

Technology Transfer

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International
Vaccine
Institute

Outline of Presentation

- **Overview of International Vaccine Institute (IVI)**
- **Technology Transfers from IVI to DCVMs**
- **Execution of Vaccine Technology Transfer – my experience from the past**



Every child should have the opportunity to receive high
quality, safe and efficacious vaccines
to
protect them from life threatening infectious diseases



IVI is a Vaccine R&D Center with a Global Health Mission

VISION

Developing countries free of suffering from infectious diseases

MISSION

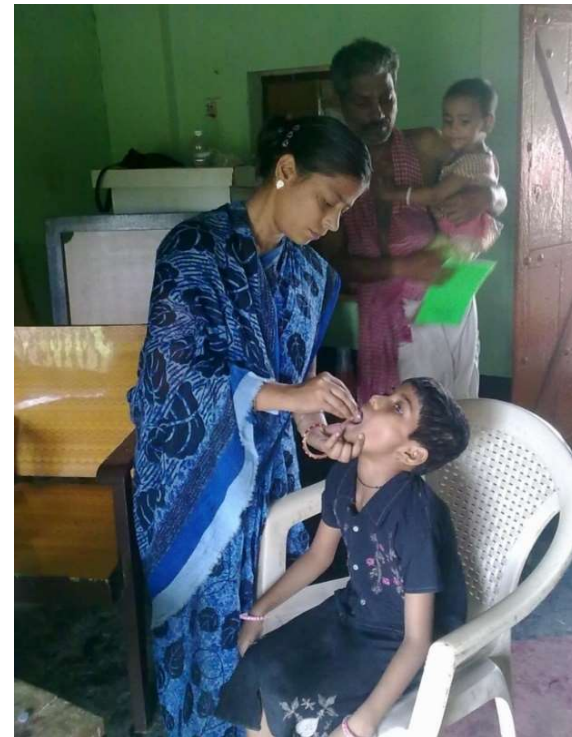
Discover, develop and deliver safe, effective and affordable vaccines for global public health

An International Organization

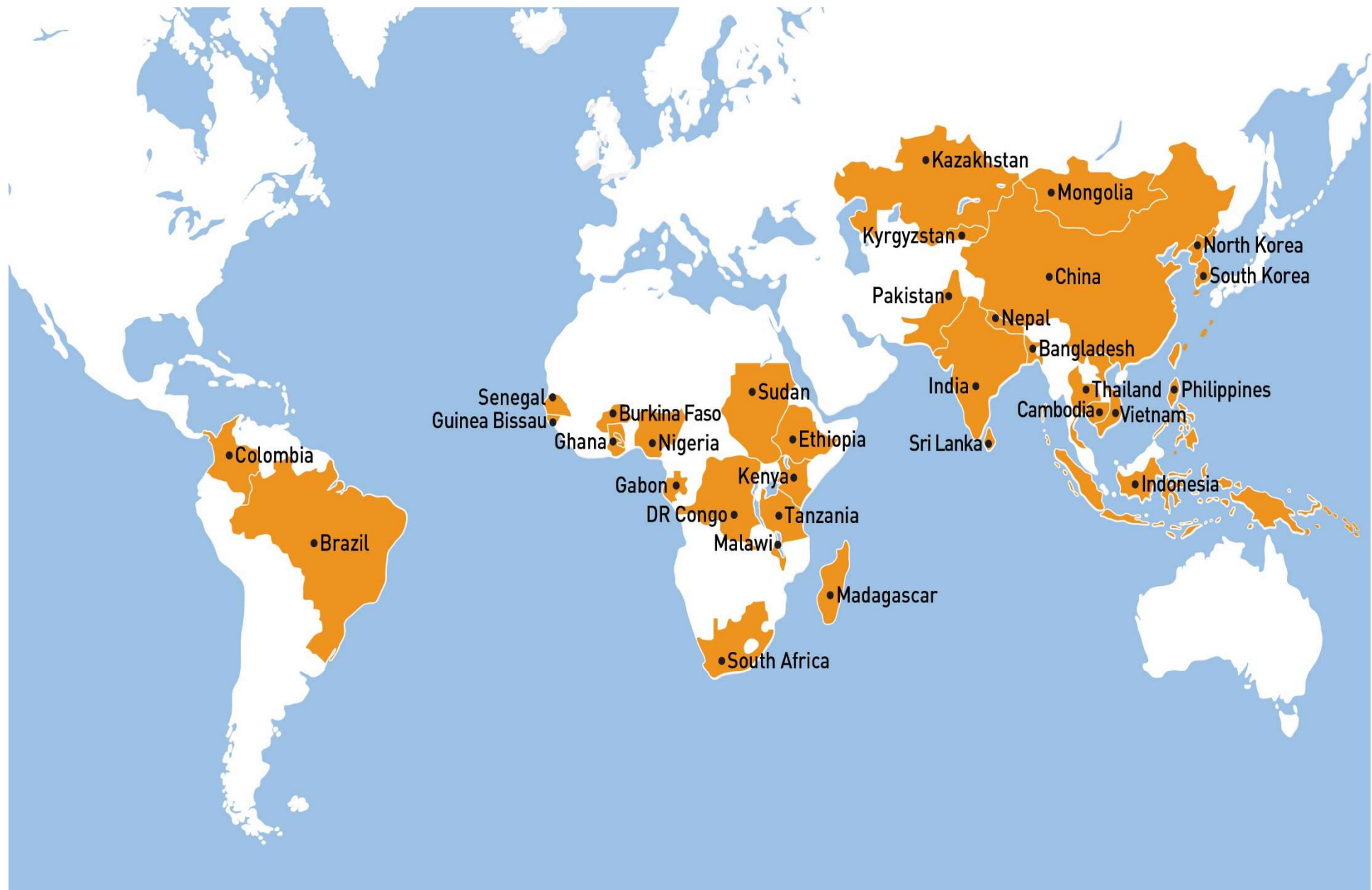
- UNDP initiative
- First international organization in Korea founded in 1997
- 35 countries and WHO as state parties

