VIPS VACCINE INNOVATION PRIORITISATION STRATEGY

VIPS Phase II executive summary: Autodisable Sharps-Injury Protection Syringes (AD SIPs)

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Gavi The Vaccine Alliance

World Health Organization

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Autodisable (AD) sharps-injury protection (SIP) syringes

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About AD SIP syringes

- AD SIP syringes are **single-use, disposable syringes** with a **mechanism that covers the needle after use to reduce the risk of accidental needlestick injury**.
- Mechanisms include **retraction of the needle into the barrel after injection or a needle shield**.
- Some syringes have **SIP features that are automatically activated,** and **others require extra activation steps by the end user.**

WHO [a]

A VanishPoint® retractable syringe (Retractable Technologies, Inc.)

PATH

BD Eclipse™ syringe (BD, Franklin Lakes, NJ) with needle shield

Stage of development

- AD SIP syringes are **commercially available**.
- A list of available World Health Organization (WHO)-prequalified AD SIP syringes can be found in the WHO Performance, Quality, and Safety (PQS) catalogue.[b]

[a] http://apps.who.int/immunisation_standards/vaccine_quality/pqs_catalogue/LinkPDF.aspx?UniqueID=f3025136-636d-4139-9773-fdbf824276e1&TipoDoc=DataSheet&ID=0.
[b] WHO PQS Category E008 auto-disable syringe for fixed dose immunisation page: http://apps.who.int/immunisation_standards/vaccine_quality/pqs_catalogue/categorypage.aspx?id_cat=37.

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Summary of key insights (1/2)

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Potential public health impact of innovation

Applicability to vaccines

- **AD-SIPs are applicable to all parenteral vaccines.**

Public health benefits

- AD SIPs have the potential to reduce **needle-stick injuries (NSIs) for all parenteral vaccines.**

Vaccine problem statements

- In the VIPS Phase II online survey, **needle-stick injuries** were identified by countries as an **important challenge** for **MR, MenA, rabies and YF** vaccines.

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Summary of key insights (2/2)

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Barriers to realise the innovation's potential impact

Costs

- AD SIP syringes are estimated to be 63% more costly than similar AD syringes without a SIP feature; a price increase of $0.025.

Technology Readiness

- **No barriers to technology readiness**.

Commercial feasibility

- AD SIP products are **commercially available from multiple manufacturers and many are WHO prequalified.**
- **Future uptake in LMICs would be driven by an anticipated WHO/UNICEF requirement** for SIP features for syringe prequalification and procurement.

Countries interest

- In the VIPS country interviews, AD-SIPs were ranked o**verall 6th out of the 9 tested innovations together with SDIs**, with immunisation staff ranking them 6th and decision makers 7th.

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AD SIPs have broad applicability to vaccines

		VIPS Phase II analysed vaccines	Vaccine Type	Presentation	Route
Vaccines **technically compatible** with AD-SIPs and analysed in Phase II	Licensed vaccines	**Penta** (or DTP containing)	Adjuvanted Inactivated subunit plus polysaccharide-protein conjugate	Liquid	IM[2]
		Hepatitis B (birth dose)	Adjuvanted sub-unit	Liquid	IM
		HPV	Adjuvanted sub-unit	Liquid	IM
		MR (or MCV)	Live attenuated	Lyophilised	SC[5]
		N. Men A (or N. Men A,C,W,Y,X)	Adjuvanted Inactivated subunit plus polysaccharide-protein conjugate , adjuvant in diluent	Lyophilised	IM
		Polio, IPV	Whole inactivated	Liquid	IM or ID[6]
		Rabies	Whole inactivated	Lyophilised	IM or ID
		Typhoid, conjugate (TCV)	PS-PCV, no adjuvant	Liquid	IM
		Yellow fever (YF)	Live attenuated	Lyophilised	SC
	Pipeline vaccines	**Ebola** (rVSV-ZEBOV)[7]	Live vector	Liquid (FROZEN)	IM
		HIV (ALVAC-HIV + bivalent Subtype C gp120)[8]	Live recombinant virus, adjuvanted recombinant protein	lyophilised prime and liquid booster (gp120)	IM
		Influenza (pandemic,VAL-506440)	Nucleic acid	Liquid	IM
		Malaria (RTS,S)	Adjuvanted recombinant protein	Lyophilised, liquid adjuvant	IM
		MTb (next gen.,VPM1002)	Live recombinant BCG	Lyophilised	ID
		RSV (Pre-F)	Recombinant protein	Lyophilised	IM
Vaccines **not technically compatible** & not analysed in Phase II		**Rota** (Oral)	Live attenuated virus	Liquid	Oral
		ETEC (ETVAX)	Whole inactivated organism	Liquid vaccine, lyophilised buffer and adjuvant	Oral

