# International Network for Vaccine Safety Surveillance (INNOVATE): An Integrated Population and Sentinel Hospital-Based Vaccine Safety Surveillance in Six Low and Middle-Income Countries

***A joint proposal by***

***INCLEN & DCVMN***

THE INCLEN TRUST INTERNATIONAL

DCVMN
Developing Countries Vaccine Manufacturers Network

# Limited Evidence - Background rates

01 **Background rates from LMICs**

Lack of background rates for serious AEFI / AESI from LMICs

02 **Population Based Background rates**

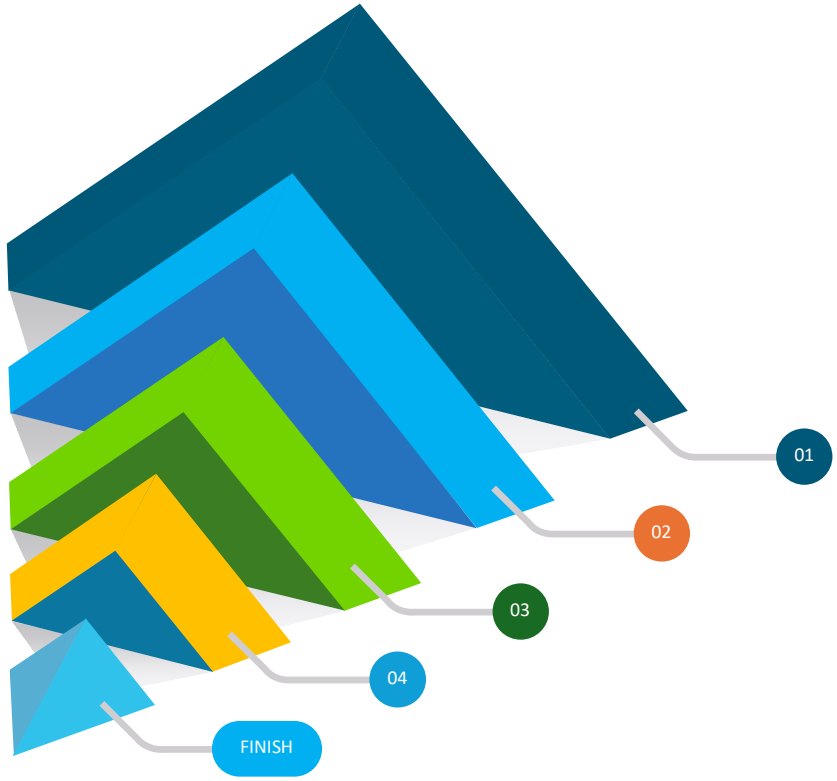
Non Availability of Population Based background Rates - Available Background Rate Data is limited to Hospital based Surveillance

03 **Standardized Case Definitions**

Lack of standardized Case Definitions to validate the cases of AESI / AEFI

04 **Stratified Case Distribution**

Age, Gender, Geography, Time and Socio Economic Stratified Case Distribution is not available



# Alignment to CEPI's 100-day mission

- *The proposed study focusses on following goal under CEPI's 100 Day Mission - "vaccines should be ready for initial authorization and manufacturing at scale within 100 days of recognition of a pandemic pathogen when appropriate".*
- *Generate Background Rates for AESI/AEFI for different Vaccine Development Platforms and not just one vaccine – age and gender stratified rates*
- *Establish **Active Vaccine Surveillance System (AVSS)** for **half a million population** representing **2 billion population – This platform will***
  - ***Pave the pathway for rapid vaccine approvals***
  - ***Platforms for Clinical trials***
  - ***Strengthen National AEFI System***
  - ***Support Enrollment of Vaccine in the public health system***
- *Partnerships with Developing Countries Vaccine Manufacturers Network (DCVMN) help in building global capacity through data sharing by translating the learning into National Policy through involvement of National AEFI Committees of the partner Countries.*

