

Microarray patches (MAP)

Comparators* : Single dose vial (liquid) and autodisable (AD) needle and syringe (N&S);
SDV + diluent + reuse prevention (RUP) reconstitution N&S and AD N&S

Section 1: Summary of innovation

1.1 Example images:



Image source: ^a



Image source: ^b



Image source: ^c

1.2. Description of innovation:

MAPs consist of an array of hundreds or thousands of micro-projections on a 'patch'. The projections are coated with, or composed of, vaccine in a dry formulation. When applied to the skin, the vaccine is delivered into the dermis and/or epidermis, which are rich in antigen presenting cell (APCs).

Several different formats of MAPs are being developed:

- With, or without, applicators; when present, the applicator can be a separate component or integrated with the MAP. The most advanced MAPs in development either have no applicator or an integrated applicator. **Therefore, MAPs with a separate applicator are not considered in this assessment;**
- Solid micro-projections coated with vaccine;
- Micro-projections formed of vaccine plus biocompatible excipients that dissolve or biodegrade in the skin;
- Hydrogel micro-projections that swell in the skin and act as a conduit for diffusion of the active ingredient from a backing layer (primarily in development for drug delivery).

In theory, MAPs could be used for administration of any type of vaccine, although there might be some vaccine-specific limitations: it might not be possible to formulate some vaccines so that they remain potent during the manufacture or storage of MAPs; some vaccines (in particular those formulated with an adjuvant) might have unacceptable levels of local reactogenicity when delivered into the skin; and in some cases, MAPs might not have the payload capacity for the vaccine plus necessary excipients, or it might not be possible to concentrate the antigen sufficiently so that it can be loaded onto the MAP.

* 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.

^a Image provided by David Hoey, Vaxxas, 15 May 2019

^b <http://micronbiomedical.com/technology/>

^c https://www.who.int/immunization/research/meetings_workshops/PDVAC_2017_Delivery_Tech_Update_Zehrung_PATH.pdf?ua=1

VIPS TECHNICAL NOTE

Category: Integrated primary container and delivery technology

Innovation: Microarray patches (MAP)


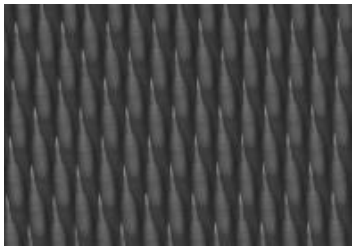
Comparators: SDV (liquid) and AD N&S;

SDV + diluent + RUP reconstitution N&S and AD N&S



1.3 Examples of innovations and developers:

Table 1.

Product name; Image	Developer (place); website	Brief description, notes
Solid, coated MAPs		
<p>Nanopatch™</p>  <p>Image source: ^a</p>  <p>Image source: (1)</p>	<p>Vaxxas, Brisbane, QLD, Australia. (1)</p>	<p>The Nanopatch consists of a puck-shaped device, containing the MAP and integrated, spring-powered applicator. The MAP is a high-density array of polymer microprojections (thousands per cm²) that are coated with vaccine. The device is applied to the skin, the applicator is pressed and the device and MAP are left in position for a period of time (currently 2 minutes, but the target is 10 seconds) before removal. ^d</p> <p>Clinical studies:</p> <ul style="list-style-type: none"> • Acceptability study, no vaccine (2) • First time in humans, monovalent influenza vaccine (1) • Phase I study, monovalent influenza vaccine (manuscript in preparation). ^{e, d}
Dissolving MAPs		
<p>No product name</p>	<p>Fujifilm, Tokyo, Japan. www.fujifilm.com</p>	<p>The array consists of microneedles 100 to 2,000 μm long, composed of polysaccharides and the active ingredient. The projections dissolve within several minutes after piercing the skin, ^f</p>

^d David Hoey, Vaxxas, personal communication, 15 May 2019

^e Tom Lake, Vaxxas, Presentation at World Vaccine Congress, 14-16 April 2019,

^f <https://www.fujifilm.com/innovation/technologies/delivery-of-solids-or-liquids/>

