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Pandemic Preparedness & Response
Vaccine Development Ecosystem Strengthening and
Use of Innovative Regulatory Approaches when Efficacy Studies are not Feasible

Summit Report

The Asia-Pacific Regional Summit

10 March 2026 - 12 March 2026

Le Méridien New Delhi, India

Executive Summary

The Asia-Pacific Regional Summit (10–12 March 2026, New Delhi, India) convened scientific leaders, regulators, ministries of health, manufacturers, and global partners to strengthen pandemic preparedness and response through (1) an end-to-end vaccine development ecosystem approach and (2) innovative regulatory approaches when traditional efficacy studies are not feasible. The program combined plenary and technical sessions, interactive breakouts, and disease-focused case studies (chikungunya, Nipah, and Kyasanur Forest disease (KFD)) to translate recent lessons—particularly from COVID-19—into practical actions for the region.

Workshop Objective 1: End-to-end vaccine development ecosystem.

The Summit reinforced that preparedness depends on connected capabilities spanning surveillance and pathogen detection, discovery research, preclinical development, clinical evaluation, regulatory oversight, manufacturing, and post-deployment monitoring. Presentations from India (Indian Council of Medical Research/Department of Health Research [ICMR/DHR]; Department of Biotechnology/Biotechnology Industry Research Assistance Council [DBT/BIRAC]), Japan (Pharmaceuticals and Medical Devices Agency [PMDA]) and the Republic of Korea (Korea Disease Control and Prevention Agency/Center for Vaccine Research [KDCA/CVR]) highlighted expanding scientific infrastructure, platform investments (including mRNA), high-containment laboratory capacity (Biosafety level [BSL]-2/-3/-4), and structured support to developers. WHO regional perspectives (South-East Asia Regional Office [SEARO] and Western Pacific Regional Office [WPRO]) emphasized current heterogeneity across Western Pacific and Southeast Asia, and opportunities to link manufacturing strengths in countries such as India and the Republic of Korea with regional demand intelligence and interoperable readiness architectures. The need to map capabilities and gaps using structured frameworks such as Coalition for Epidemic Preparedness Innovations [CEPI]'s capability framework aids in defining regional priorities.

Breakout discussions and plenary "playback" identified practical constraints that limit end-to-end readiness—such as access to preclinical material and specialized laboratory resources, domestic environmental and animal-use requirements that can delay timelines, and fragmented data systems that constrain cross-border use of clinical and real-world datasets. Participants emphasized the value of more systematic, routine collaboration, including formal information-sharing mechanisms (e.g., memoranda of understanding), multi-year roadmaps that define priority pathogens and fit-for-purpose minimal data packages for emergency contexts, support for platform-technology readiness, and technology transfer to strengthen regional manufacturing resilience.

The workshop also provided an opportunity to test the regional utility of CEPI's capability framework, with participants viewing it as a helpful way to structure discussion and survey results indicating that a strong majority found the framework to be beneficial.

Workshop Objective 2: Regulatory approaches for licensure when traditional efficacy trials are infeasible.

Across sessions, speakers highlighted that for pathogens with sporadic, unpredictable outbreaks (e.g., chikungunya and Nipah) or low incidence without human-to-human transmission (e.g., KFD), large phase 3 clinical endpoint trials may be impractical or ethically challenging. The Summit therefore emphasized a "totality-of-evidence" approach that integrates mechanistic plausibility, fit-for-purpose non-clinical models, scientifically justified immune markers and immunobridging, an adequate human safety database, and a defined post-authorization evidence-generation plan. Presentations and case examples discussed how immune CoPs can be supported by animal infectious challenge studies and passive-transfer

approaches, and how assay performance and standardization underpin regulatory interpretability. Discussions also highlighted new approach methodologies (NAMs) and the shift toward *in vitro* and analytically driven methods for certain legacy assays, alongside the continued importance of validated models for questions that require *in vivo* immune-system integration.

The case studies reviewed provided concrete regulatory and implementation lessons. For chikungunya, speakers described licensure strategies that used neutralizing-antibody protection thresholds supported by non-human primate (NHP) passive-transfer studies and seroepidemiology, accompanied by post-authorization effectiveness studies (including pragmatic and test-negative designs) and enhanced pharmacovigilance. For Nipah, regulators discussed "Animal Rule–type" evidentiary logic relying on robust animal challenge models, immunogenicity bridging, and enforceable post-authorization commitments, with additional attention to strain diversity and cross-neutralization. For KFD, speakers noted that phase 3 trials are not expected to be feasible; discussions therefore emphasized immunogenicity endpoints supported by NHP challenge work, benchmarking to related flavivirus vaccine precedents, and fit-for-purpose observational study designs once deployment occurs. Across discussions, reliance mechanisms and regulatory networks were repeatedly cited as efficiency enablers (e.g., UK International Recognition Procedure [IRP] routes; Thai FDA reliance; Association of Southeast Asian Nations [ASEAN] joint assessment activities; and PMDA's role as a WHO-listed authority supporting regional capacity building and information exchange).

Progress toward the expected outcomes:

- **Pathway to strengthen the end-to-end vaccine development ecosystem in the region**

  The Summit used CEPI's capability framework and WHO regional analyses (including regulatory maturity and International Health Regulations [IHR] core capacities) to support mapping of national and sub-regional strengths and gaps. Breakouts highlighted actionable needs including platform readiness, access to preclinical resources, scalable and sustainable manufacturing models, and interoperable data systems.

- **Consensus on alternative pathways for vaccine licensure**

  Sessions converged on a totality-of-evidence framework when randomized controlled trials (RCTs) are infeasible, with recurring elements: robust non-clinical/animal challenge data, scientifically justified immune markers and immunobridging, adequate safety databases, and detailed post-authorization evidence plans, particularly for confirmation of the CoP with real-world data.

- **Agreement on coordinated post-marketing studies and surveillance strategies**

  Across disease case studies, participants emphasized that immunogenicity- or model-based authorizations require strengthened pharmacovigilance and real-world effectiveness monitoring. Examples discussed included test-negative designs, cohort analyses, registry-linked safety surveillance, and sentinel-site approaches, with standard case definitions and laboratory confirmation as prerequisites.

- **Commitment to forming a regional regulatory alliance for sharing data and review processes**

  The Summit highlighted existing regional mechanisms (e.g., ASEAN joint assessment activities and ASEAN Vaccine Security and Self-Reliance [AVSSR] discussions) and international collaboration platforms (e.g., regulator-to-regulator dialogue, reliance pathways, and sharing of assessment reports). Participants identified the need for more routinized governance arrangements and confidentiality-enabled data sharing to reduce duplication and accelerate access.

- **Integration of regulatory decisions with public health deployment strategies**

  Public health panels emphasized that licensure is only one component of impact. Readiness requires linkage to surveillance and laboratory systems, supply, and procurement strategies (including stockpiling and advance purchase agreements), delivery capacity (cold chain, training, workforce), and risk communication to support confidence — particularly when products are authorized using surrogate endpoints.

Next steps:

Across sessions, participants emphasized that preparedness depends on sustained practice rather than one-time planning and will only be realized by translating theoretical alignment on alternative licensure pathways into sustained operational practice. As a priority next step, regulators agreed on the value of moving beyond discussion towards practical, joint regulatory reviews of concrete license applications that rely on animal challenge data and clinical immunogenicity evidence in the absence of traditional efficacy trials. Conducting such joint or collaborative reviews in peacetime would allow regulatory authorities to build hands-on experience in assessing these complex data packages, deepen shared understanding of evidentiary strengths and limitations, and identify system-level gaps or implementation challenges early. This practical experience is critical to ensuring that national regulatory frameworks are fully able to support timely approvals using a totality-of-evidence approach and to strengthening readiness across the region should a similar regulatory package require urgent review during an outbreak or public health emergency.

Importance of establishing CoPs and extensive characterization of various vaccine platforms was emphasized.

Priorities cited repeatedly include maintaining routine regulator-to-regulator and developer–regulator scientific exchange between outbreaks; harmonizing assays, reference standards, and animal model documentation (including through networks such as WHO Collaborative Open Research Consortium [CORC]); developing outbreak-ready master protocols and ethical-review pathways, and governance for data and materials exchange; strengthening health-data systems (vaccination registries, surveillance, and laboratory confirmation) to enable credible RWE; and reinforcing manufacturing and supply resilience through platform readiness, surge arrangements, and coordinated procurement models. These actions were framed as necessary to translate the Summit's technical alignment into faster, more coherent decision-making and equitable access during future public health emergencies.

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List of Abbreviations

Abbreviation	Definition
ACIP	Advisory Committee on Immunization Practices
ADC(I)	Assistant Drugs Controller (India)
ADE	Antibody-dependent enhancement
AEFI	Adverse events following immunization
AFSA	African Society for Analytical Scientists
A226V	E1 A226V mutation (chikungunya virus; associated with enhanced transmission by *Aedes albopictus*)
ANVISA	Agência Nacional de Vigilância Sanitária (Brazilian Health Regulatory Agency)
API	Application programming interface
ASEAN	Association of Southeast Asian Nations
AVSSR	ASEAN Vaccine Security and Self-Reliance
BIRAC	Biotechnology Industry Research Assistance Council (India)
BPL	Beta-propiolactone
BSL	Biosafety level
CAVEAT	Korean Advanced Center for Vaccine Development
CDC	Centers for Disease Control and Prevention
CDSCO	Central Drugs Standard Control Organization (India)
CEPI	Coalition for Epidemic Preparedness Innovations
CHM	Commission on Human Medicines (UK)
CMC	Chemistry, manufacturing, and controls
CoP	Correlate of protection
CORC	Collaborative Open Research Consortium (WHO)
COVID-19	Coronavirus disease 2019
CQAs	Critical quality attributes
CVR	Center for Vaccine Research (KDCA, Republic of Korea)
DALYs	Disability-adjusted life years
DBT	Department of Biotechnology (India)
DCGI	Drugs Controller General of India
DHR	Department of Health Research (India)
DSMB	Data and Safety Monitoring Board
E1/E2	Envelope glycoproteins E1 and E2 (chikungunya virus)
ECSA	East/Central/South African (genotype/lineage)
EDQM	European Directorate for the Quality of Medicines & HealthCare
EHR	Electronic health record(s)
ELISA	Enzyme-linked immunosorbent assay
ELISpot	Enzyme-linked immunospot (assay)
EMA	European Medicines Agency
FDA	Food and Drug Administration (United States)
FEEVA	Framework for Evidence Evaluation in Vaccine Assessment
GMO	Genetically modified organism
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice

GMT	Geometric mean titer
HERA	Health Emergency Preparedness and Response Authority (European Union)
HIS	Hospital information system
HPV	Human papillomavirus
HSA	Health Sciences Authority (Singapore)
HTA	Health technology assessment
IABS	International Association for Biological Standardization
ICMRA	International Coalition of Medicines Regulatory Authorities
ICMR	Indian Council of Medical Research
iHOMIS	Integrated Hospital Operations and Management Information Systems (Philippines)
IHR	International Health Regulations
IIL	Indian Immunologicals Limited
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IRP	International Recognition Procedure (UK)
IVI	International Vaccine Institute
JE	Japanese encephalitis
KFD	Kyasanur Forest disease
KFDV	Kyasanur Forest disease virus
KDCA	Korea Disease Control and Prevention Agency
LD_{50}	Median lethal dose
LNP	Lipid nanoparticle
MHRA	Medicines and Healthcare products Regulatory Agency (UK)
MOH	Ministry of Health
mRNA	Messenger RNA
NAMs	New approach methodologies
NEIDL	National Emerging Infectious Diseases Laboratories
NHP	Non-human primate(s)
NIE	National Institute of Epidemiology (ICMR-NIE, India)
NIH	National Institute of Health
NITAG	National Immunization Technical Advisory Group
NIV	National Institute of Virology (India)
NMRA	National Medicines Regulatory Authority (Sri Lanka)
NPRA	National Pharmaceutical Regulatory Agency (Malaysia)
NS1	Nonstructural protein 1
PAHO	Pan American Health Organization
PBPK	Physiologically based pharmacokinetic (modeling)
PCR	Polymerase chain reaction
PFU	Plaque-forming unit(s)
PhilHealth	Philippine Health Insurance Corporation
PMDA	Pharmaceuticals and Medical Devices Agency (Japan)
PRNT	Plaque reduction neutralization test (e.g., $PRNT_{50}$, $PRNT_{80}$)
PREPARE	Programme for Research in Epidemic Preparedness and Response
O/E	Observed versus Expected

QTPP	Quality target product profile
R&D	Research and development
RAG	Regulatory Advisory Group
RCT	Randomized controlled trial
RITAG	Regional Immunization Technical Advisory Group
RSV	Respiratory syncytial virus
RWE	Real-world evidence
saRNA	Self-amplifying RNA
SAGE	Strategic Advisory Group of Experts on Immunization (WHO)
SEARO	South-East Asia Regional Office (WHO)
SII	Serum Institute of India
SMART	(As used in report) safety monitoring system using sentinel sites
TBE	Tick-borne encephalitis
TGA	Therapeutic Goods Administration (Australia)
THSTI	Translational Health Science and Technology Institute (India)
UK	United Kingdom
UNSW	University of New South Wales
US	United States
U-WIN/UVIN	(As referenced) India immunization registry platforms
VLP	Virus-like particle
VRDL	Virus Research and Diagnostic Laboratory (India)
VSV	Vesicular stomatitis virus
WHO	World Health Organization
WPRO	Western Pacific Regional Office (WHO)

Day 1 - Pandemic preparedness & response vaccine development ecosystem strengthening and use of innovative regulatory approaches when efficacy studies are not feasible

1.1. Lamp lighting ceremony and welcome address

Ms. Meenu Batolar (CEPI, Singapore) welcomed participants and acknowledged senior representatives from the co-host organizations and from India's scientific, regulatory, and public health institutions, including NITI Aayog, ICMR, DBT, Central Drugs Standard Control Organization (CDSCO), and WHO SEARO. She noted the participation of experts from 25 countries and framed the Summit as a forum for exchange across vaccine research and development (R&D), manufacturing, regulation, and public health preparedness.

The welcome concluded with the traditional Indian lamp-lighting ceremony, a timeless gesture rooted in the belief that light dispels darkness and wisdom guides' action. As the flame was kindled, it symbolized the collective commitment to knowledge, clarity, and purposeful collaboration, reminding participants that progress in science and public health is illuminated not only by innovation, but by shared responsibility, trust, and the pursuit of insight for the greater good.

1.2. Co-host opening remarks

1.2.1. Professor (Dr.) V. K. Paul (NITI Aayog, India)

Professor V.K. Paul welcomed participants and acknowledged the broad regional and international representation at the Summit. He noted the value of convening scientific, regulatory, and public health leadership to strengthen preparedness in the Asia-Pacific region. His remarks underscored India's commitment to advancing vaccine development and regulatory systems through sustained cooperation, shared capabilities, and coordinated policy approaches.

Professor Paul emphasized the importance of collaboration among research organizations, regulatory authorities, ministries of health, and global partners, including CEPI and WHO, to address shared preparedness challenges.

1.2.2. Director General and Secretary Dr. Rajiv Bahl (ICMR, India)

Dr. Rajiv Bahl welcomed participants and noted that progress in disease surveillance, vaccine development, and regulatory readiness depends on sustained dialogue among scientific, regulatory, and public health stakeholders. He highlighted advances in research capacity and institutional coordination in India and across the region, while emphasizing the need to maintain momentum between outbreaks.

Dr. Bahl emphasized the value of collaboration within the Asia-Pacific region and globally to strengthen preparedness for emerging infections. He reaffirmed ICMR's commitment to generating evidence, advancing regulatory science, and supporting platforms that enable alignment among ministries of health, regulators, and development partners including CEPI and WHO.

1.2.3. Secretary Dr. Rajesh Gokhale (DBT, India)

Dr. Rajesh Gokhale welcomed participants and highlighted the importance of convening scientific, regulatory, and public health leaders to strengthen the biotechnology and vaccine-development ecosystem. He emphasized that regional and global collaboration is essential to accelerate innovation while ensuring quality, safety, and timely access to vaccines during health emergencies.

He emphasized the need for strong partnerships among government agencies, research institutions, regulators, ministries of health, and international organizations to support agile vaccine-development pathways, including for emerging technologies. He noted that continued policy coherence and alignment of regulatory approaches will be important to meet shared regional preparedness objectives.

1.2.4. Drugs Controller General Dr. Rajeev Raghuvanshi (CDSCO, India)

Dr. Rajeev Raghuvanshi highlighted the role of regulators in strengthening preparedness and enabling timely access to safe and effective vaccines. He described ongoing efforts in India to modernize regulatory systems, strengthen regulatory science, and engage with international partners to keep pace with new technologies and public health needs.

He emphasized the importance of clear communication among developers, manufacturers, and regulators, and noted that early and transparent engagement can streamline pathways without compromising standards. He also underscored the value of coordination with partners such as CEPI and WHO to promote convergence where appropriate and to support innovation across the region.

1.2.5. Officer-in-Charge Dr. Catharina Boehme (WHO SEARO)

Dr. Catharina Boehme emphasized the value of convening regulators, scientific institutions, ministries of health, and partners to consolidate lessons learned and strengthen regional health security. She highlighted the importance of building sustainable capacity and coordination across countries in the Asia-Pacific region and encouraged participants to use the Summit to accelerate alignment and deepen collaboration.

She noted that modern vaccine development requires sustained cooperation among regulators, public health agencies, researchers, and manufacturers, supported by structured scientific exchange and, where feasible, harmonized approaches.

1.2.6. Chief Executive Officer Dr. Richard Hatchett (CEPI, UK)

Dr. Richard Hatchett welcomed participants and reaffirmed CEPI's commitment to partnership across the Asia-Pacific region. He noted that recent progress in vaccine development has been facilitated by coordinated efforts among regulators, scientists, ministries of health, and manufacturers, and emphasized the need to sustain these collaborative models to improve the speed and coherence of outbreak response.

He described CEPI's role in supporting vaccine R&D, equitable access, and readiness for rapid deployment. He highlighted priorities including strengthening end-to-end vaccine ecosystems, improving regulatory agility through early dialogue, and reinforcing manufacturing resilience and cross-border coordination to enable faster translation of research into available vaccines during future emergencies.

1.2.7. Director Dr. Adam Hacker (CEPI, UK)

Dr. Adam Hacker emphasized the importance of sustained collaboration among regulators, scientific institutions, ministries of health, and manufacturers to strengthen regional vaccine-development ecosystems. He noted that coordinated planning across stakeholders supports faster development and more consistent decision-making during public health emergencies.

He highlighted CEPI's partnerships in the region and their contribution to strengthening scientific innovation, regulatory preparedness, and operational capacity. He encouraged participants to use the Summit to identify practical opportunities to reduce fragmentation and accelerate progress from discovery through development, manufacturing, and deployment.

1.3. Plenary session: CEPI mission 3.0 — collaborative partner in the global health ecosystem; partnering with Asia-Pacific

1.3.1. Chief Executive Officer Dr. Richard Hatchett (CEPI, UK)

The plenary session introduced CEPI 3.0, highlighting CEPI's role within the global health ecosystem and its commitment to deepen engagement with partners across the Asia-Pacific region. Dr. Hatchett described CEPI 3.0 as an approach to strengthen end-to-end vaccine development and accelerate the translation of scientific advances into tools for outbreak response.

The discussion emphasized the Asia-Pacific region's expanding scientific capacity, manufacturing footprint, and regulatory capability. Dr. Hatchett noted that CEPI 3.0 aims to accelerate vaccine development for known and unknown pathogens by supporting innovative research, strengthening regional networks, and promoting alignment among regulatory authorities, manufacturers, and ministries of health. Participants discussed the importance of agile regulatory pathways, cross-border coordination, and shared learning from recent public health emergencies.

1.4. End-to-end vaccine development ecosystem: capacities and capabilities in India, Southeast Asia, and the Asia-Pacific region

1.4.1. End-to-End Vaccine Development Ecosystem in India: Efforts of ICMR/DHR

Dr. Nivedita Gupta (ICMR, India) described the end-to-end vaccine development ecosystem as a core component of preparedness, spanning discovery research, preclinical development, clinical evaluation, regulatory oversight, manufacturing, and post-deployment monitoring. She highlighted India's expanding scientific infrastructure and evolving regulatory capacity and noted opportunities to shorten development timelines while maintaining quality and safety standards.

She emphasized the importance of effective interfaces among research organizations, regulators, and manufacturers to translate scientific advances into deployable products. She noted that sustained collaboration across national institutions and global partners supports platform readiness, data generation, and regulatory-science capability, and enables coordinated planning for future outbreaks.

1.4.2. End-to-End Vaccine Development Ecosystem in India: Efforts of DBT and BIRAC

Dr. Anamika Gambhir (DBT, India) and Dr. Jitendra Kumar (BIRAC, India) jointly presented this session, offering complementary perspectives from DBT and BIRAC on India's growing end-to-end vaccine development ecosystem. Their remarks emphasized the strong foundation India has built across research, development, regulatory engagement, and manufacturing, describing an ecosystem that has steadily expanded in capability and sophistication. They highlighted the important role of coordinated partnerships across government agencies, academic institutions, industry, and global collaborators, noting that these relationships support a seamless transition from early-stage scientific discovery to late-stage development and product deployment.

Both speakers underscored how recent public-health emergencies have reinforced the need for rapid, evidence-driven decision-making and closer alignment between developers and regulators. They noted that DBT and BIRAC have increasingly focused on enabling platform technologies, strengthening translational science, and supporting innovative approaches that can shorten timelines without compromising safety or quality. Their remarks also reflected a shared view that the Asia-Pacific region—and India in particular—has an opportunity to serve as both a scientific leader and a manufacturing hub, provided that stakeholders continue investing in regulatory-science expertise, clinical-trial infrastructure, and mechanisms that foster cross-border collaboration. By presenting a unified vision of a connected, resilient vaccine ecosystem, they framed the session as a call for sustained integration across the full

development pathway, emphasizing that collective effort will be essential to meeting the demands of future health emergencies.

1.4.3. End-to-end vaccine development ecosystem in the Republic of Korea

Director Dr. Yookyoung Lee (KDCA, Republic of Korea) outlined South Korea's national vaccine development ecosystem, centered on the CVR within the National Institute of Infectious Diseases under the Korean national institute of health (NIH). KDCA oversees a coordinated network responsible for infectious disease preparedness, surveillance, and response, with CVR serving as the hub for public vaccine development and structured support to industry. The center spans the full development pathway—from candidate discovery through preclinical and clinical stages—while also providing technical, regulatory, and infrastructural support to private-sector developers in collaboration with domestic and international partners.

KDCA's strategy is anchored in the 2023 National Pandemic Preparedness and Response Plan, which targets vaccine development within 100–200 days of outbreak identification. The approach emphasizes preparedness prior to outbreaks through platform readiness and infrastructure strengthening, followed by accelerated development and continuous system evaluation during emergencies. Supporting this mandate, CVR operates BSL-2, -3, and -4 laboratories, delivers high-containment laboratory training, and manages national pathogen resources to support both public health and biomedical innovation.

Platform technologies are a central focus, particularly mRNA vaccines. KDCA launched a national mRNA vaccine initiative to enable domestic mRNA vaccine development by 2028 and to support companies across preclinical and clinical development. In parallel, the Korean Advanced Center for Vaccine Development (CAVET), established in 2023, is being developed as a national vaccine library and preparedness hub, integrating AI-enabled antigen design and stockpiled trial materials to enable rapid outbreak response.

International collaboration underpins Korea's ecosystem. KDCA actively participates in CEPI-supported initiatives aligned with the global 100-days mission and positions its capabilities within CEPI's analytical framework. While Korea's technical infrastructure is well established, KDCA highlighted the need to further strengthen coordination mechanisms and operational frameworks to fully mobilize these assets. Looking ahead, KDCA aims to position Korea as a global vaccine R&D hub aligned with CEPI 3.0, with increasing emphasis on platform-based preparedness, prototype development, and regulatory innovation.

1.4.4. End-to-End Vaccine Development Ecosystem in Southeast Asia, Western Pacific Region – WHO Regional Perspectives

Dr. Jinho Shin (WHO WPRO, Philippines) presented a region-wide assessment of the vaccine and health security ecosystem across the Western Pacific, encompassing 38 countries and areas with significant geographic, economic, and regulatory diversity. To address this heterogeneity, WPRO applied a structured grouping approach using CEPI's ecosystem assessment framework, complemented by WHO analyses of regulatory system maturity and IHR core capacities, to support comparative analysis and prioritization.

Countries were grouped into three broad sub-regions: Australia and Oceania, Southeast Asia, and Pacific Island countries. Australia and Oceania largely comprise high-income countries with mature national regulatory authorities (maturity level 3 and above), demonstrating strong performance across multiple ecosystem components, including surveillance, regulatory systems, manufacturing capacity, and supply chain resilience. These systems were assessed as technically robust, with targeted strengthening required only in selected areas.

Southeast Asian countries, predominantly middle-income, showed meaningful progress in regulatory system strengthening, with several having undertaken formal self-assessments. COVID-19 experience reinforced the central role of regulatory capacity in enabling local production of vaccines, therapeutics, diagnostics, and medical devices. However, gaps remain in end-to-end coordination and supply chain resilience, highlighted by challenges such as shortages of essential ancillary supplies during the pandemic. As a result, multiple ecosystem components for this group were identified as priority areas for strengthening.

Pacific Island countries face distinct structural constraints related to geography, scale, and logistics. Local manufacturing was not identified as a priority due to feasibility limitations. Instead, high-priority needs include innovative outbreak response tools, workforce development, and adaptable delivery and deployment models. Equity considerations were emphasized, reflecting fragile logistics systems, low procurement volumes, and limited supplier incentives. During COVID-19, regional mechanisms such as COVAX played a critical role in vaccine access for Pacific populations, though platform-specific logistics challenges constrained uptake in some settings.

Across all sub-regions, several cross-cutting themes emerged, including innovation, equity, biosecurity, and sustainability. Innovation—such as digital tools, AI-enabled workforce support, and alternative energy solutions—was highlighted as particularly important for geographically remote and resource-constrained contexts. The assessment also underscored the need for cautious interpretation, given ongoing transitions in regulatory maturity and the use of different analytical lenses across datasets.

Looking ahead, WPRO highlighted opportunities to strengthen regional preparedness by linking manufacturing strengths in countries such as India and the Republic of Korea with regional demand intelligence. Enhanced regulatory cooperation in Southeast Asia, combined with interoperable regional readiness architectures, could enable the Asia-Pacific region to function as a more coordinated, resilient ecosystem capable of accelerating access to new tools while ensuring that no country is left behind.

1.4.5. Strengthening End-to-End Vaccine Development Ecosystem: Capacities and Capabilities in India and Southeast Asia

Director Dr. Manoj Jhalani (WHO-SEARO) reflected on lessons from COVID-19 and emphasized that future protection depends on strengthening the full vaccine ecosystem—from surveillance and pathogen detection through research, clinical development, regulatory pathways, manufacturing, and health-system delivery. He noted that the region, which includes a large share of the global population and infectious-disease burden, has substantial assets, including vaccine manufacturing capacity, scientific capability, diverse clinical trial populations, and increasing regulatory maturity. He also highlighted areas requiring further investment, including clinical trial networks, platform-technology capability, pathogen and data-sharing mechanisms, regulatory reliance approaches, and equitable distribution capacity.

Throughout his remarks, Dr. Jhalani emphasized the importance of strengthening cross-border collaboration through shared pathogen libraries, rapid-activation clinical trial networks, harmonized regulatory approaches, and distributed surge-manufacturing models to ensure preparedness across the region. He described WHO-SEARO's efforts to develop capability-framework tools that allow countries to map ecosystem strengths and gaps, promote structured dialogue among regulators, governments, industry, and global partners, and prioritize investments that support innovation, equity, and regional resilience. He concluded by stressing that achieving true pandemic readiness requires coordinated action across all ecosystem components—not only manufacturing but also regulatory-science capacity, real-time data exchange, and strong health-system delivery platforms—to ensure communities can rapidly access vaccines when emergencies arise.

1.5. Part 1: End-to-end vaccine development ecosystem

1.5.1. Session opening remarks - Director Dr. Rogerio Gaspar (WHO)

Dr. Rogerio Gaspar grounded his comments in lessons from COVID-19, noting that the world must resist the tendency to forget what enabled the unprecedented speed of response during the pandemic: a powerful alliance between science, the private sector, governments, regulators, and public-health agencies. He warned that despite these successes, global regulatory systems may be in a weaker place today than in 2020, citing loss of staff, aging workforces, and erosion of institutional memory. This reality, he suggested, should temper optimism around ambitious goals like the 100-Days Mission, which is achievable only if fragmented improvements across outbreaks are integrated into a cohesive, well-aligned response framework rather than treated as isolated successes.

Dr. Gaspar encouraged participants to look beyond the three diseases highlighted in the Summit agenda and instead focus on the structural components of an end-to-end vaccine ecosystem. Drawing on experience from the Regulatory Advisory Group (RAG) and WHO's R&D Blueprint, he contrasted large-scale information-sharing forums—valuable for dissemination but not conducive to meaningful dialogue—with smaller, informal exchanges among regulators and between regulators and manufacturers, where true consensus on guidelines and technical alignment emerged. He stressed that regulatory preparedness must exist before a crisis begins; systems cannot be built or scaled during an emergency. Strengthening the existing network of regulatory authorities in the region, potentially supported by a "second layer" of collaboration with partners like CEPI, is necessary to replicate the globally coordinated regulatory interactions seen during COVID-19. He also emphasized that scientific, epidemiological, and manufacturing capacities are interdependent. Strong manufacturing hubs must maintain surge capacity and sustainable business models, noting that past pandemic investments in some countries collapsed when facilities were shut down and were unavailable during COVID-19.

Mr. Gaspar concluded by urging participants to contribute candidly to the workshop's discussions, highlighting the need for structural investments across regulatory systems, manufacturing capacity, surveillance, and scientific coordination to ensure the region can respond effectively and rapidly to the next health emergency.

