Blow-fill-seal primary containers

Comparator*: Single dose vial (liquid vaccine)

Section 1: Summary of innovation

1.1 Example images:

Rommelag BFS ampoule

Image source: provided by PATH

Rommelag BFS vial

Image source: Rommelag

1.2. Description of innovation:

- Blow-fill-seal (BFS) is an aseptic filling process that is widely used to produce a variety of pharmaceuticals in polymer primary containers. In the blow-fill-seal process, a polymer resin is melted into a parison, which is blown into a mold, filled, and sealed, all in a continuous process within a single piece of equipment. This is in contrast to preformed polymer primary containers, in which the container is first produced and sterilized, and then shipped to a different site for filling and sealing.
- A wide variety of different container designs are feasible with BFS.
    - For single-dose parenteral vaccines, BFS containers can be used similar to glass ampoules, with the top twisted off and an AD N&S used to draw up and inject the vaccine. BFS containers can also be produced with septums, similar to a glass vial. Insert-molding of a septum requires a different type of BFS production equipment and results in slower, much more costly production process, and is therefore more likely to be suitable for a multi-dose presentation. The ampoule and vial formats of BFS primary containers are assessed in this technical note. Because they have different attributes they are assessed separately.
    - BFS has the potential to be used for production of compact prefilled autodisable devices (CPADs), which are reviewed in the CPAD Technical Note (TN).
    - For oral or intranasal vaccines, BFS containers can be designed as squeeze tube dropper or dispenser devices for delivery of the container's contents directly to the mouth or nostrils. This is reviewed in the BFS Dropper/Dispenser Technical Note.

* 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.

- BFS can facilitate development of container designs that are optimized for efficient packing, including conjoined single-dose containers that stack or fold within a secondary carton. Labeling space and costs can be minimized if single-dose BFS containers are designed to be rendered open by separating them from a strip that holds the label and vaccine vial monitor (VVM) for multiple individual containers (a multi-mono-dose [MMD] configuration).
- In 2019, GlaxoSmithKline's (GSK's) Rotarix oral rotavirus vaccine was the first vaccine to be WHO prequalified in a BFS container (1). The BFS presentation of Rotarix is in a 5-dose MMD strip and has a smaller cold chain volume per dose (11.8 cm^3) than the previous preformed squeeze tube presentation of Rotarix (17.1 cm^3). BFS is also currently used to package vaccine diluents, such as Serum Institute of India Pvt Ltd's (SIIPL's) live attenuated influenza vaccine (LAIV) diluent in a BFS ampoule.
- The BFS filling process exposes the container's contents to heat, and although methods exist to minimize temperatures during BFS filling, concerns have been raised about the compatibility of BFS with vaccines and other temperature-sensitive biologics. However, stability studies with a number of live and subunit liquid vaccines, including rotavirus, LAIV, respiratory syncytial virus (RSV), and pneumococcal conjugate vaccine (PCV), have demonstrated that the vaccine was not impacted by the BFS process (2,3).
- Depending on the vaccine, the container's design, and the intended storage conditions, some vaccines in BFS may require a foil overwrap to prevent gas and water vapour ingress/egress through the polymer.

1.3 Examples of innovations and developers:

Table 1.

Product name; Image	**Developer (place); website**	**Brief description, notes**
Nasovac  Image source: SIIPL[a]	**Serum Institute of India**, Pvt, Ltd (SIIPL) https://www.seruminstitute.com/	SIIPL uses BFS ampoules for packaging of diluents for some vaccines, including Nasovac for influenza. The lyophilized vaccine is in a glass vial and is reconstituted using a needle and syringe.

[a] https://www.seruminstitute.com/product_influenza_vaccines.php

Product name; Image	**Developer (place); website**	**Brief description, notes**
BFS ampoule (Image source: Global Good) 	**Global Good** https://www.intellectualventures.com/what-we-do/global-good-fund	Global Good developed a concept for a BFS ampoule for single-dose vaccines that minimizes cold chain storage by folding compactly. This design has been found in a user evaluation to pose usability challenges due to its small size, and it has not been developed to meet manufacturing/regulatory requirements such as sufficient space to apply a label and VVM (4).
BFS containers (various)  Image source: Rommelag	**Rommelag** https://www.rommelag.com/en/	Rommelag is a manufacturer of BFS equipment and has developed a variety of different BFS squeeze tube, ampoule, and vial designs.

SECTION 2: Summary of assessment for prioritisation

2.1 Key benefits:

- BFS containers have the potential to be more compact than single-dose glass vials and to reduce cold chain storage volumes

2.2 Key challenges:

- For parenteral vaccine delivery, BFS ampoule and vial designs have yet to be developed that are optimized for usability as well as minimizing cold chain volume (4).
- The cold-chain volume (compared with a vial) will be impacted by the space needed for product labelling, and whether an overwrap is required (5).