Applicability to vaccines

15 vaccines are technically compatible and have therefore been assessed with AD-SIPs (out of 17 in scope) in Phase II

- **Antigen applicability: all parenteral vaccines** given by intramuscular, subcutaneous or intradermal injection are potential candidates for AD SIPs.
- **Comparators:** to assess innovations against both 'best practice' and 'current practice', comparators were defined as:
  - **SDV[3] presentation** and **AD N&S[4],**
  - If available, the multiple-dose vial presentation commonly procured by LMICs.

[2] Intramuscular; [3] Single-dose presentation; [4] Auto-disable needle & syringe; [5] Subcutaneous; [6] Intradermal

[7] At the time of the assessment, Ebola vaccine was not yet licensed and has been analysed as a pipeline vaccine.

[8] HIV vaccine consists of two different components: a virus vector for priming doses and a subunit protein plus adjuvant. The prime and boost were therefore assessed separately.

Beyond the 17 vaccines analysed through VIPS, AD-SIPs should be compatible with a range of other vaccines

Applicability to vaccines

**Pipeline vaccines*

VIPS vaccines compatible with AD-SIPs	Vaccine type	Other vaccines likely to be compatible with AD-SIPs
HepB; pentavalent; *HIV (gp120 boost)*	Subunit, liquid, adjuvant	dT; TT; DTwP; DTaP; hexavalent; *non-replicating rotavirus; GAS; next generation malaria; CEPI vaccine platform (clamp); Shigella; ETEC*
HPV	VLP or inactivated virus, liquid, adjuvant	JE (inactivated); hepA; *non-replicating rotavirus; RSV*; *improved or universal influenza; influenza (pandemic)*
IPV	Inactivated virus, liquid	Influenza (seasonal); *RSV*
Men A	Polysaccharide-protein conjugate, lyophilised	Men ACWY(X)
MR; YF; *HIV (ALVAC viral vector prime)*	Live attenuated virus, lyophilised	MCVs; JE (live attenuated); dengue; influenza (seasonal); *CEPI vaccine platforms (live recombinant vectors); chikungunya, HSV; next generation malaria; RSV*
Rabies	Inactivated virus, lyophilised	*R&D Blueprint vaccines*
Typhoid	Polysaccharide-protein conjugate, liquid	Pneumococcal conjugate vaccine; Hib, Men ACWY (liquid); *GBS*; *Shigella*
Ebola	Live vector, liquid,	*CEPI vaccine platforms (rVSV); R&D Blueprint vaccines; HSV; next generation malaria; RSV*
Flu (pandemic)	Nucleic acid, liquid	*CEPI vaccine platforms (DNA, RNA), HSV*
RSV; Malaria (RTS,S)	Subunit, lyophilised, +/- adjuvant	*Mtb (next generation, M72)*
Mtb (next generation)	Live attenuated, lyophilised, ID admin	BCG, other vaccines for ID administration e.g. IPV, rabies

Overview of AD SIPs public health benefits based on Phase II analysis

Vaccine with an elimination agenda

Public health benefits

VIPS Criteria	Indicators	Penta	Hep B BD	HPV	MR	Men A	IPV	Rabies	TCV	YF	Ebola	HIV[5]	Influ-enza[6]	Malaria	M. Tb[7]	RSV[8]
Primary criteria – Health impact	Vaccine efficacy	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
	Vaccine effectiveness	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
	Ability of the vaccine presentation to withstand heat exposure	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
	Ability of the vaccine presentation to withstand freeze exposure	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
Primary criteria – Coverage & Equity impact	Number of fully or partially immunised (relative to target population)	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
	Ease of use: clinical perspective based on product attributes	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
	Ease of use: ability of a lesser trainer personnel to admin / self-admin.	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
	Ability to facilitate dose sparing	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
	Avoid missed opportunities and reduce vaccine wastage[1]	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
	Acceptability of the vaccine presentation and schedule[2]	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
Primary criteria – Health impact	Potential to reduce stock outs[3]	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
Primary criteria – Safety impact	Number of vaccine product-related AEFIs	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
	Likelihood of contamination and reconstitution errors	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
	Likelihood of needle stick injury	Better	Better	Better	Better	Better	Better	Better	Better	Better	Better	Better	Better	Better	Better	Better
Primary criteria – Economic costs	Commodity costs of the vaccine regimen[4]	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse
	Delivery costs of the vaccine regimen[4]	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
	Introduction & recurrent costs of the vaccine regimen[4]	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse	Worse
Primary criteria – Environmental impact	Waste disposal of the vaccine regimen[4] and delivery system	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral

[1] Based on availability of the innovation in a single-dose presentation or multi-dose with preservative; [2] To patients/caregivers; [3] Based on the number of separate components necessary to deliver the vaccine or improved ability to track vaccine commodities; [4] per person vaccinated; [5] ALVAC-HIV + bivalent Subtype C gp120; [6] VAL-506440; [7] VPM 1002; [8] Pre-fusion F protein

AD SIPs prevent needle-stick injury; addressing a single safety issue for all injectable vaccines

Public health benefits

- Since AD SIP syringes either shield or retract the needle after administration, they **reduce the likelihood of needlestick injury and transfer of bloodborne pathogens to patients, health care workers** (HCWs), **and the community** after vaccine administration.
  - Accidental needle-stick injuries (NSIs) in HCWs can occur while giving an injection or after the injection, including **handling infected sharps before and after disposal**. Certain **practices considered high risk for health care workers**, such as **recapping** contaminated needles, are associated with NSIs and have **frequently been observed** during surveys on injection practices using WHO's Injection Safety Assessment Tool.
  - In settings where SIP devices have been introduced, for every 1,000 HCWs, 9 fewer are expected to suffer a NSI over a one year period. Greater benefits can be expected in higher HIV, HBV and HCV disease prevalence/higher sharps injury frequency settings.

Overview of the ability of AD-SIPs to address vaccine specific problems identified in the VIPS Phase II country online survey[1]

Vaccine problem statements

Vaccine with an elimination agenda

	Penta	Hep B BD	HPV	MR	Men A	IPV	Rabies	TCV	YF	Ebola	HIV[3]	Influenza[4]	Malaria	M. Tb[5]	RSV[6]
Vaccine ineffectiveness/wastage due to **heat exposure**	2	2	4	1	3	2	2	1							
Vaccine ineffectiveness/wastage due to **freeze exposure**	1	1	1			1		5	3						
Cold chain requirements during outreach[2]	4	3	3	4	2	3									
Vaccine wastage or missed opportunities due to **multi-dose vial**[2]				2	1		4	2	1						
Reconstitution related **safety issues**[2]				3	4				2						
Reduced acceptability due to painful administration[2]	3	5	2			4	3								
Difficult preparation requiring trained personnel[2]		4	5				1	4							
Negative impact on the environment due to waste disposal practices[2]						5			5						
Needle-stick injuries[2]				5	5		5		4						
Contamination risk due to multi-dose vial[2]	5														
Difficult to deliver vaccine to correct injection depth[2]								3							

[1] Based on an online survey with 209 global experts and country-level stakeholders across 54 countries conducted in Q4 2019 – Q1 2020, top 5 challenges identified by countries per licensed vaccine were selected as 'vaccine problem statements' to be specifically analysed. Numbers in the table refer to the ranking order of top 1 to 5 problem statements. For pipeline vaccines, problem statements were defined by the VIPS WG. [2] Scoring based on product attributes. [3] ALVAC-HIV + bivalent Subtype C gp120; [4] VAL-506440; [5] VPM 1002; [6] Pre-fusion F protein

No different to the comparator | Better than the comparator

AD SIPs have the potential to address needle stick injuries – a top 5 vaccine problem identified by countries for MR, MenA, rabies and YF

Vaccine problem statements

- Countries identified needle-stick injuries as being the **4th highest problem for yellow fever vaccine** and the **5th highest problem for Men A, MR and rabies vaccines**.
- All four vaccines identified by countries require use of a **reconstitution syringe** to withdraw and place diluent in the vial of lyophilised vaccine, as well as the needle and syringe used for injection. This might be why NSIs were identified as a problem for these vaccines. NSIs were not identified as one of the top 5 problems for liquid vaccines**.**
- Because reconstitution syringes are not used for injections there is no risk of transmission of bloodborne pathogens, however, a SIP feature could help prevent needlestick injury during vaccine preparation. **Use of a SIP feature in a reconstitution syringe was not evaluated under VIPS.**

AD SIPs will have a higher cost than an AD syringe with no SIP feature

Costs

Commodity costs[1, 2]

An AD SIP syringe would be more expensive than an AD syringe with no SIP, so the innovation would increase the purchase costs of injection syringes.