1.5.2. CEPI 3.0 - end-to-end vaccine development ecosystem

Ms. Freya Hopper (CEPI) introduced this portion of the programme as a transition into a more interactive workshop. She explained that the focus of the session was CEPI's capability framework and emphasized that the objective was to build a shared understanding of the ecosystem approach to vaccine development, including its core components and the priorities emerging from country and regional perspectives. Participants were encouraged to move toward discussion tables, including those seated in overflow rooms, in preparation for breakout sessions and a later "playback" of key points.

She connected the discussion to CEPI's new five-year strategy under CEPI 3.0, highlighting how it aligns with the 100 Days Mission—the ambition to achieve initial vaccine authorization and scalable manufacturing within 100 days of identifying a pandemic pathogen, and to maintain similar readiness across pandemic, endemic, regional, and national outbreaks. The presenter stressed that the necessary capabilities do not exist in isolation; they must be rooted in national systems and supported by cross-country collaboration.

She clarified the distinction between "capacities" and "capabilities," describing the latter as capacities that are used, exercised, and ready to activate—much like having weights versus being able to weight-lift. To engage participants, she initiated a brief poll via the event app and then began outlining CEPI's 100-Days

Mission capability framework, which is built on pillars such as accelerated vaccine development, regulatory and policy preparedness, resilient supply, early detection, and cross-cutting elements including equity, innovation, biosecurity, and partnership models.

1.5.3. Break-out groups – partnership to meet the 100 Days Mission

Moderator: Ms. Freya Hopper (CEPI)

Following the breakout discussions, Ms. Hopper facilitated a plenary "playback" of key points from each table. Participants highlighted that, while regional regulatory networks and reliance pathways exist, collaboration remains variable and would benefit from more systematic, routinized engagement. Several groups recommended establishing more formal information-sharing mechanisms (e.g., memoranda of understanding), strengthening benefit–risk assessment processes, and improving post-authorization evidence generation—particularly for populations typically under-represented in pre-licensure datasets. Several groups remarked on the asymmetrical innovation across the region, observing that only a few countries consistently generate new approaches, while others lack the same momentum. Unlike other regions with established regulatory blocs, Southeast Asian regulators seldom convene directly, leaving most collaboration to sponsors and manufacturers.

Participants recommended forming a regional consortium or alliance to foster routine regulator to regulator dialogue, enable structured data sharing across borders, and support reliance-based decision-making during outbreaks.

Participants also discussed operational constraints affecting end-to-end readiness, including access to preclinical materials and specialized laboratory resources, and the potential for domestic environmental and animal-use requirements, especially use of NHPs, to delay development timelines. Data sharing and cross-border use of clinical datasets were identified as additional challenges; one example cited was the need for clear mechanisms to enable neighboring countries to support regulatory decisions (including immunobridging) based on shared trial data. To advance the 100 Days Mission, groups proposed developing multi-year roadmaps to identify priority pathogens and define fit-for-purpose minimal data packages for emergency contexts. Participants also encouraged continued support for platform-technology readiness and technology transfer to manufacturers in low- and middle-income countries. Across discussions, consistent themes included the need for practical governance mechanisms, transparent data exchange, and sustained regulator-to-regulator dialogue to strengthen regional preparedness.

1.6. Part 2: Use of innovative regulatory approaches when clinical efficacy studies are not feasible

1.6.1. Regulatory readiness in Southeast Asia – regulatory readiness dashboard & alternatives to RCTs in WHO-recognized countries

Ms. Meenu Batolar (CEPI, Singapore) summarized regulatory-readiness work across Southeast Asia aimed at identifying tools that national authorities can establish during inter-epidemic periods to support timely decision-making during future public health emergencies. She described CEPI-facilitated readiness workshops and tabletop exercises designed to explore relevant innovative approaches when traditional RCTs are not feasible. These exercises are intended to simulate regulatory decision-making, identify gaps between legal frameworks and operational guidance, and clarify where reliance, adaptation, or other regulatory innovations could be applied during crises. She introduced the Regulatory Readiness Dashboard, which summarizes 25 innovation approaches and indicates whether national legal frameworks support, partially support, or do not support each approach.

She emphasized that the work aims to strengthen emergency preparedness by improving regulatory processes and building trust among authorities through closed technical exchange.

Examples were noted from workshops held in India, Indonesia, Japan, the Republic of Korea, Singapore, Malaysia, Thailand, and Australia. Discussion then addressed increasing regional interest in alternatives to RCTs for vaccine evaluation, including the use of immunobridging, well-justified surrogate endpoints, and real-world evidence (RWE) to support authorization when efficacy trials cannot be conducted ethically or operationally. Participants noted that these approaches are being advanced through ongoing international scientific fora and should be translated into clear national-level decision frameworks.

1.6.2. Innovative approaches when efficacy studies are not feasible: connecting the evidence base

1.6.2.1. Case example: National Emerging Infectious Diseases Laboratories (NEIDL)

Professor Dr. Nancy Sullivan (Boston University, NEIDL, USA) discussed evidence generation when randomized efficacy trials are not feasible, emphasizing the role of fit-for-purpose animal models in supporting regulatory decision-making. She noted that immune CoP derived from NHP challenge studies can be difficult to translate if the infectious challenge dose and route do not reflect typical human exposure. Excessively high challenge doses may inflate the apparent antibody level associated with protection, and highly lethal models optimized for maximal effect may underestimate real-world vaccine benefit. She highlighted that, under some high-dose conditions, protection may reflect combined contributions from antibodies and T-cell responses; correlates should therefore be interpreted in the context of the challenge model. She emphasized that animal models should be pathogen- and platform-appropriate, include biologically relevant exposure routes, and use the lowest challenge dose that maintains model validity and statistical power.

1.6.2.2. Regulatory perspectives on CoP when efficacy trials are not feasible: Lessons from the 4th CoP meeting on next-generation influenza vaccines (Vienna, Oct 2025)

Dr. Anuradha Poonepalli (Health Sciences Authority [HSA], Singapore) summarized lessons from a Vienna meeting on CoPs and highlighted their relevance to pathogens for which efficacy trials are impractical or unethical. She noted that immune correlates can substitute for efficacy only when supported by converging lines of evidence that robustly link the marker to protection in humans. She emphasized the importance of well-characterized animal models that reflect key features of human disease and immunogenicity, complemented by additional evidence sources where available (e.g., human challenge data, epidemiological analyses, breakthrough infections, and passive immunization studies). She noted that the approach is well established across multiple diseases, with regulatory acceptability depending on the strength of the association between the marker and clinical protection.

She emphasized that assay performance and standardization are foundational for regulatory use of correlates. While absolute protective thresholds are preferable, she noted that regulators have, in some contexts, accepted strong associations without a single cutoff where data demonstrate consistent, reproducible trends (e.g., for some variant-adapted COVID-19 vaccines). She also highlighted limitations in extrapolating correlates across platforms and populations and noted that differences in formulation, delivery, or age-related immune response can affect interpretation. Composite endpoints that combine antibody, cellular, or mucosal markers may be informative but introduce additional complexity for validation and regulatory interpretation. She concluded that early engagement with regulators is important to define acceptable markers and post-authorization evidence needs.

1.6.2.3. Summaries of the African Society for Analytical Scientists [AFSA]/International Association for Biological Standardization [IABS] non-animal testing for vaccines meeting (Bangkok, Thailand, 2–4 Dec 2025) and the IABS vaccine RWE for vaccine authorization meeting (Montreal, Canada, 10–11 Dec 2025)

Dr. Dean Smith (IABS-NA Chair, Canada) summarized two technical meetings that addressed evidence generation when traditional efficacy trials are infeasible.

First, he outlined outcomes of a multi-year effort on non-animal testing methodologies, discussed at a meeting in Bangkok that convened regulators, national control laboratories, and manufacturers. He noted that several legacy *in vivo* assays are increasingly poorly suited to modern vaccines and can be difficult to operationalize during pandemics. Discussions highlighted NAMs and the shift toward *in vitro* and analytically driven approaches, similar to practices used for many biotherapeutics. He referenced the development of guidance and standard-setting activities, including work by European Directorate for the Quality of Medicines & HealthCare (EDQM) and WHO, signaling that some traditional animal assays are no longer considered fit for purpose. He also cited collaborative initiatives (including a €13 million European program) that have generated candidate assays and supporting regulatory principles and noted the potential of high-throughput and sequencing-based tools to strengthen detection of adventitious agents and product characterization.

He then summarized a Montreal meeting focused on RWE and immunobridging. He noted that immunobridging and related evidence streams are used in a substantial proportion of recent regulatory authorizations and described typical use cases, including extending indications to new age groups, supporting new formulations or regimens, and evaluating concomitant administration. He cited examples across multiple vaccines (including influenza, polio, hepatitis B, meningococcal, pneumococcal, orthopoxvirus, and chikungunya) to illustrate how immunological markers and functional assays have supported licensure decisions. He emphasized that when authorization relies on immunogenicity or animal-challenge evidence, robust post-authorization effectiveness and safety monitoring is important, and that pragmatic designs can complement traditional studies when appropriately justified.

1.6.2.4. Summary of the European Medicines Agency (EMA) non-clinical models' workshop (24–25 Nov 2025)

Dr. Marco Cavaleri (EMA) summarized discussions from a recent EMA workshop on non-clinical models and alternative evidence pathways when efficacy trials are not feasible. He noted that the workshop focused on practical approaches to strengthen preparedness, including the use of immunobridging and other non-traditional evidence sources, and the value of structured scientific dialogue among regulators. Themes aligned with other session presentations, including the need for validated assays, biologically meaningful CoP, convergence on scientific principles across agencies, and robust post-authorization evidence-generation plans.

1.6.2.5. Assessing the evidence for vaccine effectiveness

Dr. Miles Davenport (University of New South Wales [UNSW], Australia) framed his remarks around how decision-makers synthesize imperfect and indirect evidence when an ideal randomized, blinded efficacy trial is not feasible. He described the theoretical "ideal" trial as one conducted in the target population, independently replicated, and powered for clinically meaningful endpoints. In practice, trials often enroll lower-risk populations, use more feasible (but less severe) endpoints, and may rely on single datasets without independent confirmation.

He then examined alternative trial designs such as pragmatic randomized trials implemented during rollout and controlled human infection models conducted in healthy young volunteers. Both can provide

valuable data but come with mismatches—unblinded designs, different populations from the intended target group, and endpoints that differ from those of greatest regulatory interest. Dr. Davenport highlighted that animal models introduce even more uncertainty: unmatched species, different immune responses, unnatural challenge conditions. The ideal animal model is as elusive as the ideal RCT.

Rather than seeking certainty, Dr. Davenport emphasized the importance of explicitly characterizing uncertainty, quantifying it where feasible, and defining which uncertainties are acceptable under specific outbreak conditions. He described how combining evidence streams can strengthen inference, for example by demonstrating protection in animals following passive transfer of serum from vaccinated humans or by aligning signals across natural-history studies, animal-challenge models, and human immunogenicity datasets. When multiple lines of evidence converge on a consistent protective antibody level—and a vaccine induces titers above that level—confidence can increase even if individual datasets are imperfect.

Dr. Davenport closed by introducing a CEPI- and Wellcome-funded project he is co-leading with Monash University: the development of a Framework for Evidence Evaluation in Vaccine Assessment (FEEVA). The initiative reviews how Food and Drug Administration (FDA) and EMA approvals have historically used non-RCT evidence and seeks to establish best-practice guidelines for reporting and assessing animal-model and other alternative data. He encouraged attendees to participate in ongoing consultations, to ensure the project can build consensus and strengthen the ability of regulators and developers to make transparent, well-reasoned decisions under the inevitable uncertainty they will face in future emergencies.

1.6.2.6. Connecting the dots: Q&A

Moderator: Dr. Marco Cavaleri (EMA)
Panelists:
Dr. Nancy Sullivan (Boston University, NEIDL, USA)
Dr. Anuradha Poonepalli (HSA, Singapore)
Dr. Dean Smith (IABS-NA Chair, Canada)
Dr. Miles Davenport (UNSW, Australia)

The Q&A session addressed questions on interpreting evidence generated outside traditional efficacy trials.

One question focused on whether uniformly high and lethal challenge doses in NHP studies can distort CoP relative to typical human exposure doses. Dr. Sullivan noted that aligning dose and route between animal models and likely human exposure may improve both qualitative and quantitative translatability, but that historically high doses have been used to maximize statistical power with small group sizes and to maintain continuity once a model is established. She referenced recent work (including Nipah studies) exploring lower challenge doses, noting that such approaches provide reliable efficacy data requiring only modestly larger animal numbers, and may better reflect natural infection.

A second question addressed whether organoids and microphysiological systems could replace animal studies for vaccine evaluation. Panelists noted that while these technologies are advancing and can model specific tissue features, they do not currently replicate systemic immune coordination and other *in vivo* dynamics needed to assess vaccine-induced protection. The panel emphasized that new methods require validation before they can be relied upon for regulatory decision-making.

Discussion also addressed the continued role of animal models. Panelists noted that, while NAMs may reduce animal use over time, animal studies remain necessary for many vaccine-evaluation questions. The

panel reiterated the importance of applying the 3Rs (Replacement, Reduction, Refinement), including appropriate study design, humane endpoints, and avoidance of unnecessary duplication. Examples were cited where *in vitro* assays have replaced specific legacy animal potency tests when science supports equivalence.

The discussion concluded with questions on safety testing expectations and the operational constraints of high-containment studies. Panelists noted the need for pragmatic, risk-based decision-making on study requirements and agreed that post-authorization monitoring and transparent justification of evidence packages are important when approvals rely on alternative data streams.

1.6.3. Pandemic preparedness beyond COVID-19: Lessons for future emergencies

Executive Director Dr. Umesh Shaligram (Serum Institute of India [SII], India) described SII's experience during COVID-19 and discussed implications for future preparedness. He noted that the pandemic increased the expectations for speed, flexibility, and coordinated scientific exchange among manufacturers, regulators, and global health partners. He highlighted operational challenges encountered during scale-up, including rapid technology transfer, evolving regulatory requirements, and supply-chain constraints, and emphasized the importance of maintaining quality throughout accelerated timelines. He suggested that several practices used during COVID-19—such as structured regulatory engagement, flexible manufacturing approaches, and alternative evidence strategies—should be formalized and sustained beyond emergency contexts to strengthen readiness for emerging pathogens.

He emphasized the value of early dialogue among manufacturers, regulators, and ministries of health to clarify expectations and enable faster operational decision-making during emergencies, particularly for platform-based technologies and rapid scale-up scenarios. He noted that industry perspectives can inform preparedness planning in inter-epidemic periods, including work on supply-chain resilience, evidence-generation plans, and post-authorization monitoring. He highlighted opportunities to sustain investments in platform technologies and to strengthen mechanisms for timely data sharing and regulatory reliance. Overall, the discussion underscored the need to translate COVID-19-era innovations into durable processes that support preparedness across a wider range of outbreak scenarios.

1.6.4. Immunobridging for vaccine evaluation

Managing Director Dr. Sanjay Singh (Gennova, India) reviewed the use of immunobridging to support authorization of updated COVID-19 vaccines when traditional efficacy trials were not feasible. He described immunobridging as an evidence approach that leverages a previously authorized vaccine with established clinical benefit to evaluate product modifications (e.g., antigen/variant updates, new age groups, dosing schedules, formulations, or platform changes) using immunogenicity endpoints rather than clinical disease endpoints. He noted that, during the pandemic, accelerated pathways were enabled by platform familiarity and prior evidence, while safety expectations and reporting requirements remained stringent.

He outlined common elements of an immunobridging program, including selection of an appropriate comparator vaccine authorized in the relevant jurisdiction; measurement of neutralizing antibody responses and other agreed immunogenicity endpoints; and prespecified statistical criteria such as geometric mean titer (GMT) ratios and seroresponse rates, typically assessed against regulator-defined noninferiority margins. He noted design considerations in settings with high background infection (e.g., baseline serostatus and timing of sampling) and emphasized the importance of assay standardization and calibration (e.g., WHO reference standards or validated in-house assays). He also noted that immunobridging packages generally include safety data in several thousand participants, with representation of populations not included in the parent efficacy trial, and follow-up commonly extending at least 6–12 months.

Dr. Singh noted that, while neutralizing antibody titers are frequently used as primary endpoints for COVID-19 immunobridging, additional immune profiling can support interpretation where appropriate. He cited examples across multiple indications (including hepatitis B, human papillomavirus [HPV], Ebola, influenza, and chikungunya) in which bridging principles have been applied, and noted that markers such as mucosal responses, memory B-cell measures, and cellular immunity may provide complementary evidence when assays are validated and linked to protection.

Turning to Gennova's work, Dr. Singh described development of an Omicron-specific mRNA booster supported by immunobridging, using an authorized comparator vaccine (ChAdOx1). He noted that the program sought to address operational constraints relevant to low- and middle-income countries by improving temperature stability relative to ultra-cold-chain requirements. He reported that the platform was designed for storage at 2–8 °C and for extended periods at 25 °C. He summarized reported trial findings, including neutralizing antibody responses and cellular immune measures, and emphasized the value of longer immunogenicity follow-up and more detailed characterization of memory responses to inform expectations for durability.

He noted Gennova's CEPI-supported work on rabies and Nipah vaccines and stated that both programs anticipate substantial reliance on immunobridging due to the absence of feasible human efficacy studies. He described rabies work aimed at simplifying multi-dose regimens and noted that Nipah vaccine evaluation is expected to rely on NHP models and immunological markers given the rarity and severity of human infections.

In the Q&A, participants discussed the role of modeling in addressing evidence gaps. Dr. Singh cited examples in which physiologically based pharmacokinetic (PBPK) modeling has supported dose selection or extrapolation when accompanied by commitments to generate confirmatory real-world data. A further discussion focused on pediatric immunobridging in immunologically naïve children; participants noted that modeling can inform dose selection and risk mitigation, but that clinical data are generally required. Regulators highlighted additional considerations in infants due to developmental immunology. Discussion also noted that bridging strategies may be pathogen- and population-specific; for respiratory syncytial virus (RSV), panelists cautioned that infant evaluation requires particular attention to safety signals, including the historical concern regarding vaccine-enhanced disease.

1.6.5. Enabling licensure without efficacy trials: platform readiness and regulatory decision-making in emergencies

Chief Medical Officer Dr. Manabu Inoue (PMDA, Japan) outlined a core regulatory challenge in public health emergencies: authorizing a vaccine when traditional efficacy trials are not feasible. Drawing on examples from COVID-19 and mpox, he described why large phase 3 efficacy trials may be impractical during rapidly evolving or sporadic outbreaks. Incidence may peak and decline before endpoints can accrue; placebo-controlled designs can become ethically unacceptable once effective countermeasures exist; and low event rates can prevent statistically meaningful evaluation. He noted that, in these settings, regulators must determine which alternative data streams can provide sufficient evidence to support an authorization decision.

He proposed five elements that can support licensure when efficacy trials are not available:
(1) Mechanistic plausibility (a credible biological CoP)
(2) Justification of immune markers (validated or well-supported surrogate endpoints)
(3) Platform familiarity (prior knowledge from the same technology platform)
(4) An adequate safety database
(5) A defined post-authorization evidence-generation plan

He noted that, during COVID-19, pediatric authorizations of variant-adapted mRNA vaccines relied on immunobridging rather than clinical efficacy outcomes, supported by prior knowledge of mRNA–lipid nanoparticle (mRNA–LNP) platforms and accumulated safety experience. For mpox, he noted that decisions drew on existing evidence and biological plausibility for cross-protection from licensed smallpox vaccines, supported by emergency authorization pathways.

Dr. Inoue then discussed criteria for a "regulatory-ready" platform. He described key components including a defined quality target product profile (QTPP) and critical quality attributes (CQAs), a consistent manufacturing process with understood impurity profiles, prior human safety exposure, validated immune markers where applicable, and pre-agreed bridging principles. He noted that tools such as CEPI's Platform Readiness Dashboard can support structured assessment. He introduced the concept of scientific disaggregation, in which a platform is evaluated as constituent elements (e.g., encoded antigen, nucleic-acid backbone chemistry, LNP composition, and impurity profile) that may require different levels of evidence. This approach can clarify which evidence can reasonably be leveraged from prior products and which data need to be generated anew, while recognizing that platform knowledge does not eliminate antigen-specific risks.

He noted that evidence strategies vary by outbreak context: variant updates may rely primarily on immunobridging, whereas zoonotic pathogens with limited human data may require greater reliance on animal models and other non-traditional evidence sources. He emphasized that reduction in animal use should remain consistent with risk-based decision-making and lifecycle monitoring, and that NAMs require validation before they can substitute for *in vivo* data. He referenced PMDA guidance on non-clinical safety evaluation for mRNA–LNP vaccines, which supports the disaggregation approach by allowing use of existing data for unchanged platform components while maintaining the requirement to evaluate antigen-specific risks. He concluded by noting that, while global fora (e.g., WHO, International Coalition of Medicines Regulatory Authorities [ICMRA], CEPI) support convergence on scientific principles, differences in legal frameworks and post-authorization obligations can lead to divergent regulatory decisions; transparent justification and robust post-authorization monitoring therefore remain essential when approvals rely on alternative evidence packages.

In closing, Dr. Inoue emphasized that licensure without efficacy trials is feasible only under clearly justified conditions. He noted that platform familiarity can reduce, though not eliminate, uncertainty, and that transparent scientific rationale, lifecycle oversight, and clear post-authorization evidence plans are critical complements to innovation.

1.6.6. Use of preclinical data to support licensure of Janssen's Ebola vaccine (Zabdeno/Mvabea)

Dr. Jenny Hendriks (CEPI, UK) presented a case study describing how preclinical efficacy data, combined with human immunogenicity, supported licensure of a two-dose Janssen Ebola Zaire vaccine regimen when conventional efficacy trials were not feasible. She noted that while an rVSV (vesicular stomatitis virus)-based vaccine demonstrated efficacy late in the West African outbreak, the Janssen heterologous regimen (Ad26 prime followed ~8 weeks later by an MVA-based boost) could not be evaluated in field efficacy trials because outbreaks are unpredictable in location, size, and duration and the Ad26/MVA platform could offer longer durability, thus being ideal for HCWs. Regulatory evaluation therefore relied on an "Animal Rule"–type evidentiary logic and, in Europe, authorization under exceptional circumstances.

She outlined the immunobridging strategy, which required (1) an appropriate NHP challenge model and (2) identification of immune markers plausibly linked to protection. Three candidate biomarkers were evaluated: Ebola glycoprotein–binding antibodies (enzyme-linked immunosorbent assay [ELISA]), neutralizing antibodies (pseudovirus neutralization assay), and antigen-specific T-cell responses

(interferon-γ enzyme-linked immunospot (assay) [ELISpot]). Logistic regression analyses assessed the association between each marker and survival following NHP challenge. All three markers were associated with survival, but ELISA and neutralization readouts outperformed T-cell responses; multivariable models showed limited added predictive value from including the ELISpot data. Binding antibody titers measured by ELISA were therefore selected as the primary bridging marker.

Dr. Hendriks described refinements used to strengthen the bridging model, including a dose-down study in NHPs to generate a wider dynamic range of immune responses and improve estimation of the logistic relationship between marker level and survival. Although the pooled dataset included studies with variation in dose, schedule, and regimen, these covariates had limited impact on model performance. The resulting model demonstrated predictive utility for the intended regimen and informed development of an assay suitable for use in both NHP and human studies.

A critical program element was demonstrating that the ELISA could reliably quantify binding antibodies in both humans and NHPs. The team centralized testing in a single laboratory, harmonized assay conditions, evaluated cross-species parallelism, and confirmed comparable performance of secondary antibodies for detection of IgG from each species. After validation, the full NHP dataset was reanalyzed to finalize the immunobridging curve. Human immune-response data from phase 2 and phase 3 studies were then mapped onto the curve to estimate mean survival probability, with uncertainty quantified using a double-bootstrap approach. Regulators prespecified that the lower bound of the 95% confidence interval must exceed 20% to support evidence of clinical benefit. The final estimate (57.3% mean survival probability; 95% CI lower bound 41.2%) met this criterion and supported EMA licensure under exceptional circumstances. Sensitivity analyses were broadly consistent across subgroups, with lower estimates reported in West African participants, likely reflecting differences in immunogenicity.

Dr. Hendriks concluded by noting that the immunobridging methodology described in this case study does not yield a direct field efficacy estimate and that effectiveness and safety must be further characterized through post-authorization evidence generation. She emphasized that the case illustrates how fit-for-purpose animal models, analytically validated cross-species assays, prespecified statistical decision criteria, and early engagement with regulators can support access to vaccines when conventional efficacy trials are not feasible.

1.6.7. Innovative regulatory science case example: Platform and bridging evidence to expand mpox vaccine use across age groups

Dr. Victoria Jenkins (Bavarian Nordic, USA) presented the regulatory evidence base supporting the modified vaccinia Ankara–based vaccine MVA-BN (marketed as JYNNEOS/Imvanex in different jurisdictions) and discussed how platform and bridging evidence enabled expansion of its use across age groups. She noted that MVA-BN is a third-generation, non-replicating smallpox vaccine originally developed after smallpox eradication, which precluded conventional field efficacy trials. During the initial licensure period, mpox outbreaks were limited, and pediatric efficacy studies were not feasible. She highlighted that the non-replicating platform supports a safety profile suitable for populations for whom older replicating vaccinia vaccines are contraindicated (e.g., individuals with immunocompromising conditions or atopic dermatitis), while noting that benefit–risk considerations remain context-dependent.

She summarized the sequence of major authorizations, noting initial approvals by EMA and Health Canada in 2013 for smallpox prevention in adults, followed by FDA approval in 2019 for prevention of both smallpox and mpox. She noted that subsequent outbreaks accelerated additional authorizations and emergency-use decisions in multiple countries and contributed to a growing post-authorization evidence base, including clinical studies, post-marketing commitments, and RWE.

Dr. Jenkins described the evidence package supporting EMA approval under exceptional circumstances, which combined non-clinical orthopoxvirus challenge studies with extensive human safety and immunogenicity data. She referenced multiple NHP challenge studies showing protection in vaccinated animals relative to controls and noted comparative studies suggesting earlier immune responses after MVA-BN than after a replicating vaccinia comparator. These findings were complemented by a broad clinical program (more than 20 studies; approximately 9,000 participants), including evaluation in groups considered at higher risk for adverse events with older smallpox vaccines.

For FDA licensure, she noted that the evidence package included immunogenicity bridging to ACAM2000, supported by additional non-clinical studies. A pivotal phase 3 study comparing a two-dose MVA-BN regimen with a single dose of ACAM2000 demonstrated higher neutralizing antibody responses in the MVA-BN group. She noted that attenuation of the "vaccinia take" was evaluated as a secondary biological marker, but that the FDA decision relied primarily on immunogenicity endpoints and the totality of evidence.

She highlighted the contribution of RWE generated during mpox outbreak responses. She noted that large numbers of doses were administered during the 2022 outbreak in the United States and that additional use has occurred globally. Reported post-authorization surveillance and observational analyses generally described a safety profile consistent with clinical trial findings, with most events characterized as non-serious injection-site reactions. She also cited published effectiveness estimates from observational studies in multiple countries, with reported ranges varying by setting and study design (e.g., approximately 35–86% after one dose and 66–90% after two doses), noting that such estimates are subject to confounding and differences in case ascertainment.

Dr. Jenkins also outlined an ongoing pediatric development plan, including a dose de-escalation study in Uganda and the Democratic Republic of the Congo enrolling children aged 2–11 years with an adult comparator arm. She reported that interim analyses met the primary immunogenicity objective, with neutralizing antibody responses in children meeting prespecified noninferiority criteria relative to adults, and with safety findings broadly consistent across age groups. She noted that, at the time of the Summit, a formal pediatric licensure submission had not yet been completed. She concluded by emphasizing that regulators increasingly apply a totality-of-evidence approach—integrating non-clinical data, immunogenicity bridging, safety databases, and RWE—when efficacy trials are not feasible.

1.7. Day 1 Summary and Outlook for Days 2–3: Audience questions

The final session of Day 1 synthesized key technical themes and oriented participants to the case studies and cross-agency discussions planned for Days 2–3. Ms. Meenu Batolar (CEPI, Singapore) thanked participants for contributions across the day's sessions and noted recurring questions on how to interpret immunogenicity-based evidence, design animal models with improved translatability, and balance the 3Rs (Replacement, Reduction, Refinement) with the need for biologically informative datasets in emergencies. Participants also discussed how regulators weigh uncertainty when authorizations rely on alternative evidence packages and how post-authorization evidence generation can be planned prospectively.

Participants emphasized the importance of sustained regulatory collaboration and routine cross-authority dialogue, particularly in the Asia-Pacific region where capacities and legal frameworks vary. The facilitation team noted that these topics—including assay comparability, reliance pathways, model translatability, and integration of evidence streams—would be addressed in greater depth in subsequent sessions through disease-specific case studies and dedicated working discussions.

Day 2 - Pandemic preparedness & response vaccine development ecosystem strengthening and use of innovative regulatory approaches when efficacy studies are not feasible

2.1. Part 3: Chikungunya case study

2.1.1. Chikungunya case study: Setting the scene

Ms. Danielle Craig (CEPI, USA) opened day 2 by introducing the chikungunya case study and outlining its relevance to CEPI and regulatory partners. She noted that chikungunya virus was first identified in the 1950s and has received renewed attention for vaccine development following WHO's inclusion of chikungunya on its 2018 list of priority pathogens for R&D. She also noted that CEPI has convened a series of technical workshops (2020–2025) to support alignment between developers and regulators on evidence expectations for licensure.

She highlighted a central development and regulatory challenge: although chikungunya can affect large populations, outbreaks are unpredictable in time and location, which can make traditional phase 3 clinical efficacy trials difficult to execute. She described a "totality-of-evidence" approach under discussion for chikungunya vaccines that integrates non-clinical challenge and passive-transfer data (including NHP studies), clinical immunogenicity, and seroepidemiologic analyses, alongside robust CMC and safety datasets. She noted that this approach has supported increasing convergence around the use of immunological markers as surrogate endpoints, with associated expectations for labeling, risk management, and post-authorization evidence generation.

