TOTAL SYSTEM OF EFFECTIVENESS (TSE) FOR RESEARCH & DEVELOPMENT (R&D)

Minutes of the meeting

August 1, 2018 | 9:00 AM to 5:30 PM

Location – Hotel Mida Ngamwongwan

Objectives

- To understand the barriers toward vaccine R&D for low and middle incomes countries (LMICs) and the extent to which they could be addressed by TSE.
- To characterize the different R&D use cases for TSE.
- To explore potential applications of TSE within the identified R&D use case(s) and priority activities to develop TSE for R&D use.

Attendees

Name	**Organization**
Dr Auliya Suwantika	Padjadjaran University, Indonesia
Dr Birgitte Giersing	Initiative for Vaccine Research, World Health Organization
Cecilia Oh	Access and Delivery Partnership, United Nations Development Programme
Diana Beatriz Bayani	Health Policy Development and Planning Bureau, Department of Health, Philippines (HITAP interns)
Do Tuan Dat	VABIOTECH
Dr Yot Teerawattananon	Health Intervention and Technology Assessment Program, Ministry of Public Health, Thailand
Dr Pornthip Wirachwong	Biological Research Group, Government Pharmaceutical Organization, Thailand
Erik Ismail Suhaeri	Bio Farma, Indonesia
Ery Setiawan	University of Indonesia, Indonesia
Evelyn Thsehla	Researcher, Council for Medical Schemes, Pretoria, South Africa (HITAP interns)
Jacqueline O'friel	Msc student, London School of Hygiene & Tropical Medicine, UK (HITAP interns)
Dr Jarir At Thobari	Gadjah Mada University, Indonesia
Jatuporn Apichadsupapkajon	Health Intervention and Technology Assessment Program, Ministry of Public Health, Thailand

Jirata Tienphati	Health Intervention and Technology Assessment Program, Ministry of Public Health, Thailand
Jitep Kidkasetpaisal	Pharmaceutical Research and Manufacturers Association, Thailand
Naritpong Chaiwong	Pharmaceutical Research and Manufacturers Association, Thailand
Jitep Kidkasetpaisal	Pharmaceutical Research and Manufacturers Association, Thailand
Jos Luttjeboer	Asc Academics, Netherlands
Juliet Eames	Health Intervention and Technology Assessment Program, Ministry of Public Health, Thailand
Manushi Sharma	Health Intervention and Technology Assessment Program, Ministry of Public Health, Thailand
Monta Thammasat	National Science and Technology Development Agency
Pramote Akarapanon	Food and Drug Administration, Ministry of Public Health, Thailand
Amporn Charoensomsak	Pharmaceutical Research and Manufacturers Association, Thailand
Nantiya Narkwachara	Pharmaceutical Research and Manufacturers Association, Thailand
Nuntapun Subhapatarapong	Pharmaceutical Research and Manufacturers Association, Thailand
Rachel Archer	Health Intervention and Technology Assessment Program, Ministry of Public Health, Thailand
Rajibul Islam	Health Intervention and Technology Assessment Program, Ministry of Public Health, Thailand
Ritika Kapoor	National University of Singapore, Singapore
Saudamini Dabak	Health Intervention and Technology Assessment Program, Ministry of Public Health, Thailand
Siobhan Botwright	Initiative for Vaccine Research, World Health Organization
Dr Wanruedee Isaranuwatchai	Health Intervention and Technology Assessment Program, Ministry of Public Health, Thailand
Waranya Rattanavipapong	Health Intervention and Technology Assessment Program, Ministry of Public Health, Thailand
Dr. Wassana Wijagkanalan	BioNet-Asia, Thailand

Welcome by Chair

The meeting commenced with a round of introductions and declaration of conflict of interest; post this Dr Yot Teerawattananon, Chair of the meeting and Founding Leader of Health Intervention Technology Assessment Program (HITAP), Thailand provided an overview of the project (Presentation here). The details are as follows.

As innovative technologies and biological treatment are becoming available for use, policymakers worldwide will require a tool to evaluate the cost and assess the trade-offs. The concept of Total System Effectiveness (TSE) is an end-to-end analytical framework which is intended to inform future investments, purchase and advance the uptake of innovative medicine delivery technologies. He further added the TSE is a step ahead, it is an approach to priority setting; Using HTA to inform the forthcoming products and apprise manufacturers of the demand specific characteristics that a product should have. The aim of TSE is to ensure that vaccine product preferences in low and middle-income countries inform R&D, with the intention of facilitating country uptake and decreasing risk for manufacturers. Decision making is a multi-faceted process and involves a variety of stakeholders. The intent of TSE is to improve decision making at all levels from product development to in-country use by initiating a dialogue between the vaccine producers and health care programmes.