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Product name; Image	Developer (place); website	Brief description, notes
No product name	JuVIC Biotech , Seoul, Korea. http://juvicbio.com/	
MicroCor™  Image source: ^g	Corium , Menlo Park, CA, USA. http://www.coriumintl.com	The device consists of an integrated applicator and an array of projections, the tips of which are formed from the vaccine plus excipients that are biodegradable and dissolve in the skin after application. The wear-time for the device is < 5 minutes. ^g No clinical studies with vaccines have been published. Corium's lead MicrCor product is being developed to deliver teriparatide to treat osteoporosis. This has completed a phase 2a trial. ^h
MicroHyla™  Image source: (3)	Cosmed , Kyoto, Japan. http://cosmed-pharm.co.jp	The MAP consists of 200 microprojections (800 µm long) consisting of antigen and hyalauronic acid, mounted on a film backing. After application to the skin (either by finger pressure or separate applicator), the projections dissolve, releasing antigen (3,4) Clinical studies: <ul style="list-style-type: none"> • Phase I, trivalent influenza vaccine (4)
No product name	Micron Biomedical , Atlanta, GA, USA. http://micronbiomedical.com	"Peel-and-stick" patch resembling a bandaid. No applicator. The array consists of 100 microprojections, 650 µm tall, mounted on an adhesive backing. After application the

^g <http://www.coriumintl.com/home/technology/microcor/>

^h <http://www.coriumintl.com/home/technology/microcor/>

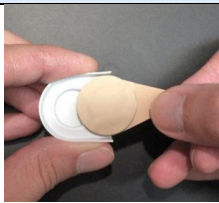

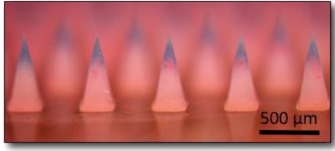
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Product name; Image	Developer (place); website	Brief description, notes
 <p>Image source: ^b</p>		<p>microprojections containing the active ingredient dissolve into the skin during the 20 minute wear time. (5) ^b</p> <p>Clinical studies:</p> <ul style="list-style-type: none"> • Acceptability study, no vaccine (6) • Phase I, trivalent influenza vaccine (5)
<p>Mimix™</p>  <p>Image source: ⁱ</p>  <p>Image source: ^c</p>	<p>Vaxess, Boston, MA, USA. http://vaxess.com</p>	<p>Band-aid-like device. No applicator. The microprojections contain the active ingredient and silk fibroin to provide structural strength and thermostability. After removal of the backing, the vaccine is released slowly from the application site which is thought to increase the immune response to the antigens. ^j No clinical studies with vaccines have been published.</p>
<p>VaxMAT™</p>	<p>Theraject, Fremont, CA, USA. http://www.theraject.com</p>	

ⁱ <http://vaxess.com>

^j <http://vaxess.com/technology/>

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SECTION 2: Summary of assessment for prioritisation

2.1 Key benefits

As an innovation type, MAPs offer several **potential** benefits reviewed in (7).

- **Ease of use:** MAPs could be suitable for use by minimally trained healthcare workers (HCWs) or even for self-administration;
- **Needle/sharps-free** administration;
- **Avoidance of reconstitution** of lyophilized vaccines, reducing the risk of errors or contamination;
- **Single-dose** presentation;
- **Combining vaccines** that would otherwise not be able to be formulated together as a liquid vaccine by incorporating them into different areas of the MAP.
- **High recipient acceptability:** including low pain on delivery.
- **Resistance to heat exposure and/or freeze-damage:** MAPs might be able to be stored and distributed outside the cold-chain, or in a controlled temperature chain (CTC). This will be vaccine- and formulation- dependent.
- **Improved vaccination coverage** if MAPs are thermostable, suitable for use in most immunization settings, or avoid 'missed opportunities' by virtue of being a single-dose presentation.

