FACTORS CONTRIBUTING TO COST-COMPETITIVENESS IN REGIONAL MANUFACTURING

THEORETICAL, OUTSIDE-IN ANALYSIS OF THE COST-PER-DOSE OF VACCINES MANUFACTURED ON THE AFRICAN CONTINENT

June 2023

INTRODUCTION

- Kroll and BDO have developed a series of economic models aimed at estimating the fully-loaded costs of end-to-end vaccine manufacturing in Africa under a range of hypothetical scenarios.

- The intention of this work was to:

1. Compare fully-loaded cost per dose estimates for a hypothetical manufacturer in Africa to likely competitors in delivering select vaccines to Africa;
2. Assess the drivers and circumstances through which the cost premium of vaccine production in Africa (as compared with likely low-cost mature competitors) could be mitigated or removed; and
3. Outline under what scenarios vaccines could be produced in Africa and sold for a price that is both sustainable for the manufacturer and affordable for purchasers.

- The remainder of our presentation will detail our model construct and select findings.

SCOPE & USE

- The analyses presented herein was performed in partnership with, at the direction of, and funded by the Bill and Melinda Gates Foundation and completed in Spring 2022.

- The analyses presented herein are purely hypothetical and constructed based on non-confidential benchmarks and process modeling information, for discussion purposes only.
  - The facility specifications and variables underlying these analyses were selected to illustrate potential cost drivers. Accordingly, these should not be construed as actual or proposed business plans.
  - Further, these analyses should not be used for commercial decision-making purposes.
  - These analysis are subject to change based on new or revised information.

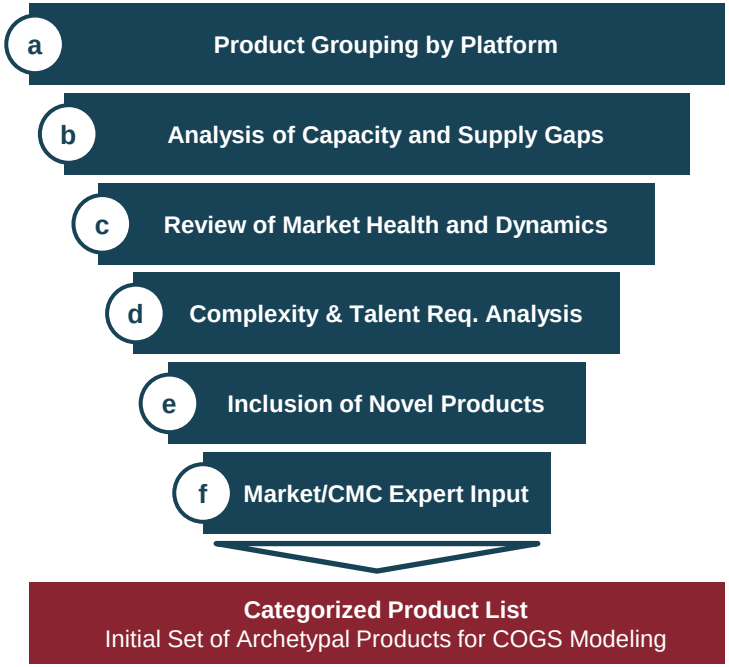
- This analysis is solely focused on production costs incurred by vaccine manufacturers.
  - These costs are just one component of the total costs in the vaccine value chain and costs themselves are just one component of the considerations underlying vaccine manufacturing in Africa.
  - Any other cost or non-cost considerations are outside the scope of these analyses.

PRODUCT AND SCENARIO SELECTION

FOCUSED COGS MODELING ON THREE DIFFERENT VACCINE TYPES

Context and Approach

- The Gates Foundation conducted an **in-depth view of current and projected market dynamics across approved and in-development vaccines**
- Prioritized products in six steps:



Findings and Output

The Foundation's findings were as follows:

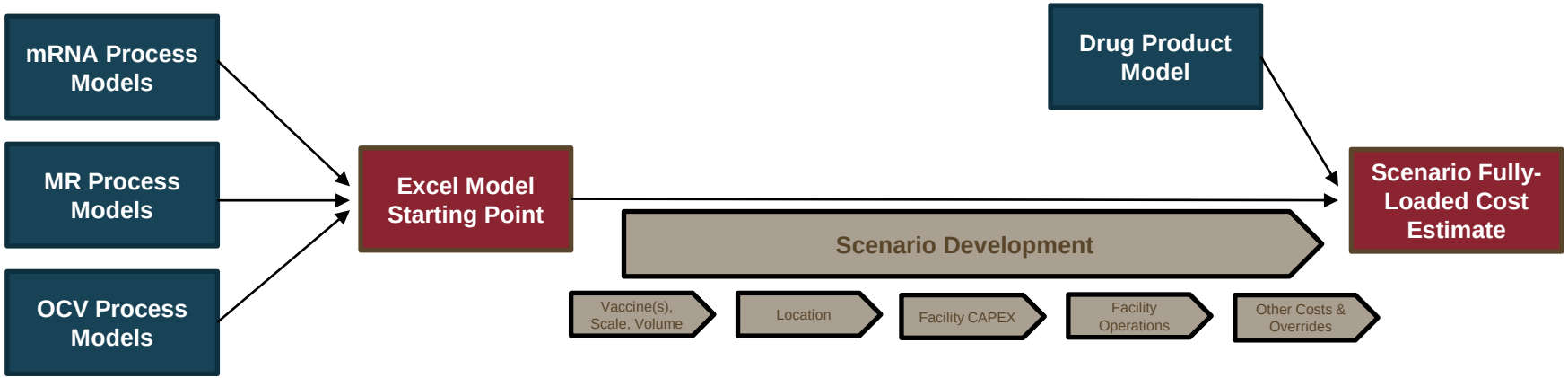
- There are currently available vaccines for **~25 diseases,** including multiple bi/multivalent combinations; approved vaccines exist in each major production platform, for example: viral/viral vector (e.g., EBOV, JE), protein/subunit (e.g., HepB, HPV), attenuated/inactivated (e.g., flu, OCV), conjugate (e.g., Hib, PCV), and mRNA (e.g., COVID-19)
- Global projections indicate that supply will exceed demand through 2030 by ~3-5x (sometimes more) for all disease **except for OCV, which contains ~100M dose gap** (of 800M needed) through 2030
- Global and Africa-specific market values and expected growth rates seem to indicate that certain products **carry a high starting market base that will grow or remain steady** over the coming decade: PCV, Hexa, Rota, MR
- Dual marketplace products with potential to sell into low- and high-income markets may **offer avenues to increase revenue** (i.e., PCV, Rota, HPV and JE)
- MR, JE, and MenA all have **limited suppliers** and would benefit from new entrants
- Focusing on **less complex products** (e.g., mono- or bivalent, already approved and produced at scale) would lead to a higher probability of success for new entrants
- Novel vaccines in development – e.g., HepC, paratyphoid, RSV, and new vaccines for HIV and malaria – have attractive markets, but can be complex to develop and/or manufacture, and time to approval and use is uncertain