- Compared to the current price of a 0.05 mL AD syringe without the SIP feature, the price of an AD syringe with the SIP feature is $0.025 higher (equivalent to a 63% increase).
- There would be no change in vaccine regimen purchase cost and safety box costs.

Delivery costs[1, 3]

Delivery costs are unchanged assuming that the packaged volume of the AD SIP syringe is the same as that of the comparator (AD syringe without SIP feature) – this depends on products and future products may differ**.**

Introduction and recurrent costs[1]

Introduction costs due to training needs:

- Training would be required to introduce AD SIPs as would be required with any innovation.
- No upfront costs, recurrent or ongoing costs.

[1] Of a vaccine regimen (per person vaccinated); [2] Includes the purchase cost of a vaccine regimen and delivery devices (injection syringes or other components needed for vaccine preparation and administration) accounting for wastage, and safety box costs; [3] Includes costs of in and out of cold chain storage and transport for a vaccine regimen including delivery technology(ies), time spent by vaccinators when preparing and administering the vaccine and by staff involved in stock management;

AD SIPs are a well-defined product already being manufactured at commercial scale

Technology Readiness

Vaccine with an elimination agenda

VIPS Criteria	Indicators	Penta	Hep B BD	HPV	MR	Men A	IPV	Rabies	TCV	YF	Ebola	HIV[2]	Influ-enza[3]	Malaria	M. Tb[4]	RSV[5]
Secondary criteria	Technology readiness[1]	Clinical development pathway complexity							No complexity							
		Technical development challenges							No complexity							
		Complexity of manufacturing the innovation							No complexity							
		Robustness: multiple developers of the technology							Highly robust							
		Robustness: multiple suppliers/manufacturers of the vaccine							N/A							

- As they are stand-alone delivery devices, AD SIP syringes **do not require a clinical development programme**.
- AD SIP products are **commercially available from multiple manufacturers.** A list of WHO prequalified AD SIP syringes is available in the WHO PQS catalogue. They all follow ISO 7886 and ISO 23908 standards.
- The innovation is a stand-alone device and **does not require partnerships** with vaccine manufacturers for commercialisation.
- By the end of 2020, **WHO** intends to announce a **forthcoming requirement to include SIP features on all syringes for injection, including immunisation syringes**.

[1] VIPS assessment of the Technology Readiness criteria was informed by consultations with the WHO/PATH Delivery Technology - WG for each innovation assessed under Phase II, as well as with consultations with regulators. [2] ALVAC-HIV + bivalent Subtype C gp120; [3] VAL-506440; [4] VPM 1002; [5] Pre-fusion F protein

Market for AD SIPs is large and well-defined if the SIP feature is required for WHO syringe prequalification

Commercial feasibility

Vaccine with an elimination agenda

VIPS Criteria	Indicators	Penta	Hep B BD	HPV	MR	Men A	IPV	Rabies	TCV	YF	Ebola	HIV[1]	Influ-enza[2]	Malaria	M. Tb[3]	RSV[4]
Secondary criteria: Commercial feasibility	Country stakeholders' interest based on evidence from existing data	No data														
	Potential breadth of the target market	Large	Large	Large	Large	Moderate/ Large	Moderate	Small/ Moderate	Small/ Moderate	Moderate	Small	Large	Small	Moderate	Large	Large
	Existence of partnerships to support development and commercialisation	Established support														
	Known barriers to global access to the innovation	No known interest														

- There are **no published data** on country stakeholder interest in AD-SIP syringes.
- **Future uptake will be likely driven by a WHO/UNICEF requirement** for SIP features for syringe prequalification and procurement. This would mean that AD syringes would no longer be WHO prequalified or available through UNICEF and only AD SIPs could be prequalified and purchased.
- **Uptake for AD SIPs in self-procuring LMICs** is **uncertain** and will likely be driven by **cost as well as advocacy efforts**.