2.2 Key challenges:

- Some MAPs have a significantly **larger volume per unit** (or per dose) than SDV and N&S, particular if the device has an integrated applicator. This could be a problem if they need to be stored or distributed in the cold-chain.
- There is some uncertainty regarding which vaccines can be used with MAPs, due to:
 - **Stability:** Some antigens may be difficult to stabilize on a MAP.
 - **Immunogenicity:** Some antigens may not produce an equivalent immune response in humans when delivered by MAPs.
 - **Payload constraints:** The volume that can be loaded onto a MAP is small (for some technologies, $\leq 20 \mu\text{l}$, compared with $500 \mu\text{l}$ for typical intramuscular (IM) or subcutaneous (SC) injection) (13,14); therefore, the bulk antigen has to be at a high concentration and this can limit the amount of antigen that can be loaded;
 - **Local reactogenicity** at the application site: Clinical studies have observed minor local reactions lasting several days following application; these were generally found to be acceptable (8,9). It is possible that inclusion of adjuvants, if they are needed, might result in unacceptable levels of local reactogenicity (15). Only **limited clinical data** are available, and more safety and reactogenicity data are needed in different ages and ethnic groups.

2.3 Additional important information:

- **Possibility of improved immunogenicity**
 - Based on preclinical data, it is possible that fewer doses and/or less antigen per dose may be required for some antigens and MAP designs to provide immune responses similar to parenteral injection (8–12) Currently, there are no published clinical data on dose-sparing

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with MAPs, although one trial evaluating dose-sparing in the clinic has been completed and a manuscript is in preparation.

- Some MAP formats might be compatible with sustained- or pulsatile release formulations (11,12)
- MAPs are likely to cost more per unit than SDV + AD N&S when first introduced and possibly when manufactured at scale. **There might, however, be savings at the systems level** if MAPs do not require the cold chain, and/or improve vaccine coverage and/or reduce vaccine wastage.
- As combination products, **each vaccine MAP product needs to be licensed** individually.
- Vaccines will **need to be (re-)formulated** for use with a MAP and adjuvants may need to be removed.
- MAPs for vaccines are at a relatively **early stage of development**. Several phase I trials have been completed for influenza vaccine, but significant obstacles need to be overcome before MAPs can be licensed and widely implemented;
- The **manufacturing processes** for MAPs are novel and MAP-specific. Significant investment will be needed to scale up manufacturing for phase III trials and commercial use;
- There is uncertainty regarding whether aseptic manufacturing will be required for MAPs or whether a low bio-burden process will be sufficient. Aseptic manufacturing is the conservative approach but will be more expensive.
- **Commercial credibility and viability:** Developers will need to produce MAPs for commercially viable markets in high-income countries (HICs), to support development of MAP–vaccine combinations of interest to low- and middle-income countries (LMICs);

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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	Liquid comparator	Lyophilised comparator	Assessment
	Does the innovation have features that may improve heat stability?	Better	Better	Solid coated and dissolving MAPs require reformulation of the vaccine into a dry state. This offers the opportunity to improve the thermostability of the vaccine but does not guarantee it. Whether or not the MAP-formulated vaccine can withstand heat exposure will be vaccine specific. Encouraging results have been obtained with MR vaccine (16) and influenza vaccine (17). In a study with MR vaccine (16) MAP formulated vaccine showed no loss of titre after storage at 40°C for 28 days, which is at least stable as published data with existing lyophilised formulations (18). In one trial, influenza-loaded dissolving MAPs were found to remain within product specifications following storage at 5°C, 25°C or 40°C for 12 months (5). In contrast, developing dried thermostable formulations of IPV, particularly IPV3 has proved to be more challenging for MAPs and other stabilization approaches (19–21)

Liquid	Lyophilised	Better than both the liquid and lyophilised comparators
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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	Liquid comparator	Lyophilised comparator	Assessment
	Does the innovation have features that may improve freeze resistance?	Better	Neutral	The need to develop new formulations of vaccines for use with MAPs also provides an opportunity to improve resistance to damage by freezing. It is likely that dry vaccine formulations will be more resistant to freeze-damage than liquid vaccines, because of their low moisture content. At least one antigen, formulated for use with a MAP has been shown to survive repeated freeze-thaw cycles (17).