Ultimately, the Foundation's directed us to model the **following products (by platform):**

mRNA	Viral	Bacterial
Prototypical mRNA Product	MR	OCV

OVERVIEW OF MODEL INFRASTRUCTURE

- We developed several models in process modeling software (SuperPro) to act as starting points for a range of scenarios.
  - Outputs from these models were then integrated into an Excel-based overlay that can flexibly adjust for key variables, in some cases using market data.
- Below is a summary of the model framework:



OVERVIEW OF STARTING PROCESS MODELS

- Below are the specs of the process models (3 vaccines at 3 scales, besides OCV) that underlie the toggle model.

	50M	100M	300M
mRNA	Single-use 13 L Scale	Single-use 26 L Scale	Single-use 78 L Scale
OCV	Single-use 300L x3	Single-use 300L x6	N/A
MR	Nevoline Nitro 200m^2	Nevoline Nitro 600 m^2	Cell-Stacks Harvest Volume M: 75L, R:30L

- These specs were chosen in coordination with the Foundation in order to optimize the generation of realistic scenarios that would assess key questions (e.g., whether new technology can offset scale advantages).

DESCRIPTION OF BASELINE AND TESTED SCENARIOS

To provide a **consistent format for comparing cost dynamics** both between products and countries, the following scenarios were modeled:

Scenario	Baseline	Africa Low Cost[2]	Africa Mid Cost	Africa High Cost
Description	*Large-scale facility using traditional manufacturing equipment and staffed with local labor*	*Medium-scale facility in low-cost African country, using local labor*	*Medium-scale facility in relatively low-cost African country hiring expat (India) labor*	*Small-scale facility in relatively high-cost African country, hiring local talent*
Scale	300M (MR, mRNA) 50M (OCV)	100M	100M	50M
Location	South Asia	Africa (low cost)	Africa (low cost)	Africa (high cost)
Labor Source	Local	Local	Expat (India)	Local
Addl. Costs	Corporate overhead (CO), research and development, and transport to Africa	Corporate overhead	Corporate overhead	Corporate overhead
Tech[1] MR	Traditional Disposable Tissue Cultureware	Modern Cost-Cutting Technology (MCCT)	Modern Cost-Cutting Technology (MCCT)	Modern Cost-Cutting Technology (MCCT)

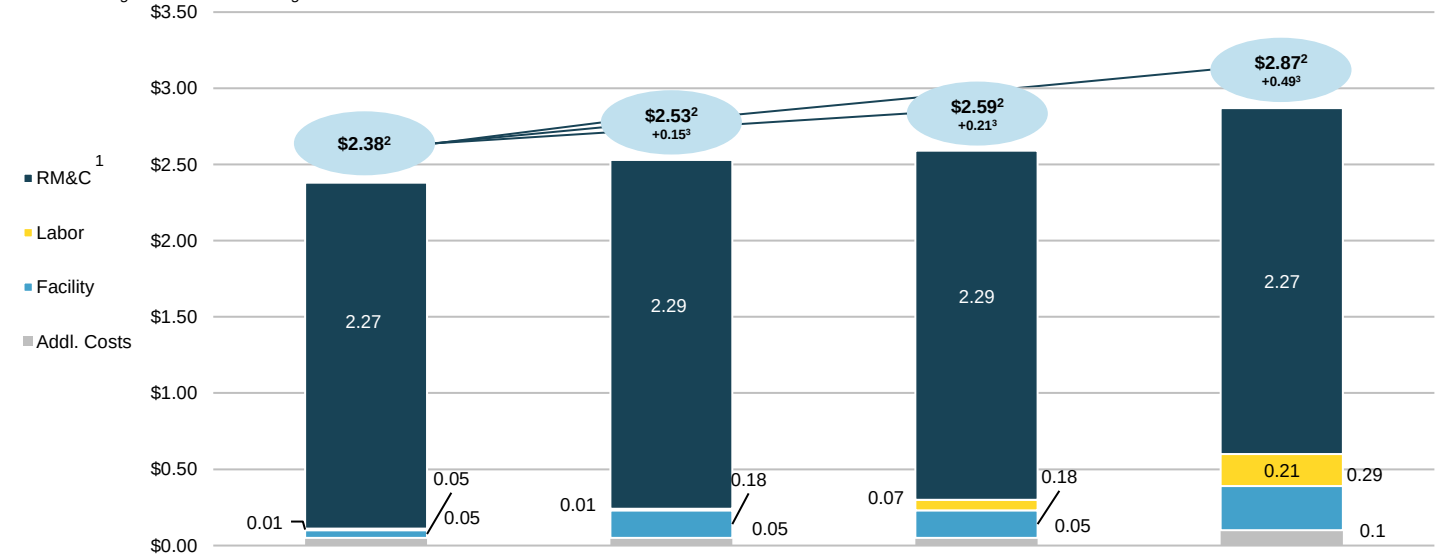
1 Technology difference only relevant in Viral scenarios where theoretical African facility may employ modern cost-cutting technology
2 Country low/mid/high cost determined by embedded location variables (labor, facility construction, tariffs)