A Global Vaccine Research Institute

- HQ and laboratory in Seoul
- Field programs in 29 countries: Asia, Africa, Latin America



IVI has a Global Footprint, with Field Programs in 29 Countries



Signatories to IVI's Establishment Agreement



Bangladesh



Bhutan



Brazil



China



Ecuador



Egypt



India



Indonesia



Israel



Jamaica



Kazakhstan



Kyrgyzstan



Lebanon



Liberia



Malta



Mongolia



Myanmar



Nepal



Netherlands



Oman



Pakistan



Panama



Papua New Guinea



Peru



Philippines



Republic of Korea



Romania



Senegal



Sri Lanka



Sweden



Tajikistan



Thailand



Turkey



Uzbekistan



Vietnam



World Health Organization

Funding

Major funders

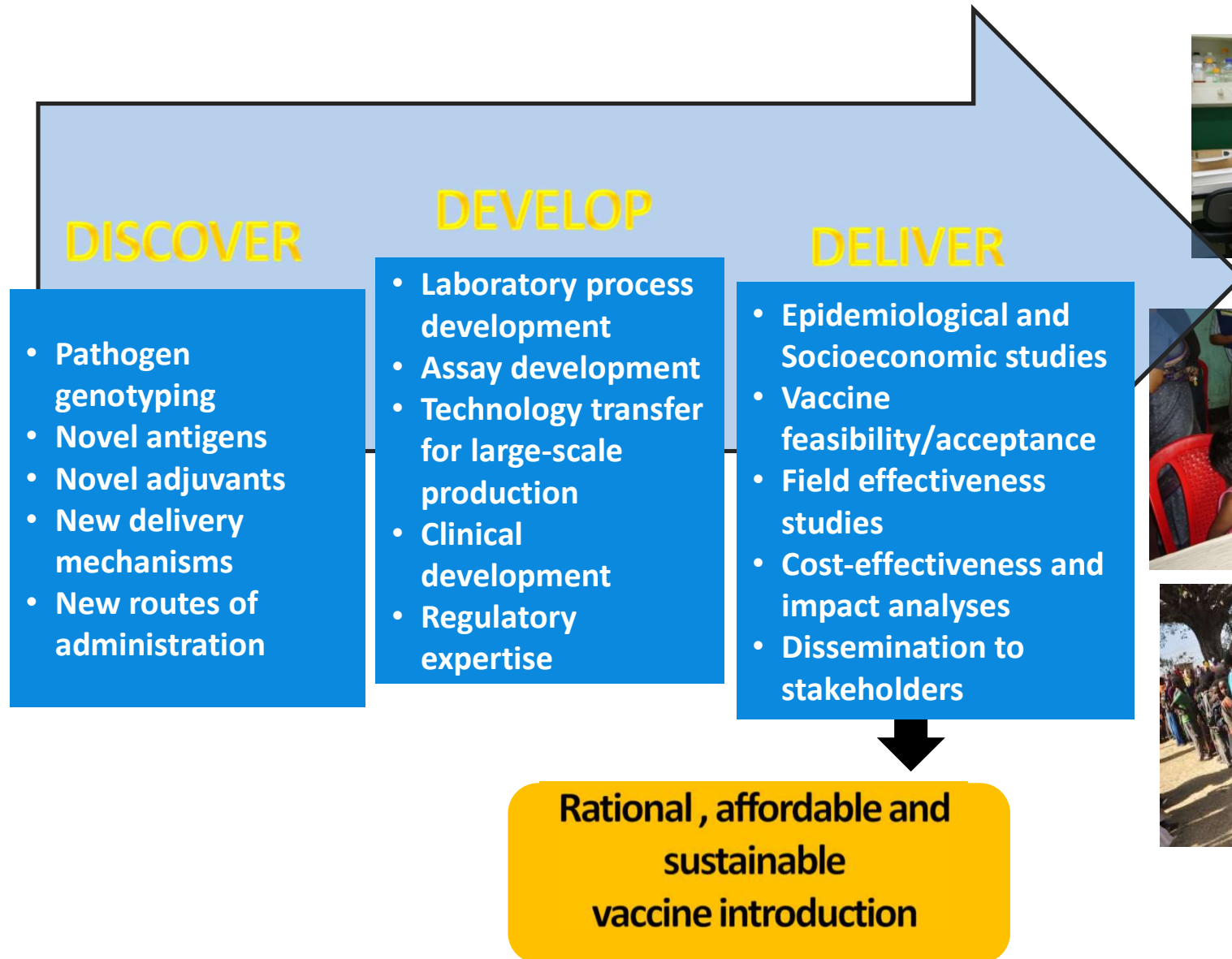
- Bill & Melinda Gates Foundation
- Korean Government (Ministry of Education)
- Swedish Government (Sida)

