Achieving the full health impact of vaccines:

Analysis of value proposition for increased thermostability

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Despite significant progress towards global immunization goals, millions of infants worldwide are still missing out on basic vaccines

Immunization Goals	Current performance against goals	
 Extend **coverage** of vaccines to all children in GAVI countries	**26%**	Share of birth cohort without DTP3 coverage in GAVI countries
	23M	Infants worldwide who lack access to vaccines
 Ensure delivered vaccines are **efficacious, effective** and simple to administer	**Significant reduction in efficacy & effectiveness**	given the operating environment (including cold chain excursions), e.g., 15-55% freeze exposure
 Minimize **total system cost** of delivering immunization	**$2.2B**	Total system cost for routine immunization in 2012
	$3.7B	Projected system cost for routine immunization in 2020

SOURCE: Map from gavialliance.org

Improving thermostability is critical to achieve immunization goals; but it must be targeted and evidence-based to increase probability of success

Thermostability & immunization goals

Increase coverage…

…by stocking vaccines at facilities that do not have cold chain equipment

Improve efficacy…

…by decreasing probability of administering efficacy-impaired vaccines

Reduce System Cost…

…by decreasing waste due to heat & freeze exposure

…by decreasing cold chain footprint

… by reducing cold chain complexity

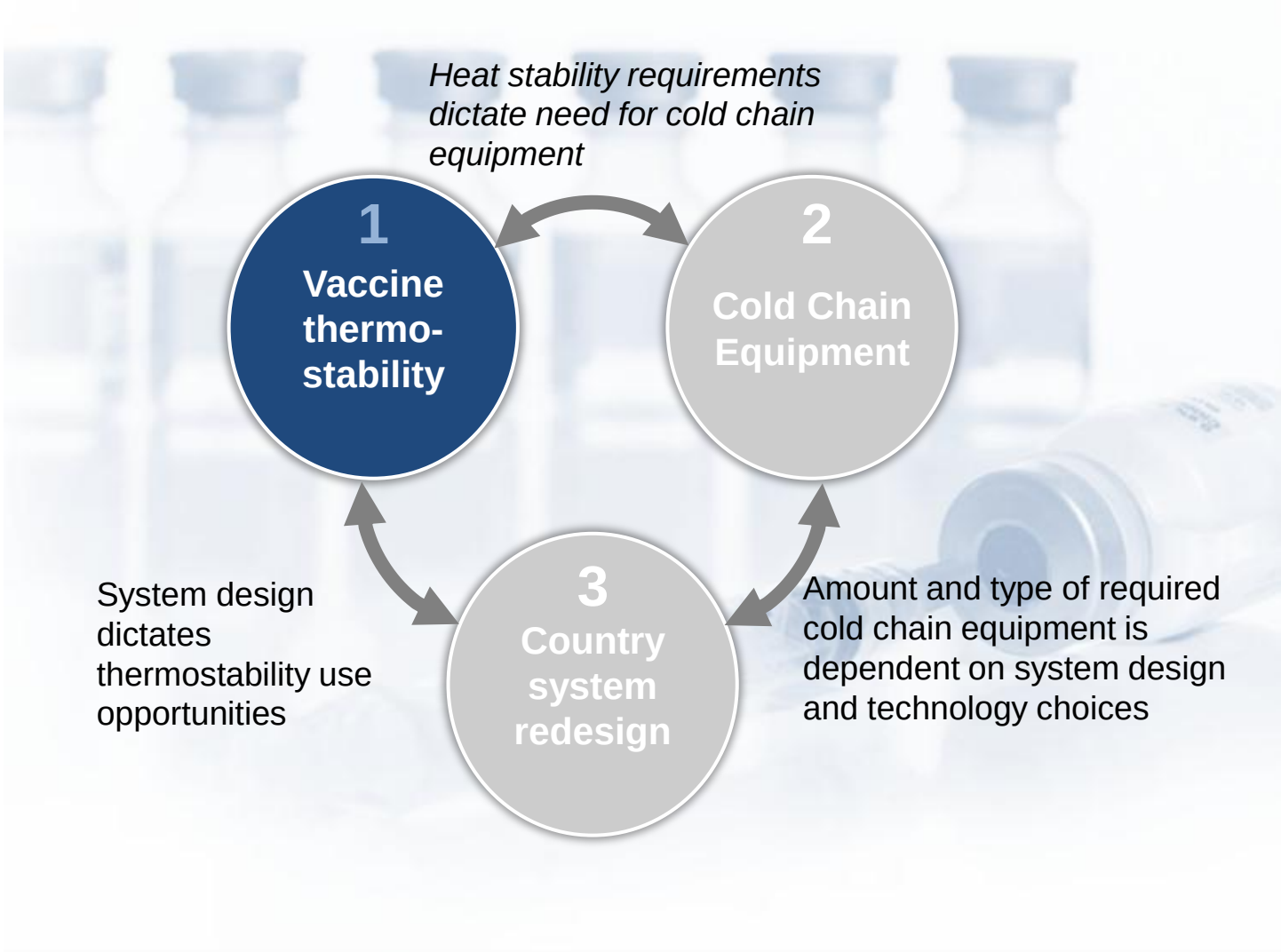
Historical & forward-looking context

- **Significant investment by the GPH community** has led to some limited benefits
  - CTC collaborations established
  - Development of freeze protection technology
- **Translating science to product has been challenging:**
  1. Lack of a systematic approach aimed at the specific use conditions of specific products
  2. Lack of end to end analysis of the value proposition for specific interventions
  3. Lack of attention to industry motivations/ incentives

A systematic look at thermostability issues required to increase probability of success

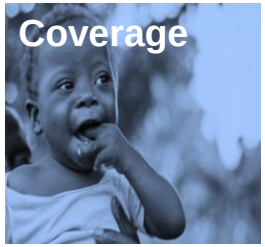
We believe that there are 3 interrelated elements that have an ability to help us achieve outcomes

Focus of this document

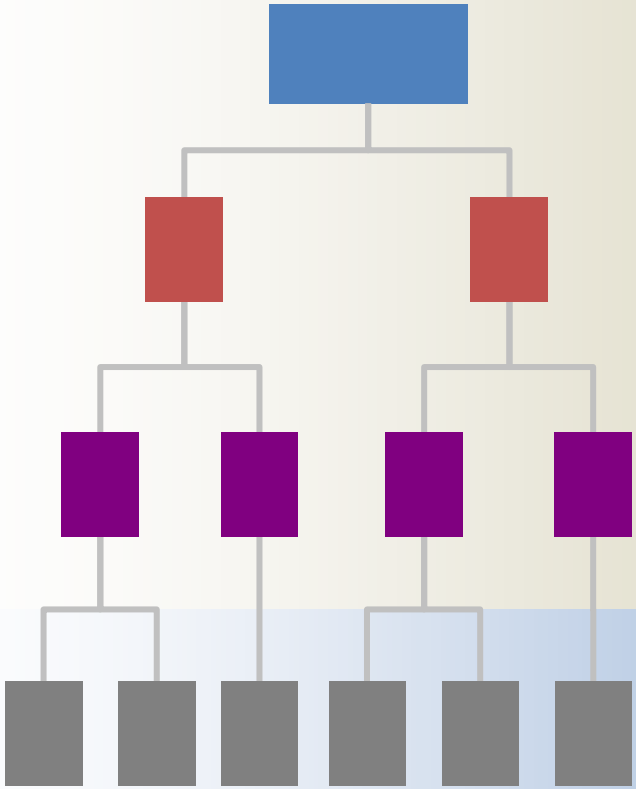


For Routine immunization the ultimate goal would be the removal all vaccines from the cold chain