2.3 Additional important information:

- BFS ampoules can be less costly to produce than single-dose glass vials (5).
- BFS eliminates issues of glass such as delamination and cracking (which results in production loss or recalls) or shattering during transport.
- Polymer containers such as BFS can be disposed of more easily by incineration than glass primary containers.
- Vaccine manufacturers must conduct stability studies and production validation to support regulatory approval of each vaccine that is switched to a BFS presentation.

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	Vial sub-type	Ampoule sub-type	Assessment
	Does the innovation have features that may improve heat stability?	Neutral	Neutral	BFS is a primary container technology and does not impact the temperature stability of the vaccine.
				***No difference** to either format relative to the comparator*

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	Vial sub-type	Ampoule sub-type	Assessment
	Does the innovation have features that may improve freeze resistance?	Neutral	Neutral	BFS is a primary container technology and does not impact the freeze resistance properties of the vaccine.
				***No difference** to either format relative to the comparator*

3.2 Coverage and equity criteria

Indicator: Ease of use[b]

*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 4.

Ease of use • *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)*	**Parameters to measure against a comparator**	**Vial sub-type**	**Ampoule sub-type**	**Assessment**
	Does the innovation avoid reconstitution and is that an improvement?	Neutral	Neutral	BFS packaging is only compatible with liquid vaccines (or the liquid diluents of dry vaccines). BFS packaging does not affect the need for a vaccine to be reconstituted. When BFS containers are used for diluents, similar reconstitution practices apply as for diluents in glass vials.
	Does the innovation require fewer vaccine product components?	Neutral	Neutral	For parenteral vaccines, an AD N&S is still required for delivery, so the number of components is unchanged.
	[c]**Does the innovation require additional components or equipment (such as scanners or label readers)?**	NA	NA	
	Does the innovation require fewer preparation steps and less complex preparation steps?	Neutral	Neutral	The preparation steps are similar as for parenteral vaccines in glass vials.

[b] 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).

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

Category: *Primary vaccine containers (without delivery device)*

Innovation: *BFS primary containers*

Comparator: *Single dose vial* (liquid vaccine)

Ease of use • *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)*	**Parameters to measure against a comparator**	**Vial sub-type**	**Ampoule sub-type**	**Assessment**
	Does the innovation improve dose control?	Neutral	Neutral	BFS packaging is not expected to impact the ability to deliver a correct dose.
	Does the innovation improve targeting the right route of administration?	Neutral	Neutral	A BFS container is not expected to change the targeting of the right route of administration. It will be important to design the ampoule so that it is not easily confused with an oral vaccine squeeze tube presentation.
				<u>No difference</u> *to either format relative to the comparator*

Category: *Primary vaccine containers (without delivery device)*

Innovation: *BFS primary containers*

Comparator: *Single dose vial* (liquid vaccine)

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.*

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 • *Assessment of the potential to reduce stock outs based on the innovation's features*	**Parameters to measure against a comparator**	**Vial sub-type**	**Ampoule sub-type**	**Assessment**
	Does the innovation require fewer components?	Neutral	Neutral	For parenteral vaccines, an AD N&S is still required for delivery, so the number of components is unchanged.
	Or does the innovation include labelling that facilitates product tracking and is it better than the comparator?	Neutral	Neutral	The innovation has no impact on product labelling.
				No difference *to either format relative to the comparator*

Category: *Primary vaccine containers (without delivery device)*

Innovation: *BFS primary containers*

Comparator: *Single dose vial* (liquid vaccine)

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.*

Table 6.

Acceptability of the vaccine presentation to patients/ caregivers • *Does the innovation include features that may improve acceptability of vaccinees and caregivers*	**Parameters to measure against a comparator**	**Vial sub-type**	**Ampoule sub-type**	**Assessment**
	Painful or not painful	Neutral	Neutral	A BFS container does not impact the recipient's pain upon vaccine injection.
	Perception of ease of administration (i.e. convenience for the vaccinees/caregivers)	Neutral	Neutral	A BFS container does not impact the recipient's experience of vaccine delivery.
	Any other tangible benefit to improve/impact acceptability to vaccinees/caregivers	N/A	N/A	
				***No difference** to either format relative to the comparator*

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.*

Table 7.