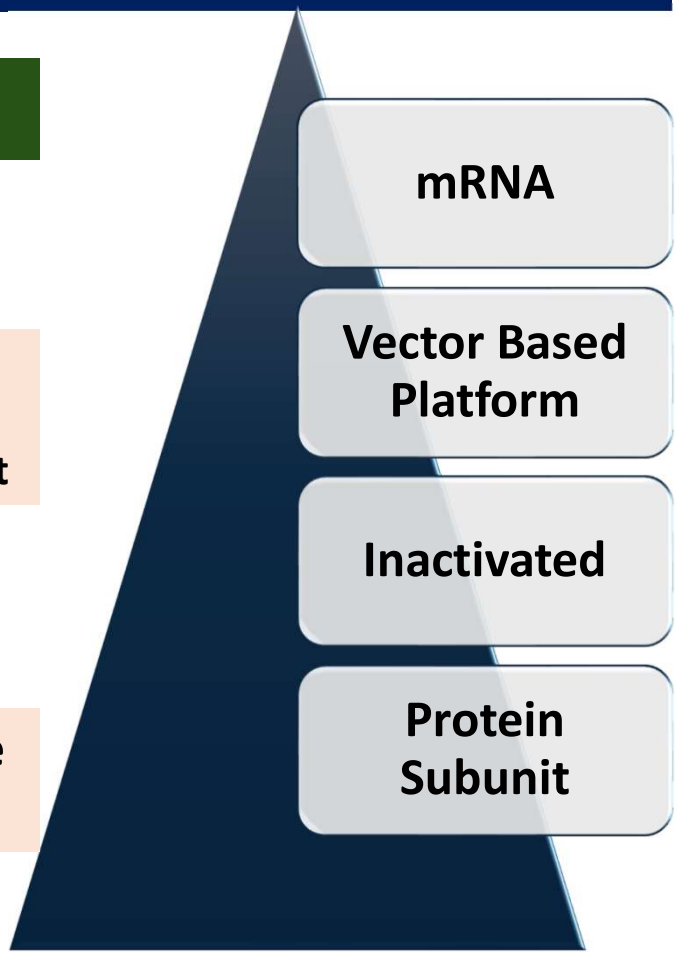
# Prepare for Future Pandemics – Platforms for Vaccine Safety Assessment

- 3 Continents
- 6 Countries
- 9 Sites
- 0.5 Million Population Coverage
- 2 Billion Representative Population

**Background Rates**

Adverse Event Following Immunization
Adverse Event of Special Interest

**Targeting Different Vaccine Development Platforms**



# Proposed Study Sites

| Site | Country | Total Population | Type |
|---|---|---|---|
| **Africa** | | | |
| Gilgel Gibe | Ethiopia | 62235 | Mix |
| Nairobi | Kenya | 63639 | Urban slum |
| University of Pretoria | South Africa | 60,000 | Urban |
| **Latin America** | | | |
| Bangu – Rio | Brazil | 680,000 | Urban |
| **Asia** | | | |
| INCLEN, Palwal | India | 245263 | Rural |
| INCLEN, Bareilly | India | 81211 | Peri Urban |
| INCLEN, Shillong | India | 87985 | Tribal |
| PIMS, Pondicherry | India | 56000 | Mix |
| Purworejo | Indonesia | 773588 | Mix |


Sensitivity: Official Use

# Goals

Engage with national regulators, CEPI, CEPI supported developers and DCVMN for evolving a sustainable mechanism of sharing the vaccine safety data as per agreed terms and conditions in alignment with the national laws.

# Objectives

1. To establish **population cohorts (~50,000)** to monitor and document all deaths and hospitalization and pregnancy related events:

**To determine the community based background rates of all cause and cause specific death and hospitalizations**

A

**To identify the public and private health care facilities chosen by the community for hospitalization of sick individuals for tracking clinical details**

