provided from a one-time WHO stockpile – so not really an indication of a sustainable market. The team therefore recommends that the SC reconsider inclusion of ID DSJIs. This Technical Note assesses and scores the DSJIs grouped into the following two subtypes: (i) DSJI for SC/IM delivery and (ii) DSJI for ID delivery.

Section 1: Summary of innovation

1.1 Examples of innovation types:

PharmaJet® Stratis (SC/IM)

Image source: Provided by PharmaJet

PharmaJet® Tropis (ID)

Image source: provided by PATH

Med-Jet™ H4

Image source: provided by PATH

1.2. Description of innovation:

- DSJIs are delivery devices that deliver vaccines in a narrow, high-pressure liquid stream that can penetrate through tissue without the use of needles.
- DSJIs can inject vaccines intradermally (ID), subcutaneously (SC), or intramuscularly (IM) from standard vial presentations, replacing use of an autodisable needle & syringe. For some DSJI platforms, different devices are required for different depths of delivery; other devices deliver to multiple depths of injection.
- Previous-generation multi-use nozzle jet injectors (MUNJIs) were used for decades in mass immunization campaigns to deliver hundreds of millions of doses of vaccines globally, including vaccines for measles, smallpox, and yellow fever. However, these devices were later found to pose

[a] Though DSJIs are most likely to be used with multi-dose vials of vaccines, for consistency with the other Technical Notes they have been scored assuming use with a single-dose vial. Use with multi-dose vial presentations will be assessed in Phase 2, if applicable based on the vaccine pairing.

a risk of cross-contamination between vaccine recipients due to the reusable fluid pathway. The new generation of DSJIs was developed to eliminate the risk of cross-contamination through use of single-use needle-free syringes (or cartridges) for each injection.

- DSJIs consist of a needle-free syringe, a filling adapter, and a reusable injector. Some designs are manually powered through an internal spring, which is reset through either an integrated mechanism or a separate reset station. Other designs are gas powered and require gas cartridges or canisters or connection to a compressed air line.
- Clinical data has been generated for DSJI delivery of various vaccines including measles, mumps, rubella (MMR), inactivated poliovirus, BCG, HPV and influenza vaccines, as well as vaccines in development for dengue and Zika (1-9).

1.3 Examples of innovations and developers:

Table 1.

Product name; Image	**Developer (place); website**	**Brief description, notes**
Stratis  Image source: provided by PATH	**PharmaJet** (Golden, CO, USA) www.pharmajet.com	The PharmaJet Stratis device consists of a reusable injector & a separate manually-powered reset station, a filling adapter (one per vaccine vial) and a needle-free autodisable syringe (one per injection.) The device has FDA 510(k) clearance, CE Mark, and WHO prequalification, as well as national clearances in countries in Asia, the Middle East, and Africa. It provides fixed-dose 0.5ml injections either IM or SC. Seqirus' Afluria seasonal influenza vaccines and Serum Institute of India Ltd's measles-containing vaccines have been re-labelled for delivery by the PharmaJet Stratis device in addition to N&S injection. The device is commercially available in several countries (HICs and LMICs), including use for seasonal influenza vaccine delivery in pharmacy clinics in the United States.
Tropis  Image source: provided by PATH	**PharmaJet** (Golden, CO, USA) www.pharmajet.com	The PharmaJet Tropis device provides fixed-dose 0.1ml injections ID. It consists of a reusable injector (with integrated manually-powered reset mechanism), a filling adapter (one per vaccine vial) and a needle-free autodisable syringe (one per injection.) The device has CE Mark and WHO prequalification, as well as national clearances in countries in Asia, the Middle East, and Africa. Clinical data is available for delivery of several vaccines, including IPV. A pilot introduction of the Tropis device is underway in early 2019 in Cuba for fractional dose IPV delivery in routine immunization through collaboration between the WHO GPEI and Cuba Ministry of Health,

Product name; Image	Developer (place); website	Brief description, notes
		and an IPV campaign was conducted with the device in March 2019 in Pakistan.
Med-Jet™ H4  Image source: provided by PATH	**Medical International Technologies, Inc** (MIT Canada) www.mitcanada.ca	The Med-Jet H4 device consists of a reusable injector, filling adapter (one per vaccine vial), and single-dose disposable syringe (one per dose). It is compressed-gas powered and requires either a gas cylinder or direct connection to a compressed air line. It provides variable doses up to 0.5ml and can deliver vaccines ID, SC, or IM, depending on the gas pressure settings. The Med-Jet H4 has device clearance in Canada, China, and other countries.