Likelihood of contamination • *Risk assessment of potential for contamination based on design of innovation and on usability data from field studies*	Parameters to measure against a comparator	Vial sub-type	Ampoule sub-type	Assessment
	Does the innovation reduce the risk of contamination while reconstituting the dry vaccine?	Neutral	Neutral (liquid vaccine) Worse (diluent for dry vaccine)	A BFS vial has a septum and a similar risk of contamination as a glass vial. The BFS ampoule does not apply to liquid vaccines so would be no different to the comparator. However, as the BFS ampoule shown in Table 1 is a presentation that contains diluent for vaccine reconstitution, in this scenario exposure of the diluent to the environment (similar to if the diluent was in a glass ampoule) could potentially increase the risk of contamination.
	Does the innovation reduce the risk of contamination while filling the delivery device?	Neutral	Worse	Opening a BFS ampoule presentation of a vaccine during filling of the delivery device would expose the vaccine to the environment (similar to filling from a glass ampoule), potentially increasing the risk of contamination occurring compared to a glass vial presentation. A BFS vial has a septum and a similar risk of contamination as a glass vial.
	[d]**Does the innovation require additional components or equipment (such as scanners or label readers)?**	N/A	N/A	

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

VIPS is a Vaccine Alliance project from Gavi, World Health Organization, Bill & Melinda Gates Foundation, PATH and UNICEF

Category: *Primary vaccine containers (without delivery device)*

Innovation: *BFS primary containers*

Comparator: *Single dose vial* (liquid vaccine)

Likelihood of contamination	Parameters to measure against a comparator	Vial sub-type	Ampoule sub-type	Assessment
• *Risk assessment of potential for contamination based on design of innovation and on usability data from field studies*	**Does the innovation require fewer preparation steps and less complex preparation steps?**	Neutral	Neutral	For parenteral vaccines, the preparation steps are similar.
	Does the innovation reduce the potential risk of reuse of delivery technology?	Neutral	Neutral	For parenteral vaccines, BFS containers and glass vials are both used with AD N&S, so the risk of device reuse is unchanged.
	Does the innovation reduce the risk of use of nonsterile components?	Neutral	Neutral	For parenteral vaccines, the use of a sterile AD N&S as the delivery device is unchanged.

		No difference *to the vial format* ***Worse*** *than the ampoule comparator*

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.*

Category: *Primary vaccine containers (without delivery device)*

Innovation: *BFS primary containers*

Comparator: *Single dose vial* (liquid vaccine)

Table 8.

Likelihood of needle stick injury	Parameters to measure against a comparator	Vial sub-type	Ampoule sub-type	Assessment
• *Risk assessment of the presence of sharps during the process of preparing and administering the vaccine*	**Does the innovation contain fewer sharps?**	Neutral	Neutral	BFS packaging does not impact the number of sharps used for vaccine delivery.
	Does the innovation use sharps for preparing and/or administering the vaccine and is that better than the comparator?	Neutral	Neutral	BFS packaging does not impact the use of sharps for preparing and administering the vaccine.
	Does the innovation include an auto disable feature and is that better than the comparator?	Neutral	Neutral	The innovation is a primary container and cannot be re-sealed. For parenteral vaccines, a standard AD N&S would be required for vaccine delivery, the same as the comparator.
	If the innovation uses sharps, does it include a sharps injury prevention feature and is that better than the comparator?	Neutral	Neutral	BFS is a packaging technology and does not provide sharps injury prevention.
	Does the innovation reduce the risk of injury after vaccine administration?	Neutral	Neutral	BFS packaging has no impact on the risk of injury after vaccine administration.
				No difference *to either format relative to the comparator*

3.4 Economic costs criteria

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

*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	Vial sub-type	Ampoule sub-type	Assessment
	Does the innovation reduce the volume per dose stored and transported in the cold chain?	Better	Better	BFS containers have the potential to be smaller in volume than single dose glass vials, but this will be highly dependent on the final design of the container and size of the tab required for labelling space. PATH estimated the potential volume per dose for an MMD BFS ampoule vaccine to be 7.8 cm^3 per dose (4). A prototype BFS vial was measured to be 9.0 cm^3 per dose (4) For a liquid vaccine in a single dose glass vial the volume per dose varies by vaccines and manufacturer but examples of the volume per dose are 10.3 cm^3 (Quinvaxem) (6) and 14.53 cm^3 (Euvax, hepatitis B) (7).
	Does the innovation reduce the volume per dose stored and transported out of the cold chain?	Neutral	Neutral	For parenteral vaccines, an AD N&S is required and is stored and transported out of the cold chain, similar to the comparator.
				***Better** than both formats relative to the comparator*

[e] The assessment of the indicator is volume-related and builds upon PATH's VTIA analysis. A directional estimation is made at this stage, and a better evaluation will be done in Phase II with more antigen-specific data.

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.

Total economic cost of the time spent by staff per dose	Parameters to measure against a comparator	Vial sub-type	Ampoule sub-type	Assessment
	Does the innovation have attributes that can save time for the vaccinator in preparing and administering the vaccine?	Neutral	Neutral	For parenteral vaccines, delivery time is expected to be similar since the vaccine preparation steps are the same as the comparator.
	[f]Does the innovation have attributes that save time for staff involved in stock management?	Neutral	Neutral	The innovation does not have any attributes that impact the time for staff involved in stock management.
				***No difference** to either format relative to the comparator*

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.*

[f] 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.