MODEL OUTPUTS

COST OF GOODS MODELING: PROTOTYPICAL MRNA

COGS Modeling Outputs, Total Cost per Dose at Respective Scenarios/Capacities in $USD

Potential Differing Sums Due to Rounding



Assumptions	Baseline	Africa Low Cost	Africa Mid Cost	Africa High Cost
Scale	300M	100M	100M	50M
Location	South Asia	Africa (low cost)	Africa (low cost)	Africa (high cost)
Labor	Local	Local	Expat (India)	Local
Addl. Costs	Overhead	Overheard	Overheard	Overheard

1 RM&C = Raw Materials and Consumables 2 Total Cost per Dose 3 Cost Relative to Baseline

Theoretical African mRNA vaccine (e.g., COVID-19) manufacturing may be competitive in either a low-cost or lowest-cost model where **local labor is employed**

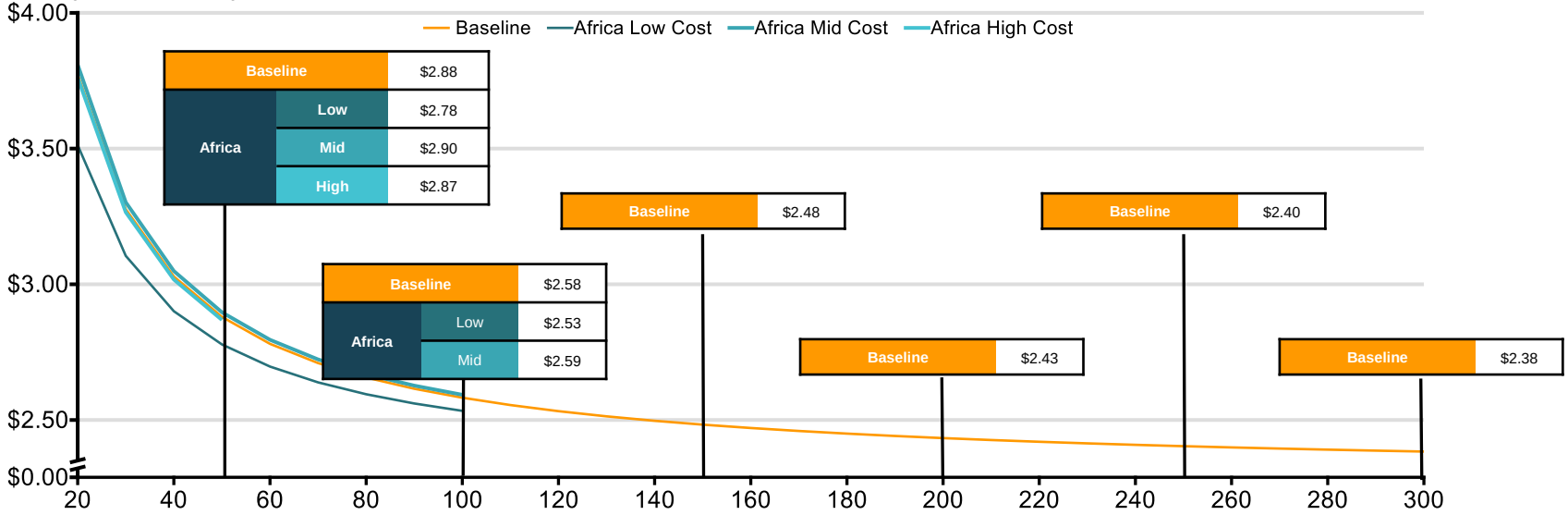
Costs of raw materials required for mRNA product production have **outsized impact on COGS** in comparison to non-mRNA manufacturing modelled, so **impact of other variables is less notable**

Modeling carries assumption that African facility will **have access to raw materials,** at same costs as baseline entity, irrespective of location