SECTION 2: Summary of assessment for prioritisation

2.1 Key benefits:

- DSJIs eliminate the use of a needle for providing an injection, reducing sharps waste and the risk of needlestick injuries.
- In many countries and use scenarios, DSJIs have been found to be significantly more acceptable to vaccine recipients and caregivers as they can reduce pain at the time of injection (10) and needle phobia (Evidence noted in section 2.4 below). In high-throughput settings such as fixed-post campaigns, DSJIs can reduce the time required to give injections (see Table 10 below). DSJIs may have particular value for ID delivery, to avoid the challenging Mantoux technique required for ID injections with a N&S (11).
- DSJIs can be used with current liquid and lyophilized vaccine presentations, and no vaccine packaging changes are required.
- DSJIs may improve coverage through increased acceptability and the novelty of the delivery method (12).

2.2 Key challenges:

- DSJIs require more components, including a reusable handpiece, and in some cases a separate re-setting station, which can increase logistical challenges. Some DSJI models are gas powered, and gas supply is challenging in many LMIC settings. These designs also have reduced portability as gas cylinders are heavy and bulky.
- The currently prequalified DSJI devices for ID and SC/IM injections are different models. If an immunization program introduced DSJIs for use for both an ID vaccine and either a SC or IM vaccine, two different reusable devices and associated consumables would have to be supplied. (Similar to the current situation of supplying different kinds of AD N&S for ID and SC/IM vaccines.)
- Like other injection devices, DSJIs are unlikely to be suitable for house-to-house delivery scenarios (13).

2.3 Additional important information:

- Clinical trial data has been generated demonstrating the safety and immunogenicity of vaccine delivery with DSJIs, including MMR (2), inactivated poliovirus (3, 5), BCG (4), HPV (9), and influenza vaccines (1,7), as well as vaccines in development for dengue (6) and Zika (8).
- Due to the method of injection, DSJI delivery often results in more local injection site reactions than N&S injection, including pain, redness, and swelling after injection. Although vaccine administration with DSJI has been reported to be less painful than AD N&S injection (see Section 2.4 below).
    - For unadjuvanted vaccines, these reactions are generally transient, mild, and well-tolerated (1,14). A phase III study in 1,250 subjects evaluating influenza vaccine delivered by IM injection of SC/IM DSJI (Stratis) reported significantly ($p < 0.001$) more pain, tenderness, itching and redness up to 6 days after vaccination by DSJI compared with needle and syringe, although the delivery method was regarded as acceptable (1). Similar findings were reported in a smaller, more recent study with a different DSJI. The jet injector was associated with significantly more pain and local redness and swelling. At day 21, 56% of those in the DSJI group said that they would prefer to receive vaccines by jet injection in the future (7).
    - DSJI delivery of reactogenic vaccines, such as those with adjuvant, increases local reactions (15). Depending on the vaccine and the recipient population, this may be unacceptable and/or pose a safety risk.
- The SAGE Polio Working Group reviewed evidence for use of the PharmaJet Tropis ID DSJI for fractional-dose IPV delivery and suggested “it will be important to gather well-documented implementation experience both in routine and campaign settings to guide future policy”, and “emphasised that the performance and pre-qualification of Tropis device was an exciting development which could have applicability to other antigens” (16).
- DSJIs have been found to often obtain more doses per multidose vial than a N&S, due to reduced wastage by vaccinators during the filling process (11).
- DSJIs are more costly than AD N&S. The increased costs per dose are accentuated in low-throughput use scenarios, as the cost of the reusable injector cannot be spread across as many recipients.
- HCWs require specific training on use of the device to provide injections (11,17).

- Several DSJIs have device regulatory clearance and two models are prequalified by WHO. Several countries have introduced DSJIs on the basis of device clearance and available clinical data. However, some countries require that vaccines be individually relabelled for DSJI delivery, which involves submission of data to the National Regulatory Authority from non-inferiority-based clinical trials by the vaccine manufacturer and can be a barrier to introduction of this technology.