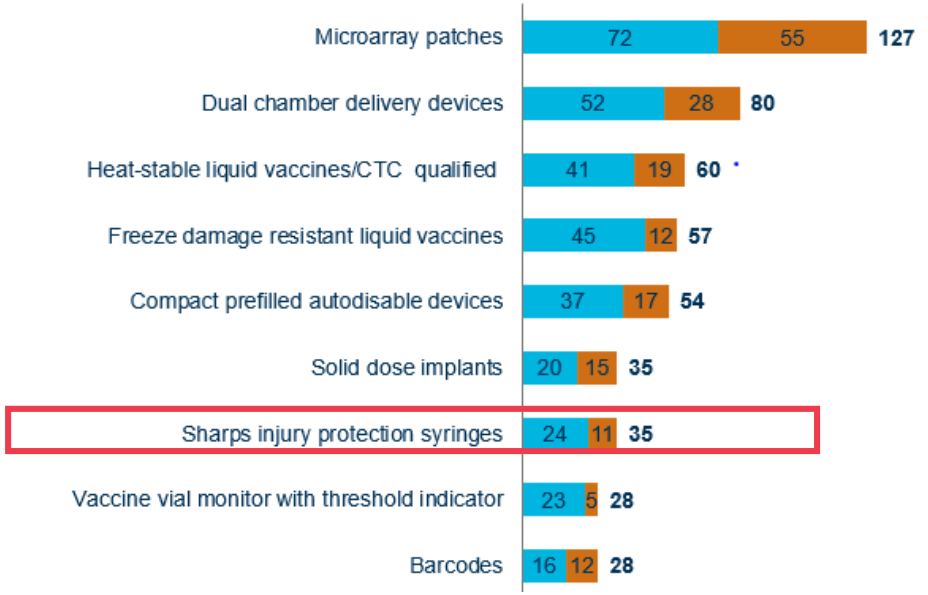
[1] ALVAC-HIV + bivalent Subtype C gp120; [2] VAL-506440; [3] VPM 1002; [4] Pre-fusion F protein

Based on VIPS country feedback[1], there is low interest in AD SIPs compared to other innovations

Countries interest

Feedback from in-person country interviews

Innovations' ranking



- AD SIPs were rated **overall** as the **#6 innovation (together with SDIs) amongst the 9 tested** in terms of having the greatest potential impact to address immunisation programme's challenges. **Immunisation staff ranked it #6**, while **decision makers ranked it #7**.

Perceived benefits

- Potential to reduce **occurrence of needle sticks injuries;**
- Make **vaccine preparation** and **administration easier;**
- Improve **waste disposal;**
- Save **health care worker (HCW) time**. (Note: AD SIPs should not impact HCW time. No rationales were given for this response during the interviews, however one other respondent mentioned that HCWs are incorrectly recapping syringes at present and this step would be averted with AD SIPs.);
- **Strong preference for the retractable AD SIPs.**

Perceived challenges

- Impact on **overall cost**;
- Immunisation staff: **complexity** of the technology use and **time to use the technology (for the needle-shield AD SIPs that require a manual step)**;
- Decision makers: **increase in price per dose** and **training needs;**
- **Safety concerns** were also raised with the **needle shield version** given that it requires manual manipulation close to the needle and that the shield could get in the way during injections.

[1] Based on in-person interviews conducted in Q4 2019-Q1 2020 with 55 immunisation staff and 29 decision makers across 6 countries to gather feedback on the 9 innovations under final evaluation

Potential impact of VIPS prioritisation

What could VIPS do to accelerate AD SIPs development for LMICs

If AD-SIPs were to be prioritised by VIPS, the Alliance could:

- Support and **advocate for the WHO's intended policy change** and assist with stakeholder buy-in and development of a supporting **procurement mechanism to help countries deal with the higher costs**.
- **Assist with introduction and roll out**, e.g. through advocacy to encourage adoption and use in self-procuring countries and helping to ensure the appropriate training mechanisms are in place for all countries.

Alternatively, VIPS could endorse AD SIPs but not prioritise them for further action by the Alliance.

Risks of not prioritising AD SIPs through VIPS

- **Loss of an opportunity for a quick win.** Prioritisation or endorsement by VIPS could help with stakeholder buy-in and accelerate countries' access to syringes with SIP features.
- No action by VIPS for this innovation could **raise questions about alignment of VIPS with WHO's initiative.**