She noted that, with licensed chikungunya vaccines now available, discussion has increasingly shifted toward post-marketing evidence needs, including real-world effectiveness and safety monitoring frameworks. She emphasized that direct scientific exchange between regulators and developers has been important for clarifying evidence requirements and for supporting efficient regulatory review.

2.1.2. Disease and epidemiology of Chikungunya

2.1.2.1. Current status and epidemiology of Chikungunya in India

Director Dr. Manoj Murhekar (ICMR- National Institute of Epidemiology [NIE], India) summarized the epidemiology of chikungunya in India, noting that the virus was first recognized in 1952 in Tanzania and that India reported early outbreaks soon thereafter, including in Kolkata, followed by epidemics across several states during the 1960s and early 1970s. He noted that reported transmission then declined, with the last documented outbreak of the earlier period occurring in 1973 in Barshi, Maharashtra. After an extended period with limited reported activity, chikungunya re-emerged in India in late 2005, followed by widespread outbreaks in 2006 and continued transmission with periodic outbreaks in subsequent years.

He described India's surveillance approach as combining routine case reporting with targeted laboratory confirmation to detect and characterize outbreaks. Suspected cases are captured through the National Centre for Vector Borne Disease Control and the Integrated Disease Surveillance Programme, with reports originating from public and private health facilities and compiled in national health-information systems. District teams review incoming data to identify clusters and trigger field investigations. He also highlighted the Indian Council of Medical Research Virus Research and Diagnostic Laboratory (VRDL) network (established from 2014), which supports early diagnosis of outbreak-prone diseases by testing routine and outbreak-related samples using syndrome-based diagnostic algorithms.

Dr. Murhekar summarized recent trends, noting that over the past five years India has reported approximately 100,000–200,000 suspected chikungunya cases annually, with Maharashtra, Karnataka,

and Gujarat contributing a substantial share of reported notifications. He reported that VRDL testing data from 2016–2025 included nearly 300,000 suspected cases, with approximately 10% laboratory-confirmed. Positivity was higher among adults aged >30 years and showed seasonal increases during monsoon and post-monsoon periods. He noted that routine national program reports do not attribute confirmed deaths directly to chikungunya; however, he cited secondary analyses (including from Ahmedabad) that have suggested potential excess mortality during large outbreaks, underscoring uncertainty in burden estimation and the need for strong surveillance and analytics.

He noted that multiple chikungunya genotypes circulate globally and that the predominant genotype in India has shifted over time. Early outbreaks were attributed to the Asian lineage, transmitted primarily by *Aedes aegypti*. Following re-emergence in 2005, the Indian Ocean lineage of the East/Central/South African (ECSA) genotype became established; he noted that the A226V mutation is associated with enhanced transmission by *Aedes albopictus*, which may have contributed to the scale and geographic spread of outbreaks. He also summarized findings from a nationwide ICMR serosurvey (2017–2018) of >12,000 samples across 15 states and 60 districts, which reported an overall chikungunya IgG seroprevalence of ~18%, with notably lower seroprevalence in eastern and northeastern states—suggesting higher susceptibility to future outbreaks in these areas. He concluded that chikungunya transmission remains widespread in India, with marked seasonality and geographic heterogeneity.

2.1.2.2. Epidemiology of chikungunya disease in Thailand (2020–2025)

Director Dr. Wichan Bhunyakitikorn (Thai Centers for Disease Control and Prevention [CDC], Thailand) described Thailand's long-standing national disease surveillance system, now digitized through the Digital Disease Surveillance System. By regulation, public and private hospitals report notifiable diseases, including chikungunya, via electronic hospital information system (HIS) connections to an application programming interface (API), enabling near real-time transmission of case data. Following automated validation and processing, aggregated data are available through public dashboards that display trends at national, provincial, and subdistrict levels. Thailand also uses event-based and syndromic surveillance to support early detection of outbreaks.

He noted that chikungunya was first detected in Thailand in 1958 in Bangkok and that the country has experienced intermittent outbreaks since then. He highlighted a large nationwide outbreak in 2009 (approximately 50,000 reported cases), predominantly affecting southern provinces, and a subsequent major outbreak in 2020 (approximately 20,000 reported cases). He noted that after 2020, transmission continued at lower levels, consistent with endemicity punctuated by seasonal peaks. The predominant genotype reported during recent outbreaks and current transmission is the ECSA lineage.

He described key drivers of transmission risk that are shared across Southeast Asia, including the distribution of competent mosquito vectors (*Aedes aegypti* predominating in urban settings and *Aedes albopictus* more common in rural areas), a tropical climate, rapid urbanization, and widespread breeding sites that complicate vector control. He noted that these factors can facilitate periodic resurgence even when overall incidence is low.

He summarized Thailand's outbreak response approach as integrating case management, vector control, and community engagement. Health facilities notify local health centers following case detection, which can trigger investigation teams to conduct household visits and implement vector-control measures (e.g., adult mosquito control activities) alongside community-based surveillance. He noted that this operational model is aligned with national approaches used for other arboviral diseases, including dengue and Zika.

He reported that surveillance since 2020 indicates that reported chikungunya cases occur predominantly among adults aged 20–60 years. Transmission is geographically widespread but typically occurs at relatively low levels, with seasonal increases during mid-year rainy months. Based on recent trends,

Thailand anticipates detection of approximately 1,000 cases in the coming year, assuming no unusual transmission events. He concluded that chikungunya remains an ongoing public health concern and noted that persistent transmission, urbanization, insecticide resistance, and climate suitability continue to complicate vector control.

2.1.2.3. Chikungunya disease and epidemiology: WHO SEARO perspective

Mr. Anil Chawla (WHO SEARO, India) provided a WHO SEARO perspective on chikungunya surveillance, regulatory preparedness, and outbreak risks across Asia. He noted that WHO's regional support spans both regulatory acceleration and surveillance strengthening, and highlighted the role of the regional laboratory network, including quality-assured surveillance laboratories co-funded with institutions such as ICMR. He also observed that South and Southeast Asia host several major vaccine manufacturers and that WHO works with countries and manufacturers to support timely introduction pathways for new vaccines when warranted.

Mr. Chawla noted emerging challenges affecting chikungunya and other vector-borne diseases in the region. He highlighted the potential effects of climate variability, insecticide resistance, and changes in vector distribution on transmission patterns, and noted that these factors can complicate vector-control strategies and contribute to geographic and temporal shifts in outbreak dynamics. He emphasized that surveillance and laboratory systems should be strengthened to detect changes in transmission and to inform timely response.

He briefly summarized vaccine-development activity for chikungunya across multiple platforms (including inactivated, viral-vector, and mRNA approaches) and noted that platform flexibility may be relevant for outbreak response if antigenic or epidemiologic conditions change. He emphasized that vaccine availability must be complemented by manufacturing readiness, regulatory agility, and cross-country coordination to enable timely access during outbreaks.

In the Q&A, participants asked about gaps between suspected and confirmed cases. Mr. Chawla emphasized that diagnostic performance depends on end-to-end system quality, including sample collection, storage, transport, and testing procedures—rather than on test kits alone. He noted that low positivity rates, false positives, inconsistent submission, and under-reporting can reflect weaknesses across these operational steps. He also noted that developers often view the reported burden as an underestimate and highlighted the importance of strengthening surveillance to better characterize true incidence.

A second question addressed whether force-of-infection modeling and environmental suitability indicators could strengthen burden estimation. Panelists agreed that disease control requires an integrated approach combining vaccination (when available), vector control, ecological monitoring, and improved surveillance. Mr. Chawla noted that, although mortality is generally low, persistent morbidity (including prolonged arthralgia) can result in substantial quality-of-life and economic impacts, reinforcing the importance of improved burden estimates.

An ICMR representative noted that serosurveys have been combined with force-of-infection modeling to estimate burden and emphasized that surveillance systems are typically designed to detect and characterize outbreaks rather than to enumerate all infections. Participants noted that under-detection remains a persistent challenge and that triangulation across syndromic surveillance, laboratory confirmation, and serologic studies is important for improving burden estimates.

The session concluded by emphasizing that sustained surveillance, laboratory quality systems, vector-control capacity, and regulatory and manufacturing readiness remain important for timely response to chikungunya and other emerging arboviral threats.

2.1.2.4. Characterization and clinical epidemiology of recent chikungunya outbreaks in Sri Lanka

Dr. Neelika Malavige (Sri Lanka) summarized recent chikungunya activity in Sri Lanka, noting a major outbreak during 2006–2008 followed by a prolonged period with few reported cases. She noted that subsequent diagnostic studies identified misclassification in syndromic surveillance, with a small proportion (approximately 2–7%) of patients clinically diagnosed with dengue testing positive for chikungunya by polymerase chain reaction (PCR). She reported that chikungunya re-emerged in late 2024, with laboratory confirmation of a substantial outbreak in 2025, concentrated initially in densely populated areas of Colombo.

She noted that national surveillance reports chikungunya activity as a proportion of monthly arboviral cases rather than as absolute case counts, with peak activity reported in June–July. She described clinical epidemiology findings from hospital and primary-care datasets: hospitalized patients were predominantly 41–60 years of age and more than half were women, while most cases were managed in outpatient settings. In a clinical study of >600 laboratory-confirmed cases from Colombo and southern primary-care facilities, 64% of patients were female, more than half were aged 41–60 years, and approximately 8% required hospitalization, consistent with the hospital-based observations.

Dr. Malavige described the clinical presentation in the recent outbreak, noting polyarticular involvement most frequently affecting the ankle, followed by small joints of the hands and the midfoot. She reported that joint pain and swelling often persisted beyond the acute febrile phase, with improvement commonly beginning after approximately 15–20 days. Functional impairment was substantial: using the Barthel Index, only ~8% of patients had full function at presentation and at 30 and 60 days after symptom onset. She noted that women experienced greater functional impairment and slower recovery than men, while recovery time did not differ significantly by age group in the study population.

She reported genomic sequencing findings indicating that 2025 Sri Lankan strains belonged to the Indian Ocean lineage but were genetically distinct from strains associated with Sri Lanka's 2008 outbreak and from strains reported in several other recent outbreaks. Mutations were observed in the E1 and E2 envelope proteins, including in regions associated with neutralizing antibody binding. She noted that ongoing work is evaluating whether these changes could influence population immunity following prior infection and, more broadly, how sequence variation should be considered when interpreting vaccine-induced immune responses.

She described Sri Lanka's laboratory-supported surveillance approach, including testing of dengue PCR- and NS1-negative samples for chikungunya through a network of tertiary hospitals and primary health centers across multiple provinces. She noted that the national Epidemiology Unit also monitors chikungunya-like illness through sentinel clinical sites. Reported activity in this system remained elevated through approximately August 2024 and then declined; a smaller resurgence was observed from January of the current year.

2.1.3. Innovative approaches: Data used to license chikungunya vaccine to include preclinical models with WHO listed authority feedback on the adequacy of the model to support preclinical efficacy studies

2.1.3.1. Innovative approaches to license a chikungunya vaccine: VLA1553 (IXCHIQ)

Dr. Shailesh Dewasthaly (Valneva, USA) described the regulatory approach used to license Valneva's live-attenuated chikungunya vaccine candidate VLA1553 (marketed as IXCHIQ). He reported that the vaccine contains a large, stable 31–amino acid deletion in the nonstructural protein 3 (nsP3), intended to support attenuation stability. He noted that the product is manufactured in Vero cells, contains no adjuvant, and is supplied as a lyophilized formulation with water for injection.

He noted that, because large, randomized efficacy trials with clinical endpoints were difficult to execute in the context of chikungunya's unpredictable outbreak patterns, licensure relied on a correlate-of-protection strategy supported by multiple evidence streams. First, Valneva presented evidence that neutralizing antibody titers were associated with protection using a passive-transfer study in NHPs: animals that received immune human sera before challenged with wild-type chikungunya virus showed reduced or absent viremia and fewer clinical signs relative to controls. Regulators (including FDA and EMA) agreed on a conservative correlate threshold of a plaque reduction neutralization test 50% titer ($PRNT_{50}$) of 1:150. Second, a seroepidemiology study in the Philippines provided supportive evidence; protective titers measured using a $PRNT_{80}$ assay were bridged to Valneva's $PRNT_{50}$ assay and were reported to align with the same threshold, supporting use of this marker as a surrogate endpoint.

Dr. Dewasthaly noted that, because authorization was based on a surrogate endpoint, the program includes post-authorization commitments intended to further characterize effectiveness and safety. He highlighted ongoing studies in Brazil, including a pragmatic effectiveness study (study 402) using a test-negative case–control design. He reported that, as of early March, approximately 7,000 participants had been vaccinated, increasing to nearly 10,000 by the time of his presentation. He stated that safety reviews to date had not identified new concerns in the reported study population. Additional post-authorization activities include continued safety surveillance and further work to support pediatric development.

He concluded that this case illustrates how a predefined CoP framework, supported by non-clinical evidence and a structured post-authorization evidence plan, can support licensure decisions for pathogens for which efficacy trials are difficult to conduct.

2.1.3.2. Development of chikungunya vaccine (recombinant and live-attenuated): VLA1555 (Butantan-Chik)

Dr. Julia da Costa Silva (Butantan Institute, Brazil) described Instituto Butantan's chikungunya vaccine program (Butantan-Chik) and the regulatory strategy for advancing it in Brazil. She noted that the candidate is a single-dose, lyophilized formulation developed in partnership with Valneva, in which Valneva supplies the drug substance and Butantan performs fill-finish and releases the final drug product. She stated that the program is intended to support access in endemic settings, with an initial focus on Brazil and potential expansion to other regions subject to regulatory approvals and supply arrangements.

She noted that, because the drug substance and parts of the clinical evidence package originate from Valneva, the Butantan dossier overlaps substantially with the IXCHIQ submission and may enable an efficient review pathway. She reported that Butantan is engaging with Agência Nacional de Vigilância Sanitária (ANVISA) on planned submission and review timelines and is also developing additional presentations, including a multi-dose format, as part of longer-term manufacturing planning. She noted that, following national authorization, Butantan intends to pursue pathways that can support broader regional access (e.g., WHO prequalification and engagement with Pan American Health Organization [PAHO]), alongside country-specific regulatory submissions and partnerships where appropriate.

Dr. da Costa Silva emphasized early scientific and regulatory engagement with ANVISA to clarify evidence expectations and operationalize post-authorization requirements. She also noted participation in the EMA OPEN framework, which supported information exchange and alignment on scientific considerations. She stated that several post-authorization activities established for IXCHIQ would be relevant for the Butantan product, depending on the final regulatory requirements and risk-management plans.

She highlighted several challenges relevant to chikungunya vaccine development and deployment. These include differences in benefit–risk considerations between endemic populations and non-endemic travelers, limited feasibility of conventional efficacy studies due to fluctuating incidence, and constraints on generating robust RWE when health data systems are fragmented. She noted that strengthening

sentinel surveillance, case reporting, laboratory confirmation, and data linkage can support both outbreak monitoring and post-authorization safety and effectiveness evaluations.

2.1.3.3. Innovative approaches to regulatory approval: Bavarian Nordic's CHIKV virus-like particle (VLP)

Dr. Victoria Jenkins (Bavarian Nordic, Switzerland) described Bavarian Nordic's chikungunya vaccine VIMKUNYA, a VLP vaccine adjuvanted with aluminum and supplied in a prefilled syringe (reported shelf life: three years). She noted that the vaccine was licensed in 2025, first by FDA and subsequently by EMA and Medicines and Healthcare products Regulatory Agency (MHRA) and is indicated for individuals aged ≥12 years. She added that additional regulatory reviews are ongoing in other jurisdictions.

She noted that, given the difficulty of conducting conventional efficacy trials for chikungunya, regulators accepted a surrogate marker framework as the basis for initial licensure. She described development of a neutralizing-antibody threshold using a passive-transfer NHP model: serum from vaccinated individuals was diluted, administered to animals, and animals were then challenged with chikungunya virus. Logistic regression analysis of viremia outcomes was reported to identify protection from viremia among animals with pre-challenge neutralizing antibody titers above 25.7 (NT_{80}). For clinical development, regulators selected a more conservative threshold (reported as 100) for phase 3 immunogenicity analyses.

Dr. Jenkins noted post-authorization requirements, including a pregnancy registry, pediatric studies, and long-term follow-up. She also described a planned phase 3 clinical efficacy study designed as a randomized, double-blind, placebo-controlled trial with an event-driven endpoint (target: 64 chikungunya cases) and enrollment of >6,000 participants across the Philippines and Thailand. She noted that seroepidemiologic monitoring is intended to support site selection and timing by identifying emerging outbreaks. Given the inherent uncertainty in outbreak occurrence, she noted that additional complementary strategies to generate effectiveness evidence are also being explored.

She noted that Bavarian Nordic has established partnerships intended to support access in endemic regions, including collaboration with Biological E (India) and with Europharma (Brazil) for regulatory submissions and distribution. In reflecting on the development program, she emphasized the value of early and sustained scientific advice with regulators, preparation of dossier components suitable for multi-agency review, and use of reliance pathways where applicable to support efficient evaluations across jurisdictions.

2.1.4. Developers: Q&A

Moderator: Dr. James McBlane MHRA, UK)
Panelists:
Dr. Shailesh Dewasthaly (Valneva, USA)
Dr. Julia da Costa Silva (Butantan Institute, Brazil)
Dr. Victoria Jenkins (Bavarian Nordic, Switzerland)

Audience questions focused on developers' experience aligning innovative evidence approaches with national regulatory expectations. Participants asked which components were most challenging to align (e.g., acceptance of preclinical models, immunobridging, and real-world effectiveness study designs), and whether a common study template or shared methodological guidance could support more consistent post-authorization evidence generation across jurisdictions.

In response, Dr. Jenkins emphasized that a key challenge was achieving regulatory acceptance of a scientifically justified surrogate marker of protection. She noted that, in the absence of an established

chikungunya correlate of protection (CoP), developing and validating a neutralizing-antibody threshold required substantial technical dialogue with regulators and shaped the design of phase 3 immunogenicity programs. She also noted that post-authorization requirements intended to confirm clinical benefit remain a major area of variability across agencies. She contrasted the approaches being pursued by different developers, including observational effectiveness studies in some settings and attempts to conduct event-driven efficacy trials in others, each with distinct feasibility constraints.

Developers noted that expectations differed across agencies (e.g., between FDA and EMA), which limited harmonization of study designs and sequencing of post-authorization commitments. One example discussed was the difficulty of initiating or progressing an effectiveness study when initial licensure occurs in settings with limited or no endemic transmission, reducing the probability of accruing endpoints in a reasonable timeframe. Participants suggested that clearer, more standardized post-authorization frameworks—defining which study designs are acceptable, when they should be initiated, and how local epidemiology and vaccine uptake should inform feasibility—could support more efficient evidence generation and reduce duplication across jurisdictions.

2.1.5. National regulatory authority perspectives on adequacy of data to support licensed vaccine: US, EU, UK, Brazil and, India

2.1.5.1. Anvisa's perspectives on adequacy of data to support licensed vaccine: IXCHIQ chikungunya vaccine assessment case

Dr. Brenda Gomes Valente (ANVISA, Brazil) summarized ANVISA's assessment of the chikungunya vaccine IXCHIQ, submitted by Instituto Butantan in 2023. She noted that ANVISA participated in the EMA OPEN initiative during the review, enabling access to EMA assessment outputs and supporting alignment on key scientific questions and uncertainties. She also noted that input from Brazil's independent arbovirus expert committee and participation in international CEPI/International Vaccine Institute (IVI)/PAHO technical workshops informed ANVISA's appraisal of the evidence package.

She reported that ANVISA granted marketing authorization in April 2025 for adults aged 18–59 years at increased risk of chikungunya; the initially proposed indication included older adults but was later revised. Because conventional efficacy trials were considered infeasible due to the unpredictable and short-lived nature of outbreaks, the dossier relied on a conservative serologic surrogate endpoint: a neutralizing antibody micro-PRNT titer ≥150, supported by non-clinical challenge studies and seroepidemiologic data. The clinical evidence package included randomized phase 3 immunogenicity and safety studies in healthy adults, an ongoing long-term extension study, and a phase 3 adolescent study conducted in endemic settings.

She noted that the review identified residual uncertainties, including the magnitude and duration of protection; protection against severe or chronic outcomes; performance in previously infected individuals; and longer-term safety, including use in older adults and people with comorbidities or immune-mediated conditions. ANVISA concluded that protection could be reasonably inferred from the serologic surrogate marker in the context of Brazil's endemic transmission and the clinical safety database available at the time of review. Authorization was therefore accompanied by post-authorization obligations, including effectiveness studies (e.g., test-negative designs), a pragmatic randomized study, enhanced safety monitoring, and updates to the risk-management plan.

She reported that, following initial rollout and post-authorization safety monitoring, ANVISA reviewed reports of serious adverse events, primarily among individuals aged ≥65 years and those with multiple uncontrolled comorbidities. Reported events included chikungunya-like illness with clinical deterioration, encephalitis, and deaths. Following evaluation, ANVISA revised the product information by removing use

in adults aged ≥60 years and adding a contraindication for people with poorly controlled chronic diseases; additional warnings and enhanced pharmacovigilance requirements were also implemented. She noted that these evolving safety considerations affected feasibility and design of planned post-authorization effectiveness and pragmatic studies in Brazil. She indicated that, for the authorized population, ANVISA considered the benefit–risk balance to remain favorable when used in accordance with updated contraindications and risk-minimization measures.

Dr. Gomes Valente concluded that ANVISA is prepared to consider innovative regulatory approaches, including use of scientifically justified surrogate endpoints, when efficacy trials are not feasible. She emphasized the importance of early engagement with developers, transparency on residual uncertainties, and clearly defined post-authorization evidence-generation and risk-management plans.

2.1.5.2. Approved chikungunya vaccines

Dr. Marco Cavaleri (EMA, EU) summarized EMA's experience in assessing chikungunya vaccines, focusing on how putative CoPs were defined and used to support approvals of VIMKUNYA and IXCHIQ. He noted that the two products relied on different assays and non-clinical models, but that EMA and FDA aligned on conservative neutralizing-antibody thresholds to reduce the risk of divergent evidentiary expectations for developers. He suggested that broader multilateral scientific exchange among regulators could further improve consistency and predictability of evidence requirements across jurisdictions.

He noted that once surrogate thresholds are defined, a central clinical question is whether trials can demonstrate that vaccinated individuals reliably achieve titers at or above those levels. For VIMKUNYA, he reported that seroresponse rates were high, with antibody rises observed within days and persistence of responses over at least six months. For IXCHIQ, he reported similarly robust antibody responses; however, he noted that interpretation of early protection differs for live-attenuated vaccines because kinetics depend on viral replication. He also compared safety profiles in general terms: VIMKUNYA showed reactogenicity consistent with an adjuvanted vaccine, while IXCHIQ was associated with chikungunya-like illness in some recipients and includes contraindications for severely immunocompromised individuals.

He noted that both vaccines received positive benefit–risk assessments, accompanied by risk-management plans and legally binding post-authorization requirements. EMA required confirmatory studies to further characterize effectiveness—an approach used when approvals rely on surrogate markers. He noted that randomized efficacy trials during outbreaks may not accrue sufficient endpoints and that complementary observational designs are therefore often needed despite methodological limitations. He emphasized the importance of planning such studies in collaboration with national regulators and ethics committees in countries likely to experience outbreaks, to enable timely activation and appropriate governance.

He also described EMA's ongoing safety review of IXCHIQ in light of post-authorization reports from vaccination campaigns, including reports from La Réunion involving older adults and individuals with comorbidities. He noted that EMA updated product information by strengthening warnings and contraindications and by reinforcing risk-minimization measures. He also noted that continued signal evaluation is ongoing as additional case reports are assessed (including reports such as aseptic meningitis in Canada), consistent with routine pharmacovigilance practice.

Dr. Cavaleri concluded by noting continuing evidence needs, including data in pregnant individuals and infants, improved estimates of disease burden and longer-term sequelae, and strengthened surveillance systems to inform vaccination strategies. He emphasized that these data, together with post-authorization monitoring, are important for refining benefit–risk assessments and for guiding public health use of chikungunya vaccines.

2.1.5.3. UK licensing of chikungunya vaccines: Regulatory routes

Dr. James McBlane (MHRA, UK) described how the UK authorized the two chikungunya vaccines in 2025, focusing on the regulatory routes used rather than re-assessing the full scientific evidence base. He explained that applicants may seek approval through a full national review or through the UK's IRP, which functions as a reliance pathway that leverages assessments by selected reference authorities. He noted that IRP has two routes: IRP A, a streamlined pathway that largely relies on the conclusions of the reference authority, and IRP B, a more detailed pathway used when additional UK-specific issues require further assessment (e.g., changes in manufacturing sites, new clinical information, or genetically modified organism [GMO] considerations).

He reported that both vaccines (IXCHIQ and VIMKUNYA) were authorized via recognition pathways, with MHRA reviewers focusing on confirming consistency between the UK submission, product information, and the reference authority's assessment. He noted that a substantial portion of the review effort related to GMO-related regulatory requirements, rather than re-evaluating the vaccines' clinical or non-clinical data.

Dr. McBlane explained that marketing authorization decisions for new active substances in the UK are supported by advice from the independent Commission on Human Medicines (CHM), as required under UK law. MHRA assessors conduct the review and formulate recommendations and questions, and CHM provides independent scientific advice to inform the final decision. He noted that applicants should therefore anticipate engagement not only with MHRA assessors but also with the broader UK advisory system when preparing submissions.

He concluded that early clarification of UK-specific requirements and alignment on the scope of reliance review can help applicants plan efficient submissions and avoid delays.

2.1.5.4. National regulatory authority perspectives on adequacy of data to support licensed vaccine: India

Deputy Drugs Controller Dr. Rubina Bose (CDSCO, India) summarized India's regulatory perspective for chikungunya vaccines, noting that while no chikungunya vaccine is currently licensed in India, several domestically developed candidates are advancing. She noted that regulatory review is led by the CDSCO, supported by national control laboratories and expert committees, including scientific advisory structures for clinical trial protocols. Reviews are conducted under India's Drugs and Cosmetics Act and the New Drugs and Clinical Trials Rules, alongside relevant WHO guidance.

She noted that candidate development is expected to follow established steps, including non-clinical evaluation, phase 1–3 clinical studies as appropriate, marketing authorization, and post-authorization requirements. Non-clinical packages typically include proof-of-concept and dose-ranging studies, safety/toxicology where relevant (including additional studies for novel adjuvants), and, where immunogenicity-based licensure is contemplated, challenge and/or passive-transfer studies to support a scientifically justified surrogate marker framework. She noted that current candidates do not include new adjuvants.

Dr. Bose noted that clinical development plans may use seamless phase 1/2 or phase 2/3 designs and typically include randomized, placebo-controlled components, dose escalation, and lot-to-lot consistency assessments. Study design should account for prior exposure patterns and the need to include relevant age groups and endemic settings. She emphasized that validated neutralizing-antibody assays are essential and that, in the absence of an established CoP, primary endpoints may include seroresponse rates or the proportion of participants achieving titers above a prespecified threshold. She noted that

efficacy trials with clinical endpoints may be feasible only in limited circumstances due to outbreak unpredictability.

She noted that, following authorization, sponsors are expected to conduct post-authorization safety monitoring and, where feasible, effectiveness evaluations using RWE approaches. She reported that four chikungunya vaccine candidates are currently in development in India: one subunit candidate based on structural proteins and three whole-virion inactivated candidates. She noted that one candidate has entered phase 3 evaluation and is supported by non-clinical safety studies, NHP challenge and passive-transfer data, and phase 1–2 immunogenicity datasets. Other candidates are transitioning from preclinical to early clinical development.

2.1.6. Vaccines in development (preclinical, clinical, manufacturing technologies, regulatory strategies) with gaps remaining to be filled

2.1.6.1. Chikungunya vaccine Zydus Lifesciences Limited

President Dr. Kapil Maithal (Zydus Lifesciences, India) introduced Zydus Lifesciences and summarized the organization's vaccine-development and manufacturing capabilities relevant to chikungunya vaccine development. He noted that the company has multiple manufacturing sites, in-house R&D capacity, and clinical-development infrastructure. He also noted access to an accredited NHP facility and an internal phase 1 clinical trial unit, which support preclinical-to-clinical translation.

He described the company's chikungunya vaccine candidate as a fully liquid, inactivated vaccine based on an Asian lineage strain, produced in WHO-sourced Vero cells and formulated with a dual-adjuvant system (aluminum hydroxide plus an oil-in-water emulsion). He noted that the intended use case is a single-dose regimen for individuals aged ≥2 years, subject to demonstration of acceptable safety and immunogenicity. He reported that the candidate has completed discovery and Good Manufacturing Practice (GMP) manufacturing of clinical material and that a phase 1 clinical trial application has been submitted.

He reported preclinical findings including neutralizing antibody responses measured through approximately 180 days, cross-neutralization against ECSA and Asian strains, and immune profiles interpreted as balanced Th1/Th2 responses in animal models. He also summarized toxicology studies in rats and rabbits, reporting no safety concerns at four- to five-fold human-equivalent doses. He noted that comparative testing in animal models against licensed chikungunya vaccines (IXCHIQ and VIMKUNYA) was conducted and reported to show similar or higher antibody levels and longer persistence for the Zydus candidate, while acknowledging that cross-study comparisons depend on assay conditions and study design.

