Meeting Minutes

A Roundtable on Consideration for Primary Vaccine Container Selection in Developing Countries – Defining the Evidence and Framework for Decision Making

May 9-10, 2012
PATH, 455 Massachusetts Ave NW Suite 1000, Washington DC
Executive Summary

Vaccine containers are often chosen based on easily identifiable and quantifiable criteria, such as procurement price or storage volume, but container choices can have additional impacts on safety, coverage, and affordability that are harder to observe. In an effort to articulate those tradeoffs, the Vaccine Primary Container Roundtable convened a group of experts from countries, agencies, academia, and the private sector in order to: present and respond to available evidence and a preliminary framework for primary container decision-making; identify the most relevant data gaps inhibiting evidence-based decision-making; understand diverse needs of stakeholders involved in container decisions; and identify opportunities for improved data and decision-making to affect product development, programs and policy.

Key themes of the discussion included:

The need to balance the country and global perspectives. Analyzing systems and data at the aggregate level can lead to programs or policies that don’t meet the needs of specific regions. For instance, in regions without an airport able to accept large cold-chain shipments, EPI managers may need to prioritize low volume above all other considerations, regardless of international recommendations.

The importance of safety impacts. Participants agreed that decision-makers often make trade-offs between safety, affordability, wastage and coverage without realizing it. While some of these trade-offs may ultimately be appropriate, they should be understood and appreciated. Making trade-offs transparent and quantifiable will ensure that they are made deliberately.

The need for accurate market forecasting to incentivize product development. Manufacturers expressed willingness to provide new presentations in response to global health community requests, but highlighted the need for accurate, consistent forecasting in order to ensure that research and development investments are appropriately directed and high up-front costs can be recouped.

The diversity of stakeholder perspectives. In considering primary containers, different stakeholders will have different needs, priorities, and resources. A useful approach to decision-making will allow for these differences, understanding that there is no one right answer for every situation. Improving the understanding and appreciation of mutual needs and constraints can help inform stakeholder choices.

Uses and structure of the draft framework. Participants agreed that different users will need differing levels of complexity. Specifying cost drivers will be helpful to many users. Ideally, the framework can help standardize the decision processes leading to new product development requests, reducing the risk for manufacturers and facilitating appropriate decisions for both manufacturers and consumers.

The need for data. Priority data gaps identified included information about safety and contamination issues, wastage rates, cold chain capacity, session sizes, and cost per administered dose. Cost per administered dose is a function of several other data inputs, such as price per dose, wastage, and cost of storage and transport; there was agreement that quantifying and monetizing these data points would be valuable.

Future proofing. Primary container design impacts but cannot solve all the issues arising from the recent addition of several new vaccines such as Rotavirus and S. pneumoniae on existing systems. Introduction of these vaccines and, from 2017, subsequent replacement of pentavalent vaccine with hexavalent DTP combinations in single rather than multidose presentations (due to interactions between thimerosal preservative and IPV) will for many countries necessitate focus on cold-chain expansion rather than trying to fit all of their scheduled vaccines within an existing infrastructure.

Next steps for this group include the dissemination of a meeting report, a policy brief, a revised decision framework, presentation at relevant conferences, and preliminary mathematical modeling of different container scenarios.
Day One: Sharing Perspectives, Setting the Stage

The opening remarks laid out key themes of the meeting, including the importance of thoughtful container decisions in resource-limited settings, the timeliness of the discussion given the global increase in new vaccine introductions, the need to identify and address the data gaps hindering evidence-based decision-making, and the difficulty of achieving optimal balance when tradeoffs are necessary.

The overarching objective of the meeting was to organize a complex landscape of stakeholders, competing domains, and data in such a way that those complexities become manageable, tradeoffs become transparent, stakeholders are satisfied, and recommending bodies can make informed decisions.

More specifically, participants set the following goals for the meeting and follow-up:

- Progress towards a decision-tree or model that (a) can be adapted for developed and developing country audiences choosing between existing options; (b) can inform product profile proposals; (c) can provide some guidance into quantifying trade-offs between options; and (d) be acceptable and workable to stakeholders with different primary needs
- Progress towards guidelines at two levels: Generic product profile guidance for industry at the beginning of the product development cycle, along with post-development decision-making guidance to help countries choose between existing options
- Improved understanding and appreciation of safety issues
- Identification of knowledge gaps
- Identification of multiple perspectives and the areas in which multiple stakeholders have overlap in their goals
- Improved understanding of the complexity of constraints for each stakeholder

There was consensus among participants that this group is not a recommending body, and the goal of this event is not to recommend a particular course of action. Instead, the goal is to improve the tools available to recommending bodies as they make their decisions.

