VIPS VACCINE INNOVATION PRIORITISATION STRATEGY

VIPS Phase I executive summary: Prefilled dry-powder intranasal (DPIN) devices

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Gavi The Vaccine Alliance

World Health Organization

BILL & MELINDA GATES foundation

PATH

unicef

Prefilled dry-powder intranasal (DPIN) devices

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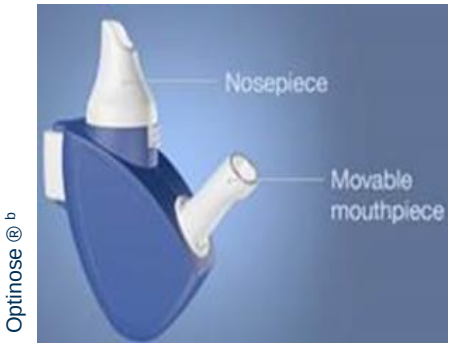
About Prefilled dry-powder intranasal (DPIN) devices

- A wide range of DPIN devices are being developed or are already on the market for delivering medicines. DPIN devices fall into two basic categories based on the activation method:
  - **Passive devices** that **use mechanical energy from fingers or thumb** to generate pressure to disperse the powder;
  - **Active devices** (breath actuated powder inhalers) that **use breath flow** to activate expulsion from the container filled with the powder to enable dispersion into the nasal passageway.
- Powders would likely reach only the nare(s) to which they are administered, and it is possible to administer doses to each nare.
- Dry powder vaccines for intranasal delivery require specialised drying methods to achieve a formulation that is aerosolizable and of appropriate particle size for efficient delivery to the nasal cavity.
- Various studies have demonstrated the feasibility of preparing dry powder aerosolized vaccines using a variety of methods such as spray-drying, bubble drying (a gentle version of spray drying), spray-freeze drying or freeze-drying methods.

Bespak [a]

Passive device (Unidose Bespak)



Optinose ® [b]

Active device
(Bi-Directional™ nasal delivery technology, Optinose®)

Stage of development

- Most of the devices **are commercially available**, however their **uses for vaccine delivery are in early phase preclinical studies** and **early phase clinical trials.**

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[a] Personal communication from Ian Anderson, Bespak, February 2015
[b] https://www.optinose.com/exhalation-delivery-systems/powder-delivery-device

Prefilled dry-powder intranasal devices scorecard

Comparator: Single dose vial (lyophilised) + diluent + reuse prevention (RUP) reconstitution needle and syringe (N&S) and autodisable N&S

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Quality of evidence: Low to Moderate

VIPS Criteria		Indicators		Priority indicators - Country consultation: RI* Facility	RI* Community	Campaigns
Primary criteria	Health impact	Ability of the vaccine presentation to withstand heat exposure	Neutral	+	++	++
		Ability of the vaccine presentation to withstand freeze exposure	Neutral			
	Coverage & Equity impact	Ease of use [a]	Mixed	+	+	++
		Potential to reduce stock outs [b]	Better			
		Acceptability of the vaccine presentation to patients/caregivers	Mixed		+	+
	Safety impact	Likelihood of contamination	Mixed			+
		Likelihood of needle stick injury	Better			
	Economic costs	Total economic cost of storage and transportation of commodities per dose	Better	+		
		Total economic cost of the time spent by staff per dose	Better	++	++	+
		Total introduction and recurrent costs [c]	Neutral			
Secondary criteria	Potential breadth of innovation use	Applicability of innovation to one or several types of vaccines	Vaccines against mucosal pathogens that can be prepared in a dry format are potential candidates.			
		Ability of the technology to facilitate novel vaccine combination	No			

* RI : Routine immunisation

++	Given significantly more importance
+	Given more importance
	Kept neutral

[a] Ease of use can prevent missed opportunities and impact ability for lesser trained personnel to administer the vaccine, including self-administration
[b] Based on the number of separate components necessary to deliver the vaccine or improved ability to track vaccine commodities
[c] Total economic cost of one-time / upfront purchases or investments required to introduce the innovation and of recurrent costs associated with the innovation (not otherwise accounted for)

Prefilled dry-powder intranasal (DPIN) devices: Antigen applicability

- DPIN devices could be applied to **vaccines that are intended for mucosal delivery** and are particularly **well suited for antigens that can be dried** and **that are immunogenic when delivered intranasally** (i.e. respiratory pathogens) **without an adjuvant**.
- **Live-vaccines are more likely to be suitable**. Non-live vaccines are likely to require a mucosal adjuvant, and none are licensed at present.
- **Live-attenuated influenza vaccine** is not a VIPS priority antigen, but it could be **well-suited for this innovation**.
- The **VSV-vectored Ebola and MR vaccines**, which are on the VIPS priority list, **might also benefit from this route of delivery,** providing a dry formulation can be developed for the Ebola vaccine.

Prefilled dry-powder intranasal (DPIN) devices:
Assessment outcomes

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KEY BENEFITS

✚✚ **Rated better than comparator on some aspects of ease of use:**

- Dry powder formulations do not require reconstitution.
- In general **require fewer components** (number of components vary between different device designs) and **less complex preparation of the vaccine.**
- May **improve dose control.**

- Potential to **reduce stock-outs** due to fewer components.

✚✚ Potentially **more acceptable** to patients and caregivers due to **painless administration of vaccine**.

- May **reduce risk of needle stick injuries** since DPIN devices are needle-free.

- **Potential to reduce delivery costs:**
  - May **reduce out of cold chain storage and transportation costs:** DPIN is prefilled and eliminate the need for reconstitution components to be stored out of the cold chain.

✚✚
  - May **save health care worker time** due to less complex preparation.

KEY CHALLENGES

- **Rated lower than the comparator on some aspects of coverage and equity**:
  - May **increase route of administration errors:** DPIN devices could be **mistaken for an orally inhaled vaccine**, resulting in **reduced efficacy of the vaccine or adverse events**.

✚✚ **Limited acceptability:** Issues related to the lack of coordination between the device activation and inhalation due to lack of patient training could impact patient acceptability, since DPIN could be perceived as more complex than the comparator.

✚ **Increase likelihood of contamination:** In spite of some easy to use benefits, there is a **risk of reuse of the nose and mouth pieces for breath activated devices.**

- **Bells Palsy has been observed as a serious adverse event following intranasal** delivery of some vaccines.

- Some DPIN devices would require a certain level of coordination by the user to activate the expulsion of powder and inhale sufficiently, this would be problematic for young infants under 3-4 years of age, so those devices would be more suitable for adolescents and adults, which limits applicability.

- **Antigen applicability**
  - Limited to mucosal delivery and antigens that can be dried and immunogenic when delivered intranasally (i.e. respiratory pathogens) without an adjuvant.

✚✚ Important attribute for at least 2 settings or for the 3 settings based on the country consultation (see slide 3)

✚ Important attribute for campaigns or routine facility-based immunisation based on country consultation (see slide 3)

Prefilled dry-powder intranasal (DPIN) devices: Rationale for prioritisation

- DPIN devices are **not recommended to be prioritised** for further analysis under Phase II.
- While their economic storage/transport and staff time costs are favorable, their **potential coverage and equity and safety benefits are mixed in relation to the comparator.**
- In addition, their **applicability to vaccines is identical or nearly identical to that of sublingual dosage forms** which are rated more highly in all categories and have fewer drawbacks than DPIN devices.
    - Sublingual dosage forms are included in the maybe' category for prioritisation and the Steering Committee is requested to provide advice on whether this innovation should be prioritised or not for Phase II.