

VIPS Phase I executive summary: Freeze damage resistant liquid formulations

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Freeze damage resistant liquid formulations



About Freeze damage resistant liquid formulations

- **Many vaccines are freeze-sensitive**, including those containing aluminium adjuvants. When vaccines containing aluminium adjuvant are frozen, the antigen-adjuvant particles agglomerate (form a cluster) and sediment resulting in the irreversible loss of potency.
- **Developing novel freeze-stable formulations** using different excipients (stabilising agents) could prevent agglomeration and stabilise the potency of vaccines.
- The addition of excipients such as glycerin, polyethylene glycol 300, or propylene glycol (PG) has been **demonstrated to reduce the freeze-sensitivity of hepatitis B vaccine** and other vaccines containing aluminum-salt adjuvants including diphtheria, tetanus and pertussis (DTP); and pentavalent (hepatitis B, DTP, Haemophilus influenza type b) vaccines.



Freeze damage resistant liquid vaccines

Stage of development

- **Excipients that could be used to improve freeze resistance** of vaccines are known and available but are **not used in any approved vaccines** – though they are used in other parenteral drugs, including for pediatric use.
- There has been **some testing and pre-clinical studies with hepatitis B, pentavalent, diphtheria, tetanus toxoid and pertussis vaccines**, but overall, the approach is at an **early phase of development**.



Freeze damage resistant liquid vaccines



^a <https://www.mylomacrowd.org/wp-content/uploads/2015/05/vials.jpg>

^b <https://www.publichealthontario.ca/en/BrowseByTopic/InfectiousDiseases/PIDAC/Pages/Infection-Prevention-and-Control-for-Clinical-Office-Practice-Multidose-Vials.aspx>

Freeze damage resistant liquid formulations scorecard

Comparator: Use without innovation (i.e. current liquid formulations)



Quality of evidence: Moderate

| VIPS Criteria | | Indicators | |
|--------------------|-------------------------------------|---|---|
| Primary criteria | Health impact | Ability of the vaccine presentation to withstand heat exposure | Neutral |
| | | Ability of the vaccine presentation to withstand freeze exposure | Better |
| | Coverage & Equity impact | Ease of use ^a | Neutral |
| | | Potential to reduce stock outs ^b | Neutral |
| | | Acceptability of the vaccine presentation to patients/caregivers | Neutral |
| | Safety impact | Likelihood of contamination | Neutral |
| | | Likelihood of needle stick injury | Neutral |
| | Economic costs | Total economic cost of storage and transportation of commodities per dose | Neutral |
| | | Total economic cost of the time spent by staff per dose | Neutral |
| | | Total introduction and recurrent costs ^c | Neutral |
| Secondary criteria | Potential breadth of innovation use | Applicability of innovation to one or several types of vaccines | All vaccines that are freeze-sensitive. |
| | | Ability of the technology to facilitate novel vaccine combination | No |

| Priority indicators - Country consultation | | |
|--|---------------|-----------|
| RI* Facility | RI* Community | Campaigns |
| + | ++ | ++ |
| | | |
| + | + | ++ |
| | | |
| | + | + |
| | | + |
| + | | |
| ++ | ++ | + |

* 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)

Freeze damage resistant liquid formulations: Antigen applicability



- Freeze damage resistant liquid formulations could be **applied to all vaccines containing aluminum-salt adjuvant** and potentially to other freeze-sensitive vaccines, such as **IPV as well.**
- **Hepatitis B vaccine** is an example of a liquid freeze-sensitive vaccine, which includes an aluminum adjuvant.

Freeze damage resistant liquid formulations: Assessment outcomes



KEY BENEFITS

- **Potentially improves freeze resistance of liquid formulations** using stabilising agents, especially for vaccines with aluminium-salt-based adjuvants, would **safeguard the potency of the vaccine if accidentally exposed to freezing temperatures** and help to **prevent vaccine wastage**.
- **Broad applicability to all liquid vaccines** containing aluminum-salt adjuvant and potentially to **other freeze-sensitive vaccines**.

KEY CHALLENGES

- The technology offers only **one benefit – freeze protection**.

Freeze damage resistant liquid formulations: Rationale for prioritisation



- Freeze damage resistant liquid vaccine formulations are included in a '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.**
- While the technology **only offers one benefit** that helps to **safeguard the potency of vaccines**, it does have application to many liquid vaccines.
- Prioritisation for phase II could **help raise the visibility of the technology to vaccine manufacturers** currently developing liquid vaccines with aluminum adjuvants.

Additional important information to be analysed in phase II (if prioritised for Phase II):

- Reformulation of vaccines can be costly and time consuming due to the need to assess the impact of the added excipient(s) on the product via laboratory and clinical studies and to obtain regulatory and WHO prequalification approvals. This technology is therefore best suited for vaccines in development which could be identified and targeted in phase II.