Liquid	Lyophilised	Better than the liquid comparator Neutral to the lyophilized comparator
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3.2 Coverage and equity criteria

Indicator: Ease of use^k

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.

^k 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).

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Table 4.

Ease of use	Parameters to measure against a comparator	Liquid comparator	Lyophilised comparator	Assessment
<ul style="list-style-type: none"> • 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) 	<p>Does the innovation avoid reconstitution and is that an improvement?</p>	Neutral	Better	<p>No reconstitution is needed with MAPs or liquid vaccines.</p> <p>However, reconstitution is needed with the lyophilised comparator, so MAPs measure better for this parameter.</p>
	<p>Does the innovation require fewer vaccine product components?</p>	Better	Better	<p>MAPs with integrated or no applicators will have fewer component than are needed for liquid or lyophilised vaccines.</p>
	<p>Does the innovation require additional components or equipment (such as scanners or label readers)?</p>	N/A	N/A	
	<p>Does the innovation require fewer preparation steps and less complex preparation steps?</p>	Better	Better	<p>MAPs with integrated or no applicators, will have fewer and less complex preparation steps than liquid or lyophilised vaccines,</p> <p>For both types of MAPs, a film or covering needs to be peeled back, the MAP is applied to the skin and pressed, it is left in place for a defined period (usually minutes), then removed and discarded.</p>

¹ This parameter is only assessed for RFID/barcodes, for all other innovations it is not applicable (N/A).

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Ease of use	Parameters to measure against a comparator	Liquid comparator	Lyophilised comparator	Assessment
<ul style="list-style-type: none"> 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) 	Does the innovation improve dose control?	Better	Better	<p>As MAP is prefilled, it potentially avoids any error that may be associated with withdrawing a dose.</p> <p>MAPs must be applied with sufficient pressure to penetrate the skin and worn for a certain period of time, e.g., 10 seconds^m, 2 minutes (1), 20 minutes (5), 6 hours (4), for delivery of the full dose into the skin, otherwise an insufficient dose may be delivered.</p>
	Does the innovation improve targeting the right route of administration?	Better	Better	<p>By design, MAPs cannot penetrate beyond the intradermal layer due to the length of the microprojections. However, AD N&S can deliver vaccines to too shallow a depth, or potentially too deep.</p>

Liquid	Lyophilised	Better than both the liquid and lyophilised comparators
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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.

^m Vaxxas, unpublished data. David Hoey, personal communication 17 May 2019.

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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	Liquid comparator	Lyophilised comparator	Assessment
<ul style="list-style-type: none"> Assessment of the potential to reduce stock outs based on the innovation's features 	Does the innovation require fewer components?	Better	Better	A MAP would have fewer components compared with liquid and lyophilised vaccines. Currently, MAPs most advanced in development have no applicator or an integrated applicator.
	Or does the innovation include labelling that facilitates product tracking and is it better than the comparator?	Neutral	Neutral	MAP packaging will incorporate all required labelling, similar to the comparator, but will not have additional 'inherent' features that facilitate tracking.

Liquid	Lyophilised	Better than both the liquid and lyophilised comparators
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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.

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Table 6.

Acceptability of the vaccine presentation to patients/caregivers	Parameters to measure against a comparator	Liquid comparator	Lyophilised comparator	Assessment
• Does the innovation include features that may improve acceptability of vaccinees and caregivers	Painful or not painful	Better	Better	MAP projections do not reach nerve endings in the skin and clinical studies have found that application is less painful than N&S and more acceptable to recipients (1).
	Perception of ease of administration (i.e. convenience for the vaccinees/caregivers)	Better	Better	In vaccine MAP clinical studies, acceptability scores were similar for MAPs and IM, but overall most subjects preferred MAPs to IM injection (1,2,6). 81–98% caretakers would accept MAPs for vaccination as demonstrated in usability study in Benin, Nepal, Vietnam (22). These results do not necessarily relate just to perception of ease of administration, but overall acceptability. If MAPs require a long wear time, this could be viewed by patients/caregivers as inconvenient.
	Any other tangible benefit to improve/impact acceptability to vaccinees/caregivers	Better	Better	Most MAPs are expected to be suitable for self-administration if required (e.g. outbreak response) (6).