He outlined a clinical development plan beginning with a phase 1 dose-escalation study in adults with safety follow-up through six months and immunogenicity assessment. He noted ongoing reproductive toxicology studies and challenge studies in IFNAR1 knockout mice and NHPs. He described a proposed phase 2 study to expand enrollment (including adolescents), refine dose/regimen selection, and evaluate cytokine responses and cross-neutralization. He noted that a phase 3 program may use placebo-controlled or active-comparator designs, include lot-to-lot consistency, and assess safety and immunogenicity as primary endpoints, with the design contingent on regulatory expectations and availability of licensed comparators. He also noted anticipated post-authorization activities, including longer-term safety follow-up, effectiveness studies, evaluation in younger age groups, and assessment of potential interference with co-administered vaccines.

2.1.6.2. Developmental vaccine- BBV87

Director Dr. Badri Narayan Patnaik (Bharat Biotech, India) described BBV87, an inactivated chikungunya vaccine candidate based on an ECSA strain and inactivated with beta-propiolactone. He noted that the liquid formulation is adjuvanted with aluminum hydroxide, stored at 2–8 °C, and has a reported 24-month real-time shelf life. The planned regimen is a two-dose schedule administered 28 days apart; a 40 µg dose was selected for the pivotal phase 3 trial. The intended target population is individuals aged 12–65 years.

He summarized preclinical studies supporting clinical development. In active challenge studies in macaques, 20 µg and 40 µg doses were reported to reduce or clear viremia following challenge with a virulent chikungunya strain. He also described passive-transfer experiments in which sera from phase 2 trial participants (20 µg and 40 µg cohorts) were infused into macaques prior to challenge; both dose cohorts were reported to suppress viremia, with stronger effects observed using sera from the 40 µg cohort. He noted that these findings support a neutralizing-antibody–based bridging rationale and suggested that a $PRNT_{50}$ titer on the order of ~100 may be associated with protection in the model, although additional validation is required to define a regulatory-acceptable threshold.

Across phase 1 and phase 2 clinical studies conducted in India and in other trial sites (Costa Rica, Colombia, Guatemala, and Thailand), he reported that no vaccine-related serious adverse events were observed. Reported local reactions were generally limited to transient pain, redness, or swelling. He stated that immunogenicity analyses showed seroconversion after the second dose.

He noted that the development strategy anticipates seeking licensure based primarily on immunogenicity endpoints, supported by active and passive-transfer animal challenge studies, given the practical challenges of conducting clinical endpoint efficacy trials for chikungunya. He noted that the initial licensure plan focuses on a two-dose regimen, with evaluation of alternative regimens for outbreak-response use as a potential future objective. He reported that CDSCO has granted permission to initiate phase 3 trials, with study activation contingent on required ethics approvals.

2.1.7. Vaccines in development: Q&A

Moderator: Dr. James McBlane (MHRA, UK)
Panelists:
Dr. Kapil Maithal (Zydus Lifesciences, India)
Dr. Badri Narayan Patnaik (Bharat Biotech, India)

Audience questions focused on how developers incorporate the role of National and Regional Immunization Technical Advisory Groups (NITAGs/RITAGs) when planning development and regulatory strategies for chikungunya vaccines. Participants asked whether, and at what stage, developers seek to understand advisory-group evidence standards (including use of vaccines licensed via surrogate endpoints) and how advisory recommendations may influence country uptake and post-authorization evidence-generation plans.

Bharat Biotech noted that prioritization of chikungunya vaccination varies across countries and that engagement strategies therefore differ by epidemiologic context and national policy processes. As an early-stage developer preparing for a pivotal phase 3 study, the company reported focusing on early engagement with national regulators and relevant public health stakeholders. It also reported interactions with authorities in countries hosting trials or planned studies (including Guatemala, Colombia, and Thailand) and noted ongoing engagement in India with CDSCO and relevant government stakeholders. The speaker indicated that, to date, engagement with advisory groups has been limited and typically occurs later in the pathway or when requested.

Dr. Jenkins noted that engagement with NITAGs must preserve advisory group independence and should be conducted transparently, typically in response to invitations or structured consultation processes. She reported that, in jurisdictions where licensure was obtained, developers may have opportunities to present data and contextual information when requested. She cited examples of engagement with the U.S. Advisory Committee on Immunization Practices (ACIP) and with NITAGs in multiple countries. She also emphasized the role of neutral conveners such as CEPI and WHO in providing structured forums where developers can share data and clarify the scientific landscape without compromising NITAG independence.

WHO SEARO noted that technical advisory groups may invite manufacturers to attend meetings as observers and, where appropriate, to present data in dedicated sessions. The speaker emphasized that such engagements should follow established procedures that maintain transparency and manage conflicts of interest.

2.1.8. Panel: Adequacy of regulatory strategies for chikungunya vaccines

Moderator: Dr. Rubina Bose (CDSCO, India)
Panelists:
Ms. G. M. D. T. Gurugalgoda (National Medicines Regulatory Authority [NMRA], Sri Lanka)
Dr. Wittawat Viriyabancha (Thai FDA, Thailand)
Dr. Pura Wena A. Clacio-Clores (Philippines FDA, Philippines)
Dr. Yuji Matsukara (PMDA, Japan)
Mr. Anil Chawla (WHO SEARO, India)

This panel brought together national regulatory authorities from Sri Lanka, Thailand, the Philippines, and Japan, alongside WHO SEARO, to discuss the adequacy of current regulatory strategies for chikungunya vaccines. Discussion focused on regulatory pathways when conventional phase 3 efficacy trials are infeasible, the role of surrogate markers and RWE, expectations for safety data, and opportunities for regional cooperation.

Panelists emphasized that regulatory flexibility must be grounded in clearly articulated scientific rationale. While no country represented on the panel applies a formal equivalent of the US FDA's Animal Rule, several regulators described mechanisms that allow authorization based on scientifically justified surrogate endpoints (e.g., immunological markers) within a totality-of-evidence framework, supported by defined post-authorization obligations such as enhanced pharmacovigilance and confirmatory evidence-generation plans.

Thailand's regulator noted that conditional approval can be considered when benefit–risk is favorable and when enforceable post-authorization commitments are incorporated into risk-management plans. Panelists also discussed reliance pathways to accelerate evaluation by leveraging assessments from reference authorities and WHO, while maintaining national decision-making autonomy. Japan's regulator noted that chikungunya is not currently a domestic public health priority, but that the same scientific principles apply; decisions may place increased weight on safety when efficacy certainty is limited and may include requests for local immunogenicity data or justification for extrapolation across populations.

The panel discussed RWE as a complementary evidence stream for confirming effectiveness and monitoring safety after authorization, particularly when approvals rely on surrogate markers. The Philippines described ongoing progress in health-data digitization, noting the existence of multiple electronic health record systems across public and private sectors. However, they highlighted fragmentation and limited nationwide integration as constraints on producing high-quality RWE at scale.

As a result, while RWE can meaningfully inform regulatory reassessment, it is unlikely to fully substitute for traditional evidence unless data systems become more interoperable and standardized.

Thailand described stronger readiness to generate RWE, including national health coverage databases, surveillance systems, and established adverse events following immunization (AEFI) reporting platforms. For conditionally approved vaccines, RWE generated under post-authorization commitments is considered essential for informing regulatory reassessment, labeling updates, and risk-minimization measures. Across regulators, there was alignment that RWE must be methodologically rigorous, embedded within existing health systems, and interpreted within a structured benefit–risk framework.

Regional coordination was identified as an enabler of efficiency and convergence. WHO SEARO emphasized the role of regional mechanisms (e.g., ASEAN, SEARO, WPRO) in supporting joint reviews, reliance models, and shared learning, while implementation remains the responsibility of member states. PMDA described contributions through regulatory training, capacity building, bilateral cooperation, and publication of assessment reports to support convergence on scientific principles across agencies.

Regional coordination emerged as another key enabler. WHO SEARO emphasized the importance of regional bodies—including ASEAN, SEARO, and WPRO—in driving regulatory convergence through joint reviews, reliance models, and shared learning. Such coordination can reduce duplication, lower costs, and accelerate access, while implementation remains the responsibility of individual member states. Japan's PMDA, as a WHO-listed authority, outlined its role in supporting harmonization through regulatory training, capacity building, bilateral cooperation agreements, and transparent publication of assessment reports. PMDA emphasized that harmonization should focus on aligning scientific principles and evidence interpretation rather than imposing uniform regulatory decisions, respecting national legal frameworks and sovereignty.

Safety evidence needs, particularly for populations often under-represented in clinical trials, were discussed in depth, including older adults, children, pregnant individuals, and people with comorbidities or immunocompromise. Panelists noted the importance of characterizing breakthrough infections, long-term safety, co-administration considerations, and potential diagnostic interference, with gaps addressed through targeted studies and post-authorization surveillance, as appropriate to national contexts.

WHO SEARO emphasized that evidence requirements and risk tolerance may differ across routine licensure, emergency decision-making, and authorization during active outbreaks. In outbreak settings where delays could result in substantial morbidity, regulators may need to act with greater urgency, prioritizing defined high-risk groups such as healthcare workers and individuals with comorbidities. In such cases, safety and efficacy requirements must be appropriate to the intended population and justified by the available evidence. Panelists noted that stepwise approaches to expanding use may be appropriate as additional evidence accrues, and that transparent justification of benefit–risk decisions is important for public confidence.

Overall, the panel highlighted broad alignment on the need for flexible, evidence-based regulatory pathways for chikungunya vaccines, complemented by fit-for-purpose post-authorization evidence generation. Regional reliance mechanisms and scientific exchange were viewed as practical tools to reduce duplication and accelerate access while maintaining rigorous national decision-making.

2.1.9. Panel: Public health perspectives on chikungunya vaccine deployment

Moderator: Dr. Jinho Shin (WHO WPRO, Philippines)
Panelists:
Dr. Pragya Yadav (ICMR, India)
Dr. Wenny Indriasari (Ministry of Health, Indonesia)
Dr. Sunate Chuenkitmongkol (National Vaccine Institute, Thailand)
Dr. Yookyoung Lee (KDCA, Republic of Korea)

This panel examined public health considerations for chikungunya vaccine deployment in the context of immunogenicity-based licensure and limited field efficacy estimates. Discussion addressed programmatic feasibility across two use cases (routine immunization and outbreak response), data needs to support policy decisions, and operational requirements to generate credible RWE.

Indonesia described its current epidemiological context and decision pathway for potential vaccine introduction. The MOH reported increased chikungunya activity in 2025 (approximately 23,000 suspected cases and 5,000 verified cases), concentrated in West Java and Central Java with peak activity from January to April. Indonesia does not yet have an approved chikungunya vaccine and therefore emphasized that equitable access depends on timely regulatory decision-making and on national introduction processes such as health technology assessment, budget impact analysis, and evidence-based recommendations from immunization advisory structures. Decentralized financing mechanisms were cited as a potential route for targeted deployment in high-burden provinces.

The panel discussed stockpiling and surge preparedness, noting the tension between outbreak unpredictability and the shelf life of finished vaccine. Thailand's National Vaccine Institute highlighted that outbreaks in some settings occur approximately once per decade, which can make stockpiling finished product inefficient if shelf life is shorter than outbreak periodicity. Participants discussed alternatives such as stockpiling bulk materials, contractual surge manufacturing arrangements, pooled procurement mechanisms, and early-warning signals to trigger production and deployment.

Regional solutions were positioned as a potential efficiency lever, but not a simple one. Within ASEAN's Vaccine Security and Self-Reliance agenda, pooled procurement and stockpiling have been repeatedly identified as priorities, with renewed discussion under AVSSR 2.0 alongside human-resource development and data-sharing. However, the session acknowledged that implementation remains incomplete, and that designing a pooled stockpile requires agreement on governance, financing, allocation principles, and —critically—credible demand forecasting. Participants noted that manufacturers seek predictability, while chikungunya epidemiology is intrinsically uncertain. Panelists suggested that regional and global partners could support forecasting methodologies and procurement models that reduce risk for both countries and suppliers.

Manufacturing readiness was highlighted as a determinant of access and response speed. Indonesia described domestic capacity across conventional platforms and newer technologies and noted a hybrid model involving a state-owned manufacturer and private-sector partners. Panelists emphasized that enabling conditions include infrastructure investment, regulatory pathways that can support rapid review, technology transfer arrangements, and procurement policies that provide demand assurance where appropriate. The implication was clear: vaccine access in outbreaks will be shaped as much by national manufacturing and regulatory systems as by clinical evidence alone.

Vaccine confidence and public communication were discussed as determinants of program impact, particularly for products authorized using surrogate endpoints. KDCA noted that hesitancy can be amplified by misinformation and by concerns about contraindications and adverse events. Importantly,

the speaker framed acceptance as being driven less by platform labels and more by confidence in decision-making: live-attenuated vaccines may raise greater concern because they contain replicating virus and can appear riskier for older adults or immunocompromised people, whereas VLP vaccines may be perceived as safer because they do not replicate—but still face questions about durability and long-term safety. Panelists emphasized that acceptance depends on confidence in the decision-making process, transparent communication of benefits and uncertainties, and visible post-authorization safety monitoring and effectiveness studies.

A recurring technical theme was the role of RWE when classical efficacy trials are difficult to conduct. ICMR noted that sporadic outbreaks and high baseline seropositivity in some settings can limit phase 3 feasibility. In this context, RWE was framed as a necessary complement, capable of measuring symptomatic infection, hospitalization, and outbreak reduction. The panel discussed how observational designs (e.g., retrospective or prospective cohorts, case–control studies, and test-negative designs embedded in surveillance systems) can estimate effectiveness, but credibility depends on standardized case definitions, laboratory confirmation, rigorous analytic methods, and transparent reporting.

Operational readiness was addressed as the "last mile" constraint that often determines whether a vaccine strategy can succeed in outbreak conditions. KDCA highlighted cold-chain readiness as a central risk—particularly in tropical and resource-limited settings—and emphasized the need for storage capacity mapping, contingency planning, and integration into existing immunization delivery systems. Workforce considerations were presented as equally limiting; frontline training must cover product characteristics, contraindications, and safety monitoring requirements; rapid training modules and supportive supervision are needed; and outbreak response can strain human resources because vaccination must run alongside surveillance, case management, and vector control. The panel further noted that evidence generation does not pause during deployment—countries need systems to monitor safety and effectiveness in near real time and to adapt policy as new data emerge, reinforcing the linkage between operational systems and credible RWE.

The session widened the lens to what is most important to strengthen in the end-to-end ecosystem to make RWE and evidence-informed policy feasible. ICMR outlined a structured view of the RWE ecosystem: linked data streams (surveillance, vaccination registries, electronic health records [EHRs], hospital outcomes, laboratory confirmation), standardized and interoperable datasets, robust epidemiological study designs with appropriate statistical controls, real-time outbreak detection, regulatory frameworks that specify acceptable approaches and validation expectations, and multisectoral collaboration with strong data governance. Audience questions tested whether modelling could compensate for data gaps; panelists acknowledged that modelling has shown partial success (e.g., during COVID-19) but remains constrained by input data quality. ICMR further emphasized that predicting chikungunya's cyclical outbreaks will likely depend on integrating vector surveillance data with geotagging and hotspot mapping—linking mosquito ecology to early warning signals—rather than relying solely on human case detection.

The panel concluded that chikungunya vaccine policy will depend on an integrated preparedness architecture that links decision frameworks (including health technology assessment [HTA] and advisory processes), supply and procurement strategies, operational delivery capacity, and fit-for-purpose RWE systems. Participants emphasized that strengthening surveillance and data linkage, improving standardization, and sustaining cross-sector coordination are important for both outbreak response and any future consideration of routine immunization strategies.

In summary, the discussion reinforced that chikungunya vaccine policy will depend on more than a licensure decision: it requires an integrated preparedness architecture that links equitable financing and prioritization, manufacturing and supply strategies (including realistic approaches to stockpiling),

operational delivery capacity, public confidence, and fit-for-purpose RWE systems. The session positioned RWE, standardization, and cross-sector coordination as pivotal enablers for both outbreak response and any future consideration of routine immunization approaches, particularly in settings where epidemiology remains unpredictable and classical efficacy trials are difficult to execute.

2.2. Part 4: Nipah case study

2.2.1. Nipah case study: Setting the scene

Ms. Meenu Batolar (CEPI, Singapore) introduced the Nipah case study and summarized why Nipah virus remains a high-consequence preparedness priority. She noted that outbreaks are typically driven by sporadic zoonotic spillover, can be associated with high case-fatality rates, and may include clusters of human-to-human transmission. She emphasized that these epidemiologic features create significant challenges for evidence generation and underscore the need for pre-established scientific and regulatory approaches.

She noted that the Summit builds on a series of prior convenings aimed at strengthening regulator-to-regulator dialogue on Nipah evidence pathways, including a regulators' roundtable in Singapore (2019), a virtual follow-up (2021), and an in-person meeting in Kuala Lumpur (2023). She added that these meetings helped maintain continuity among participating regulators and partners and supported progressive alignment on key scientific questions relevant to licensure in the absence of feasible efficacy trials.

In closing, she emphasized that sustained scientific exchange between regulators, developers, and public health partners can reduce uncertainty during outbreaks by clarifying evidence expectations in advance. She noted that maintaining these relationships and technical forums between outbreaks supports faster decision-making when cases emerge.

2.2.2. WHO- CORC paramyxoviridae

Dr. Nivedita Gupta (ICMR, India; WHO CORC paramyxoviridae lead) introduced the WHO CORC for paramyxoviridae and described its role in coordinating research and preparedness activities across high-priority paramyxoviruses, including Nipah. She noted that CORC is intended to strengthen comparability and interoperability of data generated across institutions by enabling shared scientific assets and aligned methodologies.

She outlined key CORC workstreams, including development and dissemination of reference reagents and standards, harmonization of laboratory protocols (e.g., neutralization, binding, and cellular assays), and support for quality systems that enable cross-site reproducibility. She noted that lack of standardized methods can slow scientific progress and complicate regulatory interpretation when results cannot be readily compared across laboratories or platforms.

Dr. Gupta emphasized that for pathogens such as Nipah—where outbreak data are limited and conventional efficacy trials are not feasible—laboratory evidence and animal-model data become central to evidence packages. She noted that CORC can support regulators and developers by improving confidence in preclinical and early clinical datasets through standardized assays, shared materials, and transparent reporting, thereby reducing avoidable uncertainty in interpreting immunogenicity and protection signals.

She described CORC as operating through collaborative networks with an emphasis on open science where feasible, including data sharing, precompetitive collaboration, and transparent methods documentation. She noted that these approaches are intended to support timely validation of findings,

reduce duplication, and enable more consistent interpretation across product developers and regulatory agencies, subject to appropriate governance and confidentiality arrangements.

She concluded by noting that CORC outputs are intended to support subsequent discussions on preclinical efficacy models, assay selection, and regulatory-science questions relevant to potential Nipah vaccine licensure pathways.

2.2.3. Innovative approach: Regulatory feedback on the adequacy of preclinical efficacy models and potential licensure for Nipah

Dr. Nancy Sullivan (Boston University, NEIDL, USA) discussed regulatory considerations for assessing preclinical efficacy models for Nipah vaccines when human efficacy trials are not feasible. She described how model development, documentation, and review are approached under the U.S. FDA's Animal Rule and noted the importance of developing consistent scientific principles across agencies in the Asia-Pacific region. She highlighted that coordinated data generation and sharing among partners can accelerate model development and reduce duplication.

She described the high-containment facilities and quality systems required to generate Good Laboratory Practice (GLP)-compliant non-clinical data packages. Elements she highlighted included standardized operating procedures, staff qualification and training records, animal-care oversight, instrument qualification and calibration, and independent quality assurance. She noted that robust documentation is essential because regulators may need to inspect studies years later and trace procedures, deviations, and corrective actions.

Dr. Sullivan summarized scientific principles relevant to model qualification, including discussion of one- versus two-species expectations. She noted that, historically, efficacy in two animal species was often referenced, but that a single well-justified species may be acceptable depending on the strength of the model and supporting evidence. She also discussed how challenge dose selection can influence observed CoPs: very high challenge doses can shift apparent protective thresholds upward and reduce translatability to human exposure. She noted that recent engagement with regulators has supported movement toward lower, biologically relevant challenge doses while maintaining adequate lethality and statistical power.

For Nipah, she described efforts to establish a natural history model intended to reflect key features of human disease, including respiratory involvement and, where feasible, neurologic manifestations. She noted that the program generated dose–response data across challenge doses and compared routes of administration (intranasal versus combined intranasal/intratracheal). Studies from multiple partners were integrated to identify a challenge dose low enough to avoid unrealistically stringent immune thresholds, while maintaining sufficient lethality to support statistical comparisons. She noted that power analyses suggested that, even with occasional survivors in control animals, the model could detect clinically meaningful vaccine effects and immune correlates under reasonable assumptions.

She described iterative engagement with regulators during model refinement, including a request to evaluate a 100-PFU (plaque-forming unit) intranasal challenge dose as a candidate lowest uniformly lethal dose. She noted that an initial pilot study produced one survivor, prompting additional iterations to confirm dose and operational parameters. Follow-on work was reported to produce consistently lethal outcomes with extended time to death (approximately 15 days), supporting generation of a natural history dataset intended for FDA submission and potential model qualification review. She emphasized that model development is inherently iterative and that early, proactive communication with regulators can clarify expectations and reduce rework.

2.2.4. *Nipah disease and approach: Q&A*

The session transitioned into an open Q&A, providing participants with an opportunity to clarify scientific, regulatory, and operational considerations raised during the preceding presentations. The discussion began with questions centered on the feasibility of generating sufficiently robust data packages for Nipah vaccines in the absence of traditional efficacy trials. Participants sought clarification on how animal model data, assay harmonization, and reference standards would be weighed by regulators when human clinical evidence is necessarily limited. Speakers emphasized that while no single data stream is adequate on its own, a well constructed combination of animal model outcomes, validated immunological endpoints, and coherent laboratory methods can together form scientifically defensible evidence base for regulatory evaluation.

The conversation also touched on the operational realities faced by institutions in outbreak prone countries. Representatives raised questions about how regional partners could strengthen sample sharing, access to reagents, and analytical capability—elements essential for timely data generation during an outbreak. Panelists reiterated that initiatives such as CORC and CEPI's ongoing coordination with national regulators are designed precisely to address these gaps. They noted that transparent communication, pre-established scientific networks, and early alignment on accepted laboratory methods can substantially reduce delays once an outbreak begins.

A recurring theme in the Q&A was the importance of maintaining continuity across regulatory authorities. Participants expressed interest in how ongoing dialogue—via platforms such as the regulators' huddle and CEPI facilitated communication channels—could support real time decision making when new data emerge during an active Nipah event. Speakers affirmed that the intent is to build not only scientific capability but also trusted relationships that allow regulators to consult one another rapidly, interpret uncertain data collaboratively, and navigate decisions that must often be made under considerable time pressure.

The session concluded with reflections on the evolving landscape of Nipah research and preparedness. Participants acknowledged that while scientific challenges persist, the region now benefits from a more coordinated research base, expanding laboratory networks, and increasingly engaged regulatory partners. The Q&A served to underscore that sustained dialogue—anchored in openness and technical collaboration—remains a cornerstone of effective preparedness.

2.2.5. *Vaccines in development (preclinical, clinical, manufacturing technologies, regulatory strategies) with gaps remain to be filled*

2.2.5.1. ChAdOx1 NipahB

Dr. Brian Angus (University of Oxford, UK) presented an update on the ChAdOx1 NipahB vaccine candidate and situated it within the broader portfolio of Nipah countermeasure development. He noted that the candidate uses the ChAdOx1 platform, a replication-deficient adenoviral vector previously evaluated across multiple indications. He emphasized that existing platform experience provides a substantial safety and immunogenicity evidence base that can inform regulatory review as NipahB advances.

He described the construct as encoding the Nipah virus G glycoprotein, a principal antigenic target associated with induction of functional neutralizing antibody responses. He noted that this antigen choice aligns with a broader body of henipavirus research supporting the G protein as a key target for vaccines intended for outbreak-response use.

Dr. Angus summarized ongoing preclinical evaluation, noting that multiple animal models are being used to characterize immune responses and to assess protection in challenge settings, given that human efficacy trials are not feasible for Nipah. He described characterization of humoral and cellular immunity, including neutralizing antibody titers, binding antibody profiles, and T-cell readouts, to support a bridging framework for regulatory consideration.

He noted that assay development and harmonization are important for comparability of results across laboratories and development phases. He described use of validated microneutralization assays and standardized binding assays and noted that alignment with CORC-supported reference materials and emerging international standards can support regulator confidence in immunogenicity datasets.

He also summarized manufacturing and CMC considerations, noting that the candidate can leverage established adenoviral-vector production processes and quality controls. He highlighted ongoing work on potency and release assays, stability characterization, and technology-transfer readiness as key dependencies for later-stage development and for potential outbreak deployment.

He noted that early and iterative engagement with regulators is being used to clarify expectations for non-clinical models, immunogenicity endpoints, and potential surrogate-marker approaches that could support authorization decisions during an outbreak. He emphasized that transparent methods and assay comparability are important for interpretability of evidence packages across jurisdictions.

2.2.5.2. rVSV-Nipah vaccine (PHV02)

Dr. Joan Fusco (PHV, USA) presented an update on the rVSV-Nipah vaccine candidate PHV02, outlining its scientific rationale and development considerations for a high-severity, low-incidence pathogen. She noted that PHV02 builds on the VSV vector platform, which has prior regulatory precedent and outbreak-response experience through the licensed rVSV-ZEBOV Ebola vaccine. She emphasized that prior platform knowledge can inform expectations for manufacturing and safety evaluation, while noting that Nipah-specific risks and evidence requirements must still be addressed.

She described PHV02 as expressing the Nipah virus G glycoprotein within an attenuated rVSV backbone, with the intent of inducing functional antibody responses against the viral attachment protein involved in host-cell entry. She noted that the G protein is a common antigen choice across multiple Nipah vaccine programs. She reported that early non-clinical studies have generated immunogenicity data, including functional neutralizing activity, and that protection has been explored in challenge models; detailed study results were not presented in the transcript.

Dr. Fusco highlighted development considerations specific to a replication-competent viral vector. She noted that evidence packages are expected to address vector shedding, attenuation stability, biodistribution, and suitability for populations with varying levels of immunocompromise. She emphasized that these topics affect non-clinical safety expectations, environmental risk considerations, and clinical monitoring plans, and benefit from early alignment discussions with regulators.

She noted that, as with other Nipah vaccine programs, conventional human efficacy trials are not expected to be feasible and that development therefore relies on robust animal-model data and immunologic bridging concepts. She emphasized the importance of assay harmonization and shared reference materials to support interpretability of neutralizing-antibody and cellular-response readouts across laboratories and platforms, consistent with themes discussed in CORC and regulator-to-regulator exchanges.

Operational and CMC readiness considerations were also discussed. Dr. Fusco noted that although the rVSV platform benefits from prior production experience, advancement of PHV02 depends on

development and validation of batch-release and potency assays, stability characterization, and definition of acceptable specifications. She emphasized that these elements are key dependencies for progression to broader clinical evaluation and for potential outbreak deployment.

2.2.5.3. Self-amplifying RNA (saRNA) vaccine development for Nipah

Managing Director Dr. Sanjay Singh (Gennova, India) described saRNA vaccine technology and discussed its potential relevance to preparedness for low-incidence, high-severity pathogens such as Nipah virus. He noted that saRNA platforms can encode both an antigen and replicon machinery, enabling intracellular amplification of the RNA and potentially reducing the input RNA dose required per vaccination. He emphasized that, in preparedness contexts, platform attributes such as rapid design cycles and scalable manufacturing are of interest, subject to demonstration of acceptable safety, immunogenicity, and operational feasibility.

He noted that saRNA constructs are often based on alphavirus-derived replicons and can be formulated for delivery using LNPs. For Nipah, he reported that the construct focuses on expression of the Nipah virus G glycoprotein, consistent with other programs that target the attachment protein as a key antigen for inducing functional neutralizing antibody responses. He noted that the larger size and replicative features of saRNA have implications for formulation and analytical characterization relative to conventional mRNA vaccines.

Dr. Singh summarized early immunogenicity findings from saRNA studies, noting reported induction of binding antibody responses, functional neutralizing activity, and measurable cellular immune readouts in preclinical settings. He emphasized that, as with other Nipah vaccine candidates, the evidentiary strategy is expected to rely on robust animal models and assay harmonization because conventional human efficacy trials are not feasible. He noted that alignment on assays and use of standardized reagents can improve comparability across platforms (e.g., saRNA, adenoviral vectors, and rVSV-based candidates) and support regulatory interpretation.

He identified formulation, analytical characterization, and manufacturing readiness as key development considerations. He noted that delivery systems (typically LNP formulations) may require optimization for saRNA constructs given their larger size and encoded replicon elements. He also highlighted stability characterization, scalability, and development of suitable release-testing strategies as important prerequisites for later-stage development and potential outbreak deployment and noted ongoing work to improve temperature stability and handling characteristics for use in outbreak-prone settings.

He emphasized the importance of early regulatory-science engagement for newer modalities such as saRNA, including discussion of non-clinical safety expectations, platform characterization requirements, and potential approaches to immunogenicity-based bridging. He noted that regional regulator-to-regulator dialogue can help clarify evidence expectations across agencies and support preparedness planning in advance of outbreaks.

He concluded that saRNA platforms represent an emerging approach for Nipah vaccine preparedness, with key readiness dependencies including validated assays, fit-for-purpose animal models, robust CMC packages, and clearly defined regulatory evidence pathways.

2.2.5.4. Nipah vaccines in development: Q&A

Moderator: Dr. Nivedita Gupta (ICMR, India)
Panelists:
Dr. Brian Angus (University of Oxford, UK)
Dr. Joan Fusco (PHV, USA)
Dr. Sanjay Singh (Gennova, India)

The session transitioned into an open discussion period, allowing participants to question the developers about the ChAdOx1 NipahB platform and the broader challenges associated with advancing Nipah-virus countermeasures. The conversation focused heavily on technical and regulatory-science questions that arise when developing a product for a pathogen with limited human clinical data and no feasible pathway for conventional efficacy trials.