2.4 Evidence

- In a WHO pilot using the PharmaJet Stratis device (IM/SC) to deliver measles vaccine in a campaign in Cambodia, 92% of the 5-9 year old vaccine recipients said that DSJI delivery was less painful than needle and syringe injection. 97% of parents also preferred DSJI delivery, as did 100% of the vaccinators (12).
- In clinical trials of various vaccines in infants, reduced rates of crying and increased acceptability among parents has been observed for vaccination with DSJI compared to N&S injection (primarily for ID delivery of IPV (3,18), but also for SC delivery of MMR (19) and IM delivery of IPV (3) using DSJI), while other studies found similar rates of crying following SC delivery of MMR (2) and IM delivery of pentavalent DTwP-Hib-HebP vaccine (15) for DSJI injection compared to N&S.
- In a clinical study of IPV delivered in adults, fewer vaccinees reported pain on injection with both IM and ID DSJI than IM N&S (20).
- In other studies of IM delivery of influenza vaccine in adults, DSJI delivery was associated with higher pain scores (14). One clinical study of influenza vaccine delivery in adults blinded vaccine recipients to the sight, sound, or touch of the DSJI device. A greater percentage of IM N&S delivery (73% vs 60%) rated the injection experience as “excellent” but this was not statistically significant. (The remainder of both groups rated the experience “acceptable”) (21).
- Post-market surveys conducted by PharmaJet of recipients of IM influenza vaccine with the Stratis DSJI in retail pharmacies, university and corporate flu clinics, and public health flu campaigns in the US found that 93% preferred the DSJI injection and would choose to have it for their next influenza vaccination (22).

Category: *Delivery technology (not pre-filled)*

Innovation: *Disposable syringe jet injectors (DSJIs)*

Comparators: *SC/IM DSJI subtype is compared with AD N&S;*

ID DSJI subtype is compared with BCG AD N&S

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	SC/IM Sub-type	ID Sub-type	Assessment
	Does the innovation have features that may improve heat stability?	Neutral	Neutral	The innovation is a delivery device and does not impact the heat stability of the vaccine.

SC/IM	*ID*	***No difference** for both subtypes*

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	SC/IM Sub-type	ID Sub-type	Assessment
	Does the innovation have features that may improve freeze resistance?	Neutral	Neutral	The innovation is a delivery device and does not impact the freeze resistance of the vaccine.

SC/IM	*ID*	***No difference** for both subtypes*

VIPS is a Vaccine Alliance project from Gavi, World Health Organization, Bill & Melinda Gates Foundation, PATH and UNICEF

Category: *Delivery technology (not pre-filled)*

Innovation: *Disposable syringe jet injectors (DSJIs)*

Comparators: *SC/IM DSJI subtype is compared with AD N&S;*

ID DSJI subtype is compared with BCG AD N&S

3.2 Coverage and equity criteria

Indicator: Ease of use[b]

*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 • *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)* • *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)*	**Parameters to measure against a comparator**	**SC/IM Sub-type**	**ID Sub-type**	**Assessment**
	Does the innovation avoid reconstitution and is that an improvement?	Neutral	Neutral	A DSJI does not impact the reconstitution procedure for the vaccine, similar to an AD N&S.
	Does the innovation require fewer vaccine product components?	Worse	Worse	A DSJI consists of a reusable injector/reset station, a filling adapter (one per vial), and a needle-free syringe (one per injection), in addition to a reconstitution N&S if needed for the vaccine. There are more components than for vaccine delivery with an AD N&S.
	[c]Does the innovation require additional components or equipment (such as scanners or label readers)?	N/A	N/A	
	Does the innovation require fewer preparation steps and less complex preparation steps?	Worse	Worse	A DSJI requires more steps for preparation of a dose, including resetting the reusable injector and insertion of the vial adapter into the vial.

[b] 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).

[c] This parameter is only assessed for RFID/barcodes, for all other innovations it is not applicable (N/A).

Category: *Delivery technology (not pre-filled)*

Innovation: *Disposable syringe jet injectors (DSJIs)*

Comparators: *SC/IM DSJI subtype is compared with AD N&S;*
ID DSJI subtype is compared with BCG AD N&S

Ease of use • *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)* • *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)*	**Parameters to measure against a comparator**	**SC/IM Sub-type**	**ID Sub-type**	**Assessment**
	Does the innovation improve dose control?	Better	Better	The currently prequalified fixed-dose DSJIs automatically set the dose drawn into the needle-free syringe, reducing the likelihood of an inaccurate dose volume. The user must slightly overfill the syringe in order to remove the filling tab. Inserting the filled syringe into the reusable injector sets the dose and returns overfill to the vial, minimizing vaccine wastage. However, the user must still visually observe and manually remove air bubbles to ensure a complete dose is delivered, similar to an AD N&S.
	Does the innovation improve targeting the right route of administration?	Neutral	Neutral	Targeting the correct depth of injection with a DSJI is dependent on user technique, similar to an AD N&S. DSJIs have been proposed to increase reliability of targeting the ID depth, compared to N&S injection, but data has been mixed (23,24).