Category: *Primary vaccine containers (without delivery device)*
Innovation: *BFS primary containers*
Comparator: *Single dose vial* (liquid vaccine)

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 (not otherwise accounted for)	**Parameters to measure against a comparator**	**Vial sub-type**	**Ampoule sub-type**	**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	There are no upfront or recurrent costs associated with the use of this innovation, other than (minimal) training costs which would be needed with the introduction of any innovation. However, we are not including training costs as part of the assessment in this phase.
				No difference *to either format relative to the comparator*

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 • *What vaccines/antigens does the innovation apply to, based on technical feasibility?*	**Assessment**
	This innovation could be applied to any liquid vaccine administered parenterally, or used for diluents for dry vaccines. Compatibility of a vaccine with the BFS filling process and material would have to be assessed on a case-by-case basis. Examples of priority VIPS antigens that would be well-suited for a BFS primary container include pentavalent and RSV, both currently available in single-dose presentations.

Indicator: Ability of the technology to facilitate vaccine combination

Table 13.

Ability of the technology to facilitate novel vaccine combination • *Does the innovation facilitate novel combination vaccine products?*	**Assessment**
	BFS is a primary container technology and is not expected to impact the ability to combine vaccines relative to standard glass vial packaging.

SECTION 4

4.1 Robustness of data:

Table 14.

Category	Assessment
Type of study	BFS primary containers have been used commercially at large scale in both high-income and LMIC settings for packaging a variety of pharmaceuticals. They have also been introduced in LMICs for vaccine diluents. Small-scale in country feasibility studies have been conducted by PATH on prototype parenteral BFS primary containers in Uganda and Vietnam (4). A preliminary cost of goods sold and total cost of delivery study has been conducted by PATH (5). Definitive laboratory testing on vaccine compatibility/stability with BFS has been conducted by vaccine manufacturers.
Inconsistency of results	Not enough studies have been conducted to assess consistency of results.
Indirectness of comparison • *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*	All studies were in LMIC immunization delivery settings.

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.

4.3 List of technical experts, manufacturers and/or technology developers that have reviewed and provided feedback/input to the technical notes (TN):

Table 16.

Reviewers	Organisation/contact details	Notes
Courtney Jarrahian	PATH cjarrahian@path.org	Developed TN
PATH Medical Device and Health Technology Team Debra Kristensen Courtney Jarrahian Mercy Mvundura Collrane Frivold	PATH Debra Kristensen dkristensen@path.org	Reviewed TN
Fatema Kazi	GAVI, the Vaccine Alliance fkazi-external-consultant@Gavi.org	Reviewed TN
Julian Hickling	Working in Tandem Ltd julian@workingintandem.co.uk	Reviewed TN

4.4 References:

Peer-reviewed publications of primary data, systematic reviews, other reports:

1. WHO Prequalified Vaccines website. Rotavirus Rotarix page. https://extranet.who.int/gavi/PQ_Web/PreviewVaccine.aspx?nav=0&ID=363. Accessed March 28, 2019.

2. Lin YH, Orvisky E, Hau R, et al. Feasibility evaluation of blow fill seal process and compatibility with aluminum phosphate adjuvanted recombinant RSV F nanoparticle vaccine. Presented at: 11th International RSV Symposium, October 31, to November 4, 2018; Gaithersburg, MD: Novavax; Asheville, NC [poster presentation]. https://novavax.com/download/files/posters/11th-International-RSV-Symposium/YHLin_RSV_2018_Poster_FINAL.pdf

3. Sheldon EA, Jeanfreau R, Sliman JA, et al. Immunogenicity of a quadrivalent Ann Arbor strain live attenuated influenza vaccine delivered using a blow-fill-seal device in adults: a randomized, active-controlled study. *Influenza and Other Respiratory Viruses*. 2013 Nov;7(6):1142–1150. doi: 10.1111/irv.12027.

4. PATH. *Programmatic and human factors evaluation of three blow-fill-seal parenteral vaccine container designs*. Seattle: PATH; 2018.

5. Sedita J, Perrella S, Morio M, et al. Cost of goods sold and total cost of delivery for oral and parenteral vaccine packaging formats. *Vaccine*. 2018 Mar 14;36(12):1700–1709. doi: 10.1016/j.vaccine.2018.01.011.

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7. WHO prequalified vaccines website. Hepatitis B: Euvax B page. https://extranet.who.int/gavi/PQ_Web/PreviewVaccine.aspx?nav=0&ID=68. Accessed April 12, 2019.