The full presentation from the opening remarks is available [here](#). Detailed reports and links to each participant presentation are attached as Appendix One. Key themes included the importance of safety impacts from both affordability and demand creation perspectives; the need for improved market forecasting in order to reduce manufacturer risk and facilitate new product development; and the diversity of stakeholder needs at different levels (country versus global) and across sectors. Modeling efforts and other tools for decision-making were discussed, along with the need to make those tools accessible and relevant for a range of stakeholders.

Day Two: A framework for decision-making

The second day of the meeting was discussion-based. Participants broke out into three small groups. Moderators presented a draft decision-making framework created by IVAC; participants reviewed and provided feedback on document, identifying missing components, areas for improvement, and priority data gaps. Small group feedback was presented to the full roundtable during a report-back session at the end of the day.

The draft framework as presented and the edited versions from each group are attached as Appendix Two. For ease, the group feedback is also summarized below:

Structure of framework

While one group suggested simplifying the framework and focusing on a key drivers of coverage, safety and affordability, a second group wanted more detail and a third group was satisfied with the level of detail as presented. The takeaway from this varying feedback is that different users will need differing levels of complexity, and a successful final product will allow users to interact with the framework at whatever level of detail is appropriate to their needs.
Participants also suggested that the framework should more explicitly represent some of the complex feedback loops and interactions between domains; the presented draft implied a simpler, more hierarchical process than is generally observed.

Components of framework
Participants suggested that several components should be added or more explicitly noted. Proposed vaccine characteristics to add to the existing draft framework (Appendix 2) included whether or not the vaccine is packaged with ancillary materials, the label type and clarity, route of administration, disposal requirements, and thermostability out of cold chain. Contextual characteristics to include were urban/rural status, distribution of session types (fixed, outreach, or campaign), program landscape, and the regulatory environment and technical feasibility constraints governing manufacturers. Timeliness of immunization should be included as an outcome. Groups also suggested including global supply dynamics and some measure of acceptable risk thresholds.

There was general agreement that, given the importance of cost as a driver for many other outcomes, it would be appropriate to add more specificity to the cost and pricing section. Costs for syringes and other ancillary budget items should be factored in. Additional detail is particularly important for logistics costs, as those are often borne by countries and therefore highly relevant to country decision-making.

One group proposed a more defined and central role for factors related to political environment; given that container decisions are very often made in the political realm, it is important to capture the effects that political environment can have on other domains, as well as the feedback from other domains back into the political environment.

Particular feedback loops to represent explicitly include: positive feedback from successful, safe vaccination to client-level and political demand; relationships between political environment and all other domains; and the effect of global supply dynamics.

Finally, there was a general consensus that the term “access” is unclear in this context; terms such as “successful immunization” or “immunization coverage” would be more appropriate.

Uses for the framework
It was agreed that the draft framework was most closely aligned with the decision-making process for choosing from existing presentation options. However, with some adjustments, it has the potential to inform decisions about generic product profiles and other upstream decisions, highlighting unmet needs and niches for market expansion.

In the best-case scenario, the framework can be used for upstream decision-making in order to provide manufacturers with increased lead time and reassurance that there will be a market for a product developed according to country or agency requests. Increased predictability on the demand side will facilitate appropriate prices and quantities on the supply side.

Data gaps and sources
Priority data gaps identified included information about wastage rates, cold chain capacity, session sizes, and cost per administered dose. Cost per administered dose is a function of several other data inputs, such as price per dose, wastage, and cost of storage and transport; there was agreement that quantifying and monetizing these data points would be valuable. There is a general lack of data around safety and contamination issues. Along with general data gathering difficulties, there are incentives to underreport adverse events, and patients experiencing adverse events may experience a lack of trust that discourages them from returning to the original care provider to report the problem.
Participants suggested that country-level data could be mined more effectively; even small or qualitative studies can provide valuable information. Other available sources include traditional large-scale surveys such as the DHS, along with potentially underutilized surveys from non-health disciplines.

