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Cost of goods sold and total cost of delivery for oral and parenteral vaccine packaging formats

Jeff Sedita [a,*], Stefanie Perrella [b], Matt Morio [a], Michael Berbari [b], Jui-Shan Hsu [a], Eugene Saxon [a], Courtney Jarrahian [a], Annie Rein-Weston [a], Darin Zehrung [a]

[a] PATH, PO Box 900922, Seattle, WA 98109, USA
[b] Duff & Phelps, LLC, 55 East 52nd Street, Floor 31, New York, NY 10055, USA

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ABSTRACT

Despite limitations of glass packaging for vaccines, the industry has been slow to implement alternative formats. Polymer containers may address many of these limitations, such as breakage and delamination. However, the ability of polymer containers to achieve cost of goods sold (COGS) and total cost of delivery (TCOD) competitive with that of glass containers is unclear, especially for cost-sensitive low- and lower-middle-income countries.

COGS and TCOD models for oral and parenteral vaccine packaging formats were developed based on information from subject matter experts, published literature, and Kenya's comprehensive multiyear plan for immunization. Rotavirus and inactivated poliovirus vaccines (IPV) were used as representative examples of oral and parenteral vaccines, respectively. Packaging technologies evaluated included glass vials, blow-fill-seal (BFS) containers, preformed polymer containers, and compact prefilled auto-disable (CPAD) devices in both BFS and preformed formats.

For oral vaccine packaging, BFS multi-monodose (MMD) ampoules were the least expensive format, with a COGS of $0.12 per dose. In comparison, oral single-dose glass vials had a COGS of $0.40. BFS MMD ampoules had the lowest TCOD of oral vaccine containers at $1.19 per dose delivered, and ten-dose glass vials had a TCOD of $1.61 per dose delivered. For parenteral vaccines, the lowest COGS was achieved with ten-dose glass vials at $0.22 per dose. In contrast, preformed CPAD devices had the highest COGS at $0.60 per dose. Ten-dose glass vials achieved the lowest TCOD of the parenteral vaccine formats at $1.56 per dose delivered. Of the polymer containers for parenteral vaccines, BFS MMD ampoules achieved the lowest TCOD at $1.89 per dose delivered, whereas preformed CPAD devices remained the most expensive format, at $2.25 per dose delivered.

Given their potential to address the limitations of glass and reduce COGS and TCOD, polymer containers deserve further consideration as alternative approaches for vaccine packaging.

1. Introduction

Historically, most vaccines have been packaged in glass containers. While the fill-finish process for vaccines in pharmaceutical-grade glass vials is well established, these containers pose a number of challenges, including breakage and delamination (flaking), which can affect product safety and efficacy [1,2,3]; programmatic wastage of vaccines lacking preservatives and packaged in multidose-vials [4]; appropriate disposal in low-resource settings [5,6]; and the cost per dose of manufacturing for single-dose vials relative to multidose-vials. Alternative packaging formats—including polymer containers—are increasingly used, both for oral and parenteral pharmaceuticals, and they may address some of the limitations of glass-based packaging. However, the ability of polymer containers to achieve a cost of goods sold (COGS) and total cost of delivery (TCOD) competitive with that of glass containers is unclear, especially for cost-sensitive low- and lower-middle-income countries.

Abbreviations: BFS, blow-fill-seal; COGS, cost of goods sold; CMYP, comprehensive multi-year plan; CPAD, compact prefilled auto-disable; DTP, diphtheria, tetanus, pertussis; FDA, U.S. Food & Drug Administration; HepB, hepatitis B; Hib, *Haemophilus influenza* type B; IPV, inactivated polio vaccine; MDV, multi-dose vial; MMD, multi-monodose; SDV, single-dose vial; TCOD, total cost of delivery; UNICEF, United Nations Children's Fund; US, United States; VVM, vaccine vial monitor.

* Corresponding author at: PATH, PO Box 900922, Seattle, WA 98109, USA.
E-mail address: jsedita@path.org (J. Sedita).

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Two polymer fill-finish approaches are preformed (injection-molded) polymer containers and blow-fill-seal (BFS) packaging. These containers can be formed from a variety of polymers based on the preferred container characteristics and vaccine or pharmaceutical compatibility [7]. Preformed containers are purchased as sterile, open containers from vendors, filled with the biopharmaceutical, and sealed under sterile conditions. BFS containers are formed in a continuous process during which melted resin is extruded, blown into molds, formed, filled with biopharmaceutical, and sealed within a matter of seconds [8,9,10].

Both preformed polymer containers and BFS packaging enable a broad array of designs, including some in which the primary packaging also serves as the delivery device. For oral delivery, the primary container can be opened and contents dispensed directly into the patient's mouth; e.g., currently marketed rotavirus vaccines [11,12]. Polymer containers can be manufactured as ampoules, as well as compact prefilled auto-disable (CPAD) devices, which can include an integrated needle; e.g., the Uniject™ CPAD injection system [13]. Such devices can simplify delivery, ensure the correct dose is administered, and prevent transmission of blood-borne infections associated with needle reuse [14,15]. Polymer containers also enable multi-monodose (MMD) designs—multiple single-dose containers conjoined by a shared tab with one vaccine vial monitor and product label affixed to the tab [16,17]. MMD designs could reduce manufacturing cost and cold chain volume compared with traditional glass vial packaging.