Private- & public-sector and nonprofit donors

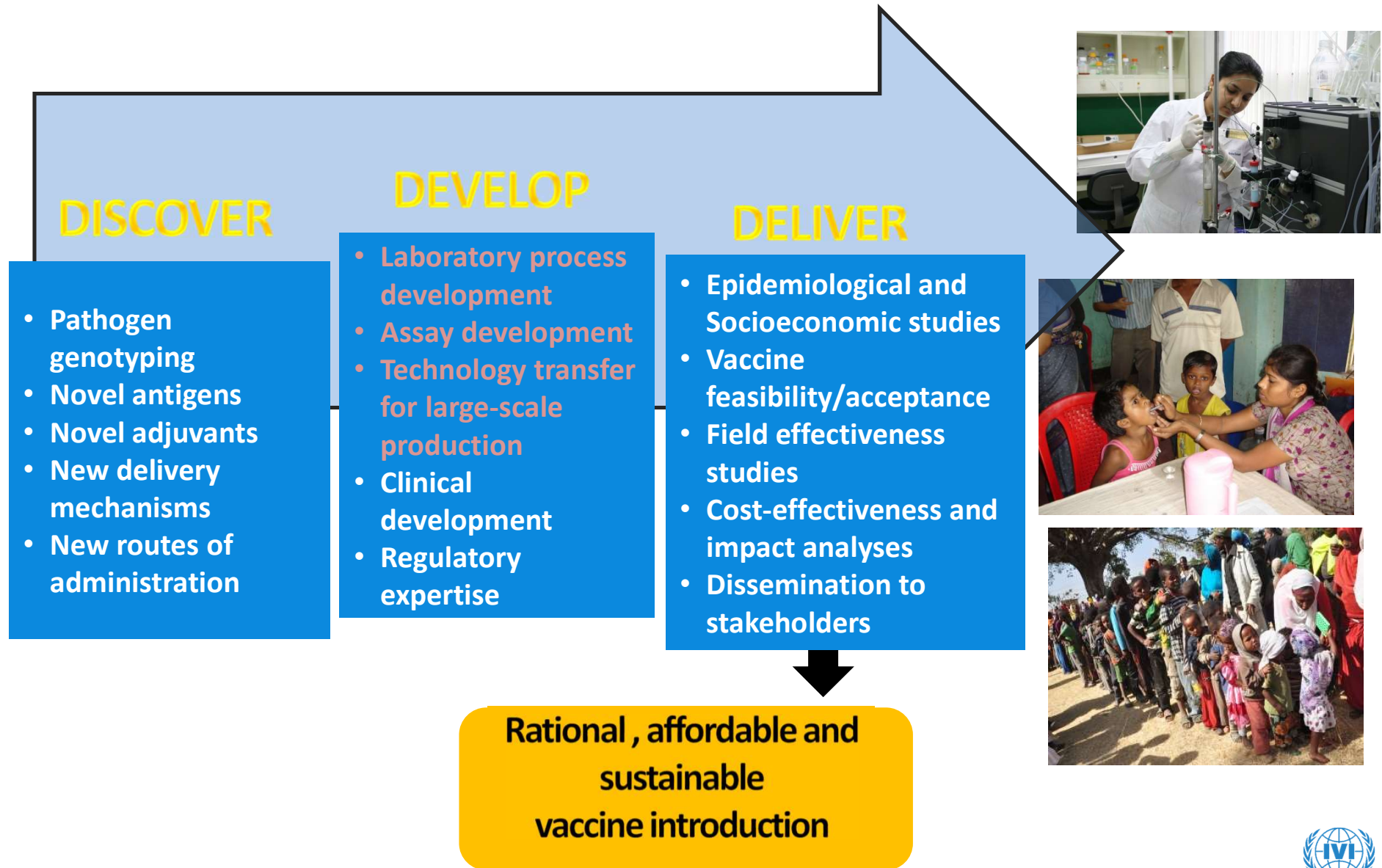
- Korea: Korea Support Committee for IVI (KSC), Samsung, LG Electronics, Kia Motors, Yanghyun Foundation, Korea Exchange Bank, Export Import Bank of Korea, KOICA
- International: German Government (BMBF), UBS Optimus Foundation, Thrasher Foundation, Rockefeller Foundation, Sanofi, Pfizer, GSK, Merck