C

B

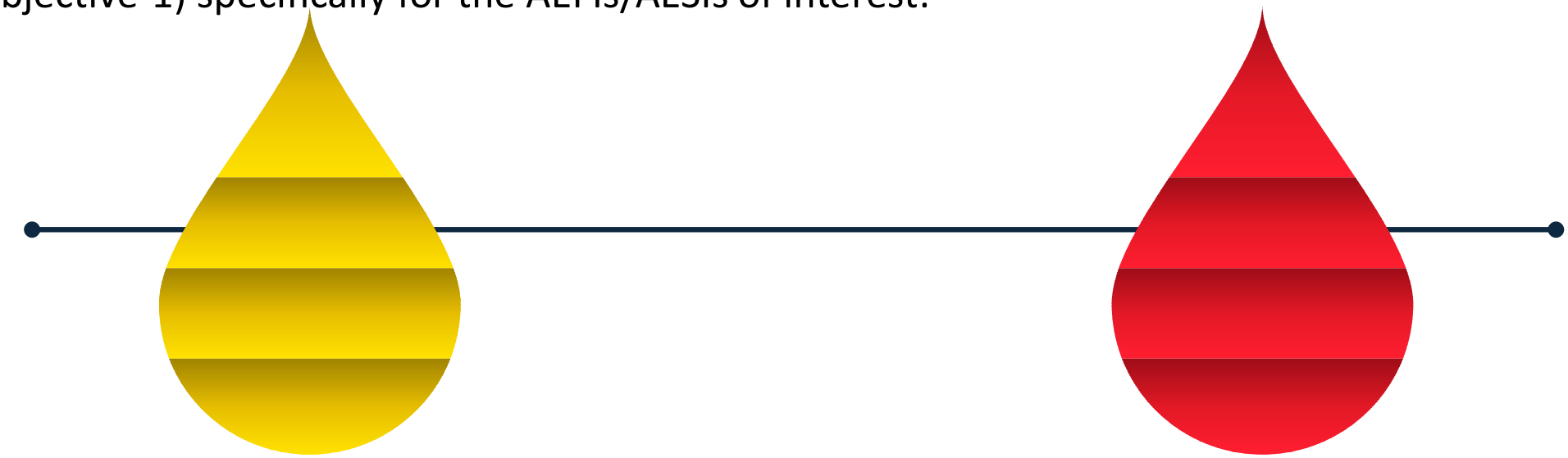
**To establish the clinical diagnosis of hospitalized and dead and determine various contributory risk factors.**

