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

June 2019
Prefilled dry-powder intranasal (DPIN) devices

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.

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

**VIPS Criteria**

**Indicators**

<table>
<thead>
<tr>
<th>VIPS Criteria</th>
<th>Health impact</th>
<th>Coverage &amp; Equity impact</th>
<th>Safety impact</th>
<th>Economic costs</th>
<th>Secondary criteria of innovation use</th>
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<tbody>
<tr>
<td></td>
<td>Ability of the vaccine presentation to withstand heat exposure</td>
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<td>Total economic cost of storage and transportation of commodities per dose</td>
<td>Applicability of innovation to one or several types of vaccines</td>
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<td></td>
<td>Ability of the vaccine presentation to withstand freeze exposure</td>
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<td>Total economic cost of the time spent by staff per dose</td>
<td>Ability of the technology to facilitate novel vaccine combination</td>
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<td>Ease of use</td>
<td>Potential to reduce stock outs</td>
<td>Likelihood of contamination</td>
<td>Total introduction and recurrent costs</td>
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<td></td>
<td>Neutral</td>
<td>Better</td>
<td>Mixed</td>
<td>Better</td>
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**Priority indicators - Country consultation**

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<tr>
<th>RI*</th>
<th>Facility</th>
<th>Community</th>
<th>Campaigns</th>
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**Quality of evidence:** Low to Moderate

**Notes:**

- Ease of use can prevent missed opportunities and impact ability for lesser trained personnel to administer the vaccine, including self-administration
- Based on the number of separate components necessary to deliver the vaccine or improved ability to track vaccine commodities
- 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

**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.
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.