Appendix 1. Summary of presentations

All presentations are available on the Vaccine Primary Container Roundtable Website: http://www.jhsph.edu/ivac/projects/primary-vaccine-container-roundtable.html#presentations

Session 1: Stakeholder Perspectives: What are the issues?

The Stakeholder Perspectives session included representation from the country, manufacturer, and health care worker perspective.

Country perspective: Bangladesh (Tajul Islam Abdul Bari, Bangladesh)
Dr. Bari’s presentation provided information on Bangladesh’s vaccine schedule, delivery system, cold chain, multidose vial policy compliance, vaccine wastage rates, and plans for new vaccine introduction. He noted that Bangladesh has no major administration safety problems, although cost, cold chain management, vaccine supply, and vaccine wastage are all important issues for the country.

- Overview of immunization in Bangladesh: Bangladesh’s target population for immunization is mainly children 0-1 years old, with TT for women of childbearing age. Most vaccines are in 10- or 20-dose vials, and all are procured via UNICEF. Pentavalent was introduced in June 2009 in single-dose vials.
- MDVP in Bangladesh is not observed at the grassroots level; only used at fixed sites with vaccine storage facilities
- There is a deficit of cold storage space at the national level, especially for Rota and HepB birth dose. At the district and upazila levels, there is excess space.
- Among EPI vaccines, wastage is at 85.1% for BCG (20 dose vial), 71.6% for measles (10 dose vial), and 1.25% wastage for Penta (single dose vial).
- If preparations are moved to higher-dose presentations, cold chain requirements decrease by 66m$^3$ at the national level, 44m$^3$ at the district level, and 6m$^3$ at the upazila level
- Looking forward, Bangladesh will be introducing MR in 5-dose vials in 2013. The switch to 5-dose MR would reduce wastage rates as compared to the 20-dose measles vials, while multi-dose penta would reduce storage needs.

Country stakeholder perspectives: Market research on vaccine attributes related to primary containers. (Debra Kristensen, PATH)
Ms. Kristensen presented data from a market research study designed to obtain country stakeholder perceptions on vaccine attributes, including presentation and packaging characteristics, with detailed insights into future human papillomavirus (HPV) vaccines.

The study was conducted in six low- and middle-income countries; respondents included country decision-makers, health systems personnel and health care workers.

- 158 respondents provided representation from Brazil, China, Ethiopia, Peru, the Philippines, and Tanzania
- Comparing a hypothetical dose 2- or 5-dose vial without preservative to a 10-dose vial with preservative, respondents reported that positive impacts would include lower wastage and fewer missed opportunities, while negative impacts included concerns about higher wastage and contamination due to lack of preservative, along with increased need for cold chain space, training, and procurement funding.
- Many respondents reported concerns about thiomersal.
- Time to administer vaccine can vary greatly between presentations
- Procurement decisions at the country level are usually based on macro issues such as storage and cold chain, but there is a need to include health care workers and health systems workers in the decision-making process.
Considerations for Primary Vaccine Containers from the IFPMA Perspective: What are the Issues?
(Jules Millogo)
Dr. Millogo spoke as a representative of the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), a nonprofit representing the research-based pharmaceutical industry worldwide. The presentation provided an overview of technical, financial, packaging, and service delivery considerations, ultimately suggesting that patient and provider considerations drive decision-making.

Technical & supply chain considerations
- The goal is to have something running on the production line at all times
- Containers need to be compatible with the existing production line components
- Components may come from all over the world; to ensure uninterrupted supply, it’s best to have multiple reliable sources
- Specifications such as fill volume, interaction between the product and container walls, thermostability, and stopper coating can affect product stability
- Think about fill volume: affects stability of the product, etc

Financial considerations
- For vaccines, the look of the container is not a selling point in the same way that it is for some other medicines
- Cost of container should only be a certain percentage of the cost of vaccine
- Changing containers can incur costs for new studies, similar to costs for developing a new product
- Cost differential between plastic and glass can be significant

Safety considerations
- Need to work within regulations for every component
- Packaging should minimize opportunity for user error
- Multiple, non-standardized containers increase opportunity for counterfeiting; standard containers are more easily recognizable.