D

**To watch for infrequent and rare signals related to the vaccination in the population cohorts**

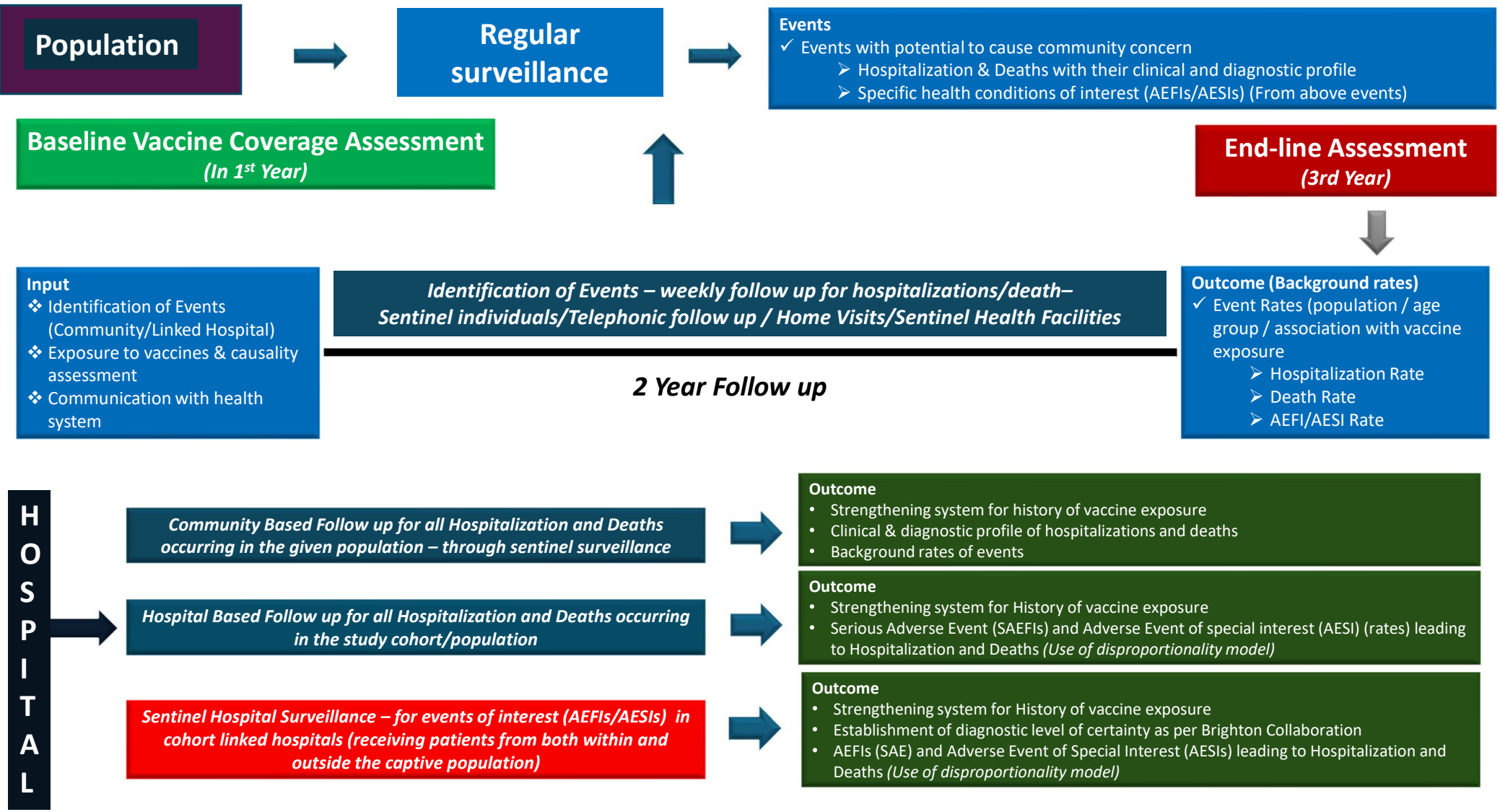
# Surveillance: Objective

**2**. To establish active sentinel surveillance at the **tertiary/secondary care hospitals (@2-3 per site)** attracting largest patient population (from the population cohort mentioned in objective-1) specifically for the AEFIs/AESIs of interest:



**A. To identify specific AEFIs/AESIs among all hospitalized (including pregnancy related events), and determine their vaccine exposure status**

**B. To determine the proportion of AEFIs/AESIs coming from the captive community cohort**



# Project Governance

**Technical Advisory Group**

- ✓ **Support the Project – Technical and Implementation Guidance to CCT and Site**

**Central Coordinating Team (Project Management)**

- ✓ **Overall Project Management**
- ✓ **Lead Protocol and Tool Development**
- ✓ **Coordination with Sites and Funder**
- ✓ **Data Management at Central level**
- ✓ **Central Case Adjudication Committee (CAC)**

**Implementation Sites**

***(Ethiopia, Kenya, South Africa, Brazil, Indonesia and India)***

- ✓ Site Level Project Management
- ✓ Coordination with Central Coordinating team
- ✓ Support Protocol and Tool Development
- ✓ Site Level Data Management
- ✓ CAC reviewing the data and causality
- ✓ Program Implementation on ground

**Field Level Data Collection**

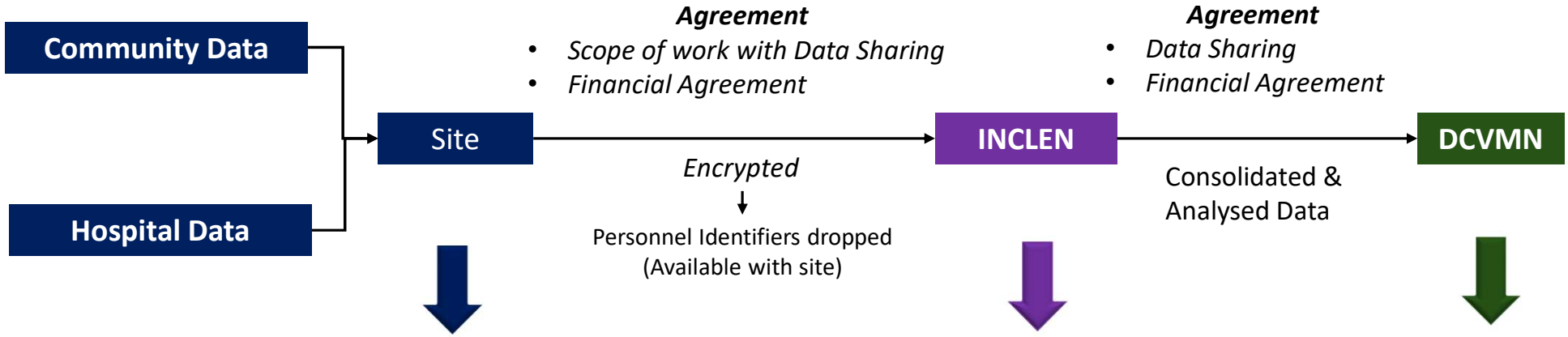
***(Site Level)***

- ✓ Field Level Data Collection
- Population Based
- Hospital Based
- System Strengthening