Participants inquired about the durability and breadth of the immune response expected from platform-based constructs such as ChAdOx1. Developers explained how immunogenicity data from comparable adenoviral-vector vaccines—along with mechanistic insights from Nipah-specific antigen design—provide a scientific basis for anticipating protection. Several questions probed the comparative performance of different animal models, with attendees seeking clarity on which models most accurately reproduce human disease, and which endpoints regulators consider most informative for a potential Emergency Use pathway.

There was considerable discussion around assay harmonization and how developers ensure that immunological readouts will be interpretable across laboratories and acceptable to regulatory authorities. Presenters emphasized the use of standardized neutralization assays, calibrated reference materials, and alignment with collaborative networks such as CORC to ensure assay reproducibility. Attendees raised concerns about data comparability when multiple vaccine candidates progress in parallel; the session reinforced that convergence on assay standards is central to enabling regulators to evaluate evidence consistently.

Operational questions also emerged, particularly regarding manufacturing scalability and timelines. Developers outlined the advantages of leveraging an established adenoviral platform with known production parameters but acknowledged that CMC readiness—especially potency assay development and lot-release criteria—remains a critical gating factor. Participants explored scenarios in which early-stage data would need to be shared quickly with regulators during an outbreak, and how such rapid interactions could be supported through existing informal communication channels and CEPI-coordinated regulatory networks.

The Q&A session underscored the collaborative approach required to advance Nipah vaccines:

- High-quality animal data
- Harmonized assays
- Transparent communication pathways
- Early regulatory engagement.

Panelists noted that the engagement shown during this meeting presented a strong foundation upon which to build future collaboration. The dialogue reinforced that while scientific challenges remain, the region's maturing infrastructure and networked regulatory capacity place developers in a stronger position to respond to future outbreaks.

2.2.6. Outbreak clinical evidence generation for Nipah virus under increased human-to-human transmission (and similar epidemiology)

Dr. Amol Chaudhari (CEPI, India) discussed approaches to clinical evidence generation for Nipah vaccines under an outbreak scenario with increased and sustained human-to-human transmission. He noted that Nipah's typical epidemiology—sporadic spillover with limited clusters and high case-fatality rates—makes conventional efficacy trials practically infeasible; however, a bigger outbreak with higher transmission rate (Nipah-X) could create both a greater need and a more feasible window to generate actionable clinical data.

He emphasized that outbreak-time data collection is most effective when scientific frameworks are established in advance. These include pre-approved clinical trial protocols with clinical endpoints including harmonized case definitions, operational infrastructure, and ecosystem alignment. He noted that alignment among regulators, health policy makers, local researchers, ministries of health, and developers on what constitutes decision-relevant information is important to ensure that data generated under time pressure support regulatory and public health decision making.

Dr. Chaudhari outlined study designs that could become feasible under larger transmission events, including adaptive observational cohorts, and various flexible options for interventional trials including single-arm trial and RCTs that could be adapted depending as appropriate to a specific outbreak scenario based on epidemiology, viral characteristics, existing evidence and local needs.

He noted that feasibility depends on operational preparedness, including expedited regulatory and ethical review processes, pre-approved protocol templates, clarity on regulatory reliance arrangements, and diagnostic and immune assay infrastructure capable of running validated assays at speed. He emphasized that without these foundations, even well-designed studies may not activate quickly enough to inform outbreak-time decisions.

He also highlighted the importance of data interoperability and cross-border coordination, noting that transmission clusters may provide limited opportunities for structured evidence generation. He referenced existing mechanisms (e.g., CEPI-convened regulator engagement and CORC-supported scientific collaboration) as enablers of rapid information sharing and aligned interpretation as new data emerge.

He concluded that outbreak-time clinical evidence generation strategies should be treated as a capability built during inter-epidemic periods, rather than as an activity initiated de novo once transmission increases.

2.2.7. Ad Hoc regulators panel on Chikungunya

Moderator: Dr. Adam Hacker (CEPI, UK)
Panelists:
Dr. Rubina Bose (CDSCO, India)
Dr. James McBlane (MHRA, UK)
Dr. Marco Cavaleri (EMA, EU)
Dr. Brenda Gomes Valente (ANVISA, Brazil)
Dr. Dean Smith (IABS-NA Chair, Canada)

This ad hoc panel opened with a set of unusually direct questions from the audience, touching the core challenges of advancing vaccines for diseases like Chikungunya, where epidemiology, data scarcity, and regulatory expectations collide. One participant asked how regulators contextualize potential safety

signals when background incidence rates for severe outcomes are poorly characterized. This question elicited one of the most technically grounded moments of the session.

Regulators explained that high-resolution background rates are not simply useful, they are foundational. Without them, interpreting rare adverse events is nearly impossible. They drew on the regulatory history of RotaShield, not merely as an anecdote but as a cautionary case study: regulators faced early safety signals but lacked precise, contemporaneous incidence data on intussusception, complicating benefit-risk assessments and accelerating the product's withdrawal. The panel emphasized that for chikungunya—where severe arthritogenic symptoms, neurological manifestations, and pregnancy complications may overlap with endemic disease burden—developers must proactively map incidence rates by region, age, sex, and clinical severity. These data enable observed-versus-expected (O/E) calculations, permitting regulators to determine whether a safety signal is meaningful or incidental.

The conversation then shifted naturally to real-world effectiveness, where the possibility of multi-country pooled evidence was met with both enthusiasm and caution. Regulators expressed that pooled analyses can be highly powerful—but only if the underlying data are harmonized from the start. They urged countries to adopt common case definitions, diagnostic criteria, surveillance thresholds, and analytic frameworks before attempting cross-country comparisons. Several panelists stressed that misaligned designs or inconsistent diagnostic assays would render pooled evidence statistically uninformative, undermining the very rationale for regional collaboration.

This prompted a broader discussion on outbreak-ready evidence generation, a theme echoed throughout the Summit. Panelists argued that chikungunya, like Nipah, requires master protocols that can be activated at the first sign of increased transmission. Such protocols should specify sampling windows, endpoints, adaptive features, and statistical triggers in advance. Regulators noted that in real outbreaks, timelines compress dramatically; approvals for protocol amendments, ethics reviews, and data-sharing arrangements cannot be improvised in crisis conditions. A pre-agreed cross-country protocol, they argued, is not simply desirable—it is the only practical path to generating meaningful clinical evidence during unpredictable chikungunya flare-ups.

Overall, the panel emphasized that credible chikungunya vaccine decision-making depends on:

(1) Baseline epidemiologic characterization to interpret safety signals

(2) Harmonized approaches to RWE generation

(3) Operational readiness to activate studies and regulatory consultation during outbreaks

Day 3 - Pandemic preparedness & response vaccine development ecosystem strengthening and use of innovative regulatory approaches when efficacy studies are not feasible

3.1. Part 4: Nipah case study (continued)

3.1.1. Nipah virus vaccines

Dr. Marco Cavaleri (EMA, EU) introduced the session by summarizing epidemiologic and clinical features of Nipah virus that shape vaccine development and evaluation. He noted that outbreaks are typically sporadic and geographically limited, affecting a small number of countries, but can be associated with high case-fatality rates. Transmission is driven by zoonotic spillover, with the potential for human-to-human spread via respiratory exposure in some outbreaks. These characteristics both increase preparedness priorities and constrain opportunities to generate conventional clinical efficacy evidence.

He noted that, given the rarity and unpredictability of outbreaks, traditional randomized clinical efficacy trials are not expected to be feasible for first-generation Nipah vaccines. Regulatory decisions are therefore anticipated to rely on well-characterized animal challenge models combined with human immunogenicity and safety data, using predefined bridging approaches to infer likely clinical benefit. He noted that controlled human infection studies are not appropriate for Nipah.

He described the African green monkey model as a stringent NHP challenge system used to evaluate candidate vaccines. Use of the Bangladesh lineage strain was noted as operationally relevant because it produces severe respiratory disease in animals and is associated with human outbreaks involving respiratory transmission. While neurologic manifestations are less consistently reproduced in animal models, he noted that severe pulmonary disease and lethality can provide informative endpoints for assessing vaccine effects. He also noted that CEPI-supported efforts are working toward a standardized model to enable more consistent evidence generation across developers.

The discussion then addressed approaches to bridge animal protection to humans. Two broad approaches were described:

(1) Deriving immune markers associated with protection directly from animal challenge studies
(2) Passive-transfer approaches in which antibodies from vaccinated humans are transferred to animals to help define a putative protective threshold.

These markers could then be used as benchmarks in human immunogenicity studies. The session emphasized that human safety evidence remains essential; participants discussed that an initial pre-licensure safety database may begin on the order of several thousand participants, with expectations informed by platform experience and the totality of evidence.

Post-authorization evidence generation was discussed as an important component of the overall strategy. While randomized placebo-controlled trials can provide robust estimates of effectiveness, the session noted that such trials may be ethically or operationally difficult once a vaccine is authorized, particularly in settings with high mortality. Alternative approaches discussed included ring vaccination strategies, cluster-randomized designs, and step-wedge or delayed-vaccination comparators, drawing on experience from Ebola outbreaks. Participants noted that these approaches can generate decision-relevant information when designed and governed appropriately.

The session also noted practical constraints for outbreak-time study designs, including the need for rapid onset of protection if ring or reactive vaccination strategies are considered. Participants discussed that even fast-acting vaccines may require days to reach maximal protection, which can affect both

intervention impact and feasibility of endpoint accrual. Candidates requiring prime–boost regimens may be less suitable for reactive use and may require different evidence strategies. Where randomized designs are not feasible, well-designed observational studies may be necessary; participants emphasized the value of developing shared core protocols and governance arrangements in advance with countries most likely to experience outbreaks.

In summary, the session emphasized that credible Nipah vaccine pathways will likely depend on robust and standardized animal models, scientifically justified immunobridging strategies, adequate human safety databases, and fit-for-purpose post-authorization study designs. Participants noted that lessons from Ebola highlight the importance of outbreak-ready protocols and pre-established partnerships to enable timely evidence generation under operational constraints.

3.1.2. Panel discussion: Adequacy of current regulatory strategies, factors to inform regulatory-benefit risk analyses, the size of the safety database, data to be generated in the early part of an outbreak, etc.

Moderator: Dr. Marco Cavaleri (EMA, EU)
Panelists:
Dr. Rubina Bose (CDSCO, India)
Dr. Erlina Fitriyani (BPOM, Indonesia)
Dr. Mohd Rezuan (National Pharmaceutical Regulatory Agency [NPRA], Malaysia)
Dr. Wittawat Viriyabancha (Thai FDA, Thailand)

This panel brought together national regulatory authorities from India, Bangladesh, Indonesia, Malaysia, and Thailand to examine feasible regulatory pathways for Nipah vaccines in the absence of traditional clinical efficacy trials. The discussion focused on the adequacy of alternative evidence strategies, including animal models and immunobridging, the handling of strain diversity, post-authorization evidence expectations, and opportunities for regional regulatory collaboration.

A core point of alignment across regulators was the recognition that Nipah virus outbreaks are sporadic, geographically limited, and associated with high case-fatality rates, making large randomized efficacy trials impractical or impossible. Regulators therefore broadly agreed that approval based on well-validated animal models combined with human immunogenicity data is both reasonable and necessary, provided decisions are grounded in a totality-of-evidence framework. This framework must integrate robust non-clinical challenge data, scientifically justified immune markers (such as neutralizing antibodies and, where relevant, cellular responses), consistent immunogenicity across studies, and the epidemiological context of the disease.

Thailand's regulator emphasized openness to surrogate markers of protection when supported by strong scientific justification, standardized and reproducible assays, and validation through international expert bodies such as WHO. Any such approval would be accompanied by enhanced pharmacovigilance and real-world effectiveness monitoring to confirm performance in practice. Indonesia's regulator similarly expressed openness to immunogenicity-based pathways where a credible immune CoP can be established, noting that such correlates may be inferred from non-clinical challenge studies, passive transfer experiments, or comparisons with related vaccines. However, Indonesia highlighted the limitations of animal-derived correlates and stressed that human data should be generated whenever feasible to strengthen confidence.

India's CDSCO underscored that, given India's epidemiological relevance for Nipah, Indian-specific data are essential. While surrogate markers derived from validated animal models and NHP studies may be used to infer protection, CDSCO expects immunobridging studies conducted in the Indian population and

mandates post-marketing confirmatory studies to verify real-world effectiveness and safety. India indicated flexibility in accepting supportive data from other affected countries, particularly for comparative safety and immunogenicity, but reaffirmed that final regulatory decisions must be anchored in nationally generated evidence.

Malaysia's regulator acknowledged that applying an "Animal Rule-like" approach for Nipah would be a first for the agency, but accepted the rationale given the infeasibility of efficacy trials. Malaysia anticipates relying heavily on evaluations by reference regulators and expressed alignment with the scientific principles articulated by neighboring authorities. Conditional authorization was viewed as feasible in principle, with appropriate post-authorization commitments.

A substantial portion of the discussion addressed Strain diversity and cross-protection, particularly the Bangladesh and Malaysian Nipah strains, with India also emphasizing relevance of the Indian strain. Regulators broadly agreed that the Bangladesh strain—associated with more uniform and severe disease in animal models—provides a strong basis for defining mechanisms of protection. Bridging across strains using cross-neutralization data and comparative immunogenicity was viewed as acceptable in principle, provided evidence demonstrates similar immune responses across strains. However, regulators emphasized that *in vitro* data alone are insufficient; animal challenge data and early-phase human immunogenicity studies remain important for confirming cross-protection and maintaining public confidence.

Indonesia and Thailand highlighted that while direct challenge data for each strain would be ideal, scientifically sound justification based on shared mechanisms of protection and comparable neutralization profiles could support bridging approaches. India reiterated expectations that vaccines developed domestically should be based on the Indian strain while demonstrating cross-reactivity with other relevant strains, and that imported vaccines must similarly show cross-reactive immunity alongside Indian population immunogenicity data.

The panel also explored Regional collaboration and shared evidence generation, with this meeting establishing key network partners. Regulators expressed strong support for developing regional core protocols for outbreak-triggered studies, noting that such collaboration could reduce duplication, streamline reviews, and accelerate access while preserving national regulatory sovereignty. Thailand and Indonesia pointed to existing experience with joint assessments and reliance mechanisms as proof that collaboration can enhance efficiency and capacity building. At the same time, regulators stressed that participation in joint reviews requires full access to underlying data, with India emphasizing that meaningful engagement is only possible when complete dossiers are shared.

From a global perspective, the moderator highlighted EMA's interest in fostering multinational scientific advice and joint discussions—drawing on mechanisms such as PRIME and the EMA Emergency Task Force—and encouraged deeper engagement between Asian regulators and global reference agencies. Malaysia noted that ASEAN already has collaborative review mechanisms in place, suggesting that regional cooperation for Nipah would build on established precedent rather than create new structures from scratch.

Audience discussion reinforced the need to balance scientific necessity with development efficiency, particularly regarding country-specific immunogenicity studies. While regulators acknowledged that immunogenicity differences can exist across populations, there was agreement that requirements should be justified case-by-case to avoid unnecessary burdens on developers, with greater reliance on shared regional data where appropriate.

In closing, the panel reached broad consensus that initial approval of Nipah vaccines based on validated animal models and immunobridging is both workable and appropriate, given the disease's epidemiology.

regulators emphasized that post-authorization studies—observational effectiveness assessments, enhanced pharmacovigilance, and outbreak-specific data collection—are essential to confirm benefit–risk and guide public health use. There was strong and consistent openness to regional and international collaboration, with recognition that coordinated evidence generation and shared scientific dialogue will be critical to ensuring timely, credible, and equitable access to Nipah vaccines while maintaining rigorous regulatory standards.

The panel concluded that authorization pathways for Nipah vaccines will likely require standardized animal models, scientifically justified immunobridging approaches, and clearly defined safety and post-authorization evidence expectations. Participants emphasized that continued regulator-to-regulator dialogue and shared technical work on assays, models, and outbreak-ready study protocols can improve consistency and timeliness of decision-making during future events.

3.1.3. Panel discussion: Public health perspectives for Nipah vaccine deployment under increased human-to-human transmission scenarios

Moderator: Dr. Sylvie Alonso (Programme for Research in Epidemic Preparedness and Response [PREPARE], Singapore)
Panelists:
Dr. Nivedita Gupta (ICMR, India)
Dr. Pragya Yadav (ICMR, India)
Dr. Madhur Gupta (WHO SEARO, India)
Dr. Anuradha Poonepalli (HSA, Singapore)
DG Azuana Binti Ramli (Ministry of Health [MOH], Malaysia)
Dr. Wichan Bhunyakitikorn (MOH, Thailand)

This panel examined the public -health and operational dimensions of preparing for future Nipah vaccine deployment, focusing on evidence requirements, surveillance readiness, supply strategies, vaccination prioritization, and community acceptance. Bringing together regulators, public-health authorities, and WHO representatives, the discussion complemented earlier regulatory panels by addressing how scientific and regulatory decisions translate into practical outbreak response.

The session opened with a regulatory perspective from Singapore, where the HSA outlined its approach to evaluating Nipah vaccines in the absence of feasible clinical efficacy trials. HSA emphasized alignment with global regulatory practice, noting that scientifically justified immune correlates or surrogate markers—supported by validated animal challenge models and statistically derived CoPs—can be used in place of efficacy data, provided these are extrapolated appropriately to humans and supported by immunogenicity studies. Singapore highlighted prior experience using this framework for mpox vaccines and indicated readiness to review Nipah vaccines during peacetime under priority review, as well as during outbreaks through its Pandemic Special Access Route, which allows rolling submissions and accelerated decisions. HSA also clarified that it does not require local clinical studies and can accept multicountry or foreign-generated data, consistent with its reliance-based approach.

The discussion then turned to regulatory collaboration and preparedness, with Singapore describing routine engagement with international and regional regulators through platforms such as the Access Consortium, ASEAN joint assessments, and collaboration with WHO, FDA, EMA, and the UK MHRA. These mechanisms were presented as critical for harmonizing evidence expectations, aligning study designs, and avoiding duplication—particularly in emergency settings where rapid decision-making is essential.

A major portion of the session focused on surveillance systems as the foundation of preparedness. India's ICMR described a post-COVID shift from pathogen-specific to syndromic surveillance, supported by priority pathogen lists for key clinical syndromes such as acute encephalitis, diarrhea, fever and severe respiratory illness. Through its network of 167 virus research and diagnostic laboratories, India conducts routine testing for Nipah using standardized algorithms, enabling rapid detection, as demonstrated by recent containment of an index case in West Bengal. This system is reinforced by India's National One Health Mission, which integrates human, animal, and environmental surveillance and supports multidisciplinary outbreak investigations.

Additional context from ICMR highlighted the substantial strengthening of India's laboratory and response infrastructure since earlier Nipah outbreaks, including expanded BSL-3 and BSL-4 capacity, mobile high-containment units, workforce training, and development of point-of-care diagnostics. These investments were described as enabling early containment at the index case and maintaining readiness through integrated surveillance and rapid response protocols.

Other countries outlined complementary approaches. Malaysia described a One Health surveillance system linking human health authorities with veterinary and wildlife agencies, including targeted sampling of bats, monitoring of pigs as intermediate hosts, and mandatory reporting of unexplained encephalitis and severe respiratory infections. Thailand noted that, despite having no recorded Nipah cases, it has incorporated Nipah into national preparedness planning, requiring rapid reporting of any detection and conducting syndromic and wildlife surveillance, with laboratory capacity expansion underway. Singapore reported continuous baseline One Health surveillance, including monitoring of bats, wastewater, and environmental sources, alongside strengthened laboratory and BSL-4 readiness and established outbreak -response protocols.

The panel then examined vaccine supply strategies and procurement during outbreaks, recognizing that countries differ markedly in manufacturing capacity. Malaysia emphasized lessons from COVID-19, prioritizing advance purchase agreements over large domestic stockpiles to ensure availability while minimizing wastage from expiry. Under this model, manufacturers retain stock offshore and supply doses rapidly when needed, supported by clear contractual terms on pricing, logistics, and exit conditions. India, by contrast, described a deliberate decision not to stockpile Nipah vaccines due to resource constraints, instead focusing on maintaining readiness among domestic manufacturers to enable rapid scale-up within weeks. India also highlighted work with CEPI to define vaccine use cases and prepare communities for acceptance, noting that demand for vaccines may remain low before outbreaks, while monoclonal antibodies often see rapid uptake once cases appear.

Procurement strategies were further explored. Thailand indicated that no final decision has been made on stockpiling or procurement, given the rarity of Nipah, and emphasized that public-health measures such as hygiene, sanitation, and education remain primary. Malaysia referenced ASEAN's pooled procurement experience for mpox, noting both its benefits and the critical lesson that regulatory readiness must precede procurement to avoid delays in deployment.

The discussion then turned to vaccination strategies and target populations. India emphasized prioritization of healthcare workers, populations in forest-fringe areas with bat exposure, and individuals with occupational risk. The possibility of rapid antibody responses from some vaccine candidates raised the prospect of vaccinating close contacts during outbreaks. Thailand and Malaysia similarly favored targeted or reactive vaccination approaches, including ring vaccination for high-risk groups, rather than routine immunization, given the disease's epidemiology. Panelists noted that the speed of onset of protection may influence strategy, with fast-acting vaccines better suited to outbreak response.

WHO SEARO outlined its role in supporting countries across preparedness, development, and deployment, highlighting regulatory strengthening, coordinated inspections, integration with the WHO R&D Blueprint, support for advance manufacturing commitments, technology transfer through the Health Technology Access Pool, and capacity building. WHO emphasized that these coordinated actions—spanning regulation, manufacturing, trials, and Vaccine confidence and risk communication were discussed as determinants of deployment feasibility, particularly for products authorized using surrogate endpoints. Panelists noted that acceptance is influenced by perceived risk, trust in institutions, and the clarity and consistency of communication. They emphasized the importance of transparent communication on benefits and uncertainties, timely publication of safety information, and visible post-authorization monitoring to support public confidence.

The panel concluded that preparedness for Nipah vaccine deployment extends beyond regulatory authorization and depends on integrated surveillance, laboratory readiness, fit-for-purpose supply strategies, predefined prioritization frameworks, and outbreak-ready operational protocols. Participants emphasized that these capabilities should be established during inter-epidemic periods to enable timely action if transmission increases.

3.2. Part 5: Kyasanur forest disease case study

3.2.1. Kyasanur forest disease

Dr. Sarah Cherian (ICMR, India) introduced KFD as a tick-borne zoonosis of the Western Ghats and summarized the historical context for its recognition. She noted that KFD was first detected in 1956–57 in Shimoga (Karnataka), coinciding with deaths among black-faced langurs and red-faced bonnet monkeys, which served as early sentinel events indicating circulation of a previously unrecognized pathogen.

She noted that reported transmission subsequently expanded beyond the initial focus area and is now established across parts of the Western Ghats, including affected areas in Karnataka, Kerala, Tamil Nadu, Goa, and Maharashtra. She attributed this geographic spread to ecological and anthropogenic factors, including deforestation, wildlife movement, and increased human activity in forested environments.

Dr. Cherian described Kyasanur Forest disease virus (KFDV) as a tick-borne flavivirus (family *Flaviviridae*) with an approximately 11-kb, positive-sense RNA genome that encodes a polyprotein processed into three structural and seven nonstructural proteins. She noted that KFDV is phylogenetically related to other tick-borne encephalitis (TBE) complex viruses, including Alkhurma hemorrhagic fever virus and TBE virus. She also noted that the pathogen is categorized as a biosafety risk group 4 agent, reflecting containment requirements.

She summarized the transmission ecology, noting that >15 *Haemaphysalis* tick species have been implicated, with *H. spinigera* and *H. turturis* described as major vectors. She noted seasonal patterns in the tick life cycle (eggs: June–September; larvae: October–December; peak nymph activity: January–May) that align with peaks in human and simian infections. Humans are infected primarily through bites from infected nymphs and are considered dead-end hosts; human-to-human transmission is considered unlikely.

Clinically, she described KFD as a biphasic illness. The initial phase may include fever, headache, hepatomegaly, gastrointestinal symptoms, hemorrhagic manifestations, and thrombocytopenia. She noted that approximately 80–90% of patients recover after 1–2 weeks, while others progress to neurological complications including seizures, ataxia, cranial nerve palsies, altered sensorium, and meningoencephalitis. She noted that no specific antiviral therapy is available and that management is supportive.

Dr. Cherian summarized epidemiologic patterns and historical outbreaks, citing 550 cases in 1981 and more than 20,000 affected during the 1983–84 surge. She reported case-fatality rates ranging from approximately 3% to 15% across reports. She highlighted higher risk among forest-exposed populations, including hunters, forest workers, farmers, and wildlife-park personnel.

She summarized genomic work conducted by ICMR-NIV, including whole-genome and partial-gene analyses from human, tick, and monkey samples. Reported bioinformatic analyses (including phylogeography and molecular clock methods) suggest two major temporal lineages (1957–1972 and 2006–2017), low overall nucleotide divergence (~2%), and relatively slow evolutionary rates. She also noted evidence of positive selection at specific sites, including in the envelope protein and the NS5 polymerase, and described analyses indicating repeated spillovers and bidirectional viral movement across Karnataka, Goa, Kerala, Maharashtra, and Tamil Nadu.

She noted that a formalin-inactivated, tissue-culture KFD vaccine has been used in Karnataka since the 1990s. The program requires two primary doses and annual boosters administered ahead of the peak nymph season; she noted limitations in vaccine acceptance and durability. She stated that, despite modest reported effectiveness, this vaccine remains the only licensed preventive tool. She also noted reports of long-lasting T-cell memory among naturally infected individuals (persisting for decades), which may inform considerations for next-generation vaccine design.

Dr. Cherian concluded by emphasizing that KFD prevention and response require an integrated One Health approach that links tick management, public health outreach, genomic surveillance, and ecological monitoring, alongside development of improved vaccines and other countermeasures. She noted that sustained surveillance and coordinated preparedness planning are important to reduce risk in affected communities.

3.2.2. KFD: Current status and development of vaccine

Dr. Pragya Yadav (ICMR, India) summarized the current status of KFD in India and reviewed progress toward next-generation vaccine development, linking recent epidemiologic findings, laboratory capacity, and evidence-generation strategies relevant to licensure.

She described India's expanding high-containment and diagnostic capacity relevant to KFD, including a national BSL-4 facility in Pune and additional high-containment facilities, alongside a growing network of One Health–aligned BSL-3 laboratories across the Western Ghats. She noted that this capacity supports coordinated testing of human, tick, and wildlife samples and strengthens situational awareness through integrated assessment of human cases, monkey die-offs, and tick activity.

Dr. Yadav noted that KFD is a tick-borne viral hemorrhagic fever with no documented human-to-human transmission, and that humans are considered dead-end hosts infected primarily through nymphal tick bites. She reported that Karnataka remains the primary contributor to notified cases, with Maharashtra, Kerala, Goa, and Tamil Nadu reporting lower but persistent activity. She stated that recent reports suggest lower mortality in the past decade than in earlier periods but cited a 2024 outbreak (147 cases and four deaths) as evidence of continued risk, particularly among individuals with comorbidities.

She summarized recent seroprevalence findings, reporting low seropositivity in parts of Karnataka (approximately 2–4%) and higher seropositivity in an outbreak cohort in Maharashtra (~50%), interpreted as consistent with undetected circulation over time. She also reported longitudinal follow-up of 72 cases indicating that naturally acquired antibody responses may wane within approximately 3–4 years, which may limit accumulation of population-level protection in endemic areas.

Dr. Yadav then reviewed the legacy formalin-inactivated KFD vaccine program in Karnataka, which required two primary doses plus annual boosters and was reported to have limited durability and uptake. She stated that in 2022 the Drugs Controller General of India (DCGI) discontinued the vaccine, citing limitations in the immunogenicity evidence base and continued occurrence of outbreaks despite vaccination. She noted that this decision increased focus on developing next-generation candidates with more robust supporting data and alignment with contemporary regulatory expectations.

She described supporting research conducted to inform vaccine development, including cohort studies characterizing viremia kinetics, leukopenia and thrombocytopenia patterns, and interferon type I responses. She also noted immunology findings highlighting CD8+ T-cell activation and the limited durability of antibody responses following natural infection. In parallel, genomic surveillance and phylogenetic analyses were reported to show low genetic divergence across sampled lineages and to support selection of stable, higher-titer viral isolates for vaccine seed development.

She described animal-model work, including controlled infections in bonnet macaques, which were reported to reproduce key features of KFD (including hemorrhagic manifestations and gastrointestinal viral loads) and to generate IgM/IgG kinetics consistent with infection. She noted that these NHP models may support future challenge studies intended to generate efficacy-relevant evidence. She also noted exploration of additional platform approaches, including viral vectors, adjuvanted subunit constructs, and computational immunogen design.

Dr. Yadav then described development of a next-generation whole-virus candidate vaccine in partnership with Indian Immunologicals, ICMR, and ICMR-NIV, formulated as a beta-propiolactone–inactivated, alum-adjuvanted product. She reported that seed-strain selection considered stability, achievable titers, and representation of circulating sub-lineages. Dose-ranging studies in mice (6–24 μg) were reported to support selection of an 18 μg alum-adjuvanted formulation, and challenge studies across multiple clades were reported to show protection in the tested models.

She reported that the candidate has entered phase 1 evaluation in KFD-endemic districts, described as a randomized, double-blind, placebo-controlled study at sites including JSS Mysore and KMC Manipal. The protocol enrolls healthy adults aged 18–49 years and evaluates a two-dose regimen administered 20 days apart. Primary objectives include safety and reactogenicity; immunogenicity endpoints include neutralizing antibody responses measured by $PRNT_{50}$. Follow-up extends through Day 366. She noted that progression to phase 2 is contingent on review of emerging data, including independent safety oversight (Data and Safety Monitoring Board [DSMB]).

Looking ahead, she described planned NHP challenge studies intended to generate efficacy-relevant evidence for a low-incidence pathogen for which phase 3 clinical endpoint trials are not expected to be feasible. She noted that ongoing engagement with CDSCO is being used to clarify requirements for integrating animal-model evidence and human immunogenicity within potential immunobridging frameworks to support eventual licensure.