Liquid	Lyophilised	Considerably better than both the liquid and lyophilized comparators
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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.

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Table 7.

Likelihood of contamination	Parameters to measure against a comparator	Liquid comparator	Lyophilised comparator	Assessment
<ul style="list-style-type: none"> Risk assessment of potential for contamination based on design of innovation and on usability data from field studies 	<p>Does the innovation reduce the risk of contamination while reconstituting the dry vaccine?</p>	Neutral	Better	<p>No reconstitution is needed with MAPs or liquid vaccines. However, reconstitution is needed with the lyophilised comparator, so MAPs measure better for this parameter.</p>
	<p>Does the innovation reduce the risk of contamination while filling the delivery device?</p>	Better	Better	<p>MAPs do not require filling of a delivery device, which minimizes the contamination risk. However, MAPs could be contaminated by the user touching the microprojections before application.</p>
	<p>Does the innovation require fewer preparation steps and less complex preparation steps?</p>	Better	Better	<p>MAPs are likely to require fewer steps than AD N&S and SDV.</p>
	<p>Does the innovation reduce the potential risk of reuse of delivery technology?</p>	Neutral	Neutral	<p>Dependent on the design, MAPs may be re-applied, but in general the safety risks associated with reuse are expected to be low. Some MAP designs will be AD, to prevent re-use.</p>
	<p>Does the innovation reduce the risk of use of nonsterile components?</p>	Neutral	Neutral	<p>MAPs do not include the use of nonsterile components.</p> <p>It has been suggested that MAPs could be manufactured under low bio-burden rather than aseptic conditions. However, this approach will only be acceptable to regulatory authorities once sufficient data have been generated to show that this is safe. Therefore, the overall risk has been assessed to be neutral relative to the comparator.</p>

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Liquid	Lyophilised	Better than both the liquid and lyophilised comparators
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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	Parameters to measure against a comparator	Liquid comparator	Lyophilised comparator	Assessment
<ul style="list-style-type: none"> Risk assessment of the presence of sharps during the process of preparing and administering the vaccine 	Does the innovation contain fewer sharps?	Better	Better	<p>In response to a stakeholder survey, including members of WHO’s Immunization Practices Advisory Committee, the assumption is that MAPs will be considered biohazard waste that can be disposed of within the clinical waste system. Suggesting, a MAP would not contain sharps.</p> <p>There is a risk with solid-coated MAPs that they could be contaminated with, and transfer, bodily fluids or tissues from the vaccinee, after they have been removed. As such, solid coated MAPs might be regarded as medical sharps waste after use. However, this has not been determined.^{n,o} Some MAPs require an applicator to generate the force required to penetrate the skin (2). Therefore, transfer of infections is likely to be possible through open wounds only.</p>

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Likelihood of needle stick injury	Parameters to measure against a comparator	Liquid comparator	Lyophilised comparator	Assessment
<ul style="list-style-type: none"> Risk assessment of the presence of sharps during the process of preparing and administering the vaccine 	Does the innovation use sharps for preparing and/or administering the vaccine and is that better than the comparator?	Better	Better	Same as above
	Does the innovation include an auto disable feature and is that better than the comparator?	Neutral	Neutral	Some MAP designs incorporate a feature to prevent reuse.
	If the innovation uses sharps, does it include a sharps injury prevention feature and is that better than the comparator?	Better	Better	Refer to top row above for explanation. Since MAPs are sharps-free a SIP feature would not be indicated.
	Does the innovation reduce the risk of injury after vaccine administration?	Better	Better	Most MAP designs do not pose a risk of injury after they have been used. Dissolving microneedles will remain in the vaccine, and solid microneedles require an applicator to generate sufficient force for penetration (2).