COST OF GOODS MODELING: PROTOTYPICAL MRNA

Scenario Cost Curves, Total Cost per Dose in $USD

Potential Differing Sums Due to Rounding



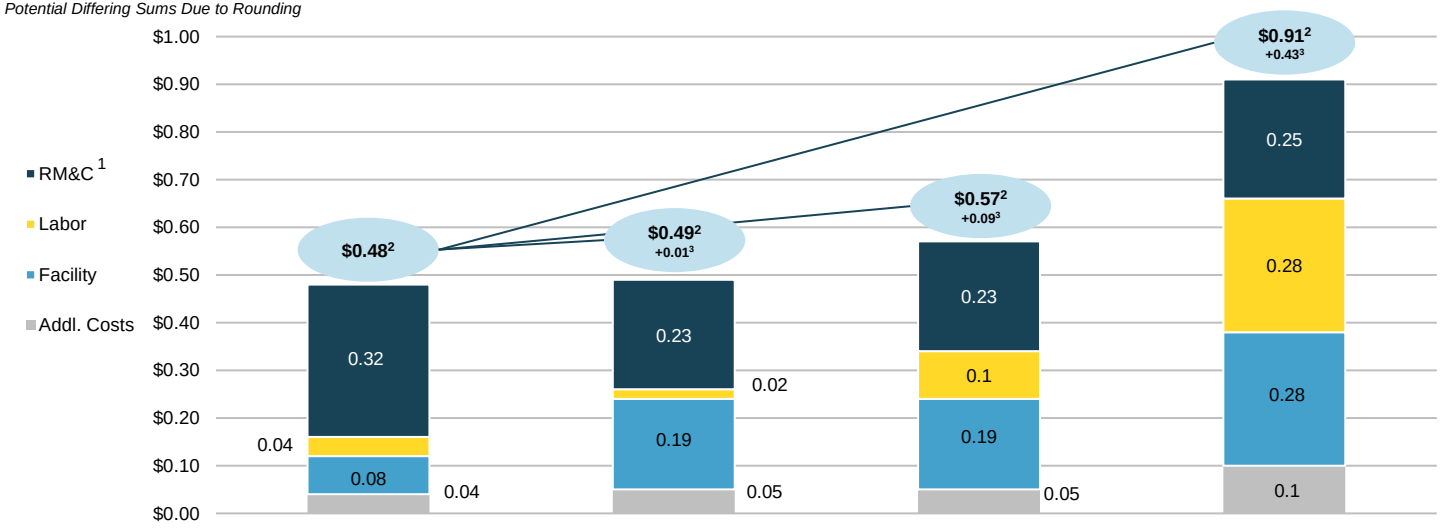
For Reference:

Assumptions	Baseline	Africa Low Cost	Africa Mid Cost	Africa High Cost
Scale	300M	100M	100M	50M
Location	South Asia	Africa (low cost)	Africa (low cost)	Africa (high cost)
Labor	Local	Local	Expat (India)	Local
Addl. Costs	Overhead	Overhead	Overhead	Overhead

COST OF GOODS MODELING: MR (VIRAL)

COGS Modeling Outputs, Total Cost per Dose at Respective Scenarios/Capacities in $USD

Potential Differing Sums Due to Rounding



Assumptions	Baseline	Africa Low Cost	Africa Mid Cost	Africa High Cost
Scale	300M	100M	100M	50M
Location	South Asia	Africa (low cost)	Africa (low cost)	Africa (high cost)
Labor	Local	Local	Expat (India)	Local
Addl. Costs	Overhead	Overhead	Overhead	Overhead

1 RM&C = Raw Materials and Consumables 2 Total Cost per Dose 3 Cost Relative to Baseline 4 Prices presented as in-year costs (i.e., not standardized to 2022 $USD); 2023 contracted price; all scenarios assume lyophilization of products produced

Source: UNICEF Supply Division Pricing Data

MR manufacturing is most competitive when **lower-cost local labor is employed**

The **use of modern cost-cutting, technology** significantly impacts competitiveness vis a vis the large-scale facility's use of traditional processes, making it feasible to compete at lower scales

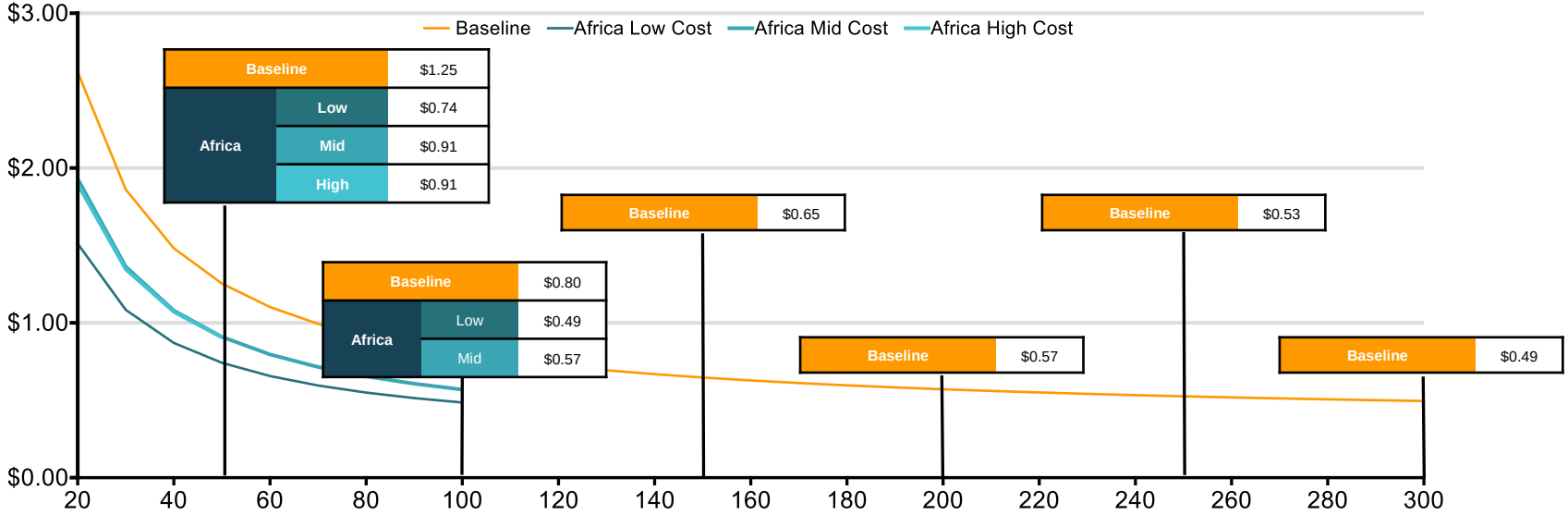
UNICEF has procured 5-dose MR products from SSI since 2018, with **prices increasing significantly in recent years** over the six-year contracted period to date[4]:

- **2018:** $0.82
- **2019:** $0.82
- **2020:** $0.82
- **2021:** $0.90 (+9.8% YOY)
- **2022:** $0.99 (+10.0% YOY)
- **2023:** $1.09 (+10.1& YOY)

COST OF GOODS MODELING: MR (VIRAL)

Scenario Cost Curves, Total Cost per Dose in $USD

Potential Differing Sums Due to Rounding



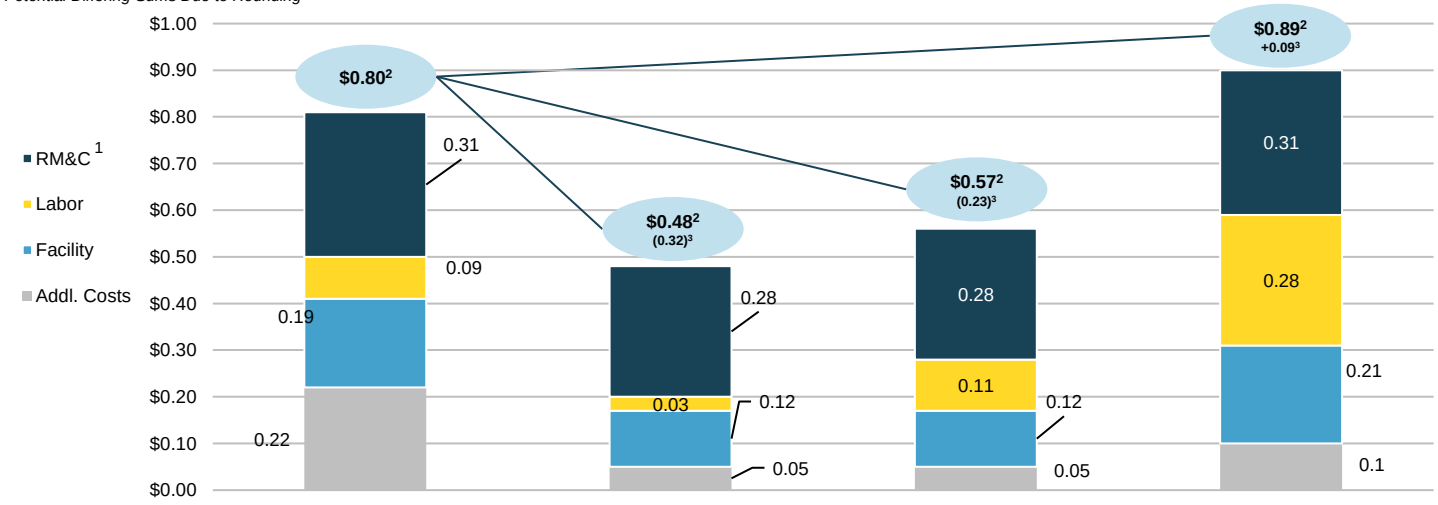
FOR REFERENCE:

Assumptions	Baseline	Africa Low Cost	Africa Mid Cost	Africa High Cost
Scale	300M	100M	100M	50M
Location	South Asia	Africa (low cost)	Africa (low cost)	Africa (high cost)
Labor	Local	Local	Expat (India)	Local
Addl. Costs	Overhead	Overhead	Overhead	Overhead

COST OF GOODS MODELING: OCV (BACTERIAL)

COGS Modeling Outputs, Cost per Dose at Respective Scenarios/Capacities in $USD

Potential Differing Sums Due to Rounding



Assumptions	Baseline[4]	Africa Low Cost	Africa Mid Cost	Africa High Cost
Scale	50M	100M	100M	50M
Location	South Asia	Africa (low cost)	Africa (low cost)	Africa (high cost)
Labor	Local	Local	Expat (India)	Local
Addl. Costs	Overhead	Overhead	Overhead	Overhead

Given the **typical volumes among OCV producers** (i.e., not exceeding 50M at an existing supplier), comparator to large-scale facility less relevant