She concluded by noting that vaccine development is being complemented by strengthening of field surveillance, diagnostic networks, laboratory capacity, and clinical-research platforms intended to support rapid activation of studies in endemic areas. She emphasized that these capabilities are relevant both for evidence generation during development and for post-authorization monitoring if a vaccine is introduced.

3.2.3. Vaccines in development (preclinical, clinical, manufacturing technologies, regulatory strategies) with gaps remaining to be filled

3.2.3.1. KFD vaccine development: process optimization, preclinical and clinical evaluation

Dr. Raju Sunagar (Indian Immunologicals Limited [IIL], India) introduced IIL and described the organization's role in translating KFD vaccine research into a GMP-manufactured clinical product. He noted that IIL produces human and veterinary vaccines from multiple manufacturing sites and that its facilities include BSL-3 capability, supporting development and manufacture of inactivated viral vaccines and associated quality-control testing.

He described the partnership model with ICMR and ICMR-NIV in which ICMR-NIV provides the viral seed and characterization, ICMR supports program direction and financing, and IIL leads industrial development under GMP. He reported that the viral isolate was received on 30 April 2024 and that subsequent work included establishing master and working seed banks, scaling Vero-cell production, validating beta-propiolactone (BPL) inactivation, conducting purification steps (including DNase treatment and chromatography), producing GMP clinical batches, and preparing the documentation to support phase 1 entry.

He noted that, in the absence of KFD-specific WHO guidance, the team used established regulatory precedents for inactivated flavivirus vaccines—particularly Japanese encephalitis (JE)—to inform key CMC and product-quality expectations. He stated that JE specifications were used as a reference for defining inactivation validation, purity and residuals, stability, potency, and release-testing requirements, supporting a structured approach to dossier development.

He described two development planning tracks: a conventional pathway aligned with standard timelines for process development and clinical manufacturing, and an accelerated pathway intended to leverage existing reagents, cell banks, and platform processes to shorten timelines where feasible. He noted that accelerated approaches depend on prior platform readiness and early alignment on assay and documentation requirements.

Dr. Sunagar summarized the preclinical evidence supporting clinical entry for a beta-propiolactone–inactivated, whole-virion KFD vaccine formulated with aluminum hydroxide. He reported dose-ranging studies in BALB/c mice using 6, 12, 18, and 24 µg antigen doses, each of which induced binding and neutralizing antibody responses. In a reported 1 LD_{50} challenge model, complete survival was observed in the 18 µg and 24 µg groups, whereas lower-dose groups showed lower survival. He also reported additional challenge work at higher inocula (e.g., 1,000 LD_{50}) and follow-up through approximately 150 days and stated that aluminum hydroxide outperformed aluminum phosphate in comparative adjuvant testing in the reported studies.

He described key CMC and manufacturing activities, including seed-bank generation, Vero-cell upstream process development and scale-up, inactivation validation, purification process definition, and completion of release testing and stability studies required to support a GMP clinical batch. He noted that supporting documentation included identity, purity, potency, safety, stability, and process-validation information consistent with expectations for inactivated flavivirus vaccines.

He reported that a phase 1 clinical study has been authorized and initiated in KFD-endemic districts, described as a randomized, double-blind, placebo-controlled trial at sites including JSS Mysore and KMC Manipal. Healthy adults aged 18–49 years receive two 18 µg doses administered 20 days apart. Primary objectives are safety and reactogenicity; immunogenicity is assessed using $PRNT_{50}$ neutralizing antibody titers. Follow-up extends through Day 366, with progression to phase 2 contingent on review of emerging data, including independent safety oversight (DSMB).

He described planned next steps including expansion to phase 2 based on phase 1 findings and a NHP challenge study (e.g., 0/28-day schedule) to generate efficacy-relevant evidence for a low-incidence pathogen for which clinical endpoint efficacy trials are not expected to be feasible. He noted that ongoing engagement with CDSCO is being used to clarify expectations for integrating human immunogenicity data and NHP challenge outcomes within potential immunobridging frameworks.

3.2.3.2. Developing a KFDV candidate vaccine using a VSV-based viral vector platform

Professor and Dean, Dr. Jayanta Bhattacharya (Translational Health Science and Technology Institute [THSTI], India) introduced the THSTI and described its role in translational vaccine R&D, assay development, and preclinical model support. He noted that THSTI operates GLP-aligned enabling platforms (including bioassay and bioprocess capabilities) and has supported standardized bioassays for multiple vaccines in India, including participation in CEPI-supported laboratory networks.

He then outlined THSTI's KFD vaccine program, noting that the institute's mandate is to advance candidates through translational R&D rather than commercial manufacture. The team is developing a VSV viral-vector approach, citing platform attributes such as genetic flexibility and absence of genomic integration. He noted that early VSV–KFD constructs were developed in collaboration with Rocky Mountain Laboratories under Dr. Heinz Feldmann, and that THSTI has continued vector engineering and preclinical evaluation in India.

Dr. Bhatia Principal Scientist Dr. Bharti Bhatia (THSTI, India) described the antigen and construct design. Consistent with flavivirus vaccine approaches, the envelope (E) glycoprotein was selected as the primary antigen. She reported that the KFDV E gene was inserted into an existing rVSV backbone between the nucleoprotein (N) and phosphoprotein (P) genes. The construct retained the Ebola glycoprotein (GP) used to pseudotype the vector. She noted that antigen expression was confirmed and that THSTI established an in-house murine disease model to support preclinical evaluation.

She summarized reported preclinical findings in mice. In a mouse challenge study using a 1,000 LD_{50} inoculum of wild-type KFDV, a prime–boost regimen was reported to provide complete survival, with viral replication in brain tissue reported as below the assay detection limit. In passive-transfer experiments, sera from vaccinated animals administered 24 hours prior to challenge were reported to provide >90% survival and reduced brain viral loads in recipient mice.

She also described a reported NHP study in pig-tailed macaques, referenced as a non-lethal model used by Rocky Mountain Laboratories. Vaccinated animals were challenged and were reported to show lower viral loads and improved clinical scores relative to controls. She noted that study details included administration of 10^7 PFU by subcutaneous and intravenous routes, and that interpretation depends on the challenge model and endpoints used.

Dr. Bhatia also reported exploratory cross-neutralization analyses motivated by KFDV's genetic relatedness to Alkhurma hemorrhagic fever virus. She noted that *in vitro* neutralization patterns were reported to be broadly similar across the tested viruses in the described assay system, and emphasized that additional work would be needed to assess the generalizability and potential implications for cross-protection.

She noted a development consideration related to the construct's use of Ebola GP for pseudotyping. Because Ebola is not endemic in India, she noted that vaccine-induced anti-Ebola antibody responses could complicate national serosurveillance or interpretation of serologic findings. She described this as a regulatory and programmatic concern and noted that THSTI is exploring re-engineering options to retain desired rVSV platform characteristics while avoiding inclusion of antigens that could confound surveillance or limit acceptability.

Dr. Bhattacharya concluded by noting that THSTI's work also contributes enabling capabilities relevant beyond a single candidate, including harmonized assays, GLP-aligned preclinical capacity, NHP model support, and vector-engineering methods intended to accelerate translational research for KFD and other priority pathogens.

3.2.4. Outbreak protocols, RWE, and the feasibility of generating efficacy-relevant data

3.2.4.1. KFD: Safety signals, outbreak protocols, potential for efficacy-relevant data, and real-world effectiveness

Moderator: Dr. Marco Cavaleri (EMA, EU)
Panelists:
Dr. Manoj Murhekar (ICMR-NIE, India)
Dr. Nivedita Gupta (ICMR, India)
Dr. Kasi Shankar Venugopal (CDSCO, India)

This session focused on evidence strategies for evaluating KFD vaccines once candidates enter clinical development and, potentially, public health use. Dr. Murhekar summarized key epidemiologic constraints relevant to study design, noting that fewer than 10,000 cases have been documented in India, that transmission occurs primarily through infected nymphal ticks, and that outbreaks are seasonal (typically December–May) with geographically heterogeneous clustering. Panelists noted that these features make conventional randomized phase 3 efficacy trials difficult to execute.

Panelists discussed approaches to interpreting potential safety signals for KFD vaccines in the context of limited background incidence data. As reference points, they cited licensed flavivirus vaccines used in India, including JE vaccines (e.g., JenVac and IXIARO). Reported phase 2/3 data for JenVac included AEFI after the first dose (predominantly mild events such as fever, myalgia, headache, cough, and gastrointestinal symptoms) with lower frequencies after the second dose. For IXIARO, pooled analyses across multiple phase 3 trials were described as showing local and systemic reactogenicity rates comparable to an alum-placebo control, with low proportions of severe events. Panelists noted that such comparator patterns can help contextualize expected reactogenicity and inform post-authorization pharmacovigilance plans for KFD vaccines.

Dr. Cavaleri noted that outbreak-time efficacy trial designs used for directly transmissible pathogens (e.g., ring vaccination strategies for Ebola) are not directly transferable to KFD because KFD has no human-to-human transmission; exposure risk is driven by environmental tick ecology rather than proximity to an index case. A modified reactive approach targeting occupationally exposed groups in areas where cases occur (e.g., forest workers, firewood collectors, and grazers) was discussed as a possible deployment model. However, panelists noted that heterogeneous tick exposure, dispersed settlement patterns, and low overall incidence can limit both feasibility and statistical power for outbreak-time efficacy evaluations.

Given the constraints on outbreak-time studies, panelists discussed immunobridging as a likely pathway for inferring clinical benefit, supported by NHP challenge studies and validated neutralization assays. This would require defining a scientifically justified protective threshold (or decision benchmark) for KFD, supported by integrated evidence from preclinical challenge studies, human immunogenicity data, and comparator information from licensed flavivirus vaccines where appropriate.

As an example of field effectiveness evidence, the panel referenced a large observational evaluation conducted in the early 1990s following introduction of the first formalin-inactivated KFD vaccine. The study followed >200,000 individuals across 284 villages in three endemic districts in Karnataka and reported lower incidence among vaccinated groups compared with unvaccinated groups:

- 25.22/100,000 among unvaccinated individuals
- 5.22/100,000 after one dose
- 1.66/100,000 after two doses

Panelists noted that, while these data were non-randomized and subject to confounding, they illustrate that structured observational or cluster rollout approaches may be considered for future vaccines if programmatic conditions and case detection support meaningful analysis.

The panel discussed RWE generation once a KFD vaccine is deployed. Participants noted that digital immunization registries and strengthened surveillance systems can enable analytical designs that were previously difficult to implement, provided vaccination status and laboratory confirmation are reliably captured. Examples of feasible designs discussed included:

- Test-negative case-control studies (comparing vaccination status of febrile KFD-positive and KFD-negative individuals)
- Cohort-based incidence comparisons between vaccinated and unvaccinated groups
- Outbreak-time case-control studies to estimate effectiveness and monitor safety signals during clusters

Panelists noted that embedding these designs within routine surveillance and immunization information systems can support both effectiveness estimation and post-authorization safety monitoring, subject to appropriate governance, data quality, and analytical rigor.

3.2.5. KFD vaccines

Dr. Marco Cavaleri (EMA, EU) provided a technical briefing on evidence pathways that could support evaluation and potential authorization of KFD vaccines, building on the preceding panel discussion on immunobridging, safety benchmarking, outbreak protocols, and RWE.

He noted that for some viral diseases (e.g., dengue), clinical efficacy data can be generated through large, well-controlled phase 3 trials. For KFD, however, chronically low case numbers, sporadic and localized outbreaks, and the absence of human-to-human transmission constrain feasibility of such trials. He therefore highlighted immunobridging as a relevant pathway and cited JE as an example where regulators have accepted comparative neutralizing-antibody responses in lieu of direct efficacy evidence, provided assays are appropriate and comparators are well characterized.

He noted that KFD vaccine development may be able to leverage multiple evidence sources, including observational evidence from the legacy inactivated KFD vaccine program, contemporary human immunogenicity datasets for new candidates, and supportive NHP challenge data where available. He emphasized that no single evidence stream is sufficient in isolation and that a totality-of-evidence approach would likely be required to justify immunogenicity endpoints and interpret protection benchmarks.

- Observational evidence from legacy vaccine use
- Functional antibody responses and other immunogenicity readouts
- Comparative immunogenicity benchmarks (e.g., against relevant flavivirus comparators where appropriate)
- Supportive animal-model findings

He noted that KFD's low and geographically dispersed incidence limits feasibility of pre-authorization randomized efficacy trials and may also constrain post-authorization randomized studies. In this context, well-designed observational studies are expected to be an important approach for estimating effectiveness and monitoring safety in real-world settings, provided that vaccination status and laboratory confirmation are reliably captured.

As an example from a related tick-borne flavivirus, he referenced European experience with TBE vaccines, which were authorized using neutralizing-antibody responses as key endpoints. He noted that subsequent observational studies in routine use have reported high effectiveness, supported by surveillance systems that document vaccination status and apply designs such as test-negative, cohort, and case–control studies.

He also noted the importance of monitoring durability of protection and booster needs over time. Drawing again on TBE practice as an example, he noted that booster recommendations can be informed by periodic immunogenicity follow-up and, where feasible, serosurveys or registry-linked analyses:

- Accurate documentation of vaccination status
- Systematic case detection
- Embedding observational study designs within routine surveillance
- Minimizing confounding and bias at every stage

In closing, he reiterated that KFD's epidemiology is likely to necessitate immunogenicity-based pathways supported by a totality of evidence, complemented by fit-for-purpose observational studies to characterize real-world effectiveness and safety over time.

3.2.6. Panel discussion: Advancing KFD vaccines—regulatory, public health, and development scenarios

Moderator: Dr. Marco Cavaleri (EMA, EU)
Panelists:
Dr. Nivedita Gupta (ICMR, India)
Dr. Pragya Yadav (ICMR-NIV, India)
Dr. Rubina Bose (CDSCO, India)
Dr. Kasi Shankar Venugopal (CDSCO, India)
Dr. Madhur Gupta (WHO SEARO, India)

This panel brought together regulators, public health authorities, and developers to discuss evidence-generation and authorization scenarios for next-generation KFD vaccines. Discussion focused on feasible regulatory pathways given KFD's low incidence, the role of immunogenicity-based endpoints and animal-model data, requirements for safety and post-authorization monitoring, and the operational and policy enablers needed to support deployment in endemic areas.

Panelists noted that conventional randomized clinical efficacy trials are generally infeasible for KFD due to sparse and geographically dispersed cases and the absence of human-to-human transmission. They discussed immunobridging as a likely approach for inferring clinical benefit, supported by a totality of evidence that may include preclinical challenge data, human immunogenicity and immune profiling, observational evidence from prior vaccine use, and comparator benchmarks from other flavivirus vaccines where appropriate.

Regulators described available national pathways for life-threatening, geographically limited diseases and emphasized the importance of early alignment on decision-relevant endpoints, assay requirements, and evidence thresholds. One speaker noted that, if immunogenicity and bridging plans proceed as intended and data are sufficiently robust, an authorization decision could potentially be considered on an accelerated timeline; however, this would remain contingent on the completeness and quality of the evidence package and on national legal requirements.

CDSCO described the regulatory framework under India's New Drugs and Clinical Trials Rules, including provisions that can enable accelerated pathways for serious diseases with unmet need. Panelists discussed that, if a phase 3 clinical endpoint trial is not feasible, authorization could be considered based on immunogenicity endpoints supported by non-clinical and NHP evidence, provided that appropriate post-authorization obligations are defined. Development plans were described as integrating phase 1 and phase 2 studies with parallel NHP work to support immunobridging and to inform endpoint selection for later-stage evaluation.

Operational constraints were also discussed, including availability of bonnet macaques and scheduling of NHP studies. Panelists noted that where NHP work is delayed, enhanced human immunoprofiling and assay development may help maintain decision readiness by strengthening interpretation of early clinical datasets.

Safety evidence and lifecycle monitoring were a major focus. Panelists discussed the need for a sufficiently sized and appropriately characterized pre-licensure safety database, benchmarked where relevant against licensed flavivirus vaccines, followed by enhanced pharmacovigilance and post-authorization studies. India's emerging digital immunization and safety-monitoring capabilities (including immunization registries such as U-WIN/UVIN, where implemented) were noted as potential enablers of registry-linked safety and effectiveness analyses, subject to data quality, coverage, and governance.

Given constraints on randomized designs, panelists described observational approaches—such as test-negative case–control studies, cohort analyses, and outbreak-triggered case–control evaluations—as likely methods for estimating real-world effectiveness and monitoring safety. They emphasized that credibility depends on standardized case definitions, laboratory confirmation, and reliable capture of vaccination status.

Panelists referenced the historical field evaluation of the legacy inactivated KFD vaccine as an example of how structured observational evidence can be generated in endemic districts. They noted that such analyses are non-randomized and may be confounded, reinforcing the need for prospective protocols and analytic plans for future candidates.

Manufacturing and partnership models were discussed, including India's capacity to support GMP production and scale-up through public–private collaboration. Panelists described ICMR's role in supporting early-stage research and evidence generation (including assays and NHP studies) and noted that technology transfer and quality standardization mechanisms may be relevant if broader manufacturing or multi-site production is pursued.

The panel also discussed the potential value of regulator-to-regulator coordination to support efficient multi-country evaluation and deployment, including reliance approaches where appropriate and harmonization of post-authorization study protocols, while maintaining national decision-making authority.

Communication and public trust were discussed as determinants of vaccine uptake. Panelists emphasized the need for clear, consistent messaging from regulators and public health authorities on benefits, uncertainties, contraindications, and safety monitoring, particularly when authorization relies on immunogenicity-based endpoints.

The discussion closed by noting the role of surveillance systems in both pre-licensure evidence generation and post-authorization monitoring, including year-round sentinel sites in affected states and the potential use of sequencing for pathogen-negative samples where operationally feasible.

3.3. Part 6: Bringing it all together to support the 100 Days Mission

3.3.1. Panel discussion: Bringing it all together to support the 100 Days Mission

Moderator: Dr. Adam Hacker (CEPI, UK)
Panelists:
Dr. Rajiv Bahl (ICMR, India)
Dr. Jinho Shin (WHO WPRO, Philippines)
Dr. Dean Smith (IABS-NA Chair, Canada)
Dr. Marco Cavaleri (EMA, EU)
Dr. Nancy Sullivan (Boston University, NEIDL, USA)
Dr. Rajeev Raghuvanshi (CDSCO, India)

The final panel served as a capstone discussion synthesizing themes from the 3-day Summit. Panelists reflected on cross-cutting requirements to support the 100 Days Mission, including sustained collaboration across regulators, developers, and public health institutions; fit-for-purpose evidence strategies when efficacy trials are infeasible; strengthened post-authorization monitoring; and operational preparedness to activate studies and manufacturing during outbreaks.

3.3.1.1. Collaboration as a foundational enabler

Panelists noted that the Summit format—bringing together regulators, scientists, developers, and public health practitioners—supported practical exchange on evidence expectations and operational readiness. They emphasized the importance of sustaining these relationships between outbreaks through routine information sharing, structured scientific advice, and continued work on data and assay comparability, which can improve timeliness and consistency of decisions during future events.

3.3.1.2. Regulatory science and alternative evidence pathways

The panel discussed how regulatory approaches have evolved to accommodate pathogens for which conventional efficacy trials are infeasible. Examples cited across agencies included:

- Use of immunogenicity endpoints and scientifically justified surrogate markers in place of classical efficacy trials
- Rolling reviews and other accelerated assessment processes
- Accelerated pathways for serious diseases with unmet need
- Reliance mechanisms and regulatory networks that enable sharing of assessments and scientific reasoning

Panelists noted that these approaches are already used in routine regulatory practice, including for products supported by animal models, surrogate markers, and other non-randomized evidence streams. They emphasized that flexibility does not remove evidentiary requirements; rather, it shifts emphasis toward clarity of scientific rationale, assay validity, and enforceable lifecycle evidence-generation plans.

3.3.1.3. Safety, effectiveness, and post-authorization evidence infrastructure

For pathogens where efficacy trials are difficult to conduct, the panel noted that evidence packages often place greater weight on:

- Well-defined immunobridging endpoints and validated assays
- Fit-for-purpose non-clinical packages
- Deeply characterized immunogenicity profiles
- Post-authorization safety monitoring and effectiveness studies

Panelists discussed pharmacovigilance and RWE generation as critical complements to immunogenicity-based pathways. They noted that post-authorization monitoring is resource intensive and depends on end-to-end systems that can capture vaccination status, adverse events, and outcomes over time, including in remote settings. Participants emphasized that these capabilities require sustained investment, integration into routine health systems, and clear allocation of responsibilities across manufacturers, regulators, and public health institutions.

3.3.1.4. Preparedness prerequisites for the 100 Days Mission

The panel identified prerequisites that can enable faster development and decision-making during outbreaks. These include:

- Pre-mapped immunological correlates and validated assays
- Readily accessible virus isolates, reagents, and challenge models
- Pre-agreed regulatory markers and endpoints
- Platform technologies primed for rapid adaptation
- Strengthened surveillance that can detect unusual events in real time

- Established mechanisms for regulatory reliance and shared evaluations
- Activation-ready clinical-trials networks.

3.3.1.5. Manufacturing readiness and technology transfer

The panel noted that manufacturing capacity and supply resilience are determinants of response speed. Discussion highlighted the value of platform-ready manufacturing processes, surge arrangements, and technology transfer frameworks that can be activated rapidly, alongside quality systems and regulatory readiness to support multi-site production when needed.

3.3.1.6. Public communication and trust

Finally, the panel emphasized that effective risk communication is integral to preparedness. Participants noted that public acceptance depends on trust in decision-making processes, clarity about benefits and uncertainties, and transparency about contraindications and safety monitoring. Consistent messaging across regulators and public health authorities was described as important, particularly when authorizations rely on surrogate endpoints or rapidly evolving evidence.

3.4. Closing remarks

In closing remarks, speakers emphasized that preparedness depends on sustained practice rather than one-time planning. They encouraged participants to maintain technical networks established through the Summit, continue routine scientific exchange between outbreaks, and translate lessons into practical actions across surveillance, regulatory readiness, manufacturing, and evidence-generation systems.

Participants emphasized that preparedness will only be realized by translating theoretical alignment on alternative licensure pathways into sustained operational practice. As a priority next step, regulators agreed on the value of moving beyond discussion toward practical, joint regulatory reviews of concrete license applications that rely on animal challenge data and clinical immunogenicity evidence in the absence of traditional efficacy trials. Conducting such joint or collaborative reviews in peacetime would allow regulatory authorities to build hands-on experience in assessing these complex data packages, deepen shared understanding of evidentiary strengths and limitations, and identify system-level gaps or implementation challenges early. This practical experience is critical to ensuring that national regulatory frameworks are fully able to support timely approvals using a totality-of-evidence approach and to strengthening readiness across the region should a similar regulatory package require urgent review during an outbreak or public health emergency.

4. Appendices

Appendix 1: Steering Committee and Preregistered Participants

Scientific Steering Committee:

Dr. Nancy Sullivan, Director, NEIDL, USA
Dr. Robin Levis, Deputy Director, Division of Viral Products, OVRR/CBER, US FDA,
Dr. Marco Cavaleri, Head of Health Threats and Vaccine Strategy, EMA, WHO CoRC Lead Flaviviridae
Dr. Dean Smith, Section Head, Vaccines, Health Canada,
Prof. (Dr.) Vinod K Paul, Member, Niti Aayog, Government of India (GoI)
Dr. Nivedita Gupta, Scientist – G, ICMR, WHO CoRC lead for Paramyxoviridae, MoH, GoI
Dr. Rubina Bose, Deputy Director Controller India, CDSCO, MoH, GoI
Dr. Kamakshi Chhaithri, Scientist – D, DBT, Ministry of Science and Technology, GoI
Dr. Anil Kumar Chawla, Scientist (Vaccine Regulation, Safety and Management) IVD/CDS, WHO-SEARO
Dr. Anuradha Poonepalli, Clinical Lead / Regulatory Consultant, Health Sciences Authority, Singapore
Dr. Adam Hacker, Director and Global Head of Regulatory Affairs and Quality, London, CEPI
Ms. Catherine Hoath, Global Regulatory Affairs Strategy Lead, Regulatory Affairs & Quality Dept, USA, CEPI
Ms. Danielle Craig, Head Regulatory Affairs Americas, Regulatory Affairs & Quality Dept, USA, CEPI
Ms. Meenu Batolar, Global Regulatory Affairs – Asia Pacific Lead, Singapore, CEPI
Dr. Debra Yeskey, Global Regulatory Affairs & Intelligence Lead, Regulatory Affairs & Quality Dept, USA, CEPI
Dr. Vikas Aggarwal, Senior Global South Partnerships Lead, Public Partnerships Department, London, CEPI
Dr. Amol Chaudhari, Clinical Development Science Lead, Clinical Development Department, India, CEPI

Preregistered Participants:

Title	First Name	Last Name	Designation	Company Name
Dr	Badri	Patnaik	Director Medical Affairs	Bharat Biotech
Dr	Krishna	Mohan	Whole Time Director	Bharat Biotech International
Mr.	Guru	Guru	Assistant Regulatory Officer	Bhutan Food and Drug Authority
	Jigme	Tenzin	Chief Regulatory Officer	Bhutan Food and Drug Authority
	Saraswathi	Gundabathula	Regulatory Affairs - Head	Biological E Limited
Dr	Subhash	Thuluva	Sr.VP & Head -Clinical Devlopm	Biological E Ltd
Mr.	Asheesh	Kaundal	Drugs Inspector	CDSCO
Ms	Haritha Sameeraja	Nagampalli	Drugs Inspector	CDSCO
Mr	Neelesh	Namdeo	Drugs Inspector	CDSCO
Ms	D	Hemalatha	Assistant Drugs Controller (I)	CDSCO HQ New Delhi
Ms	Lipika	Roy	Drugs Inspector	CDSCO, Head Quarter
Mr	Vinod	Gupta	Drugs Inspector	CDSCO, India
Mr.	Dhayalamurthi	Siva	Drugs Inspector	CDSCO
	Kasi Sankar	Venugopal	Assistant Drugs Controller (I)	CDSCO
	Shivadev	Dasi	Drugs Inspector	CDSCO
	Priya	Pandey	Drugs Inspector	CDSCO Directorate General of Health Services Ministry
	Freya	Hopper	Senior Strategy Lead	CEPI
	Richard	Jarman	Programme Leader	CEPI
Dr.	Kamakshi	Chaithri	Scientist D	DBT
Dr.	Anamika	Gambhir	Scientist 'G'/Adviser	Department of Biotechnology, Ministry of Science and Technology, Govt. of India
Mr	Narayan Prasad	Dhakal	Director General	Department of Drug Administration

Assistant Professor	Wei Chuen	TAN-KOI	Assistant Professor	Duke-NUS Medical School Centre of Regulatory Excellence
Dr	Dr. Abhijit	Kadam	Scientist D	ICMR-National Institute of Translational Virology and AIDS Research
Prof. Dr.	Sheela	Godbole	Director	ICMR-National Institute of Translational Virology and AIDS Research
Dr.	Labanya	Mukhopadhyay	Scientist-C	Indian Council of Medical Research
Dr.	Apoorva	Pandey	Scientist- C	Indian Council of Medical Research
Professor	Raghavan	Varadarajan	Professor	Indian Institute of Science
Mr	Muhammad	Luhur	Biological Product Evaluator	Indonesia FDA
Dr	In-Ohk	Ouh	Senior Researcher	KDCA
Dr	Brent	Yamamoto	Principal Investigator	Mapp Bio
Dr	Rebecca	Routh	Head of Regulatory Affairs	Mapp Biopharmaceutical, Inc.
Ms.	Tenzin	Wangmo	Regulatory Officer	Medical Product Division, Bhutan Food and Drug Authority
	Julian	Bonnerjea	Vaccine Project Lead	MHRA
Dr.	Nimesh	Gupta	Chief, Vaccine Immunology Lab	National Institute of Immunology
	G.M.Dilini	Gurugalgoda	Pharmaceutical Assessor	NMRA
	Safiya	Mohd Razif	Sen Principal Ass. Director	NPRA
Dr.	Sunate	Chuenkitmongkol	Deputy Director	National Vaccine Institute
Mr.	Kumar	Gaurav	Sr. G.M. - Reg & Govt. Affairs	Panacea Biotec Ltd.
Professor Dame	Sarah	Gilbert	Saïd Professor of Vaccinology	Pandemic Sciences Institute, University of Oxford
Dr	Yangmu	Huang	Deputy Director	Peking University
Dr	Manabu	Inoue	Chief Medical Officer	PMDA
Mr.	Kengo	Kawachi	Reviewer	PMDA
Dr	Sumegha	Asthana	Head, PANPREP	PHFI Instiiute of Public Health Sciences
Ms	Inthiraporn	Choadee	Pharmacist, Practitioner level	Thai Food and Drug Administration
Prof	Leo	Poon	Chair Professor	The University of Hong Kong
Ms	Ngawang	Dema	Technical Officer, EDM	WHO

Appendix 2: Detailed summary—Chikungunya panel on regulatory strategies, benefit–risk considerations, safety database size, and early-outbreak evidence needs

Moderator: Dr. Rubina Bose (CDSCO, India)
Panelists:
Ms. G. M. D. T. Gurugalgoda (NMRA, Sri Lanka)
Dr. Wittawat Viriyabancha (Thai FDA, Thailand)
Dr. Pura Wena A. Clacio-Clores (Philippines FDA, Philippines)
Dr. Yuji Matsukara (PMDA, Japan)
Mr. Anil Chawla (WHO SEARO)

1) **Could regulatory pathways such as the U.S. FDA's Animal Rule or EMA's conditional approval enable accelerated authorization in East, South, and Southeast Asia based on immunological markers, rather than large phase 3 trials that may not be technically or ethically feasible?**

Thailand (Dr. Wittawat Viriyabancha):

He stated that innovative regulatory pathways can support preparedness when large efficacy trials are not feasible, while emphasizing the need to maintain scientific rigor. He noted that Thai FDA has strengthened its regulatory framework for vaccines and innovative medicinal products to support R&D for preparedness-relevant products. While Thailand does not have a direct equivalent of the U.S. Animal Rule, he described mechanisms intended to support regulatory agility. For example, conditional approval may be granted to vaccines or medical products with a favorable benefit–risk profile, with clearly defined post-authorization commitments (e.g., additional studies, enhanced pharmacovigilance, and registries incorporated into risk-management plans). He also noted that emergency use authorization can be applied once the government declares a public health emergency, allowing accelerated timelines.