Liquid	Lyophilised	Better than both the liquid and lyophilised comparators
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3.4 Economic costs criteria

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

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	Liquid comparator	Lyophilised comparator	Assessment
	Does the innovation reduce the volume per dose stored and transported in the cold chain?	Worse	Worse	<p>The volume of MAPs will vary between different formats (e.g. without an applicator or with an integrated applicator) and the design of the packaging to protect the MAP from the environmental and mechanical damage.</p> <p>Vaccine Technologies Impact Assessment (VTIA) modelling by PATH used a range of volumes informed by various developers' prototype MAP designs: 5, 10 and 25 cm³ (PATH 2018). This can be compared with the volume of a SDV for Quivaxem vaccine of 10 cm³ per dose^p or measles vaccine of 21.09cm³ per dose^q. This input will need to be updated on developer and vaccine-specific basis.</p> <p>We assume that MAPs may be similar in size or larger than a SDV, especially if they have an applicator. So, if the MAP must be stored in the cold chain at any point, the volume stored in the cold chain would increase compared to a SDV.</p> <p>For some vaccines, MAPs may be more thermostable and enable storage in a CTC. Thermostability, and therefore dependence on the cold-chain, is likely to be vaccine specific.</p> <p>Encouraging data for extended CTC storage conditions (months) have been obtained with MR vaccine(16), and influenza vaccine(17). In</p>

^p https://extranet.who.int/gavi/PQ_Web/PreviewVaccine.aspx?nav=0&ID=6

^q https://extranet.who.int/gavi/PQ_Web/PreviewVaccine.aspx?nav=0&ID=145

Category: Integrated primary container and delivery technology

Innovation: Microarray patches (MAP)

Comparators: SDV (liquid) and AD N&S;
SDV + diluent + RUP reconstitution N&S and AD N&S

<p>Total economic cost of storage and transportation of commodities per dose</p>	<p>Does the innovation reduce the volume per dose stored and transported out of the cold chain?</p>	<p>Better</p>	<p>Better</p>	<p>contrast, developing dried thermostable formulations of IPV, particularly IPV3, has proved difficult, although short term CTC storage may be possible.</p> <p>MAPs without an applicator or with an integrated applicator do not have any components stored out of the cold chain unlike SDVs which require a syringe for delivery and /or reconstitution. For lyophilized vaccines in SDVs the diluent is also typically stored out of the cold chain except at the service delivery level. So, the volume stored out of the cold chain will be reduced for MAPs compared to the SDVs.</p>
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<p>Liquid</p>	<p>Lyophilised</p>	<p>Mixed for both the liquid and lyophilised comparators</p>
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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.

<p>Total economic cost of the time spent by staff per dose</p>	<p>Parameters to measure against a comparator</p>	<p>Liquid comparator</p>	<p>Lyophilised comparator</p>	<p>Assessment</p>
	<p>Does the innovation have attributes that can save time for the vaccinator in preparing and administering the vaccine?</p>	<p>Better</p>	<p>Better</p>	<p>A MAP without an applicator or with an integrated applicator will have fewer preparation steps than a liquid vaccine in a SDV.</p> <p>A MAP will also not require any reconstitution and so will have fewer preparation steps than a lyophilized vaccine in a SDV.</p> <p>At this phase, we assume that the wear time of the MAP does not affect the vaccinator time to administer the vaccine since the wear- time will be device/formulation-specific, and either be</p>

VIPS TECHNICAL NOTE



Category: Integrated primary container and delivery technology

Innovation: Microarray patches (MAP)

Comparators: SDV (liquid) and AD N&S;
SDV + diluent + RUP reconstitution N&S and AD N&S

				very short (seconds rather than minutes), or fit into the clinic flow.
	Does the innovation have attributes that save time for staff involved in stock management?	Neutral	Neutral	MAPs do not have any attributes that save time for staff involved in stock management.