# Study Phases and Timelines

| Preparatory Phase (0 – 5 months) | Implementation Phase (6 – 32 Months) | Consolidation Phase (33 – 35 Months) |
|---|---|---|
| • Finalization of the study sites & population cohort to be assembled<br>• Obtaining administrative and regulatory permissions<br>• Sub-award contract finalization between Central Coordinating Team and partners.<br>• Protocol, Tools, SOPs and EDC development<br>• Training of Trainers<br>• Recruitment of staff at sites<br>• Data Management and Statistical Analysis Plan | • Site Level trainings<br>• Site Level SOPs<br>• Assemble the population cohort,<br>• Obtain rates of the health events that are associated with hospitalization and deaths,<br>• Explore the association with vaccine exposures and hospital based active surveillance for indicator AEFIs/AESIs<br>• Regular review of data quality, data entry timeliness. | • Data analysis (ongoing in real time) and<br>• Report writing (last 3 months for consolidation)<br>• Publication in peer reviewed Journals<br>• Interaction with DCVMN for dissemination of findings |

# Data Sharing Plan



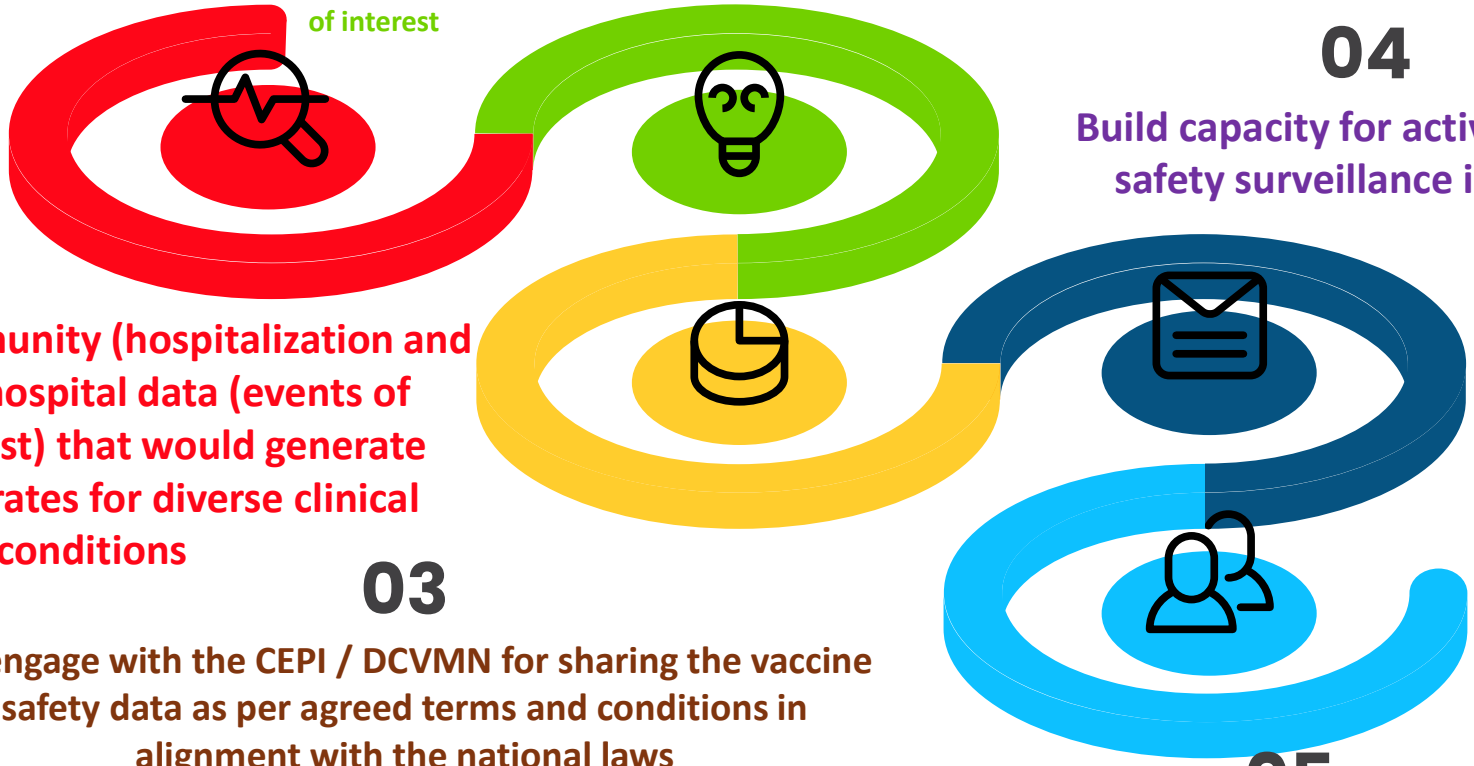

| | | | |
|---|---|---|---|
| Activities | • Project Implementation<br>• Preapproved Forms | Project Management – Project Planning, Implementation, Coordination and Data Management including Data Analysis | Financial Support |
| Dissemination | National Policy<br>Health System | National Policy<br>WHO / CEPI<br>Vaccine Manufacturer | Vaccine<br>Manufacturer |