While other studies have considered the potential cost of vaccine manufacturing for the developing world or compared the cost of vaccine administration for a single polymer container with that of glass vials, no studies have compared both the fill-finish cost and the total cost of delivery across a variety of alternative packaging formats with those of single- and multi-dose glass vials [18,19].

The aim of our study was to quantify the economic differences among vaccine presentations for low- and lower-middle-income country markets, as defined by the World Bank [20], by evaluating the COGS from a manufacturing perspective and the TCOD from a programmatic perspective for glass vials, preformed polymer containers, and BFS packaging. In addition, we considered a number of prototype packaging formats, which may help establish an evidence base to support efforts to implement these technologies as vaccine packaging formats. Our model used IPV and rotavirus vaccine as representative examples of parenteral and oral vaccines, respectively.

2. Methodology

The overall modeling flow is shown in Fig. 1. To create a useful comparison, the analysis estimates costs on an annual basis over a period of steady production at equivalent volumes for each presentation.

2.1. Cost of goods sold

For oral vaccine packaging presentations, we evaluated four primary containers designed for a 2 mL dose: BFS MMD ampoules, preformed polymer tubes, a single-dose glass vial, and a ten-dose (20 mL) glass vial (Fig. 2). The BFS MMD device consisted of five single-dose ampoules joined by a tab. The preformed polymer tubes were packaged as single-dose, individually labeled tubes.

For parenteral vaccine packaging presentations, we evaluated five primary containers designed for a 0.5 mL dose: BFS MMD ampoules that require a separate needle and syringe for delivery, a BFS CPAD device of an MMD design with a separately packaged custom needle assembly, a preformed polymer CPAD device with an integrated needle, a single-dose glass vial, and a ten-dose (5 mL) glass vial (Fig. 2).

The BFS containers were prototype designs with features anticipated to be required for regulatory approval, such as sufficient labeling space; however, none of these has yet been used as primary packaging for vaccines. Preformed polymer tubes and preformed CPAD devices are commercially available.

Secondary packaging for each oral and parenteral container design was optimized to reduce cold chain volume. It was assumed that parenteral vaccines in polymer packaging required overwrap—given the potential impact of gas exchange on the small volume—but that those in glass would not require overwrap. For oral presentations, no overwrap was included. All formats were packaged 50 doses per secondary package, except ten-dose glass vials, which were packaged 50 vials (500 doses) per secondary container.

Our COGS analysis—with inputs from manufacturers and industry experts—estimated postformulation through tertiary packaging costs incurred by a manufacturer, assuming an annual production volume of 50 million doses of vaccine. Fill-finish costs included the following categories:

(1) **Facilities, equipment, and overhead** included depreciation of capital expenditures (capitalized over a 20-year and 10-year economic useful life for facilities and equipment, respectively) and ongoing annual overhead costs for repairs and maintenance, utilities, and indirect and corporate overhead for a dedicated 50 million annual throughput filling line in a United States (US) brownfield facility.
(2) **Raw materials** included presentation-specific primary, secondary, and tertiary packaging materials, foil overwrap (polymer parenteral presentations only), labels, and cartons (secondary and tertiary).
(3) **Direct labor** included fill line operators, fill line clearance, and packaging line operators. Costs were based on hourly labor rates and the time required to fill 50 million doses, assuming a 500 L batch size for rotavirus vaccine (2.0 mL per dose) and a 125 L batch size for IPV (0.5 mL per dose).

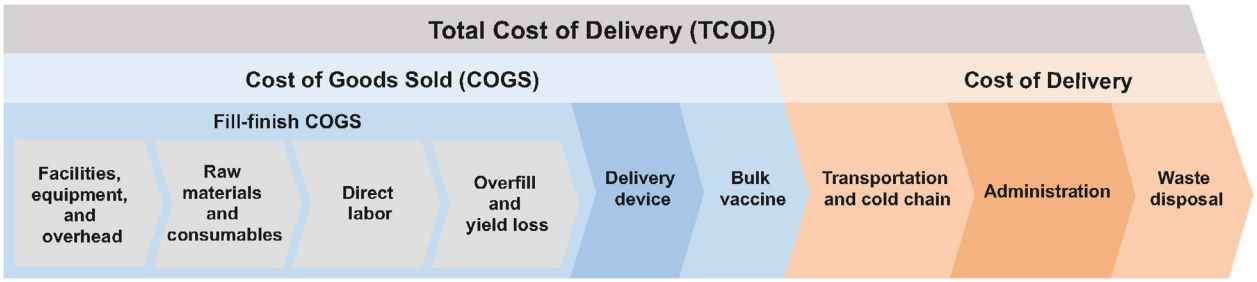

Fig. 1. Depiction of the model flow and boundaries of each model.

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