Considerations for Primary Container Decisions: DCVMN Perspective
(Suresh S. Jadhav)
Introduces the DCVMN, an alliance of vaccine manufacturers from developing countries that aims to ensure a consistent supply of quality vaccines for developing countries. Presents manufacturers perspectives on cost, vial size, and preservatives. Discusses implications for transition from multidose vials to single dose presentations.

- Developing Country Vaccine Manufacturers Network (DCVMN) was formed as a result of WHO activity
- Theoretically, manufacturers have the ability to make all dose presentations; choice is driven by purchasers (countries, agencies, public and private businesses)
  - UN, international governments, and philanthropic agencies tend to prefer MDVs
  - Domestic markets prefer single dose
  - Manufacturers use multiple strategies to balance economic goals while ensuring affordable price to end user
- Single dose presentations for newer vaccines have cost and operational implications
  - Major cost considerations
  - Potential shortage of vaccines if facilities are unable to cope with increased storage, transport, and service delivery requirements
  - It is possible to go to single dose, but at the end of the day it depends on the country and the health care providers.
- Thiomersal issues could become more relevant
- Cost will remain important as competing priorities and limited resources restrict health budgets
• Cost comparisons between presentations don’t include syringe and glove costs.
• It would be helpful to quantify value of health care worker time to administer vaccines. More studies needed to accomplish this accurately in a developing country setting.
• Anecdotally, while health workers may find it preferable to administer a lower number of injections per visit, mothers may want to do as many as possible in a single trip in order to minimize total trips.
• In the future, increased access to information and changes in client demand may necessitate single-dose vials regardless of other factors
• Cost differential between presentations varies according to manufacturer, calculation method, and ancillary costs included. In addition, as demand for single-dose vials increases, cost will decrease. The calculations are therefore not straightforward.
• In countries with high levels of outreach vs. fixed post sites, wastage from multi-dose vials is a direct result of the system.
• Five-dose measles vials have been successful in India – is this something warranting a further look?
• At the end of the day, there’s always a syringe. Who fills it? A machine or a worker?
• Vial size and shape is partially dictated by existing equipment; it will likely not be feasible to re-design a container to such an extent that it requires an entirely new system of production and distribution.
• With any re-design or repackaging effort, manufacturers must have a consistent demand and a predictable market in order to make the initial investment worth it.
• Health care workers are scared to waste vaccine, and MDVP compliance is therefore lowered. There is a mismatch between the policy and the reality of limited supply on the ground.
• There is a need for feedback from on-the-ground workers, for both policy and product design. A logistician, health worker, and EPI manager may have different priorities, purposes, and concerns, and coverage must be considered—a health worker likely to actually open the vial in the field?
• The chosen presentation should meet the needs of timely (i.e. as per vaccination schedule) as well as high overall coverage.
• Looking to the future, certain countries (e.g. Jordan) that intend to introduce single dose presentations based on expected improvements in safety, access and affordability but understand that trade-offs need to be made and managed.

Session 2: Issues Related to Primary Container Decisions

Primary Container Considerations for Prequalification (Andrew Meek, World Health Organization)
Outlines mandatory, critical, and preferred vaccine characteristics concerning programmatic suitability for WHO prequalification. Addresses issues with removal of thiomersal, including lack of alternatives and consequences of removal on immunization programs. Also describes prequalification and future challenges for Synflorix 2-dose presentation.
Key points include:
- Programmatic Suitability for Prequalification (PSPQ) evaluates the technical and programmatic aspects of a vaccine and its container
  - Characteristics can be mandatory, critical, or preferred
  - Requirements vary by vaccine type and administration route
- Mandatory characteristics (unconditionally required for prequalification) relevant to container decisions include: presence of adequate preservative in vials greater than two doses; packaging in
materials that can be safely disposed of in the field; and packaging and delivery in appropriate formats to reduce adverse events, such as an auto-disable syringe or ready-to-use format