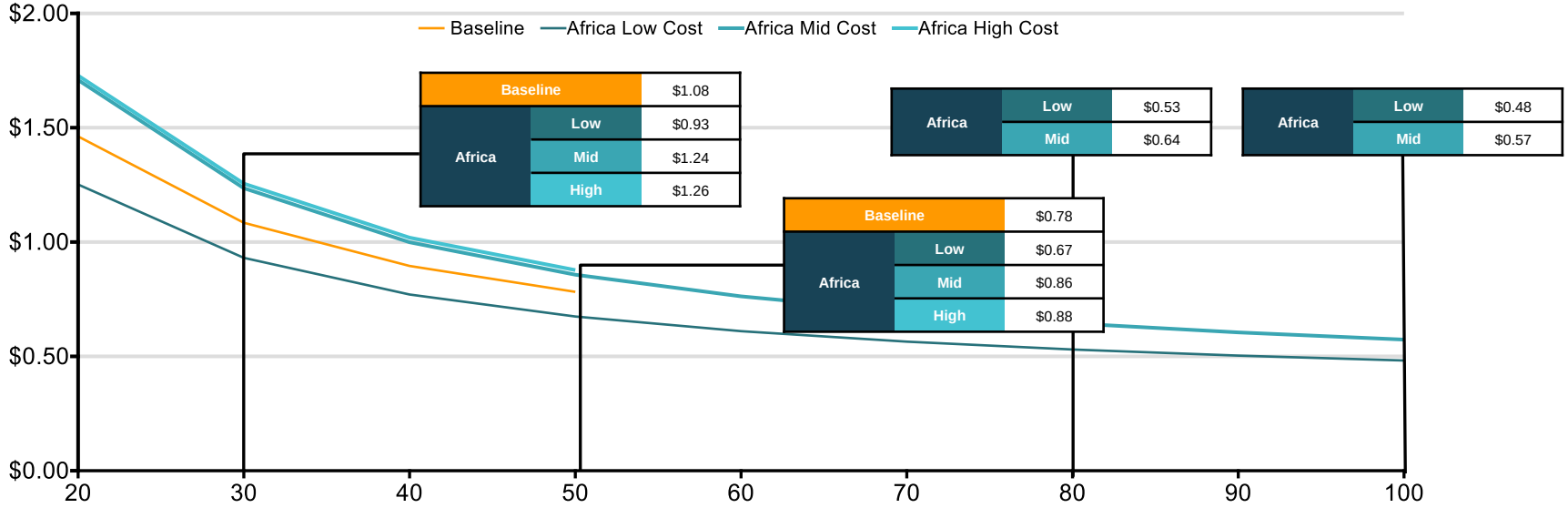
Stainless steel reduces costs compared to single use technologies for microbial operations given repeated cost of consumables

1 RM&C = Raw Materials and Consumables 2 Total Cost per Dose 3 Cost Relative to Baseline 4 Baseline scenario not based on process mode but estimated as stainless steel facility with 50M dose capacity located in India and employing local Indian labor; facility capex estimated to be ~$5.8M by taking 75% of capex for 300M stainless scenario; for Africa scenarios, estimated at 75% for 50M and 85% cost for 100M. No additional capex assumed, cost includes $5M in corporate overheard and ~$1M in transportation costs, no R&D, licensing or grants included

COST OF GOODS MODELING: OCV (BACTERIAL)

Scenario Cost Curves, Cost per Dose in $USD

Potential Differing Sums Due to Rounding



FOR REFERENCE:

Assumptions	Baseline	Lowest Cost	Low Cost	Mid Cost
Scale	50M	100M	100M	50M
Location	South Asia	Africa (low cost)	Africa (low cost)	Africa (high cost)
Labor	Local	Local	Expat (India)	Local
Addl. Costs	Overhead	Overhead	Overhead	Overhead

ASSESSMENT OF KEY VARIABLES

DETAIL ON VARIABLES IMPACTING COGS

Detail to follow

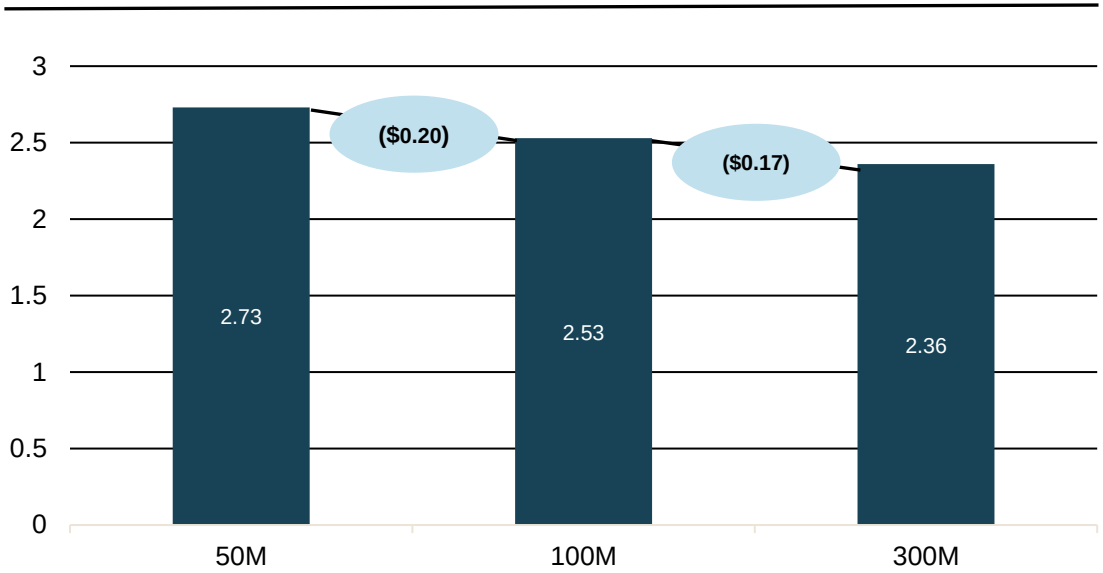
Variable	Description	Options	General Impact
Scale	Annual production volume in number of doses per active DS line; assumes 100% utilization	• 100M • 50M	Greater volume leads to lower COGS, as fixed costs (e.g., overhead, shared space) are spread over a greater # of doses
Location 1 **Facility Capex**	Manufacturing plant country location and associated CapEx costs of facility creation, assumes greenfield development	Ethiopia; Rwanda; Senegal; South Africa	Does not change heavily location to location on a per dose basis at sufficient volume
Location 2 **Labor**	Cost of direct and indirect (i.e., administrative) labor based on labor source (e.g., local in-country labor versus talent from abroad)	Ethiopia (low cost); Rwanda (low cost); Senegal (mid cost); South Africa (high cost); Expat (India); Expat (US)	Labor costs vary greatly inter- and intra-continentally; local labor is always more cost competitive vis a vis US or Euro ex-pat labor, but certain countries may be costlier than India ex-pat labor
Manufacturing Technology (MR Only)	MR DS production has the option of utilizing modern cost-cutting manufacturing technology to reduce COGS and increase competitiveness, particularly at lower scales.	• Modern Cost Cutting Tech (50M and 100M Capacity) • Traditional Disposable Tissue Cultureware (300M Capacity)	Lower scale processes using new technology can be competitive with higher scale traditional processes at respective capacities