This approach is a step in the future. This meeting is aimed to receive feedback on how the TSE approach can inform R&D, to understand the barriers toward vaccine R&D for low and middle incomes countries (LMICs) and the extent to which they could be addressed by TSE. Next, to characterize the different R&D use cases for TSE. Lastly, to explore potential applications of TSE within the identified R&D use case(s) and priority activities to develop TSE for R&D use.

Introduction to Total System Effectiveness (TSE)

Dr Birgitte Giersing who is a Technical Officer at the Initiative of Vaccine Research at the World Health Organization (WHO) set the outline for her presentation (Presentation here). Reiterating what Dr Yot had said, Dr Giersing explained that the primary focus of this meeting is to receive feedback on the TSE concept. Her presentation divided into two parts - first, to introduce the concept of TSE and how it may inform R&D to the participants, and second to give an idea of what activities will be undertaken for the rest of the day.

Setting the tone for the presentation she explained that despite the success of immunization programmes globally, many children still remain unvaccinated.

"Even though we have very successful global immunization programs, there are still 20 million children under 5 each year that are either not vaccinated at all or they don't finish their vaccination courses"

Vaccine products that better address barriers to immunization in low and middle-income countries (LMICs) could support countries to reach immunization targets. In the future, countries are likely to have

access to a choice of differentiated products which should enable them to improve reach to the un-immunized cohort of children in each context. She explained with the help of a graph that, conceptually, the logistical challenges in vaccine delivery increase as we move from densely populated areas to remote areas, or areas of conflict, where populations are more difficult to access. It is these populations that constitute a large proportion of the 20 million children per year that are under- or unimmunized. Therefore, it is of foremost importance that we find innovative solutions and platforms for vaccine delivery which improve the reach of the product to these populations.

Currently, in the case of Rotavirus, we have a diversity of licensed vaccine options present for vaccine delivery. They differ in terms of price per regimen, a number of doses per regimen, storage requirements, supply chain footprint etc. This puts the policymakers in a dilemma about which vaccine is best for what type of population. Given the selection and the choice of technologies present (and many in the pipeline); How do countries evaluate what they need? How do policymakers identify which ones are likely to be more useful and where the public money should be directed? How do manufacturers determine the market for the vaccine that they are developing?

The TSE is an approach that aims to answer these questions. Allowing the countries/policymakers to communicate the specific needs of the country is one of the core ideas around which the TSE approach was developed.

TSE should enable decision-makers to evaluate the full set of trade-offs, including the cost to buy the vaccine (which may be more expensive in the case of an innovative product) and the cost of delivering the product (which may be reduced if the product is easier to transport and deliver) ; and to make explicit the parameters which influence the vaccine decision making, allowing for prioritization of vaccine products that address program challenges. This should support R&D decision-makers select from multiple options and inform go/no-go decisions during the product development process.

The concept of TSE could potentially benefit the vaccine manufacturers and technology developers in linking preferences of LMICs (potential market demand) to product attributes to. It has the potential of facilitating the decision making process and informing donors and procurement stakeholders regarding prioritization of future products that may help to achieve immunization targets.

To inform strategic R&D decisions that meet public health needs, of LMICs, the World Health Organization develops Preferred Product Characteristics (PPC) for new vaccines. This guidance identifies the target populations, possible immunization strategies, and desired clinical data for use of the vaccine in LMICs, as well as ensuring that vaccine presentation and packaging is suitable for low-resource settings to encourage vaccine uptake in these contexts. The PPCs, presentation and the packaging recommendations form an essential part of vaccine developers' Target Product Profiles (TPPs). Companies can use these PPCs to assist in defining their candidate specific target product profiles.

This was followed by a round of open discussions. Following are the key points:

Q) Based on the discussions and explanation TSE seems theoretical, it will be interesting to see the results of the pilot case specifically regarding the uptake and the challenges.