# Expected Outcome

## 02

**Relate these events to vaccine exposure in clinical trials, phase IV safety surveillance and routine AEFI surveillance**

- **Application of disproportionality models to determine causal linkage between vaccine exposure and events of interest**



## 01

**Using the community (hospitalization and death) and hospital data (events of special interest) that would generate background rates for diverse clinical conditions**

## 03

**To engage with the CEPI / DCVMN for sharing the vaccine safety data as per agreed terms and conditions in alignment with the national laws**

## 04

**Build capacity for active vaccine safety surveillance in LMICs**

## 05

**A consortium of vaccine trial platforms across 6 countries and 9 sites**

# *Thank You*

# Panelists

| S.no | Panellist | Questions |
|---|---|---|
| 1 | **Patricia** | **Main Challenges of AEFI Surveillance in Low- and Middle-Income Countries:**<br>What are the main challenges of AEFI surveillance in low and middle income countries? What is the importance of population based background rates of AEFI's / AESI's ? |
| 2 | **Katharine** | **Vaccine Safety Surveillance Methodology**<br>**Preamble: Since Randomized Control Trial are not always feasible**<br>How can a robust observational study design and methodology for Active vaccine surveillance bring about confidence across the stakeholders? What should be done to leverage the proposed study to build capacity in LMIC Settings? |
| 3 | **Alexander** | **Data Sharing**<br>How should data sharing will be governed between the stakeholders - industry partners, regulators, academia, National technical advisory groups and the community, which comply with national and international laws? |
| 4 | **Reza** | **Data Access**<br>How do you propose to have an access to the data as a vaccine manufacturer, regulators, academia, community member, marketing authorization holders or local health system? How this data access can be used to bridge knowledge and communication gap between different stakeholders? |
| 5 | **Viska Indriani** | **Harmonization of Causality Assessment Between Project and National Adverse Event Following Immunization Committee**<br>How can this study can bring about harmonization in the causality assessment processes and methods within the country and globally? |
| 6 | **Abhishek** | **Vaccine Safety Surveillance Network**<br>How this platform of nine sites located in six countries be used for future vaccine trials and to meet CEPI's 100 day mission and future pandemic preparedness? |

# AESI For Consideration

| SPEAC - AESI / AEFI list | | | Platforms | | | |
|---|---|---|---|---|---|---|
| **S.no** | **Body Organ** | **AESI / AEFI** | **mRNA** | **Adenovectors** | **Live attenuated** | **Protein subunit** |
| 1 | Cardiovascular and Endovascular | Myocarditis | **X** | | | **X** |
| | | Pericarditis | **X** | | | **X** |
| | | Poly Serositis / Face and Neck Swelling | **X** | | | |
| 2 | Hematologic | Thrombosis / Thromboembolism | **X** | **X** | **X** | |
| | | Haemmohagic Disease | | | | |
| | | Thrombocytopenic Thrombosis Syndrome | | **X** | | **X** |
| | | Capillary Leak Syndrome | | **X** | | |
| | | Vaccine associated Immune Thrombotic Thrombocytopenia | | **X** | | |

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| 3 | Immunologic | Anaphylaxis | **X** | **X** | **X** | **X** |
| | | Single Organ Cutaneous vasculitis | | **X** | | |
| | | Vaccine Associated Enhanced Disease | | | | |
| 4 | Neurologic | Generalized Convulsions | **X** | **X** | **X** | **X** |
| | | Aseptic meningitis | | | **X** | |
| | | Acute Encephalitis / Encephalomyelitis | | | **X** | |
| | | Myelitis | | | **X** | |
| | | Dizziness and Tinnitus | | **X** | | |
| | | Gullian Barre Syndrome | **X** | **X** | **X** | **X** |
| 5 | Musculoskeletal | Aseptic Arthritis | | **X** | | |