A CONSISTENT WITH OTHER VACCINES, COGS IMPACTED BY ECONOMIES OF SCALE AND FACILITY UTILIZATION

Increasing the scale of the manufacturing plant and **spreading fixed costs (e.g., indirect overhead) over a greater number of products** will lead to lower COGS per dose

Scale Influence on mRNA Scenario

Cost per Dose in $USD[1]



1 All assumptions other than scale locked as location in Rwanda, use of local labor and production at 100% utilization at given capacity

CONSISTENT WITH OTHER VACCINES, COGS IMPACTED BY ECONOMIES OF SCALE AND FACILITY UTILIZATION

The simplified chart below provides an example of how the interplay between scale and utilization can have a significant impact on per-dose costs:

	Scenario 1	Scenario 2	Scenario 3
Facility Capacity	50M	300M	300M
Annual Depreciation	$3.0M	$5.0M	$5.0M
Facility Volume	40M	240M	40M
Facility Utilization	80%	80%	13%
Depreciation Cost Per Dose ($)	$0.08	$0.02	$0.13

- Larger scale facilities will always be cheaper than otherwise equivalent smaller scale facilities, assuming production at high utilization.
- That said, it is important to construct a facility that matches demand for the vaccine being produced, as costs of unused capacity can increase cost bases and lead to higher per-dose costs.
- Over-diversification of suppliers will not allow any one manufacturer(s) to capture sufficient demand to realize economies of scale and may not be cost effective or sustainable.

B1 LOCATION: RECEIVING SUBSIDY/GRANT FUNDING TO COVER FACILITY COSTS CAN DRAMATICALLY REDUCE COSTS PER DOSE

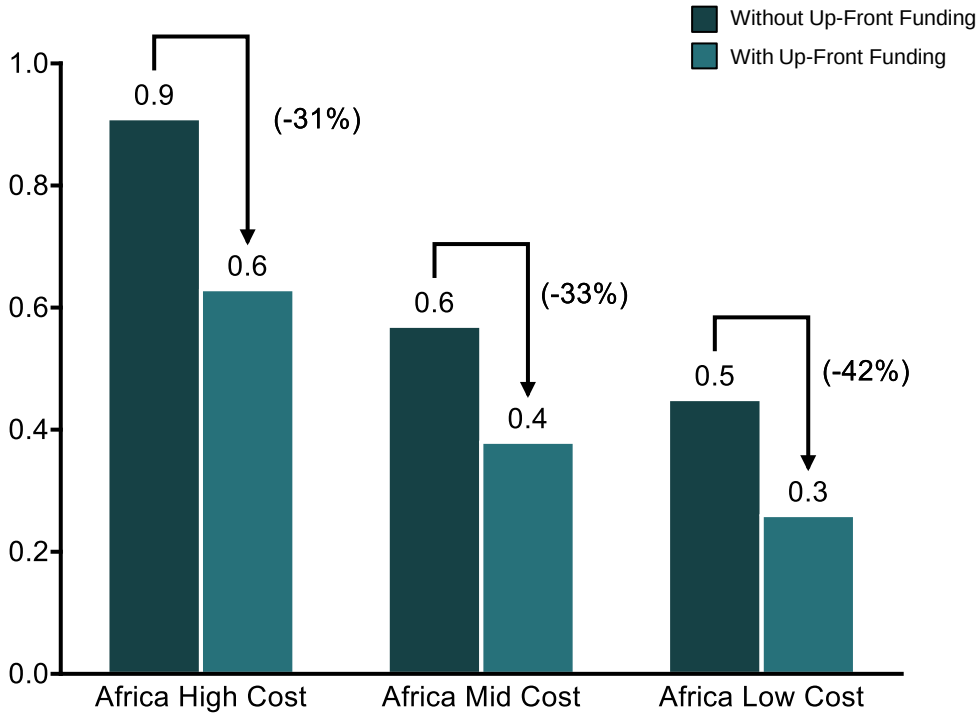
Overview

Facility costs can dominate the cost-per-dose, especially where scale is suboptimal and idle capacity is reserved.