SC/IM	*ID*	***Mixed*** *for both subtypes*

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Category: *Delivery technology (not pre-filled)*

Innovation: *Disposable syringe jet injectors (DSJIs)*

Comparators: *SC/IM DSJI subtype is compared with AD N&S;*

ID DSJI subtype is compared with BCG AD N&S

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.*

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 • *Assessment of the potential to reduce stock outs based on the innovation's features*	**Parameters to measure against a comparator**	**SC/IM Sub-type**	**ID Sub-type**	**Assessment**
	Does the innovation require fewer components?	Worse	Worse	A DSJI consists of a reusable injector or handpiece, a filling adapter (one per vial), and a needle-free syringe (one per injection), in addition to a reconstitution N&S if needed for the vaccine. Some DSJIs also require a separate reset station for resetting the spring, or access to compressed gas (see table 4). There are more components than for vaccine delivery with an AD N&S.
	Or does the innovation include labelling that facilitates product tracking and is it better than the comparator?	Neutral	Neutral	A DSJI does not impact product labelling.

SC/IM	*ID*	***Worse** for both subtypes*

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: *Delivery technology (not pre-filled)*

Innovation: *Disposable syringe jet injectors (DSJIs)*

Comparators: *SC/IM DSJI subtype is compared with AD N&S;*
ID DSJI subtype is compared with BCG AD N&S

Table 6.

Acceptability of the vaccine presentation to patients/ caregivers • *Does the innovation include features that may improve acceptability of vaccinees and caregivers*	**Parameters to measure against a comparator**	**SC/IM Sub-type**	**ID Sub-type**	**Assessment**
	Painful or not painful	Neutral	Better	Surveys of vaccine recipients have generally indicated reduced pain at the time of injection for DSJIs compared to N&S, but not always (12,14,20,21). In vaccine clinical studies in infants, delivery by DSJI has resulted in similar or less crying after injection than N&S delivery (2,3,15,18,19). Pain reduction is consistently observed for ID DSJI delivery. There are some studies with heterogenous data for SC/IM DSJI injection whereby pain of injection was observed to be less, others with no difference, and some for which pain was reported to be higher than N&S injection. This is therefore scored as neutral. In future analysis, pain of injection, as well as the risk of local site AEs occurring after injection, would need to be reviewed in a vaccine-specific and population-specific manner.
	Perception of ease of administration (i.e. convenience for the vaccinees/caregivers)	Better	Better	Surveys of caregivers and vaccinees have demonstrated significant preference for DSJIs compared to N&S, due to reduced needle-phobia, crying, and speed of delivery (12,18,19,22).
	Any other tangible benefit to improve/impact acceptability to vaccinees/caregivers	N/A	N/A	

SC/IM	*ID*	***Better*** *for SC/IM subtype* ***Considerably better*** *for ID subtype*

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 • *Risk assessment of potential for contamination based on design of innovation and on usability data from field studies*	**Parameters to measure against a comparator**	**SC/IM Sub-type**	**ID Sub-type**	**Assessment**
	Does the innovation reduce the risk of contamination while reconstituting the dry vaccine?	Neutral	Neutral	A DSJI has no impact on the reconstitution process, similar to an AD N&S.
	Does the innovation reduce the risk of contamination while filling the delivery device?	Neutral	Neutral	For a single dose vial, contamination risk during filling is likely to be similar. If multidose vials are used, contamination risk may potentially increase if the open vial with attached vial adapter is not properly handled and stored. (Storage recommendations are to insert a new, clean DSJI syringe into the vial adapter to block the open channel.)
	Does the innovation require fewer preparation steps and less complex preparation steps?	Worse	Worse	A DSJI requires more steps for preparation of a dose, as the filling adapter must first be inserted into the vial, followed by attachment of the needle-free syringe. The additional handling step could increase the chance of contamination occurring during preparation, though this risk is anticipated to be small.