Liquid	Lyophilised	Better than both the liquid and lyophilised comparators
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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	Parameters to measure against a comparator	Liquid comparator	Lyophilised comparator	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	No. Similar to the comparator, there are no upfront or recurrent costs required with this innovation (other than training costs which would be required with any innovation).

^r 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.

VIPS TECHNICAL NOTE



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SDV + diluent + RUP reconstitution N&S and AD N&S

(not otherwise accounted for)				
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		No difference to both the liquid and lyophilised comparators
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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
<i>To what types of vaccines/antigens does the innovation apply to, based on technical feasibility?</i>	<p>This innovation could theoretically be developed to deliver any parenteral vaccine; however, each antigen must be individually assessed for compatibility; some antigens may not be stable or immunogenic in a MAP. The payload that can be delivered by a MAP might also limit which vaccines can be successfully used with this innovation. Reactogenicity might also limit the number of vaccines that can be used with MAPs. MAPs deliver antigens to the dermal and epidermal layers of the skin and immune responses to the antigens are initiated here. In addition, there might be tissue-damage from MAP application. Therefore, local reactogenicity is expected to be greater than that seen with IM/SC injection, and might be unacceptable for vaccines that contain adjuvants.</p> <p>Examples of VIPS priority antigens that could be suitable include MR and rabies.</p>

Indicator: Ability of the technology to facilitate vaccine combination

Table 13.

Ability of the technology to facilitate vaccine combination	Assessment
	<p>Yes. MAPs may be compatible with existing combination vaccines and novel combinations. For example, trivalent influenza vaccine MAPs and MR vaccine MAPs have been developed (4,5,16). Other combinations, such as pentavalent DTP-Hib-HepB vaccine, are likely to be more technically challenging to combine on a MAP.</p> <p>In theory, MAPs could allow 'combination' of vaccines that can't be co-formulated in a liquid or lyophilised formulation because the individual vaccine components could be loaded in/on distinct micro-projections in different areas of the patch. There are no data yet to support this possibility.</p>

Category: Integrated primary container and delivery technology
 Innovation: Microarray patches (MAP)
 Comparators: SDV (liquid) and AD N&S;
 SDV + diluent + RUP reconstitution N&S and AD N&S

SECTION 4

4.1 Robustness of data:

Table 14. Category	Assessment
Type of study	<ul style="list-style-type: none"> Peer-reviewed publications of phase I clinical trials and an end-user acceptability study PATH previously conducted a COGS analysis for an IPV MAP. Several costing analyses have been completed for MAP technology based on current prototype designs and assumptions based on varying production volume.
Inconsistency of results	Consistent results
Indirectness of comparison <ul style="list-style-type: none"> 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 	Phase I trials were conducted in HICs End-user study was conducted in LMICs (Benin, Nepal, Vietnam)
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
N/A	N/A	No interviews conducted.

VIPS TECHNICAL NOTE



Category: Integrated primary container and delivery technology

Innovation: Microarray patches (MAP)

Comparators: SDV (liquid) and AD N&S;
SDV + diluent + RUP reconstitution N&S and AD N&S

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
Julian Hickling	Working in Tandem Ltd julian@workingintandem.co.uk	Developed the TN
Fatema Kazi	GAVI, the Vaccine Alliance fkazi-external-consultant@Gavi.org	Reviewed the TN
Mark Prausnitz	Regents' Professor, School of Chemical and Biomolecular Engineering, Georgia Institute of Technology, GA USA.	Reviewed the TN
PATH Medical Device and Health Technology Team Debra Kristensen Courtney Jarrahan Mercy Mvundura Collrane Frivold	PATH Debra Kristensen dkristensen@path.org	Reviewed the TN

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Category: Integrated primary container and delivery technology

Innovation: Microarray patches (MAP)

Comparators: SDV (liquid) and AD N&S;
 SDV + diluent + RUP reconstitution N&S and AD N&S

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Category: Integrated primary container and delivery technology

Innovation: Microarray patches (MAP)

Comparators: SDV (liquid) and AD N&S;
SDV + diluent + RUP reconstitution N&S and AD N&S

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