He also described use of reliance pathways, noting that Thai FDA can leverage assessment reports from reference regulatory authorities to accelerate evaluation, provided scientific justification is strong and post-authorization activities are ensured. He emphasized that innovative pathways should be anchored in a clear evidence rationale and accompanied by enforceable lifecycle obligations.

Japan (Dr. Yuji Matsukara, PMDA):

He noted that chikungunya cases in Japan are limited and are primarily imported, with no observed domestic transmission to date. He added that competent mosquito species are present in Japan and that climate change could increase future risk.

He stated that when clinical endpoint trials are not feasible, PMDA may accept surrogate immunological endpoints if they are scientifically justified. He emphasized that proposed CoPs or protective thresholds should be supported by robust evidence and appropriate assay performance.

He noted that PMDA may request inclusion of Japanese participants in immunogenicity trials or a justification for extrapolation from other populations, given the possibility of population differences in immune responses.

He emphasized that safety evidence is essential and noted that safety concerns contributed to vaccine hesitancy during COVID-19. He stated that when efficacy certainty is limited, regulators may place increased weight on safety characterization and risk-management measures.

He added that post-authorization commitments are important for confirming effectiveness and monitoring safety once vaccines are deployed. He noted that PMDA has not received chikungunya vaccine applications to date, but that licensure could be considered if scientific evidence is sufficient and public health needs change.

Moderator (Dr. Bose):

She summarized that both Thailand and Japan described mechanisms that allow use of surrogate immunological markers under defined conditions, with an emphasis on safety, transparent scientific justification, and post-authorization obligations. Thailand also highlighted reliance pathways, while Japan noted possible expectations for local immunogenicity data or justification for extrapolation.

2) **RWE: Could RWE be used to confirm effectiveness in your agency? Can such data be collected in your health system (e.g., via electronic health records)?**

Philippines (Dr. Pura Wena A. Clacio-Clores):

She stated that the Philippines has made progress in electronic health records (EHRs) and data digitization, but that systems are not yet uniformly implemented nationwide.

She cited examples of systems in use, including iClinicSys in rural health units and iHOMIS (Integrated Hospital Operations and Management Information Systems) in government hospitals. She noted that private hospitals and some private clinics use various validated EHR systems compatible with Department of Health and PhilHealth reporting requirements.

She noted that the EHR landscape remains fragmented across public and private sectors and that improved integration would be needed to generate high-quality RWE at scale. She emphasized that while RWE may not fully substitute for pre-authorization evidence, it can contribute meaningfully when collected systematically and analyzed with appropriate methods.

Thailand (Dr. Wittawat Viriyabancha):

He stated that clinical trial evidence remains central to regulatory decisions, but that RWE can complement decision-making, particularly after authorization. He noted that Thailand has multiple RWE sources, including the universal health coverage database, national surveillance systems, and AEFI reporting platforms.

He added that many hospitals have EHR systems, and that further coordination with stakeholders is needed to standardize and integrate data for analysis.

He noted that for conditionally approved products, RWE is particularly important post-authorization and can inform reassessments, labeling updates, and risk-minimization measures. He emphasized that RWE does not replace pre-authorization evidence but can strengthen the overall evidence base when designed and governed appropriately.

3) **Can regional bodies (e.g., ASEAN, SEARO, WPRO) support harmonized regulatory review, procurement, and distribution of chikungunya vaccines?**

WHO SEARO (Mr. Anil Chawla):

He stated that regional bodies such as ASEAN, SEARO, and WPRO can support regulatory convergence through joint reviews, reliance models, and shared learning. He noted that WHO engages with these networks, while implementation remains the responsibility of member states.

He added that regional coordination can reduce duplication and support more timely access when aligned with national processes.

Role of PMDA as a WHO-listed authority

The moderator asked whether PMDA, as a WHO-listed authority, could support regional harmonization.

Japan (Dr. Yuji Matsukara, PMDA):

He stated that regulatory harmonization can support preparedness for public health emergencies and that PMDA contributes to harmonization across the region through capacity building and information exchange.

He described PMDA's training programs, including recurring courses for regulators from across Asia and, in some cases, in-country training tailored to local needs. He emphasized the importance of bilateral cooperation and ongoing technical exchange.

He noted that PMDA has established bilateral cooperation arrangements with multiple countries in Asia to facilitate exchange of regulatory insights and experience in product review. He stated that these collaborations have supported development of legal frameworks in some countries that allow expedited review of products already approved by reference authorities, including Japan, under defined conditions.

He emphasized that PMDA respects each country's independence in regulatory decision-making and that harmonization efforts should focus on aligning scientific principles and interpretation of evidence rather than producing identical decisions across legal frameworks.

He added that PMDA publishes assessment reports in English and can respond to inquiries from other authorities under appropriate confidentiality arrangements, supporting transparency and shared learning.

4) Additional safety data: What additional safety data are needed for vulnerable populations?

The moderator asked what additional safety data are needed for vulnerable populations.

Philippines (Dr. Pura Wena A. Clacio-Clores):

She noted that additional vaccine safety data may be needed for vulnerable populations, including older adults, children, and pregnant individuals. She highlighted the following areas of interest:

- Incidence and clinical characteristics of breakthrough infections in vaccinated individuals.
- Immunological interactions during co-administration with other vaccines, particularly other flavivirus vaccines.
- Serological cross-reactivity and potential diagnostic interference with other flavivirus infections.
- Risk of antibody-dependent enhancement (ADE), which, although theoretical, has been observed experimentally and must be carefully assessed.
- Incidence of severe reactogenicity in older adults (≥65 years), especially those with underlying medical conditions.
- Safety data for adults over 65 years with acute, chronic, or uncontrolled comorbidities.
- Comprehensive safety data in pregnancy, including pregnancy outcomes, effects on offspring, and the incidence of spontaneous abortion.
- Safety data in children under 12 years of age, for whom evidence is currently lacking.

She noted that where evidence is limited for these populations, additional information may be requested from sponsors either as part of submissions, through labeling updates (e.g., pregnancy use), or through defined post-authorization study commitments.

She added that some of these data may also be generated through post-authorization surveillance and observational studies to evaluate safety outcomes in wider use.

WHO SEARO (Mr. Anil Chawla):

He emphasized the importance of distinguishing among regulatory contexts, including routine licensure, emergency decision-making during pandemics, and authorization during active outbreaks. He noted that in settings with no available vaccines and a risk of escalation, regulators may need to act rapidly while maintaining scientific justification and appropriate safeguards.

He stated that clearly identifying priority populations is central to determining appropriate safety evidence needs. He noted that initial use might prioritize healthcare workers and other high-risk groups, with subsequent expansion guided by evolving evidence and context-specific benefit–risk considerations.

He noted that stepwise approaches—supported by clearly defined evidence requests and risk-management measures—may be appropriate before expanding use to broader populations. He also referenced roles for regulators and mechanisms such as WHO prequalification in clarifying expectations and supporting evidence generation across settings.

He concluded that these contextual considerations are relevant for regulators, policymakers, and other stakeholders when interpreting evidence and planning introduction strategies.

Moderator summary

The moderator summarized that the discussion focused on regulatory pathways and alternatives to large phase 3 efficacy trials, the role of RWE, regional coordination mechanisms, and expectations for additional safety data—particularly for vulnerable populations.

Regulatory pathways and alternatives to efficacy trials

Participants discussed whether mechanisms analogous to the U.S. FDA's Animal Rule could be applied when randomized phase 3 trials are infeasible due to low or sporadic incidence. The discussion emphasized that any pathway relying on surrogate endpoints requires clear scientific justification, fit-for-purpose assays, and defined post-authorization obligations to address residual uncertainty.

Country perspectives

Thailand FDA
The moderator noted that Thailand described conditional approval as an option when benefit–risk is favorable, accompanied by defined post-authorization commitments and enhanced pharmacovigilance. Thailand also highlighted reliance pathways and emergency use authorization mechanisms under declared public health emergencies.

Japan/PMDA
The moderator noted that Japan described acceptance of immunogenicity endpoints as surrogate evidence when clinical efficacy trials are infeasible, provided markers and thresholds are scientifically justified. Japan highlighted the importance of safety characterization, potential expectations for local immunogenicity data or justification for extrapolation, and the role of post-authorization evidence generation in endemic settings.

RWE

Both the Philippines FDA and Thai FDA described RWE as a complementary evidence stream, particularly given constraints on conducting randomized efficacy trials for chikungunya.

Philippines FDA: The Philippines described RWE as potentially useful for confirming effectiveness when studies are methodologically rigorous. The panel noted that electronic health record systems are not yet fully integrated nationwide, which limits the ability to generate RWE at scale.

Thai FDA: Thailand described national data sources that could support post-authorization effectiveness and safety monitoring, including universal health coverage databases, surveillance systems, and AEFI reporting platforms. The panel noted that for conditionally approved products, RWE generated under risk-management plans can inform reassessment and risk-minimization measures.

The moderator summarized that both regulators emphasized RWE as a complement to clinical trial evidence, with differing levels of readiness based on national health data integration.

Additional safety data needs

Across regulators, there was consensus on the need for targeted safety data to fill existing evidence gaps. Critical areas include:

- Breakthrough infections and their clinical characteristics
- Long-term safety
- Co-administration with other vaccines
- Risks such as ADE and serological cross-reactivity
- Safety in special populations:
    - Older adults
    - Children under 12
    - Pregnant or breastfeeding individuals
    - Immunocompromised persons

The moderator summarized that these data inform both regulatory decisions and public health policy and may be generated through a combination of pre-authorization studies and post-authorization surveillance and observational analyses.

PMDA's regional role and harmonization

The moderator summarized that PMDA described its role in supporting regional regulatory capacity building through training, networking, and bilateral cooperation. PMDA emphasized that while harmonization can align scientific principles and facilitate reliance, each authority retains independence in decision-making.

The moderator also noted WHO SEARO's emphasis on regional coordination to support multicountry studies and post-authorization evidence generation, alongside national implementation.

Appendix 3: Detailed summary—Chikungunya panel on public health perspectives for outbreak response, additional data needs, and programmatic feasibility in the absence of a point estimate of efficacy

Moderator: Dr. Jinho Shin (WHO WPRO, Philippines)
Panelists:
Dr. Pragya Yadav (ICMR, India)
Dr. Wenny Indriasari (MOH, Indonesia)
Dr. Sunate Chuenkitmongkol (National Vaccine Institute, Thailand)
Dr. Yookyoung Lee (KDCA, Republic of Korea)

1) Are there mechanisms in place to ensure equitable access across countries with varying income levels?

Indonesia (Dr. Wenny Indriasari, MOH):

She provided an overview of the situation in Indonesia. As a tropical and geographically diverse country, Indonesia experiences multiple mosquito-borne diseases, including malaria, dengue, and chikungunya. She reported that chikungunya cases increased significantly in 2025, with approximately 23,000 suspected cases and 5,000 verified cases—substantially higher than the 2024 figures (approximately 2,300 cases). The highest numbers were reported in West Java and Central Java, with peak activity from January to April during the transition from the rainy to the dry season.

She noted that Indonesia does not yet have an approved chikungunya vaccine. She described national mechanisms for introducing a new vaccine into the immunization program, including HTA, budget impact analysis within the overall fiscal envelope, and evidence-based recommendations from NITAG. She noted that while outbreak response mechanisms exist, chikungunya-specific estimates (e.g., disability-adjusted life years (DALYs) averted compared with other diseases) have not yet been formally assessed.

She noted that, based on Indonesia's dengue experience—in which not all vaccines were covered by the central government—high-burden provinces were able to fund vaccines using provincial budgets. She indicated that a similar approach could be considered for chikungunya in high-burden regions.

She stated that programmatic feasibility across countries with varying income levels depends on timely regulatory decision-making, effective partnerships, and clear policy commitments that prioritize populations at highest risk. She noted that these conditions can support more equitable access once a vaccine is available and countries are prepared to deploy it.

2) Discuss regional and national stockpiles for chikungunya outbreak preparedness.

Thailand (Dr. Sunate Chuenkitmongkol, National Vaccine Institute):

She noted that chikungunya outbreak preparedness is challenging because outbreaks are unpredictable. She stated that in Thailand and Sri Lanka, outbreaks have occurred approximately once per decade, and referenced Indonesia's recent outbreak as an example of substantial activity. She noted that stockpiling—whether national or regional—may be considered, but requires careful planning.

She stated that stockpiling requires planning at both national and regional levels. She noted that for national stockpiling, feasibility varies by country depending on financing systems and operational readiness. For regional stockpiling, she referenced the ASEAN Vaccine Security and Self-Reliance (AVSSR) initiative and noted that the National Vaccine Institute is the focal lead for the vaccine security component. She stated that AVSSR discussions have included pooled procurement and stockpiling, although a regional mechanism is not yet in place. She added that AVSSR 2.0 includes this strategy alongside human resource development and data sharing.

She stated that ASEAN is holding focused discussions on establishing procurement and pooled stockpiling mechanisms, with support from regional partners. She noted that ASEAN stakeholders have reviewed

other models (e.g., PAHO, Africa CDC, and Health Emergency Preparedness and Response Authority [HERA]) to assess potential applicability to the ASEAN context.

She noted that because chikungunya outbreaks are infrequent, stockpiling finished product can be challenging. She identified shelf life as a key constraint: if shelf life is 3–5 years while outbreaks occur roughly every 10 years, countries may need to purchase and potentially replace doses without using them immediately, with associated financial implications.

She noted that longer shelf life could improve feasibility, but emphasized that manufacturers often seek clearer demand forecasts, which remain difficult given unpredictable outbreaks. She stated that ASEAN member states have worked to estimate demand but have not yet reached a conclusion. She noted that partners, including CEPI, may support forecasting approaches and engagement with manufacturers.

Moderator (Dr. Shin):

He noted that stockpiling raises practical questions, including whether to stockpile finished vaccine or to use contractual arrangements for bulk materials and surge production, and emphasized the relevance of these choices for agile outbreak response.

3) How can local manufacturing capacity be boosted?

Indonesia (Dr. Wenny Indriasari, MOH):

She described Indonesia's current vaccine manufacturing capacity and the policy tools used to strengthen domestic production.

She reported that Indonesia has capacity for approximately 380 million vaccine doses, spanning conventional platforms and newer technologies such as mRNA. She described a hybrid manufacturing architecture with three manufacturers—one state-owned and two private—intended to support risk-sharing: BioFarma focuses on development and research, while other partners focus on access-oriented production supported by technology transfer.

She described a strategy to strengthen domestic manufacturing that includes sovereign investment for infrastructure (e.g., state capital injections), regulatory reforms intended to support accelerated approvals, structured technology transfer partnerships, private-sector engagement, and demand assurance through procurement policies and local content requirements.

4) What are public perceptions and potential hesitancy regarding chikungunya vaccines, especially live-attenuated versus VLP platforms?

Republic of Korea (Dr. Yookyoung Lee, KDCA):

She noted that vaccine hesitancy is not unique to chikungunya and affects many immunization programs. Following COVID-19, the Republic of Korea experienced increased public attention to contraindications and adverse events, including misinformation, which influenced perceptions.

She stated that public perceptions depend on familiarity with the platform, perceived safety, and outbreak urgency. She noted that live-attenuated vaccines can raise concerns among some communities because they contain a weakened virus, including concerns about potential risks for older adults or immunocompromised individuals if decision processes are not well communicated.

She added that VLP vaccines are often perceived as safer because they contain no replicating virus. She noted that newer platforms can still raise questions about durability, effectiveness, and longer-term safety.

She concluded that acceptance depends strongly on confidence in the decision-making process. She stated that trust increases when policies are grounded in credible evidence and authorities communicate clearly about benefits and uncertainties. She noted that ongoing safety monitoring and real-world effectiveness studies, with transparent reporting, can strengthen confidence over time.

5) Do you believe gaps in efficacy data can be filled through RWE?

India (Dr. Pragya D. Yadav, ICMR):

She stated that RWE can play an important role in addressing gaps in direct efficacy data for chikungunya vaccines, but should complement—rather than fully replace—clinical trials where trials are feasible.

She noted that conducting phase 3 trials is difficult because chikungunya outbreaks are geographically and temporally unpredictable, making it challenging to select trial sites where sufficient cases will accrue within a reasonable timeframe. She stated that incidence varies by region and year, which can require large sample sizes and extended follow-up periods that increase cost and operational complexity. She also noted that outbreaks can rise and fall quickly, limiting the window for enrollment.

She noted additional challenges, including high baseline seropositivity in some populations (e.g., an 18% seroprevalence estimate reported in India), which can lower incident case counts and reduce power to measure vaccine effectiveness. She also noted that ethical considerations during outbreaks may limit feasibility of placebo-controlled trials.

She noted that RWE can be generated through retrospective and prospective cohort studies, case–control studies, and test-negative designs using surveillance and health system data. She stated that these approaches can estimate outcomes such as symptomatic infection, hospitalization, and outbreak reduction, and can reflect performance across diverse populations.

She added that RWE enables evaluation of longer-term effectiveness and post-authorization safety, which may be difficult to capture fully in pre-licensure trials.

She noted that observational evidence can be affected by confounding and selection bias. She emphasized that credible RWE requires high-quality surveillance, standardized case definitions, robust epidemiological designs, and transparent analytical methods. She noted that COVID-19 provided examples of how such approaches can be implemented and interpreted.

6) What are anticipated operational challenges (e.g., cold chain, training, human resources), and how are they being addressed?

Republic of Korea (Dr. Yookyoung Lee, KDCA):

Introducing a chikungunya vaccine during an outbreak presents several operational challenges. As noted, ensuring sufficient cold-chain capacity is particularly critical in tropical and resource-limited settings. Comprehensive mapping of storage capacity, contingency planning for supply interruptions, and integration of the vaccine into existing immunization systems are essential for a resilient delivery strategy.

Frontline personnel must be adequately trained on product characteristics, contraindications, and safety-monitoring requirements. Clear technical guidelines, rapid training modules, and supportive supervision are necessary to ensure safe, consistent implementation. Human resources may already be overstretched during outbreaks, as surveillance, case management, vector control, and vaccination campaigns typically occur simultaneously. Strengthening staffing mechanisms and improving coordination across programs can help reduce system strain and support continuity of services.

Another important challenge is generating real-time evidence while vaccination is underway. As observed during COVID-19, vaccination programs may proceed even as scientific knowledge continues to evolve. Countries must have systems in place to monitor safety, effectiveness, and potential viral changes in real-world settings, enabling timely policy adjustments when new evidence emerges.

Operational readiness, continuous data analysis, and transparent communication are essential—not only for effective vaccine deployment, but also for maintaining public confidence in government-led vaccination strategies.

7) What is most important to strengthen in the broader end-to-end ecosystem to enable this RWE work?

India (Dr. Pragya D. Yadav, ICMR):

For chikungunya vaccine, the most critical requirement is a robust end-to-end RWE ecosystem, and this ecosystem must ensure that real-world data are reliable, interoperable, analytically robust, and acceptable to regulators, with the following essential elements.

- First is a high-quality and integrated real-world data system, which has good-quality real-world data collected from multiple sources, including a surveillance system that detects chikungunya cases, a vaccination registry of who received the vaccine, electronic health records, hospital databases capturing outcomes, and laboratory systems confirming infections. When these data sources are linked together, researchers can compare infection rates between vaccinated and unvaccinated people during outbreaks to estimate how well the vaccine works in real-life settings.

- Second is standardized and compatible data collection. Studying chikungunya vaccine data from different systems requires standardized and connected datasets with common case definitions, similar laboratory testing methods, uniform vaccination records, and databases that link surveillance and health data.

- Third, and most important, is strong epidemiological study designs. Based on observational data, strong study designs are needed to reduce bias and ensure reliable results. Common approaches to assess vaccine effectiveness include test-negative case-control studies, retrospective cohort studies using health records, and outbreak-based effectiveness studies. In addition, appropriate statistical methods and weighting can help control confounding and make findings closer to those obtained from randomized trials.

- Fourth point is real-time surveillance and outbreak detection.

- Fifth is regulatory frameworks and policy acceptance. This was discussed in great detail. The value of real-world evidence depends on clear regulatory frameworks that support vaccine-effectiveness assessments. Key requirements include a clear analysis plan, high-quality data, well-defined study designs, and independent validation of results.

- Last point is multisectoral collaboration and data governance, which includes close collaboration between public-health agencies, research institutions, hospitals, labs, vaccine manufacturers, and regulatory authorities. Strong data governance is essential to ensure privacy, ethical use of data, and safe sharing of information across institutions.

Questions from the audience:

Regarding public-health implications of chikungunya: Can modeling mitigate these policy implications? The questioner noted that there are good pre-existing real-world data (outbreaks, sero-epidemiology, safety, and clinical-trial immunogenicity data). If such data are available at the national level, can modeling mitigate these issues, and what would be the acceptance of translating model-based evidence into policy?

India (Dr. Pragya D. Yadav, ICMR):

Dr. Yadav stated that such an approach would be valuable and that many participants would like to see these data become feasible. She noted that during the COVID pandemic, similar approaches were attempted, with some success but not an ideal outcome. She added that if such an approach becomes feasible for chikungunya, it would be welcome and would warrant continued effort in that direction.

India (Dr. Nivedita Gupta, ICMR):

Dr. Gupta noted that chikungunya occurs in cyclical patterns in India, but that the periodicity is uncertain and has varied across recent years. She stated that if vector data were systematically integrated—given that chikungunya is a vector-borne disease—through geotagging and hotspot mapping of mosquito

breeding, it could support identification of probable hotspots for chikungunya and dengue. She emphasized that this cannot be done in a silo and must include both diseases. She added that if chikungunya virus could be detected in mosquitoes early and outbreaks could be predicted, modeling could contribute; however, this would require a great deal of high-quality data to feed into models. She noted that prediction would rely first on strengthened vector surveillance, such that when vector breeding crosses a threshold, human outbreaks follow, and stated that reaching this point remains a longer-term objective.

For chikungunya and many viral diseases, neutralizing antibodies are easy to measure and used as surrogate markers. If one adds other components to vaccines that show preclinical efficacy and do not decrease neutralizing antibody titers or raise safety concerns, would regulators consider that acceptable? Especially since T-cell responses and other markers are hard to measure in large clinical trials.

EMA (Dr. Marco Cavaleri):

Dr. Cavaleri indicated that in principle, yes, it can be done. You can add new components and justify why, as long as you achieve the required level of neutralizing antibodies and maintain the overall safety profile.

Are recommending bodies prepared to make recommendations based on vaccines approved using surrogate markers (i.e., CoPs) rather than direct protection data? This is a common challenge in NITAG decision-making and in interactions between regulators and NITAGs. Strategic Advisory Group of Experts on Immunization (SAGE) has a working group on chikungunya vaccines.

Despite endemicity in Asia, will countries take a reactive approach—waiting for outbreaks—rather than broad routine vaccination?

Thailand (Dr. Sunate Chuenkitmongkol, National Vaccine Institute):

In Thailand, NVI and ACIP work closely with epidemiology bureaus to advise during outbreaks that require vaccines for control. The speaker noted that, as in COVID, many heterologous schedules were used and all data were provided to ACIP for scientific review. The speaker added that implementation is challenging due to competing priorities—dengue being a major one. Stockpiling chikungunya vaccine may be considered, but broad rollout depends on understanding target groups and disease burden.

Moderator Summary

The moderator noted that RWE is pivotal for chikungunya vaccines because outbreaks are sporadic and unpredictable. The moderator emphasized that data standardization across systems, epidemiological study design, and real-time surveillance are essential for reliability and comparability of findings.

The moderator noted that clear regulatory frameworks and policy acceptance help ensure RWE is appropriately used to support vaccine approvals and recommendations. The moderator added that multisectoral collaboration and strong data governance are foundational, and highlighted that the experiences shared reflect Asia-Pacific commitment to advancing vaccine development and preparedness for vector-borne diseases.

The moderator encouraged continued collaboration, prioritization of rigorous study designs, and investment in integrated surveillance systems to strengthen responses to emerging health threats and help ensure effective vaccines reach those who need them most.

Appendix 4: Detailed Summary—Nipah panel discussion on the adequacy of current regulatory strategies, factors to inform regulatory benefit–risk analyses, the size of the safety database, and early-outbreak evidence needs

Moderator: Dr. Marco Cavaleri (EMA, EU)
Panelists:
Dr. Rubina Bose (CDSCO, India)
Dr. Erlina Fitriyani (BPOM, Indonesia)
Dr. Mohd Rezuan (NPRA, Malaysia)
Dr. Wittawat Viriyabancha (Thai FDA, Thailand)

Moderator (Dr. Marco Cavaleri):

What considerations would inform potential approval of a Nipah vaccine without clinical efficacy data (e.g., approval based on an animal model with immunobridging to humans), and what regulatory route(s) exist for such early approval?

Thailand (Dr. Wittawat Viriyabancha, Thai FDA):

Thai FDA noted that Nipah outbreaks are sporadic, geographically limited, and highly lethal, making traditional efficacy trials impractical. The agency indicated openness to approvals based on scientifically justified immune markers (e.g., neutralizing antibodies and/or cellular responses), provided correlates are supported by robust non-clinical challenge data and consistent immunogenicity. It emphasized that surrogate markers should be assessed within a totality-of-evidence framework incorporating human immunogenicity, relevant animal models, and epidemiologic context. Thai FDA also highlighted the importance of assay standardization and reproducibility, ideally supported by WHO or other international expert bodies. It noted that enhanced pharmacovigilance and real-world effectiveness monitoring would be expected post-authorization to confirm performance in practice.

Indonesia (Dr. Erlina Fitriyani, BPOM):

BPOM stated that it is open to using immunogenicity data as evidence of effectiveness when a well-established immune CoP exists. In outbreak settings where human efficacy trials are not feasible, BPOM noted that correlates may be inferred from non-clinical studies, passive protection studies, comparisons with similar vaccines, or (where available) human challenge data, while emphasizing that correlates derived from animals may not fully reflect human immunity. BPOM confirmed that it is open to using animal-model data for initial Nipah vaccine approval provided the evidence is scientifically robust and sufficiently justified, and indicated that it would also consider alternative data sources beyond traditional clinical trials in emergency situations. BPOM noted, however, that it does not currently have a formal conditional or special approval pathway, while indicating openness to developing such mechanisms in the future.

India (Dr. Rubina Bose, CDSCO):

CDSCO emphasized that Nipah outbreaks in India are small, sporadic, and unpredictable, making traditional human efficacy trials impractical. The agency indicated openness to use of surrogate markers derived from non-clinical studies—including validated animal models and passive-transfer studies in NHPs—to infer protection. CDSCO noted that a defined neutralizing-antibody threshold would be preferable; however, it indicated that other immunogenicity measures (e.g., seroconversion) may be considered when thresholds cannot be established. CDSCO stated that, for regulatory decision-making, human immunobridging studies conducted in the Indian population are expected given local epidemiology and population diversity. It also noted expectations for post-authorization confirmatory studies (e.g., phase 4 trials, observational studies, or active surveillance) to verify real-world effectiveness and safety after approval.

CDSCO added that candidates developed outside India may be considered if dossiers include complete non-clinical packages, but reiterated that immunobridging in the Indian population remains essential for

final approval given the disease's relevance to India. It noted that data from other affected countries may support evaluation, particularly for comparison of safety and immunogenicity. CDSCO also referenced available priority approval pathways and outbreak-specific provisions, while reiterating expectations for Indian data followed by post-authorization studies to confirm effectiveness and safety in the local context.

Malaysia (Dr. Mohd Rezuan, NPRA):

NPRA noted that this would be the first time applying an Animal Rule–type approach, but indicated agreement with the rationale given the infeasibility of large efficacy trials for Nipah. NPRA noted that Malaysia does not have an established process for such approvals and would therefore rely heavily on evaluations by reference regulators (e.g., FDA and MHRA). It stated that the agency is broadly aligned with the evidence elements described by other panelists and indicated confidence that developers' approaches follow international standards. NPRA indicated that conditional authorization could be considered using this approach and stated that there are no objections in principle to adopting it, given appropriate supporting evidence and post-authorization expectations.

Moderator (Dr. Marco Cavaleri):

The moderator noted broad alignment on a feasible path for Nipah vaccine approval and asked whether regulators would be comfortable addressing strain differences (Bangladesh vs Malaysia) primarily through cross-neutralization and immune-response comparisons, rather than requiring separate efficacy demonstrations for each strain.

Thailand (Dr. Wittawat Viriyabancha, Thai FDA):

Thai FDA acknowledged that strain differences may affect transmission and vaccine performance. It noted that early *in vitro* and preclinical data can indicate cross-protection, but stated that broader evidence is generally expected, including animal challenge studies and immunogenicity assessments against relevant circulating strains, before authorization. It also noted that, even under emergency use authorization or conditional approval, additional real-world effectiveness data would be expected to confirm cross-protection and support benefit–risk assessment, and that maintaining public confidence requires balancing flexibility with scientific rigor. Regarding the Malaysia strain specifically, Thai FDA indicated that direct challenge data are ideal, but that a scientifically sound justification based on cross-neutralization and CoPs could also be acceptable.

Indonesia (Dr. Erlina Fitriyani, BPOM):

BPOM stated that for different Nipah strains, *in vitro* or early preclinical data alone are insufficient. It indicated that antibody cross-reactivity studies are needed to assess whether neutralizing responses extend across strains, given the potential for differences in immune responses. BPOM also stated that animal challenge studies are expected to demonstrate protection, alongside phase 1–2 human safety and immunogenicity data and relevant immune correlates or surrogate markers (e.g., neutralizing antibody titers and/or cellular immune responses).