- Critical characteristics (conditionally required for prequalification) include: standardized dose volumes; adequate preservative status in 2-dose or reconstituted vials, and antigenic stability in reconstituted multidose presentations
  - If a presentation fails critical characteristics, it will go to committee for review and may pass via that route; these characteristics can therefore be a grey area.
- Preferred vaccine characteristic (best case scenario, provides a guide for likely future requirements) include: small packed volumes; CPAD; less than 10 doses per vial for non-campaign settings and more than 10 doses per vial for campaigns; packaging of vials with ancillary materials; and non-burdensome temperature and storage requirements.
- Vaccine Presentation and Packaging Advisory Group (VPPAG) Generic Preferred Product Profile for Vaccines
  - Provides recommendations for vaccine producers and developers on presentation and packaging of new vaccines for use by public-sector programmes in developing countries
  - Some recommendations are based on evidence, but gaps in the supporting data remain
- Thiomersal in multi-dose vials: international efforts to ban mercury may result in prohibition on thiomersal use
  - Without new, effective preservatives, a thiomersal ban would force a switch to single- or two-dose vials, impacting capacity, costs, and coverage
    - No clear alternative to thiomersal currently exists
    - New preservatives would require new trials
    - Given the significant up-front costs of a new formulation, there would be no economic incentive for companies to reformulate traditional low-cost vaccines
- Synflorix: novel 2-dose liquid presentation without preservative
  - Post introduction studies show no indication of increased AEFIs related to product misuse, but some incorrect storage & waning of health worker knowledge
  - Countries need to be informed of the benefits and risks of the presentation and have the responsibility for assuring programmatic readiness and regular training to use such a presentation.

_Cold Chain (Transport & Storage) & Disposal Volumes, Current Status & Future Trends in Cold Chain._ (Souleymane Kone, World Health Organization)

This presentation provides an overview of major elements in immunization systems, along with information about the operations impact of vaccine characteristics such as price, presentation, and formulation. Data from the Democratic Republic of Congo (DRC) and Chad demonstrate the challenges of vaccine volume changes and increased workload. Key points include:

- Vaccine presentations can have major impacts on immunization systems. Storage and transport, health worker training requirements, injection safety, and waste management are all affected.
- Storage needs increase with dose size, though compact auto-disable syringes have lower storage requirements than single-dose vials
  - In a simulation of vial size changes in the DRC, using a 10-dose pentavalent presentation requires 20 walk-in cold rooms (WICR) while a CAD presentation requires 49 WICR and a single-dose vial requires 65 WICR.
- Managing increased shipment and storage volume requires increased personnel hours
  - In Chad, new vaccine introduction resulted in a 5-fold increase of the workload at central level.
- Waste generation increases as doses per vial decrease; syringe use and disposal stays constant, while number of vials disposed of will increase.
- Current presentations of new vaccines are simpler and less bulky than they were in their first incarnations, but challenges of increased storage and workload remain
- It’s important to consider service delivery needs; many countries have geographically large catchment areas for each service delivery point, potentially affecting session size or need for outreach efforts

**Immunization Session Attendance, Vaccine Wastage and Coverage (Philippe Jaillard, Agence de Médecine Préventive)**

This presentation provides data from an AMP study on session size and wastage in urban and rural areas of Burkina Faso (2009). Data indicate that session organization differed by setting, and that vaccine vial size drives session planning, affecting session size and type. Key points include:

- **Session characteristics**
  - Urban sessions were 67% of total immunization sessions and 77% of doses administered
  - Outreach strategy more frequent in rural sessions (40.5%) than in urban settings (14.8%)
- **Vaccine availability at sessions**
  - Liquid vaccines were offered at most sessions
  - Lyophilized vaccines were offered between twice a week and once per month at fixed sessions, and dependent on attendance at outreach sessions
  - A “vial effect” is observed with multi-dose measles and BCG; session sizes cluster in multiples of 10 or 20 to minimize wastage from 10- and 20-dose vials
  - No clustering observed with single-dose pentavalent
- **Vaccine wastage**
  - Overall, wastage was lower than expected at the national level
  - More wastage happens at the store level than at the session level
- **Immunization coverage**
  - Coverage rates were similar for measles and pentavalent vaccines
  - While both pentavalent and measles coverage were high, measles coverage rates drop when only timely doses are included (early dosing is likely to have reduced efficacy).