RI Thermostability Benefits

	Today	All RI vaccines stable
 Coverage	Parents travel long distances to immunization points (or need expensive outreach)	Ability to stock unequipped health posts and increase coverage
 Efficacy	**1-3%** of vaccines become inefficacious due to heat exposure **15-55%** of vaccines subject to freeze	No excursions, hence no reductions in efficacy
 Total System Cost	**~$15-40M** wastage per year **~$110M** spent per year on cold chain equipment	**$125-150M** cost savings per year

However, even benefits from more limited thermostability can be achieved



Common supply chain structure	Typical resupply	Max time spent
National	3 months	Up to 4 months
Regional	3 months	Up to 4 months
District	3 months	Up to 4 months
Health-posts	1 month	Up to 2 months[1]

>12 months[2] stability enables removal of CCE at any supply chain level & fundamental re-design of the system

>2 months stability enables removal of CCE at health posts and stocking of vaccines at unequipped facilities

Up to 2 months stability enables diverse use cases, reduction in wastage and potential simplification of outreach

1 For majority of facilities; ~20% of facilities (most very remote) will need up to 3 months given 100% buffer stock policies; assumes facilities follow FEFO policies
2 Potential to reduce overall time to 6-9 months through system changes (e.g., informed push, de-layering)

SOURCE: Team analysis, expert interviews

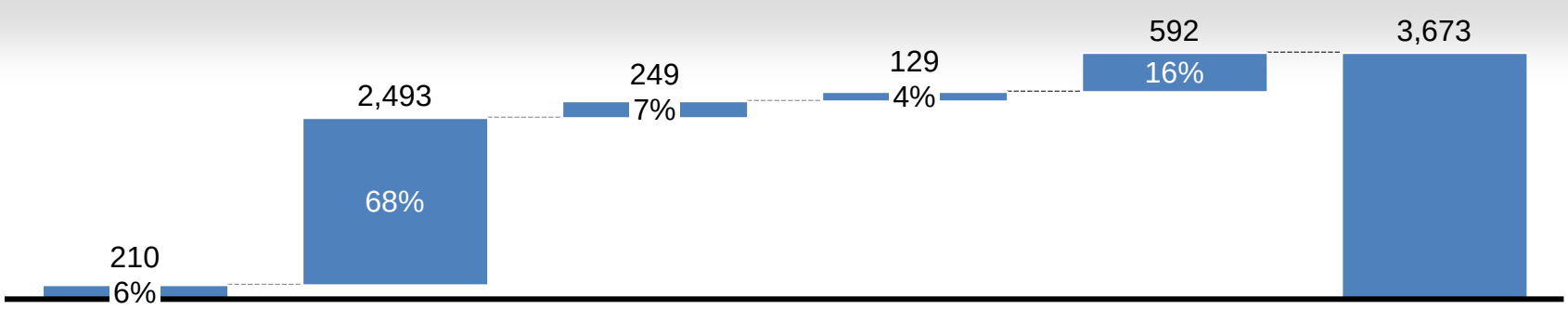
Without stability across a critical mass of RI vaccines, coverage, efficacy and cost benefits would be significantly lower

Immunization goals	All RI vaccines stable	Only 1-2 vaccines stable
 Coverage	**Ability to stock unequipped healthposts and increase coverage**	Still need to **maintain CCE** If only a subset of vaccines are stocked more broadly, parents must go to **multiple health posts** for full schedule (unclear impact on coverage)
 Efficacy	**No excursions, hence no reductions in effectiveness**	**Possible increase in excursions** for non-stable vaccines due to added complexity of cold chain management
 Total System Cost	**$125-150M cost savings per year**	**Limited savings from downsizing some equipment ($10-20M per year)**

To assess benefits, we estimated breakdown of total system costs

2020 - Main sources of cost

USD M, % of total



- Disease surveillance **2%**
- Program mgmt. **2%**
- Social mobilization **1%**
- Training **1%**

- Vaccines administered **59%**
- Wastage **8%**
- Supplies (e.g.; syringes) **2%**