A) This is the first phase of the pilot in Thailand and Indonesia. The expected outcome of this initial phase is to learn about the translatability and applicability of the TSE. One limitation of TSE is that it identifies the product which is adaptable to the context, but not how it can be delivered. The concept and tools will evolve with the learning experience from all the countries. TSE is intended to enable a broader dialogue with all the stakeholders.

Q) Along with the downstream factors which have an impact on the accessibility of the product there are some valid global stakeholders which influence the market. Even though countries are becoming more self-sustained there are relevant players like Gavi, which play an important role in shaping the country policy. Therefore, to understand the challenges clearly, it is important to liaise with relevant global parties. Does TSE accommodate for that?

A) This is a country pilot specifically for Thailand. The results from a global perspective will be consolidated in the later stages. Currently, the TSE initiative has a diversity of partners including Gavi and UNICEF. The challenge currently is to find an 'optimum' list of interventions and the demand should be led by governments. The TSE aims to facilitate this process.

Q) Does the TSE help to address the delivery shortcomings in a country?

A) Currently, the TSE is aimed to understand the prioritization of the products and the factors affecting the selection/sequencing of the products. But we do think that understanding the delivery challenges better will be important to help to understand why certain products are identified.

Q) How can TSE help provide technical input to the manufacturers?

A) The TSE is aimed at aligning government demand with manufacturers to create an optimum environment for clear communication and R&D strategy, i.e. if producers understand country preferences, they can design products in line with the country needs, thereby increasing the likelihood of uptake and returns on investment, and the government ensures 'value for money' and addresses the accessibility issues.

Plenary I - Understanding the context and current drivers of vaccine R&D in the region

This session was facilitated by Dr Birgitte Giersing (WHO) and the panellists were from the manufacturing firms – Pharmaceutical Research and Manufacturer Organisation (PReMA), Vabiotech, BioNetAsia, and Bio Farma.

Each representative presented their case and thoughts on the topic. The summary of the key discussions is as follows:

Presentation by Amporn Charoensomsak, PReMA (Presentation here)

- Childhood vaccination gives significant societal benefits for instance in the United States of America alone a whopping amount of USD1.4 trillion was saved. New portfolio of almost 270 vaccines are under development to prevent and treat diseases.

- R&D is resource intensive and time-consuming exercises and the return of investment will incentivize to a sustainable R&D for unmet needs.
- The need for greater public and private partnerships was highlighted. An effective collaboration is equalled to a win-win collaboration; this will help both the parties to function in harmony and achieve their goals.

Presentation by Do Tuan Dat, Vabiotech

- Vabiotechis one of the leading companies in the field of research, production and trading of vaccines and biologicals for human use in Vietnam with production facilities meeting the WHO-GMP, GSP and GDP standards;
- In his experience, the government hugely underestimates the costs associated with vaccine development. In a case where the government and the company work hand in hand to identify product need, specify the product characteristics it will ensure that there will be product uptake once it is out in the market.
- The monetary incentive should be linked with the R&D so as to promote innovation and achieve vaccine coverage to the remotest of regions.

Presentation by Dr Wassana Wijagkanala, BioNetAsia

- Dr Wassana introduced her firm to the audience. BioNet-Asia is a vaccine company focused on technological innovation and market access. In its state-of-the-art vaccine plant in Thailand, they are also building a unique expertise in genetic engineering, protein conjugation, cell-culture and vaccine formulation with several products in the pipeline.
- Further, she emphasized the importance of viable public-private partnerships to promote the indigenous production of vaccines in Thailand

Presentation by Erik Ismail, Bio Farma (Presentation here)

- Bio Farma is an Indonesian state-owned enterprise based in Indonesia which produces vaccines and sera to support immunization domestically and other countries. This firm has entered a pre-qualification list of the WHO and has supplied vaccines to multiple countries through various international organizations such as UNICEF and PAHO.
- For the indigenous industry to make quality products and for the consumers to get competitive prices it is important to have competition in the market. The laws and regulation should be aligned in the interest of manufacturers in such a way that returns on investment are ensured.
- Further, he added that effective partnerships in this field between the government and the manufacturers will ensure that both the parties achieve their goals. Vaccine targets for the government and return on investments for the vaccine producers.

This was followed by a round of open discussions.