Category: *Delivery technology (not pre-filled)*

Innovation: *Disposable syringe jet injectors (DSJIs)*

Comparators: *SC/IM DSJI subtype is compared with AD N&S;*
ID DSJI subtype is compared with BCG AD N&S

Likelihood of contamination • *Risk assessment of potential for contamination based on design of innovation and on usability data from field studies*	**Parameters to measure against a comparator**	**SC/IM Sub-type**	**ID Sub-type**	**Assessment**
	Does the innovation reduce the potential risk of reuse of delivery technology?	Neutral	Neutral	A DSJI has an autodisable feature on the needle-free syringe, so the risk of reuse is similar to an AD N&S.
	Does the innovation reduce the risk of use of nonsterile components?	Worse	Worse	The filling adapter is intended to be used on a single vial, but could be reused which would increase risks of contamination.

SC/IM	*ID*	***Worse*** *for both subtypes*

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.*

Table 8.

Likelihood of needle stick injury • *Risk assessment of the presence of sharps during the process of preparing and administering the vaccine*	**Parameters to measure against a comparator**	**SC/IM Sub-type**	**ID Sub-type**	**Assessment**
	Does the innovation contain fewer sharps?	Better	Better	A DSJI eliminates the needle for vaccine injection.
	Does the innovation use sharps for preparing and/or administering the vaccine and is that better than the comparator?	Better	Better	If a vaccine requires reconstitution, a reuse prevention (RUP) N&S will still be required for preparing the vaccine. A DSJI eliminates sharps for vaccine injection.

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Likelihood of needle stick injury • *Risk assessment of the presence of sharps during the process of preparing and administering the vaccine*	**Parameters to measure against a comparator**	**SC/IM Sub-type**	**ID Sub-type**	**Assessment**
	Does the innovation include an auto disable feature and is that better than the comparator?	Neutral	Neutral	A DSJI needle-free syringe has an autodisable feature, similar to an AD N&S.
	If the innovation uses sharps, does it include a sharps injury prevention feature and is that better than the comparator?	Better	Better	A DSJI device is sharps-free and a SIP feature would not be required unlike the comparator which is an injectable, but does not include a SIP feature.
	Does the innovation reduce the risk of injury after vaccine administration?	Better	Better	A DSJI has no sharps, so there is no risk of injury to the vaccine recipient, HCW, or community with a used sharp after vaccine administration.

SC/IM	*ID*	***Better*** *for both subtypes*

3.4 Economic costs criteria

Indicator: Total economic cost of storage and transportation of commodities per dose[d]

*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.*

[d] 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: *Delivery technology (not pre-filled)*

Innovation: *Disposable syringe jet injectors (DSJIs)*

Comparators: *SC/IM DSJI subtype is compared with AD N&S;*
ID DSJI subtype is compared with BCG AD N&S

Table 9.

	Parameters to measure against a comparator	SC/IM Sub-type	ID Sub-type	Assessment
Total economic cost of storage and transportation of commodities per dose	**Does the innovation reduce the volume per dose stored and transported in the cold chain?**	Neutral	Neutral	DSJI delivery has no impact on the volume of vaccine stored in the cold chain because the same vaccine vial is still used whether using a DSJI or AD N&S.
	Does the innovation reduce the volume per dose stored and transported out of the cold chain?	Worse	Worse	DSJI needle-free, custom syringes are smaller than an AD N&S. However, since DSJI delivery also requires a filling adapter (one per vial) and a reusable injector device, the total volume per dose stored out of the cold chain is increased for the DSJI compared to an AD N&S/BCG AD N&S when single dose vials are used. The volume for the reusable injector device is shared among multiple doses and so is a very small volume per dose. It should be noted that the scoring is based on SDV as the comparator. However, DSJIs are most likely to be used with MDV. In this more realistic scenario of use, the total volume per dose is lower compared to AD N&S when multi-dose vials are used, as only one filling adapter is used per vial and its volume is shared among multiple doses.

SC/IM	*ID*	***Worse** for both subtypes*

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 10.