- Transport **2%**
- Handling & logistics personnel **4%**
- Storage/CCE **<1%**

- Cold chain equipment **3%**
- Facilities **1%**

- On-site vaccination **6%**
- Outreach **6%**
- Other Vx-related activities **2%**
- Supervision & management **2%**

1 Based on WHO spend guidance per child and countries' ability to reach 90% of that spend guidance
2 Assumes rota, HPV, pneumo, & IPV have been rolled out to all GAVI countries
3 Transport & supply chain labor costs based on HERMES model
4 Based on demand segmentation for fridges and total cost of ownership values from PATH

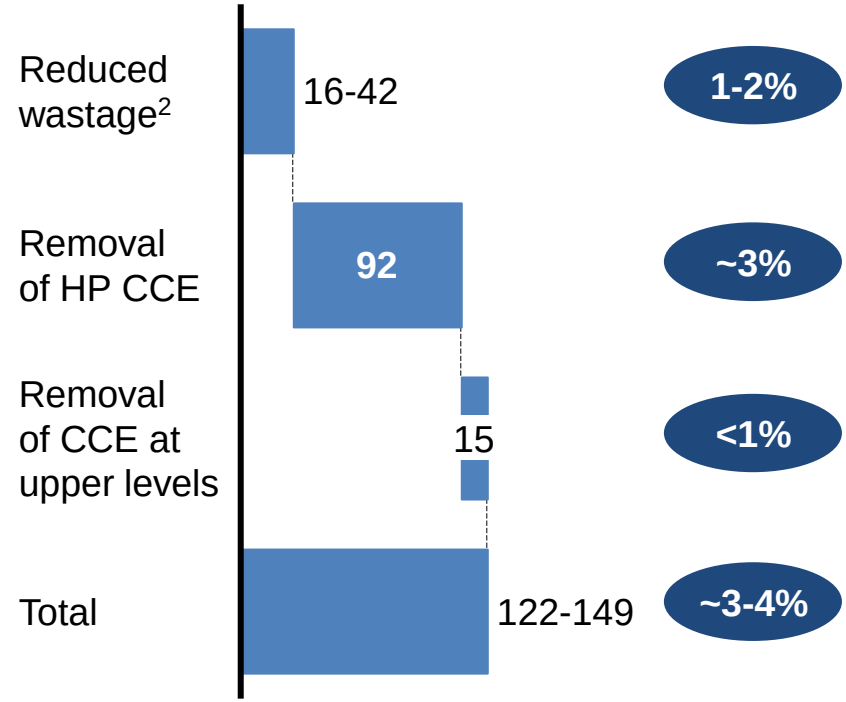
SOURCE: TSC Model

With fully stable portfolio, we could save up to ~$150 M/yr; with a sub-set stable, the savings are significantly lower

XX% Percent of 2020 total system cost

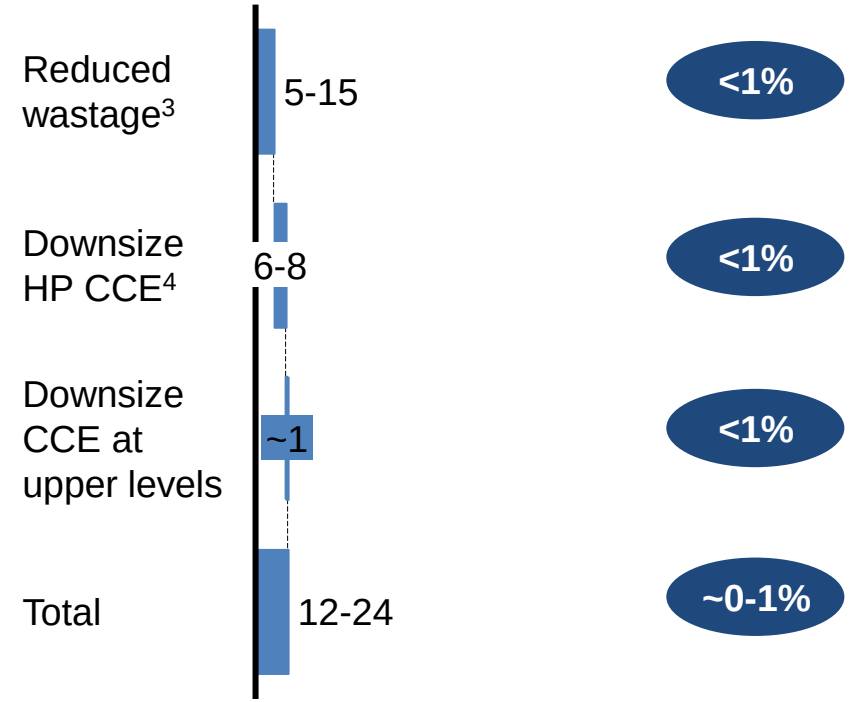
Potential cost savings with fully stable portfolio