- The vaccine availability or accessibility which is restricted due to impediments at every stage of the vaccine development process. Some factors associated with this are:
    - Manufacture of conventional drugs involves relatively simple procedures from manufacture to the supply chain. Biologics such as vaccine require highly sophisticated

processes and specific standards for vaccine production. This implies huge monetary investments thereby making R&D commercially unattractive. There should be a model of vaccine development which attempts to address the imbalance between the public health needs and a commercial incentive to the manufacturers and developers.

- Considering the large development costs attributed to vaccine development and the high attrition rate of projects in the pipeline, there may be few vaccines entering the market in the coming years from industry. There may be other projects under development by research institutes, Product Delivery Partnerships (PDPs), and biotech companies and by other smaller vaccine manufacturers. However, without a significant investment (which many of the stakeholders may not have access to), the chances of successful products reaching the market remain limited. With so many global priorities competing for investments, product development is almost certain to take a strong hit.
- In Thailand, the process of price negotiation of vaccines follows a complex purchasing process with many stakeholders, including public authorities and recommendation bodies, prescribers and end users. It is important for the vaccine developers that the end price of the vaccine is negotiated appropriately to ensure returns on vaccine investment thereby guaranteeing steady investment in innovation.
- National regulatory systems should be more accommodating towards the demands of the manufacturers. Incentivizing the R&D to boost local manufacture of vaccines so that the immunization programs in the country can be sustained by domestic production.
- Manufacturers face the challenges to balance the supply and demand sides of the local market. The global supply and demand is the second priority.

- TSE could be a tool or mechanism to help manufacturers to a better informed on the product development strategies, by articulating products characteristics that are important for their country's market, as well as LMICs. However, local context such as country priority, demand forecasting, evidence, decision criteria, and capacity is crucial and needed.

Case study: Rotavirus vaccine development in Indonesia

The case study on the development of Rotavirus vaccine in Indonesia was presented by Dr Jarir At Thobari, University of Gadja Mada, Indonesia (Presentation here). Although over the years the hospitalization of children due to Rotavirus Diarrhea has decreased, in comparison to the rest of the world the burden of Rotavirus related diarrhoea in Indonesia continues to be very high. The aim of the Rota vaccine development was to mimic the broad protection achieved after two natural rotavirus infection.

In a study conducted to examine the acceptability of Rotavirus vaccine among parents and caregivers. The important characteristics which influence vaccine uptake in Indonesia are:

- Cost of the vaccine
- Recommendation of the vaccine by health professionals
- Mode of administration of the vaccine

- Halal vaccine
- Vaccine safety

It is important that country-specific demands are taken into account. For instance, Indonesia has a Muslim-majority population, therefore, the manufacturers there, have to supply halal medicines.

Next, he explained about the Rotavirus vaccine development where there were a series of clinical trials in Australia and New Zealand. Consultations with stakeholders including community leaders and the point of halal vaccines were further corroborated. The Immunisation Technical Advisory Group in Indonesia (ITAGI) is the premier body which gives recommendations regarding the vaccination needs of the country. It communicates with the manufacturers and the ministry of health on the programmatic needs for the vaccine in Indonesia.

Although several stakeholders are involved in determining the preferred product characteristics of vaccines, the process is largely unstructured. The TSE approach could fill and streamline this gap.

Plenary II - Role of the public sector in influencing the research & development

This session was facilitated by Birgitte Giersing (WHO) and panelists were Cecilia Oh, Access Delivery Partnerships (ADP), United Nations Development Programme (UNDP) and Monta Thannasatta, National Science and Technology Development Agency (NSTDA), Thailand.

Presentation by Cecilia Oh, ADP, UNDP

It is important to look at three key areas when talking about access to vaccines:

- Innovation
- Affordability
- Actual delivery

Simply, having a vaccine in the pipeline or even on the market that meets a priority need and is suitable for use in a low- and middle-income country will not automatically solve the world's access problems. Companies and other stakeholders have a joint responsibility to ensure that there are mechanisms in place to ensure the vaccine's quick roll-out, thus ramping up coverage of vaccines upon market introduction. A holistic approach which combines the interest of all the stakeholders is required. To stimulate the development of innovative products for public health, more concerted actions are needed, with the various stakeholders working in a synchronized manner to link the upstream and the downstream arguments.

Product Development Partnerships (PDPs) are important instruments to enhance the availability of vaccines in developing countries. Many PDPs have overcome the potential barriers posed by patents by developing and implementing intellectual property management frameworks that facilitate product development while ensuring affordable prices.