**Primary Vaccine Container Selection in Developing Countries: Safety Issues (Neal Halsey, Johns Hopkins Bloomberg School of Public Health)**

Dr. Halsey addressed the potential for adverse events following immunization, laying out likely relationships between vaccine presentations, preservatives, and outcomes such as infection from contamination and needle sticks. Key points include:

- Adverse events and errors in vaccine administration occur everywhere, although no true rate data exist.
  - Contamination of multi-dose vials (with and without preservatives) has resulted in outbreaks and deaths globally.
- Surveillance systems and staff training and supervision are often inadequate; simpler vaccine administration methods reduce errors.
  - We don’t have a good capacity of detecting, investigating, and addressing adverse events associated with vaccines
  - There are incentives to underreport and suppress documentation of mistakes
Prefilled single-use syringes are easiest and safest, but also expensive and bulky.

- Adherence to vaccine policies is not universal
  - Observed breaks with safety protocol include withdrawal needles being left in MDVs (throughout complete vial use) to speed administration.
  - Knowledge about safety is often lacking.

- Contamination concerns
  - Toxic shock syndrome deaths in India were observed following injection with contaminated measles vaccine
    - Characteristics of the measles vial made it a good incubator for bacteria: multidose presentation increased opportunities for contamination, and nutrients in the diluent created an ideal environment for bacterial growth
    - Recent incidents (2008) include infections from measles vaccine reconstituted the day before administration
  - Error rates go up during mass vaccination campaigns
  - Immediate program costs are high, and long-term repercussions include increased credibility for anti-vaccine lobby

- Other forms of user error
  - Diluent was packaged in identical vials as paralyzing agent; 2 children died and 3 clusters of children collapsed after receiving injections containing paralyzing agent instead of diluent
  - Lack of standardization across countries and settings increases opportunity for user error

- Preservative options in MDVs
  - In analysis of alternatives to thiomersal, several alternate preservatives reduced bacterial growth
  - Different effects at different time points and temperatures
  - Even effective preservatives may have manufacturing and delivery vulnerabilities

- Maintaining public confidence is our highest priority
  - Need to make it a high priority to have surveillance, reporting and supervision
  - Without demand, efforts to increase coverage will not be successful
  - Where possible, unit dosing is the simplest and safest way to go

Bruce Lee: Modeling and inputs for development of a framework

Dr. Lee presented the Vaccine Modeling Initiative’s HERMES, a computational tool to design, plan, and manage vaccine supply chains. His presentation demonstrated the use of HERMES to simulate the impact of rotavirus and pneumococcal vaccine introduction in Niger and Thailand. Important supply factors considered included cost, vial size, capacity utilization, and vaccine availability.

- The HERMES software platform can generate an interactive simulation model of any supply chain
  - Integrates WHO/OPTIMIZE tools
  - Container characteristics used as model inputs include size, antigen, weight, thermo-stability, and diluent requirements
  - Model also includes health service delivery location and type, cold storage and transport availability, and other components of a vaccine logistics system
  - Can run on any laptop computer

- Why a simulation model?
  - Represents the dynamic nature of the immunization system; the ability to include feedback loops allows for the assessment of complex relationships
- Allows for a high level of detail when data are available
- Allows for representation of random events that may affect outcomes (power failures, etc)
- Allows for representation of decision-making; for instance, the simulation can assign a value representing how likely it is that a health care worker will open a vial for any given number of children
- Allows generation of multiple measures of interest to different stakeholders: did not want to tie anyone down to one particular model
- Provides a set of tools to look at vaccine supply chain issues and simulate delivery in different settings
  - Niger and Thailand simulations: introducing pneumococcal and rotavirus vaccines
    - Introducing new vaccines can result in reduced availability at service points
    - Existing bottlenecks are exacerbated if you add an additional vaccine
    - The higher the volume per dose of new vaccine, the greater the initial negative effect from introduction; bottlenecks increase with larger vial sizes
    - In supply chains currently operating below maximum capacity, new introduction will have smaller negative effects