Annual cost savings[1]
USD, M



Potential cost savings with 2 stable vaccines (IPV and rota)

Annual cost savings[1]
USD, M



1 On a projected 2020 base
2 Assumes closed vial wastage could be reduced by 20-60% depending on current VVM
3 Assumes closed-vial wastage for rota reduces by 20-60% and for IPV by 20-40%
4 Assumes 3-dose regimen of rota with 17.1 cm3 per dose & 1-dose regimen of IPV with cold chain footprint of 2.4 cm^3; marginal cost per liter of CCE is $1.50-$2.00
SOURCE: TSC Model

Must be balanced against R&D costs and increase in manufacturing costs

Therefore, expanding the cold chain to unequipped facilities may offer a less risky and cost effective path to increasing coverage…

	Increasing stability	Doubling facilities with CCE
 Timeline	▪ **Minimum 10+ years**	▪ Could rapidly start
 Risk	▪ **Very high risk**	▪ CCE available and relatively established
 Financial	▪ **Several hundred million dollars**[1]	▪ **~$35-60M** annually[2]

Existing cold chain footprint has important limitations; BMGF and its Alliance partners are actively working on addressing these challenges

1 Assuming 6 vaccines, each with 2 manufacturers, and ~$30-50M per product would yield a high-level estimate of ~$400-600M

2 For ~130k new facilities. Cost is lower than current expense because 1) newly equipped facilities tend to be smaller, 2) it is assumed that newly equipped facilities would avoid most expensive equipment (solar battery and absorption). Other costs would be incurred to stock more facilities (transport, healthcare workers, etc.) but these are equal across both scenarios

However, we might still be able to improve RI outreach with existing stability

Current situation

- Most healthpost perform day-long outreach sessions at least once a month; sometimes several times per week
- Vaccines are transported in cold boxes
  - Small portion of overall cost, but requires healthposts to make ice
- Unused vaccines are returned to the fridge at the end of the day

Opportunity

- Most RI vaccines have stability of 7 days or higher
- RI outreach could potentially be performed without ice
  - Simplify CCE technologies (no freezer compartments)
  - Improve coverage

Challenges & Next Steps

- **Logistics**: Vaccines often come back; creates a logistical challenge to avoid same vial repeatedly taken out
- **Multidose vials:** Risk of contamination of opened vials kept at ambient temperature
- **Behavior change**: Need to convince HC and parents that cold chain is not required

***Further analysis** is required to assess tradeoffs, e.g., measure actual amount of vaccines returned from outreach sessions*

1 OPV has VVM 2

Way forward

1

Encourage manufacturers to increase/document heat stability for priority vaccines in development, to reduce wastage and enable new use cases

- Build in heat stabilizers and ensure label matches stability
- Continue work with Bharat / InventPrise on liquid rota
- Continue work on ASO1 adjuvant with GSK through VaxDP

2

Focus resources on ensuring broader immunization goal are met through a combination of interventions – cold chain, system redesign

3

Consider smaller 'seed investments' in drying technologies to move technologies forward / enable 'serendipitous' discoveries

4

Continue to monitor and provide measured funding to disruptive technologies that offer real promise of moving the entire RI vaccine suite to greater stability