Direct subsidy or grant funding would provide a local African vaccine manufacturer the ability to **significantly reduce costs per dose via discounting facility depreciation and expenses** from cost per dose calculations, improving competitiveness

Debt financing requires repayment and thus carries through to cost-per-dose; interest cost itself negligible in proportion (assuming 5% or less)

Est. Impact of Full Facility Subsidy, MR Cost per Dose, $USD[1]



1 Assumes Africa Mid-Cost Scenario; 100M Scale Facility in Low-Cost Country Utilizing Expat (India) Labor
Source: World Bank

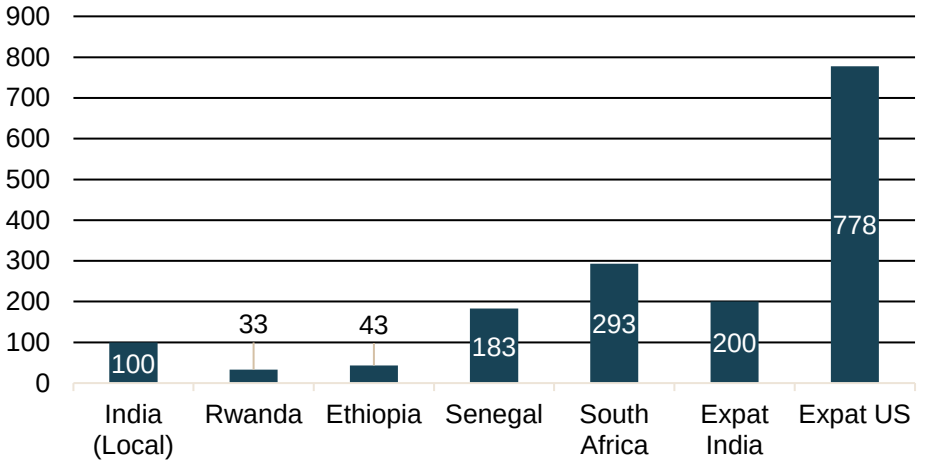
B2 LOCATION (LABOR): OPPORTUNITY EXISTS TO LOWER COGS OVER LONG-TERM BY BUILDING LOCAL TALENT BASE

Relative Labor Costs by Country

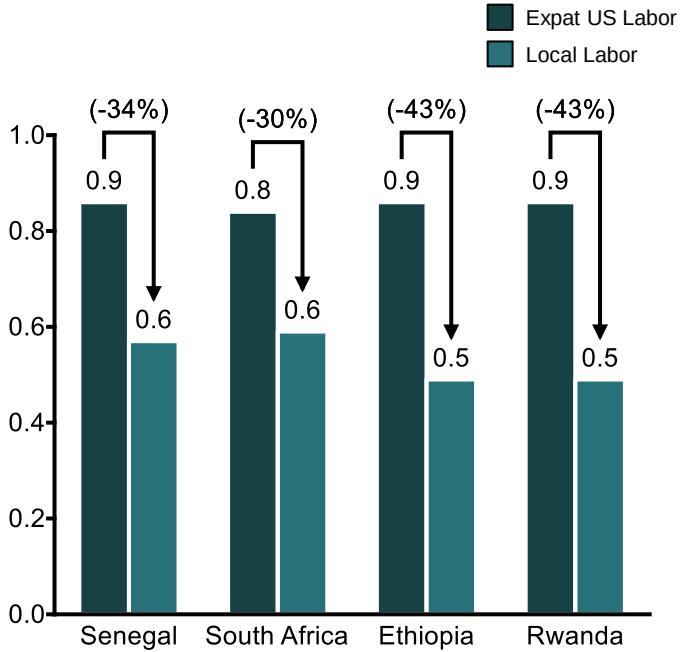
United Nations Industrial Development Organization (UNIDO) labor statistics indicates that **costs of labor vary heavily between expat and local sources**

Developing local talent versus relying on Expat labor, particularly those sourced from US / Europe is expected to lead to cost savings in production

Labor Adjustment Relative to Local India, % Premium/Reduction[1]



Impact of Labor on Cost of Goods for producing MR[2]



Above deltas assume 100% of labor comes from a single source, but likelihood is workforce will come from various sources

1 Percent cost relative to local Indian labor locked at '100%' (i.e., 43% for Ethiopia can be interpreted as approximately ½ the labor cost of local India); US costs are 4x India-based labor based on internal benchmarks, and 2x for Expat US intended to account for any additional salary/bonus/relocation costs 2 Assumes 100M Scale Facility Operating

SUMMARY: FOSTERING A SUSTAINABLE VACCINE MARKET FOR AFRICAN MANUFACTURERS REQUIRES MITIGATING KEY COST DRIVERS

- Cost per dose analysis implies that any viable African manufacturer will need to achieve **high scale and employ local labor;** as such, addressing **market access and workforce development programs** are critical to feasibility

	Variable	Impact	Implications
Key cost factors	**Labor source** 	• Expat (i.e., US, EU) labor is **expensive relative to local labor**, driving up costs for facilities reliant on external staffing • Labor costs vary **widely between countries internationally and within Africa** with certain regions (e.g., East Africa) offering much more competitive labor costs versus others (e.g., South Africa)	• Local **workforce development programs** in Africa will be crucial to enable sustainable, cost-competitive, operations long-term • Establishing a **clear, feasible, workforce transition roadmap** from any external (i.e., expat) to local labor is critical to ensuring costs become more competitive over time
	Facility scale 	• At smaller scales, **facility depreciation and operational costs make COGS less competitive** (especially in scenarios operating at <50M doses per year) • Costs can be mitigated by utilizing **modern cost-cutting technology** but required demand still exceeds most national cohorts	• Facility will likely need to access **regional (i.e., SSA) and/or global markets i**n order identify enough demand to sustain larger scale (e.g., 100M) operations • Utilization of cost-cutting manufacturing technology can help increase competitiveness at lower volumes but **may not serve as a long-term solution** given competitors access to similar technologies • **Grant funding of facilities** can have major positive impact on future cost per dose

Additional Takeaways

- Inclusion of any idle capacity will **require heavy subsidization by external donors** given high costs of maintaining idle pandemic capacity
- Where raw materials and consumable cost dominate, difference of location has less proportional impact on cost-per-dose
- Additional manufacturers of any product researched, at volumes at or less than 100M doses annually, are **not expected to carry any negative implications** for market health

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