Total economic cost of the time spent by staff per dose	Parameters to measure against a comparator	SC/IM Sub-type	ID Sub-type	Assessment
	Does the innovation have attributes that can save time for the vaccinator in preparing and administering the vaccine?	Neutral	Better	A DSJI requires more steps for preparation of a dose but may reduce the actual administration time in high-throughput settings than when using an AD N&S. In ID injection campaign delivery studies in Pakistan and the Gambia, DSJIs have been found to reduce the time required for vaccination (11). An IM influenza vaccine campaign mock-use study in the US found that delivery time was similar to IM N&S (17). Delivery time was also reported to be similar in a measles vaccine campaign in Cambodia (12). However, DSJIs have been found to increase time in lower-throughput scenarios, such as clinical trials, compared to administration with an AD N&S (3,7). Overall, we assume that DSJIs may save time for vaccinators when administering ID injections and will be neutral for IM/SC injections compared to when using an AD N&S.
	[e]Does the innovation have attributes that save time for staff involved in stock management?	Neutral	Neutral	A DSJI does not have any attributes that save time for staff involved in stock management.

SC/IM	*ID*	***No difference*** *for SC/IM subtype* ***Better*** *for ID subtype*

[e] 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: *Delivery technology (not pre-filled)*

Innovation: *Disposable syringe jet injectors (DSJIs)*

Comparators: *SC/IM DSJI subtype is compared with AD N&S;*

ID DSJI subtype is compared with BCG AD N&S

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.*

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**	**SC/IM Sub-type**	**ID Sub-type**	**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	Neutral	There are no additional upfront or recurrent cost associated with the DSJI. The costs of the DSJI device (the innovation) would be captured in the commodity costs in phase 2. Also, as with any innovation, vaccinators would need to be trained on how to use the device. Note that we are not including commodity or training costs as part of the assessment in this phase.

SC/IM	*ID*	***No difference*** *for both subtypes*

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 • *What vaccines/antigens does the innovation apply to, based on technical feasibility?*	**Assessment**
	This innovation is most likely to be suitable for delivery of vaccines that do not contain reactogenic components, such as adjuvants. Reactogenic components increase local reactions, which may be unacceptable and/or pose a safety risk depending on the target population. DSJIs may also increase immunogenicity of nucleic acid vaccine candidates. Examples of VIPS priority antigens that would be well-suited for DSJI (SC/IM) delivery include MR and yellow fever. Serum Institute of India's MMR vaccine (Tresivac-NF) is labelled for delivery with DSJI (25). Examples of VIPS priority antigens that would be well-suited for DSJI (ID) delivery include IPV, and rabies. For IPV a fractional dose delivered ID can stretch the vaccine supply through dose-sparing strategies during vaccine shortages. DSJIs may also increase immunogenicity of nucleic acid vaccine candidates.

Indicator: Ability of the technology to facilitate vaccine combination

Table 13.

Ability of the technology to facilitate novel vaccine combination • *Does the innovation facilitate novel combination vaccine products?*	**Assessment**
	A DSJI does not impact the ability to combine vaccines.

SECTION 4

4.1 Robustness of data:

Table 14.

Category	Assessment
Type of study	Non-inferiority clinical trials; small-scale pilot introduction studies; post-market surveys.
Inconsistency of results	Moderate. There is some variability between studies regarding pain and local reactogenicity of DSJIs relative to the comparator, even when comparing DSJIs delivering to the same depth of administration.
Indirectness of comparison • *Indicate the setting in which the study was conducted (low, middle or high income setting);* • *Comment if the data is on non-vaccine application of the innovation*	Studies have been conducted with DSJIs on vaccine delivery in LMICs and HICs, including Brazil, Cambodia, Canada, the Gambia, India, the Netherlands, Pakistan, South Africa, and the United States.

Overall assessment:	*Moderate*	

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

Table 15.

Expert/type	Organisation/contact details	Notes
NA	NA	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 (TN):

Table 16.

Reviewers	Organisation/contact details	Notes
Courtney Jarrahian	PATH cjarrahian@path.org	Developed and reviewed TN
PATH Medical Device and Health Technology Team Debra Kristensen Courtney Jarrahian Mercy Mvundura Collrane Frivold	PATH Debra Kristensen dkristensen@path.org	Reviewed TN
Fatema Kazi	GAVI, the Vaccine Alliance fkazi-external-consultant@Gavi.org	Reviewed TN
Julian Hickling	Working in Tandem Ltd julian@workingintandem.co.uk	Reviewed TN

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Peer-reviewed publications of primary data, systematic reviews, other reports:

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