Session 2 Discussion: Questions, comments and clarifications

- Single-dose lyophilized vaccines could still carry some risk of bacterial contamination if they are not used within the correct time window after reconstitution
- Patients with AEFI don't go back to the same clinic; AEFIs are therefore underreported
- Reuse of reconstitution syringes can be a significant problem if health workers are not educated about safety implications
- If any kind of adverse event occurs, countries need to react quickly and proactively to address concerns, including unfounded concerns; social and internet media can lead to a snowball effect
- Even very small clusters of adverse events can generate a huge amount of publicity; if not dealt with appropriately, these incidents can erode public trust
- Representing behavior in HERMES is possible, but accurate representation depends on accurate data and on-the-ground reporting, which is often lacking.
- Aspects of the HERMES model could be adapted for use as a management tool
- Each day is simulated individually, allowing for inclusion of factors like seasonal fluctuations in demand, effects of a rainy day, and so on
- A system may generally operate within capacity, but if it has troughs or peaks that take it beyond capacity at certain times or in certain areas, it's not fully meeting demand
- Niger, Thailand, Vietnam, Senegal, Kenya, and Chad have already have been simulated. The HERMES team is attempting to review available data to see where the gaps are for simulations in other areas; ideally, there would be a set list of necessary inputs that must be collected in order to successfully run the program, along with a clear protocol for how to run it in each country.
- The model hasn’t included challenges that come with sourcing from more than one supplier
Appendix Two. Draft Framework and Breakout Group Revisions.

*Draft Framework – Presented to breakout groups*
**Group 1 Revisions**

**Successful System Immunization ACCESS**

- Needle Stick Rate
- MISSED OPPORTUNITY RATES
- Infant Information Systems

**Sustainable AFFORDABILITY**

- Raw Materials Available
- Product Price
- Fixed Cost
- Storage
- Transport
- Manufacturer Capacity
- Manufacturer Feasibility

**SAFETY**

- Public Acceptance
- Health Facility
- Health Worker Training

**Group 2 Revisions – Chart A**

**ACCESS**

- Deliverability
- Coverage

**AFFORDABILITY**

- COST PER DOSE
- MISSED OPPORTUNITY RATES
- PRICE PER DOSE

**SAFETY**

- Accepted Threshold of Risk
- Quality Perception (Thiomersal)

**Group 2 Revisions – Chart B**
Group 3 Revisions

**ACCESS**

- Point of Service Supply
- Wastage Rates
- Missed Opportunities
- Shelf Life After Open
- Doses per Container
- HCW Decision Making
- Average Session Size and Type
- Political Environment
- Policy and Experts Recommendations
- Donor and Agency Funding
- Numerical Concerns
- Contaminant Infection Rate
- Blood-Borne Disease
- Contaminant Infection Rate
- Need for Vaxed Child
- HCW Training Levels
- Wastage
- Ease of Use
- Efficacy
- Liquid or Lyo
- Easily Identifiable Containers

**AFFORDABILITY**

- Price per Dose
- Cost per Vaxed Child
- Added Costs of Monitoring Visit
- MFG Delivery
- MFG Cost per Container
- Doses in Series
- Temperature Requirement
- Delivery Costs (Logistical & Initial)
- Container and Package Volume
- Other Market Forces
- Cost per Vaxed Child
- Manufacturer Cost Capacity to Adapt
- Heat Stability Out of Cold Chain Characteristics
- Container Temperature
- Container Package Volume
- Technical Feasibility
- Dimensions: Vial diameter - Vial height
- Labeling Issues
- Doses per Container
- Administration Route
- Ease of Use
- Efficacy

**SAFETY**

- Safety
- Disease Prevention/ Lives Saved
- Infrastructure (Trends)
- Buy-in
- Political Environment
- Syringe Costs: Rural/Urban
- Syringe Costs: Logistical & Initial
- Heterogeneity
- Need for Stick Rate
- Contaminant Infection Rate
- Blood-Borne Disease
- Fixed vs Outreach EPI or PRI not Campaign

**OUTCOMES**

- Outcomes
- Infrastructure (Trends)
- Policy and Experts Recommendations
- Peer Influence
- Thrombosis Concerns
- Heterogeneity
- Ease of Use
- Efficacy

**STANDARDS**

- Standards
- Disease Prevention/ Lives Saved
- Infrastructure (Trends)
- HCW Training Levels
-Need for Stick Rate
- Contaminant Infection Rate
- Blood-Borne Disease
- Fixed vs Outreach EPI or PRI not Campaign

**GROUP 3 REVISIONS**

- Disease Prevention/ Lives Saved
- Infrastructure (Trends)
- Policy and Experts Recommendations
- Peer Influence
- Thrombosis Concerns
- Heterogeneity
- Ease of Use
- Efficacy

**GROUP 3 REVISIONS**

- Disease Prevention/ Lives Saved
- Infrastructure (Trends)
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