Moderator (Dr. Marco Cavaleri):

The moderator noted that available evidence suggests the two Nipah strains likely share a mechanism of protection, which could support reliance on Bangladesh-strain animal-model data, while noting that additional Malaysia-strain data could help maintain public confidence. The moderator further noted that BPOM indicated preliminary comfort with an approval approach based on a Bangladesh-strain animal model and characterization of CoPs, provided the vaccine shows similar immune responses across strains, supported at least by phase 1 or phase 2 human immunogenicity data.

India (Dr. Rubina Bose, CDSCO):

CDSCO stated that vaccines developed in India should be based on the Indian Nipah strain, but should also demonstrate cross-reactivity with Bangladesh and Malaysia strains given regional relevance. For imported vaccines, CDSCO indicated that non-clinical evidence of cross-reactive immunity is expected and that, if clinical efficacy data are not available, an immunogenicity study in the Indian population based on a correlate-of-protection framework would be needed. Overall, CDSCO emphasized strain-

appropriate development, cross-reactivity data, and Indian-population immunogenicity evidence before approval.

Moderator (Dr. Marco Cavaleri):

The moderator stated that the Bangladesh strain produces more uniform and severe disease in animal models, providing a strong basis for establishing protection mechanisms. The moderator noted that if the mechanism of protection is shared across strains and neutralization profiles are similar, bridging from Bangladesh-strain data to Malaysia- and India-relevant strains could be feasible without requiring separate animal models; however, if meaningful differences in neutralization emerge, additional data and discussion may be needed. The moderator emphasized a rational, science-based approach to demonstrate protection across Bangladesh, Malaysia, and India strains.

Malaysia (Dr. Mohd Rezuan, NPRA):

NPRA noted that Nipah virus strains differ in transmissibility, with the Bangladesh strain described as the most infectious. It indicated that characterization data across relevant strains are expected before strains are used in animal models or human trials, and referenced lessons from COVID-19 regarding viral evolution and strain emergence. NPRA stated that as long as developers can demonstrate protective immunity across strains, the agency would have no objection to accepting such data; however, it emphasized the need for clear evidence and characterization to understand potential strain differences prior to approving related studies or submissions.

Indonesia (Dr. Erlina Fitriyani, BPOM):

Indonesia similarly stated that it is open to regional collaboration, highlighting its existing participation in joint assessments with other Asian regulators, which has accelerated vaccine approvals during outbreaks. Collaboration enables shared perspectives and capacity building, but Indonesia emphasized that final decisions rest with each nation's own regulatory authority and national committees, ensuring no compromise of regulatory sovereignty.

Moderator Summary

Dr. Cavaleri closed the panel discussion with broad agreement among regulators that initial Nipah vaccine approval based on well validated animal models is both reasonable and workable. All agencies recognized that human efficacy trials are not feasible and supported relying on animal model protection data—provided that developers can demonstrate that protection extends across multiple Nipah strains, not only the one used in the model. How best to handle bridging to human immunogenicity data remains an important next step, with a shared focus on ensuring that clinical development is scientifically robust yet efficient. There was also a strong and consistent openness to regional collaboration. Regulators expressed willingness to work together on data review, information exchange, and joint discussions to build confidence in regulatory decisions—while still maintaining each agency's full independence and authority. Collaboration could also support the creation of regional core protocols for post approval or outbreak triggered studies, helping countries coordinate evidence generation when cases occur. Post approval studies were recognized as essential for confirming effectiveness and guiding public health actions. Regulators further emphasized their readiness to collaborate not only within the region but also with agencies outside Asia, including through mechanisms that allow multinational participation in scientific advice. The moderator highlighted that the EMA is eager to include Asian regulators in such discussions, allowing all sides to share insights and strengthen confidence in regulatory decisions.

Appendix 5: Detailed summary—Nipah panel discussion on public health perspectives on factors to consider for outbreak response, additional data to support vaccine use, and related considerations under scenarios of increased human-to-human transmission

Moderator: Dr. Sylvie Alonso (PREPARE, Singapore)
Panelists:
Dr. Nivedita Gupta (ICMR, India)
Dr. Pragya Yadav (ICMR, India)
Dr. Madhur Gupta (WHO SEARO, India)
Dr. Anuradha Poonepalli (HSA, Singapore)
DG Azuana Binti Ramli (MOH, Malaysia)
Dr. Wichan Bhunyakitikorn (MOH, Thailand)

Moderator question: How would Singapore evaluate a Nipah vaccine, and what evidence requirements would apply?

Singapore (HSA):

HSA stated that its approach aligns with that of other regulators: because traditional efficacy trials are not feasible, scientifically justified immune correlates or surrogate markers—supported by validated animal-challenge models and statistically derived CoPs—may be used in place of efficacy data. HSA noted that these correlates would then be bridged to humans and supported by human immunogenicity studies. HSA cited prior experience applying this framework for mpox vaccines, where animal-model data, immunogenicity, and historical cross-protection informed approval with post-authorization conditions such as effectiveness monitoring during outbreaks. HSA noted that Singapore maintains baseline Nipah surveillance and is open to reviewing vaccines during inter-epidemic periods under priority review. During outbreaks, HSA indicated that it can use its Pandemic Special Access Route, which enables rolling submissions and rapid approval, as used during COVID-19. HSA also stated that it does not require local clinical studies and can accept multicenter or foreign-generated data, consistent with past practice.

Moderator question: How does Singapore engage with other regulators in the region, and is such collaboration routine—particularly for outbreaks that could affect Singapore?

Singapore (HSA):

HSA stated that it regularly collaborates with international and regional regulators through multiple platforms. It noted that during COVID-19, it participated in the COVAX RAG and remains an active member of the Access Consortium (with Australia's Therapeutic Goods Administration [TGA], Health Canada, the UK MHRA, and Switzerland), conducting joint reviews, sharing workload, and producing joint assessment reports while retaining independent regulatory decisions. HSA also described ongoing discussions with the U.S. FDA, EMA, and the UK, and participation in the ASEAN Joint Assessment Group, noting completion of a recent joint review. HSA indicated that it can also engage with WHO to monitor outbreaks. Singapore emphasized using these platforms during emergencies to harmonize requirements, align on study endpoints and designs, and avoid duplicative or conflicting expectations across countries.

Moderator question: From a public health preparedness perspective, what Nipah surveillance systems are in place in panelists' countries?

India (ICMR; Dr. Nivedita Gupta):

Dr. Gupta stated that India transitioned from pathogen-based to syndromic surveillance after COVID-19. She noted that priority pathogen lists have been developed for major clinical syndromes, including acute encephalitis, diarrhea, fever and acute respiratory illness. Across India's 167 Virus Research and Diagnostic Laboratories, selected sites routinely test weekly samples for Nipah using an established algorithm, which enabled rapid recent detection of a Nipah case in West Bengal. She also described India's National One Health Mission, under which multidisciplinary outbreak-response teams investigate

spillover events and animal reservoirs. She added that India is working with domestic manufacturers to ensure affordable diagnostics for broad deployment.

India (ICMR; Dr. Pragya Yadav):

Dr. Yadav provided historical context, noting that during India's first major Nipah outbreak, high mortality and limited biocontainment capacity hindered response. She stated that India has since strengthened its infrastructure by establishing BSL-3 and BSL-4 laboratories, deploying mobile BSL-3 units, training healthcare and laboratory workers, and developing point-of-care diagnostics in collaboration with industry. She noted that India now has a BSL-3 network of 23 laboratories capable of testing 39 pathogens, including Nipah. She stated that these coordinated efforts—along with awareness campaigns and rapid field investigation capacity—have enabled containment of outbreaks at the index case and ongoing readiness through refined testing algorithms and integrated surveillance.

Malaysia (MOH):

Malaysia described Nipah surveillance using a One Health approach, coordinating the Ministry of Health with the Department of Veterinary Services and the Department of Wildlife and National Parks. Surveillance was described as including priority sampling of bats, periodic sampling of pigs (the intermediate host in the 1998 outbreak), and human surveillance for unexplained acute encephalitis and severe acute respiratory infections, which must be reported.

Thailand (MOH):

Thailand stated that although it has not had Nipah cases, it has learned from India's response and integrated Nipah into its preparedness system. Hospitals and laboratories must report any Nipah detection within three hours to the Department of Disease Control. Thailand described One Health surveillance of wildlife and livestock and syndromic surveillance for encephalitis and respiratory disease. Laboratory capacity was described as currently limited to a few BSL-3 laboratories, with expansion planned. Thailand noted that any decision to use vaccines would involve the National Vaccine Institute and the ACIP.

Singapore (MOH/HSA):

Speaking on behalf of public health authorities, HSA noted that Nipah is a notifiable disease in Singapore and is subject to continuous baseline One Health surveillance, including monitoring bats, wastewater, and environmental sources. Singapore was described as strengthening laboratory and BSL-4 capacity and maintaining outbreak-response protocols. During an outbreak, Singapore was described as increasing border and animal-import surveillance; while no Nipah vaccines are currently available, MOH would consider stockpiling or advance purchase agreements in the future.

Moderator question: How would countries ensure vaccine supply if a Nipah vaccine were approved during an outbreak, particularly where local manufacturing capacity is limited?

Malaysia (MOH):

Malaysia stated that COVID-19 highlighted the importance of securing both availability and affordability of vaccines. To be better prepared, Malaysia indicated it would prioritize advance purchase agreements with manufacturers. Rather than stockpiling large quantities domestically—which requires storage space and risks expiry—Malaysia preferred agreements in which manufacturers hold stock at their own facilities and supply doses when needed. Malaysia indicated that a small domestic stockpile could be maintained, but that the bulk would remain offshore. It emphasized the need for clear contractual terms (e.g., pricing, logistics, and exit clauses) to ensure timely and reliable access when outbreaks occur.

Moderator note: The moderator noted challenges related to expiration dates. Malaysia agreed, noting that during COVID-19, manufacturers produced fresh batches upon request, highlighting the importance of balancing small local reserves with secure offshore supply backed by strong agreements.

India (ICMR; Dr. Nivedita Gupta):

Dr. Gupta stated that India has decided not to stockpile a Nipah vaccine due to resource constraints. Instead, she indicated that the national strategy is to maintain readiness among domestic vaccine manufacturers so that doses can be produced rapidly within weeks when needed. She noted that manufacturers are encouraged to keep products development-ready, complete at least phase 1 trials, and remain positioned to supply other countries that may choose to stockpile. She added that ICMR is working with CEPI to define use cases for a Nipah vaccine, including identifying priority populations and developing protocols to prepare communities for vaccine acceptance. She noted that vaccine uptake may be low before an outbreak, whereas demand for monoclonal antibodies increases rapidly once cases appear; she therefore emphasized the importance of community sensitization and careful target-population planning alongside continued support for domestic manufacturing capacity.

Moderator question: What procurement approach would countries prefer if a Nipah vaccine became available?

Thailand (MOH):

Thailand stated that it has not yet reached a conclusion on procurement strategy. Internal discussions have focused first on whether any national stockpile is needed, given the rarity of Nipah in the region. Thailand indicated that the first priority would be public health measures—hygiene, sanitation, and education—before vaccination. It noted that decisions about use of a Nipah vaccine would be led by public health specialists and the National Vaccine Institute, followed by ACIP recommendations. If vaccination were deemed necessary, Thailand indicated that procurement options would then be considered; given the disease's rarity, it suggested a regional stockpile may be more practical than maintaining a national supply.

Malaysia (MOH):

Malaysia described a recent ASEAN experience with pooled procurement for mpox, coordinated by Brunei using leftover COVID-19 funds. Malaysia noted that this approach supported regional stock security and improved pricing through economies of scale; however, it also highlighted a key operational lesson: when mpox vaccines arrived in Malaysia, they lacked domestic regulatory approval, delaying use. Malaysia therefore emphasized that pooled procurement for Nipah would require rapid regulatory readiness so that procured vaccines can be used immediately during outbreaks.

Moderator question: If a Nipah vaccine became available—either during an outbreak or in response to an imported case—how would countries approach vaccination, and which populations would be prioritized?

India (ICMR; Dr. Nivedita Gupta):

Dr. Gupta stated that healthcare workers would be the first priority group. She added that vaccination could also target people living in forest-fringe areas with high bat exposure and individuals with occupational risks, such as those frequently entering forested zones. She noted that some candidate Nipah vaccines appear to induce antibody responses within days, suggesting that close contacts of confirmed cases could also be vaccinated during outbreaks. She stated that broader population vaccination is unlikely to be justified beyond these groups.

Thailand (MOH):

Thailand emphasized that vaccination strategy depends on the nature and level of the threat. It noted that Nipah infection is typically linked to specific high-risk exposures rather than widespread transmission; accordingly, Thailand stated it would prioritize targeted immunization and ring vaccination, drawing on prior outbreak-response models. Thailand also noted that the rarity of Nipah provides time to evaluate data carefully before deploying a vaccine.

Moderator note: The moderator noted that strategy may also depend on how quickly the vaccine induces protection: candidates requiring prime–boost schedules may be better suited for preventive use, while vaccines offering rapid protection could support reactive, outbreak-focused vaccination.

Malaysia (MOH):

Malaysia stated that, based on current candidates that appear to generate fast protection, reactive vaccination of high-risk groups would be the preferred and most cost-effective approach. Malaysia emphasized that healthcare workers and laboratory staff should be prioritized, referencing Malaysia's 1998 experience in which fear among medical personnel underscored the importance of ensuring that frontline workers feel protected and confident in continuing duties during outbreaks.

Moderator question: How does WHO support public health agencies during emergencies and in inter-epidemic periods?

WHO SEARO:

WHO SEARO stated that the COVID-19 pandemic transformed global regulatory collaboration, creating unprecedented cooperation among regulators, manufacturers, and international agencies. Building on this experience, WHO described support to countries that includes: regulatory strengthening (including benchmarking, continuous support, and establishing agile emergency use authorization pathways); coordinated regulatory inspections and harmonized processes across agencies; integration with the WHO R&D Blueprint (including preparedness of clinical trial protocols, manufacturing-site readiness, and deployment frameworks through outbreak-response mechanisms); support for advance manufacturing commitments and partnerships with CEPI, Gavi, and others for vaccine development and procurement; efforts to establish global vaccine stockpiles and foster technology transfer through the Health Technology Access Pool to expand biomanufacturing capacity across Southeast Asia; and broader capacity building. WHO noted that India, Thailand, and Indonesia have significant vaccine-manufacturing potential and referenced India's role in supplying a substantial proportion of WHO-prequalified vaccines. WHO emphasized that these multilayered strategies—regulatory support, manufacturing readiness, coordinated trials, and international collaboration—are important for strengthening regional preparedness for a future Nipah vaccine.

Moderator question: What factors drive vaccine hesitancy, and why might acceptance of a Nipah vaccine be low even for high-risk populations?

India (ICMR; Dr. Nivedita Gupta):

Dr. Gupta stated that vaccine hesitancy in India is strongly influenced by perceived risk and visible mortality. She noted that when COVID-19 vaccines were first rolled out in early 2021, uptake was low, including among healthcare workers, and increased only after the high mortality of the Delta wave. She added that when the milder Omicron wave arrived later, booster uptake declined, illustrating that fear of severe disease and death drives acceptance. She also noted that negative media coverage, misinformation about rare adverse events, and viral social-media narratives can amplify hesitancy and overshadow balanced benefit–risk information. She stated that this environment has complicated recruitment for India's ongoing large dengue vaccine trial, particularly in some southern states where skepticism is higher. She emphasized that for a Nipah vaccine targeting a rare disease, acceptance may be even lower unless focused on specific high-risk groups, and highlighted the need to integrate community engagement, benefit–risk communication, and behavioral insights into vaccine development plans from the outset. She also noted the value of structured protocols to understand barriers to uptake and to sensitize communities early so that prioritized groups are prepared to accept vaccination when needed.

Moderator question: Do other countries foresee challenges in public acceptance of a Nipah vaccine, given that target populations would likely be limited rather than the general public?

Thailand (MOH):

Thailand stated that its concerns are similar to India's and emphasized that healthcare and public health professionals play a decisive role in influencing vaccine uptake. Thailand noted that if these professionals are confident and consistently recommend vaccination, public hesitancy can be reduced.

Malaysia (MOH):

Malaysia emphasized that acceptance depends on communication, trust, and clear explanation of benefits and risks, and highlighted the importance of public trust in regulators, particularly regarding safety monitoring. Malaysia also noted that if communication fails during a crisis, mandatory vaccination policies could be implemented under emergency or disaster conditions to protect public safety, as occurred in some contexts during COVID-19.

Singapore (HSA):

Singapore noted that trust and transparency are crucial, especially when approvals occur via expedited pathways. It noted that during COVID-19 some people interpreted rapid authorization as cutting corners; Singapore described addressing this through transparent communication, explaining that evaluations still met rigorous safety and efficacy standards. Singapore also noted routine publication of adverse-event reports and contextualization of risks (e.g., myocarditis risk from vaccination versus infection), which supported maintenance of public confidence.

WHO SEARO:

WHO SEARO emphasized that strong, well-coordinated communication strategies are essential during emergencies and in inter-epidemic periods. It highlighted India's national immunization program as an example, noting that designated spokespersons engage state-level policymakers with consistent, evidence-based messages about new vaccines, supported by written policy briefs. WHO emphasized that community engagement, trust building, involvement of local leaders, and transparent reporting of adverse events are critical to counter misinformation. It noted that deliberate efforts to deliver positive, evidence-based messaging when new vaccines are introduced can help balance negative media narratives and maintain public confidence.

The moderator agreed that trust must be built before crises occur, noting that once an outbreak begins there is limited time to address hesitancy. The moderator closed the discussion by thanking panel members for their contributions.

Appendix 6: Detailed Summary - Panel: advancing KFD vaccines—regulatory, public health, and development scenarios

Moderator: Dr. Marco Cavaleri (EMA)
Panelists:
Dr. Nivedita Gupta (ICMR, Delhi, India)
Dr. Pragya Yadav (ICMR-NIV, Pune, India)
Dr. Kasi Shankar Venugopal (Assistant Drugs Controller India [ADC(I)], CDSCO, India)
Dr. Madhur Gupta (WHO SEARO, India)

Moderator introduction and question: The moderator outlined the session's focus on vaccine development, the regulatory role in potential approval, and the public health implications of implementing vaccination campaigns. The moderator asked whether lessons from similar vaccination programs could guide the approach for a KFD vaccine, what regulatory pathways and realistic timelines for licensure and deployment might be expected, and what minimum data requirements and post-authorization expectations should be anticipated.

India (CDSCO):

CDSCO stated that for indigenously developed products, India has a targeted 30-day regulatory review timeline, as defined in the New Drugs and Clinical Trials Rules. CDSCO noted that the same pathway has been used for KFD, and that phase 1 approval has already been granted. Regarding the future pathway, CDSCO indicated that an accelerated approval process would be considered because KFD is India-specific and life-threatening; under this approach, a waiver of phase 3 trials may be considered, with post-authorization studies expected to generate additional safety and effectiveness data.

CDSCO added that the earlier KFD vaccine was approved in the 1980s before Schedule Y regulations were established. It noted that the vaccine was ultimately considered insufficiently effective, partly due to limited immunogenicity data, and was withdrawn. CDSCO also noted that ICMR has since isolated a new strain, enabling development of the current candidate vaccine.

WHO SEARO:

WHO SEARO noted that India has extensive experience with KFD and that the disease is geographically confined to the Western Ghats, enabling focused vaccine trials and targeted immunization strategies. WHO SEARO highlighted policy and regulatory lessons from COVID-19, including emergency use authorizations, accelerated pathways, rolling reviews, and regulatory flexibility for platform technologies, noting that similar approaches could be adapted for KFD. WHO SEARO emphasized India's political and technical leadership, particularly from ICMR and the National Institute of Virology, and noted ongoing maintenance of active research pipelines.

Based on current progress, WHO SEARO suggested that if bridging studies and updated immunogenicity and manufacturing data are satisfactory, licensure could be feasible by 2026. It noted, however, the need for a robust pharmacovigilance and safety-monitoring framework post-authorization. WHO SEARO added that adoption in other regional countries could follow within the next one to two years.

Moderator follow-up: The moderator noted that the proposed timeline appeared optimistic and, noting that 2026 is the current year, asked CDSCO for its perspective.

India (CDSCO):

CDSCO stated that the Safety Monitoring Board has reviewed the available safety data, and noted expectations that the manufacturer would soon submit the phase 2 protocol along with the phase 1 report, indicating continued progress toward the projected timeline.

India (ICMR):

ICMR stated that the IIL team, after completing 56 days of follow-up in phase 1, would move into phase 2 studies and, in parallel, expects to generate NHP data. ICMR noted that phase 1 results and NHP challenge data would guide next steps. It emphasized adopting a strategy similar to the COVID-19 vaccine development approach, integrating early phase 1–2 human data with small and large animal studies for regulatory decision-making. ICMR noted that phase 3 trials are not expected to be feasible, and that an approach analogous to Chikungunya vaccine—relying on immunogenicity and post-authorization follow-up—may be needed. ICMR added that the earlier idea of ring vaccination based on monkey deaths is no longer considered appropriate and that updated strategies should be developed based on current evidence. ICMR noted that the discussion helped reshape thinking and guide future plans.

Moderator question: The moderator sought clarification on the development sequence and asked whether phase 2 design would depend on animal data alongside phase 1 data.

India (ICMR):

ICMR clarified that phase 1, phase 2, and animal studies are expected to proceed in parallel, as approvals to start these activities have already been obtained. It noted, however, that regulatory authorization for programmatic use would be considered only once bonnet macaque challenge data and phase 1–2 results are available.

Moderator note: The moderator emphasized the importance of defining the primary immunogenicity endpoint for phase 2, likely based on neutralizing antibodies. The moderator also noted that it may be informative to review the prior vaccine's limited immunogenicity information alongside observed effectiveness after one or two doses, to help guide selection of cutoff thresholds for phase 2 immunogenicity endpoints.

India (ICMR):

ICMR noted that a major delay resulted from bonnet macaques being reclassified under the Wildlife Protection Act, which prevented timely access to the species. As a result, ICMR indicated that detailed immune profiling is being conducted in humans and alternative animal models, with the intent to correlate findings once macaque data become available. ICMR acknowledged challenges in defining immunogenicity endpoints given the lack of usable historical immunogenicity data from the earlier vaccine era, when modern diagnostic and cellular immune tools were not available. It indicated that new human immunogenicity data, mouse-model challenge results, and future NHP studies are expected to be needed to establish meaningful CoPs.

Moderator summary note: The moderator recognized the need for a pragmatic approach given the constraints and noted that stakeholders appeared committed to moving quickly. The moderator concluded that the discussion indicated alignment toward an expedited approval pathway due to clear medical need.

WHO SEARO:

WHO SEARO highlighted the importance of strong post-authorization safety surveillance once a KFD vaccine is approved and drew parallels to WHO's experience with the indigenously developed Bharat Biotech rotavirus vaccine in India. It noted that repeated concerns about intussusception led WHO and national partners to design a SMART safety surveillance system using a network of 11–12 sentinel sites coordinated by THSTI, with contributions from regulators and hospitals following a common protocol. WHO SEARO stated that data from multiple sources—including post-authorization regulatory data—were triangulated, resulting in a comprehensive benefit–risk white paper that informed WHO's global guidance and helped resolve the safety concerns due to the large sample size and robust methodology. WHO SEARO emphasized that a similar proactive pharmacovigilance approach, using sentinel surveillance and/or rigorous phase 4 studies, would be important for monitoring the safety of a future KFD vaccine.

India (ICMR):

ICMR noted that while KFD is an important public health problem, the vaccine program also represents a broader strategic goal: establishing a national framework for developing vaccines for diseases with pandemic potential, including diseases that may require licensure without phase 3 clinical trials. ICMR suggested that KFD may become among the first vaccines in India to follow such a pathway and that the experience could help build the ecosystem needed for accelerated vaccine development. ICMR also highlighted practical challenges in achieving "100-day development" timelines in India, noting that development involves two regulatory systems—the DCGI and the Review Committee on Genetic Manipulation (RCGM)—both with stringent requirements. It noted that stakeholders are examining which processes can be streamlined, such as reducing unnecessary batch requirements in animal studies, with the goal of identifying steps that can be safely modified to support expedited pathways, using KFD as a model.

Moderator note: The moderator welcomed the integration of pandemic preparedness into this work and noted that the regulatory agency appeared positioned to support accelerated and rolling review processes.

India (CDSCO):

CDSCO stated that early-stage vaccine development in India has recently been simplified. It noted that previously, developers needed prior permission at multiple steps, but that the Government of India now allows self-notification for initial phases related to PCT and HWDC establishment. After self-notification to CDSCO, developers can directly approach state authorities to obtain required licenses, making the early development process faster and less burdensome.

Moderator question: The moderator redirected attention to the critical need for post-authorization surveillance infrastructure, noting that such systems are essential for generating reliable RWE. The moderator asked whether CDSCO requires companies to conduct these studies and whether public health authorities provide infrastructure to support them, noting that reliance on manufacturers alone can be problematic. The moderator emphasized that public health systems may need to provide independent surveillance networks, such as sentinel sites, to ensure high-quality data.

M**oderator**: emphasized that regional collaboration is valuable because it makes regulatory processes more efficient and strengthens confidence in decisions involving innovative and atypical approaches, such as those needed for Nipah vaccines. He noted that even the EMA benefits from hearing perspectives from other regulators like the FDA and Health Canada, especially for complex dossiers. Sharing views allows regulators to learn from each other while still making independent national decisions, which remains unchanged.

India (Dr. Rubina Bose, CDSCO):

CDSCO noted that while India has participated in WHO led multinational studies such as the Solidarity trials, it has not previously taken part in joint regulatory assessments with other agencies. For Nipah vaccine approvals, CDSCO emphasized that any product must still meet all Indian regulatory requirements, including submission of a full product dossier and compliance with national norms. Although India participates in multicenter trials, final regulatory decisions are made independently, based on CDSCO's own evaluation. Clinical trial protocols are reviewed by an advisory committee, which ensures suitability for the Indian population, and decisions cannot be based solely on other regulators' assessments.

Malaysia (Dr. Mohd Rezuan, NPRA):

NPRA said that developing a core regional protocol is a good idea, and they are open to considering it. However, any shared protocol would still need to be reviewed by Malaysia's own regulatory committee to ensure that it fits the needs and characteristics of the local population. They remain open to suggestions but emphasize that local suitability will guide their final decisions.

Moderator (Dr. Marco Cavaleri):

Dr. Cavaleri expressed strong optimism about future regional collaboration on Nipah vaccine regulation, noting that the disease presents an excellent opportunity to build concrete cooperative frameworks. He explained that regulators outside the region, including EMA, may also review Nipah vaccine submissions and highlighted mechanisms such as PRIME and the EMA Emergency Task Force, which proactively engage on emerging health threats. He emphasized EMA's commitment to inviting regulators from other regions to participate in scientific advice discussions so everyone can share views in a single setting—benefiting both regulators and developers. He encouraged greater use of such joint opportunities and stated EMA's desire to work closely with regional partners in future meetings.

India (Dr. Rubina Bose, CDSCO):

Dr. Bose emphasized that participating in joint scientific discussions is valuable for building regulatory confidence and reviewer capacity. However, India can only meaningfully participate if it has full access to the complete data package, including the full dossier. Without full data access, CDSCO cannot justify involvement or contribute effectively. Manufacturers must therefore agree to share all confidential data.

Moderator (Dr. Marco Cavaleri):

Dr. Cavaleri acknowledged this, noting that regulators can only be invited to joint discussions when developers consent to sharing confidential information. Since developers must ultimately engage with multiple regulators anyway, early agreement on data sharing benefits everyone**.**

Malaysia (Dr. Mohd Rezuan, NPRA):

Dr. Rezuan added that ASEAN already has mechanisms for collaborative review—such as the Pharmaceutical Product Working Group (PPWG) and the ASEAN Joint Assessment (AJA) procedure—so regional joint assessment and discussion on Nipah vaccine approval would not be new for them.

Moderator (Dr. Marco Cavaleri):

Dr. Cavaleri welcomed this, stating that strengthening ASEAN collaboration will support not only regional decision making but also global engagement. He noted that successful models like AVAREF show the value of such cooperation and expressed interest in deeper engagement with regulators in Asia.

Questions from the audience:

Miles Davenport, Australia:

Dr. Davenport asked about the need for country specific immunogenicity studies, noting that Australia vaccinates diverse populations without considering ethnic or geographic differences. He asked what evidence supports requiring immunogenicity or safety studies in each region.

Thailand (Dr. Wittawat Viriyabancha, Thai FDA):

Dr. Viriyabancha responded that preauthorization data for Nipah are limited, so decisions rely on animal challenge models and immunogenicity data. However, after authorization, RWE—including observational studies, national surveillance, and health database analyses—is essential to understand vaccine effectiveness in practice.

Moderator:

Dr. Cavaleri indicated the question focused on the scientific necessity of multiple country level immunogenicity trials. He noted that many such studies lack strong justification and create unnecessary burdens for developers, who cannot conduct trials in every country. While immunogenicity differences can exist—as seen with the Ebola vaccine between Sierra Leone and the U.S.—they are not always significant. Therefore, regions should determine when additional local studies are truly needed and when data from another country (e.g., Bangladesh, Malaysia, Thailand) can be accepted.

India (Dr. Rubina Bose, CDSCO):

Dr. Bose emphasized that India's ethnic diversity, variable outbreak history, and differing baseline immunity can affect vaccine performance. India has evidence of vaccines performing differently in northern vs. southern regions. As a producing country, India must conduct some domestic clinical trials, and imported products require bridging studies. However, during outbreaks or pandemics, CDSCO can use alternative regulatory pathways to enable rapid access while still ensuring safety and effectiveness.