Presentation from Monta Thannasatta, NSTDA

Monta explained the Newly Emerging Disease - Re-emerging Disease Program which was led by NSTDA in collaboration with the universities and government agencies in Thailand. The program aims to create knowledge and products that can promptly solve problems related to and address newly emerging and re-emerging diseases as well as increasing research capability so that the country is self-reliant and stable.

The dengue program at NSTDA is one of the most advanced research collaborations in Thailand involving medical experts from a number of research institutes. This vaccine R&D program produced clinical lots of tetravalent vaccine candidates and conducted phase I clinical trial. In addition, immunological assays are being developed and evaluated for their correlation with immune protection. Two potential Good Manufacturing Practices (GMP) production facilities: one private vaccine company, the other is the national GMP pilot facility.

Key operation plans include conducting R&D work to create dengue vaccine prototypes to be tested in humans by 2016, focusing on improving research to create dengue serotype 2 vaccines and test tetravalent vaccines in monkeys. Finally, a patent resulting from the collaboration was recently licensed to Bionet – Asia for further development of the dengue vaccine.

Key points from the discussions are stated below.

- The NSTDA is a model case for the developing countries to receive support from the government. Peer countries like Indonesia where the government lends modest support to the vaccine producers and other procedures for procuring funding support are lengthy and tedious; it becomes difficult for firms to secure funding.
- While R&D efforts in recent years have begun to show promising results in producing innovative health technologies for various diseases, there has been little consideration for addressing downstream challenges. The introduction and scale-up of new health technologies place a significant burden on health systems in LMICs and are often hindered by policy and regulatory barriers, as well as capacity gaps. Such challenges have prevented new and existing health technologies from reaching millions of people in need. Governments, therefore, need to identify and address the specific factors that impede access and delivery and ensure that appropriate systems are in place and functioning properly to assure the affordability quality, safety and appropriateness of new health technologies.
- Having partnerships as a model to facilitate access to medicines was agreed to be a common factor which will benefit all the stakeholders. Public-private partnerships and PDPs are vehicles suitable for delivering healthcare and strengthening healthcare systems. These multi-stakeholder efforts are able to ensure product registration, increase local production and distribution capacity, and ensure governance for global health, e.g., adoption of new health technologies in national treatment policies in disease-endemic countries.
- TSE is a whole system approach, starting with the needs of the immunization programme in the country to shape the candidates that are in the pipeline. focuses on informing the decision-

making process about which vaccine or vaccines are best suited to a country to increase equitable coverage.

- One of the problems is lack of funding from the government to support R&D.

Summary of the discussion by Chair

TSE could be an effective platform to initiate a constructive dialogue between technology suppliers, producers, manufacturers, the stakeholders which invest heavily in the making of the product and the government or the policymakers, the technology suppliers, health care providers; this will not only drive innovation but also foster sustainable partnerships resulting in safeguard of public interests. It is public good which will be the stepping stone for future collaborations both global and local.

Using the Thailand country use case to determine preferred product characteristics

Dr Ritika Kapoor, National University of Singapore presented the results of the TSE pilot project in Thailand (Presentation here). The TSE pilot project for Thailand was based on a hypothetical case where five Rotavirus vaccines with different characteristics were taken into consideration. For the Thai pilot project, an Excel-based model for rotavirus product selection was used. The presentation was divided into five main sections:

- *Multi-Criteria Decision Analysis (MCDA) for Thailand* which includes safety, health impact, budget impact, delivery cost, and cost-effectiveness.
- *Parameters influencing MCDA Criteria*: These are divided into i) vaccine specific characteristics and ii) other criteria. For instance, safety is directly proportional to the relative risk of intussusception, a number of doses and vaccine schedule which are vaccine specific characteristics.
    - The health impact is directly influenced by the vaccine efficacy, a number of doses, duration of protection, the socioeconomic status and the coverage.
    - The budget impact of the vaccine is determined by the costs associated with its storage, doses etc.
    - The delivery cost is more influenced by the price of electricity, petrol, number of deliveries etc.
    - The cost-effectiveness of the vaccine is dependent on the vaccine and other criteria.
- *Vaccine Products Characteristics:* The criteria mentioned above were mapped to the characteristics of the vaccine above has helped shape we are considering for the hypothetical Thailand base case. Some of the factors which are utmost important are - relative risk of intussusception, vaccine efficacy, number of doses, duration of protection, vaccine schedule, commodity cost, the volume of the vaccine, a method of cooling, number of doses per vial.
- *MCDA Rankings*: Weights were assigned to each of the parameters which were explained above and the vaccines were scored on this basis. In this hypothetical situation, the weight of 20% was assigned to each vaccine. The final score was calculated by multiplying the score with the weight. While performing the analysis two scenarios were considered i) original criteria ii) Thai criteria chosen by the stakeholders in the May meeting. With the original criteria, RVV-3 ranked as the

first choice for policymakers. The results of applying the Thai criteria were similar RVV-3 ranked first followed by RVV-2. The team performed a sensitivity analysis by altering the value of each parameter to conclude which parameter influences the ranking the most.

- *Significant Vaccine Parameters Impacting MCDA Rankings:* The following parameters influenced the ranking of the vaccine RVV2 which ranked second in this model.
    - Safety is influenced by a relative risk of intussusception and number of doses.
    - The health impact is dependent on vaccine efficacy and duration of protection.
    - The Budget impact is shaped by commodity cost, vaccine efficacy, number of doses, duration of protection.
    - Cost-effectiveness of the vaccine is most influenced by the commodity cost, then the vaccine efficacy, followed by a number of doses and lastly duration of protection.

Thus, from the pilot, it was concluded that:

- The cost of developing the medical products is very high and leads to high-cost health technology and subsequently a barrier for product accessibility.
- This study corroborates that performing an early stage HTA to inform R&D, can help identify preferred product characteristics, making R&D efficient by decreasing the cost and accelerating the product uptake.

This was followed by an open discussion:

Q) Does the model investigate a) the co-morbidity costs & b) Is uncertainty of risk addressed in this model?

A) This is a work in progress. The pilot does not address the issue to co-morbidity. Regarding uncertainty, as this is a value-based pricing approach a novel product can be priced as per its worth. The intention of TSE is to characterise identify how the vaccine would be used and therefore the demand, thereby reducing the risk for manufacturers.

Q) How about the unquantifiable parameters such as acceptability of vaccine?

A) This is a limitation of the model.

Q) How early on do you recommend that HTA should be used in the manufacturing process.

A) As early as possible, but the key is to know the decision-making criteria thoroughly. If the mechanism is not well established and explicit the change may not be immediate. If the technology developers align their products with the need of the governments, it is likely to receive funding and be accepted into the EPI.

Group work 1: Developing a Target Product Profile for Rotavirus Micro Array Patch

Several country scenarios were given, and the participants were asked to identify characteristics for the Rotavirus Micro Array Patch (MAP). The exercise and the discussions are summarized below:

Country 1 - Most unvaccinated children live far from the health centre in rural areas, served by health facilities with nonfunctional cold chain equipment leading to frequent stock-outs and wastage. Most drop out due to mothers not returning for the second dose of the vaccine due to lack of awareness of the vaccines schedule and long distances to health facilities in rural areas, which requires mothers to travel for a few days to vaccinate the children. Only vaccinators can deliver vaccines and there is a shortage of vaccinators in rural areas

County 2- Parents often unaware of the vacation schedule and do not return for the 2nd dose of vaccination. Although a strong community health worker programme has increased the availability of health workers able to deliver the vaccine, community health workers must deliver a number of interventions beyond vaccination, thus do not have time to follow up on unvaccinated children. This is exacerbated by pockets of highly mobile populations and rapid migration to urban slums. Much of the population lives in urban areas with access to health facilities with functioning cold chain storage.

County 3 - There is a shortage of health workers especially in rural areas. High staff turnover, especially across the border means that many health workers are poorly trained without adequate supervision, meaning that many health workers are unaware of the rotavirus vaccination schedule and so do not deliver the second vaccine dose when mothers come to health facilities for the second dose of DTP. The country faces issues with outdated cold chain equipment, resulting in high rates of wastage and frequent stock-outs.

Next vaccine specific characteristics were discussed.

Stability - If we make the criteria too high for instance +40 degree thermostability for 2 months this may set the bar too high and innovation developers will perceive this as unattainable. Thus, it is important to set an optimum target which is achievable. The ideal instructions or targets should be used as a reference but the optimum conditions depend on country-specific conditions/factors. A vaccine that can survive three days without refrigeration is desirable so that it can be delivered to remote areas by the controlled temperature chain (CTC) label.

Doses – To ease the delivery of the vaccine and therefore increase the reach and compliance with the complete course, one dose vaccine is ideal. Also, the vaccine should be compatible with other vaccines like DTP, this will make the delivery easier.

Delivery - Aspirationally, the patch can be administered by the mother or other non-trained health support staff. However, it may be the case that this required supervision or administration (in some cases) by a trained professional even for the most marginally complicated technology. In a study conducted on the acceptability of the MAP, it was found that the mothers were reluctant to administer the MAP by themselves as they felt more confident if the medicine was administered by a healthcare professional.

Cold chain volume per dose: This patch does well as it is small and light. Minimum 20 cm cubed, optimal 12 cm cube

Group work 2: Using MCDA to inform vaccine R&D

The purpose of this exercise was to illustrate how an MCDA exercise from a country product selection decision could be used to inform preferred characteristics for manufacturers. Participants were guided through criteria selection, weighting and scoring for MCDA.

A hypothetical example was used in the exercise. The MCDA decision matrix used by a hypothetical country to evaluate the choice of vaccines was shown. Participants then defined characteristics for a vaccine product in development, by adjusting product characteristic to see whether the product could outperform existing products according to country priorities and examining trade-offs (for example, is cold chain volume or efficacy more important? What are acceptable thresholds? Do acceptable thresholds change with changes in other characteristics?)

It was concluded that when the weights are very low it is unlikely that changing the data input will be reflected in the value of the outcome. Finally, this has a great potential and very beneficial for countries to integrate into their decision-making processes.

Closing remarks

Dr Yot Terrawattananon, Chair closed the day by acknowledging all the participants for their contribution. He further added that this is the start of the many policy-relevant discussions on this topic. The TSE holds the immense scope in streamlining the decision making the process not only in Thailand but all LMICs. He concluded by announcing to the participants that the TSE steering committee meeting will be held in Geneva and the discussions and lessons learnt from this meeting will be shared at a global platform.

Workshop feedback

The participants were requested to share their comments on 'the workshop' and the 'TSE concept' on post-it notes. A brief summary of the comments is as follows. Detailed feedback here.

i) The workshop

The general response to the workshop was positive. Although, a few participants requested that the workshop could have been more practical with hands-on training on the model with several scenarios. There were also requests to have more representation and participation from a wider group of stakeholders and policymakers. It was suggested that more discussions about how the results of the model could inform/help navigate the R&D landscape and financing decisions in reality. How WHO envisions the theory of change from this data? The deliberations should be more linked to the real processes and steps of decision making in reality.

ii) The TSE concept

The participants agreed that the TSE is an innovative approach and will be useful for integrating cost evaluations with the manufacturing processes. An important concern raised was to have 'TSE for dummies'. The overall concept is intriguing but a bit difficult to grasp; a basic training would be beneficial.

Some participants questioned the robustness of the MCDA; in future, more information on MCDA was requested.

Annexure

1. Presentation – BioFarma : https://1drv.ms/b/s!AlO7P7co8CYzhX7X8fHS0Ul-1Xxk
2. Presentation – University of Gadja Mada, Indonesia: https://1drv.ms/b/s!AlO7P7co8CYzhX99vIlMzGpUFtxl
3. Presentation – PrEMA: https://1drv.ms/b/s!AlO7P7co8CYzhX3au26TTTlC5YgL
4. Presentation – HITAP: https://1drv.ms/b/s!AlO7P7co8CYzhgKx25znUfK7Wj7q
5. Presentation – WHO: https://1drv.ms/b/s!AlO7P7co8CYzhgN4ovvgsz3gFfkG
6. Presentation – NUS: https://1drv.ms/b/s!AlO7P7co8CYzhgTAXrAdJLW_WwUF
7. Exercise - https://1drv.ms/b/s!AlO7P7co8CYzhgHYRc6Ei7RDaP_m
8. List of participants - https://1drv.ms/x/s!AlO7P7co8CYzhgfiOG3CxVayOosN
9. Agenda of the meeting: https://1drv.ms/w/s!AlO7P7co8CYzhkF6_32NO1PNY6m6
10. Workshop feedback: https://1drv.ms/w/s!AlO7P7co8CYzhkIJw4vCrCzww28v