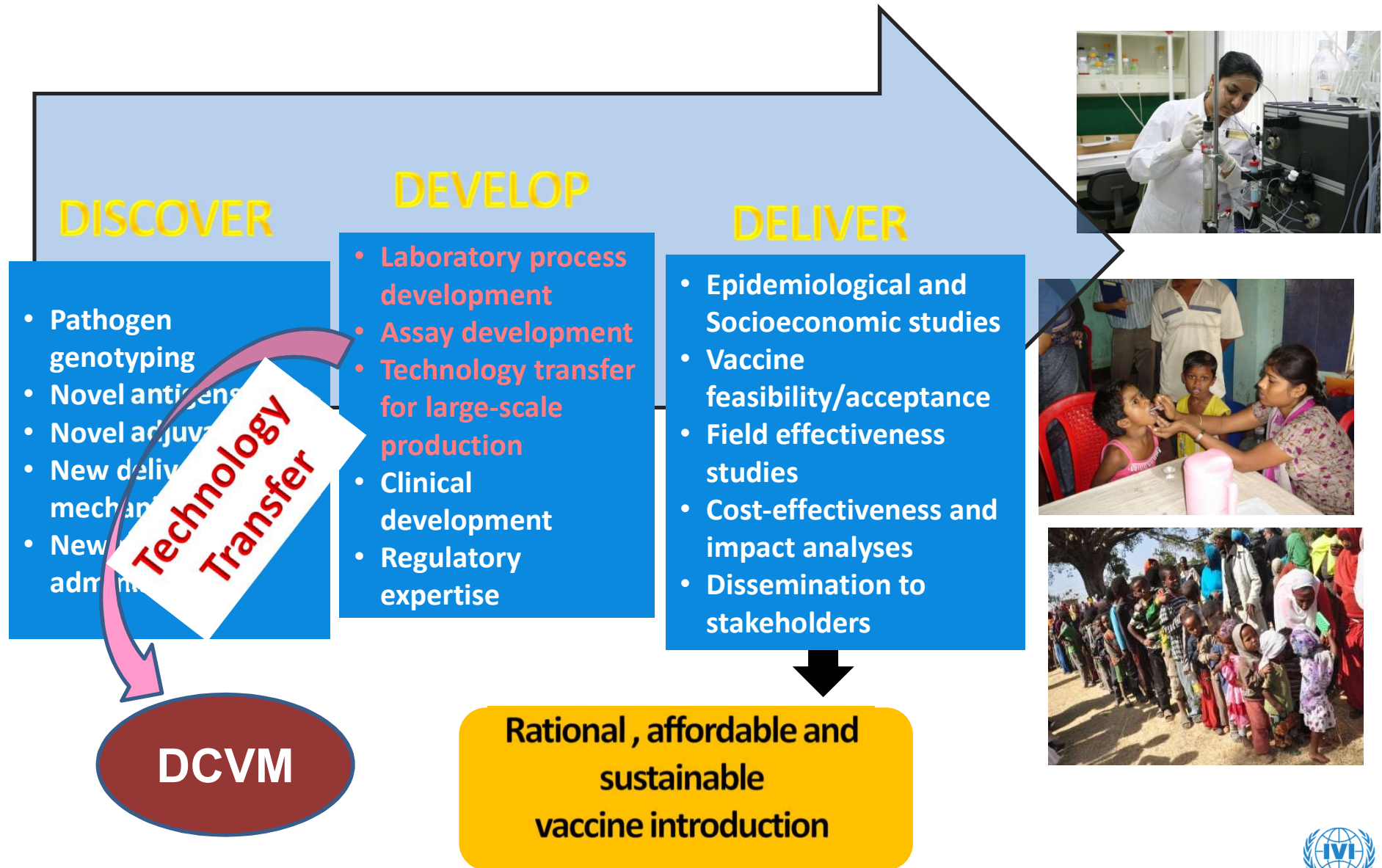
IVI Full Spectrum: Bench to Delivery



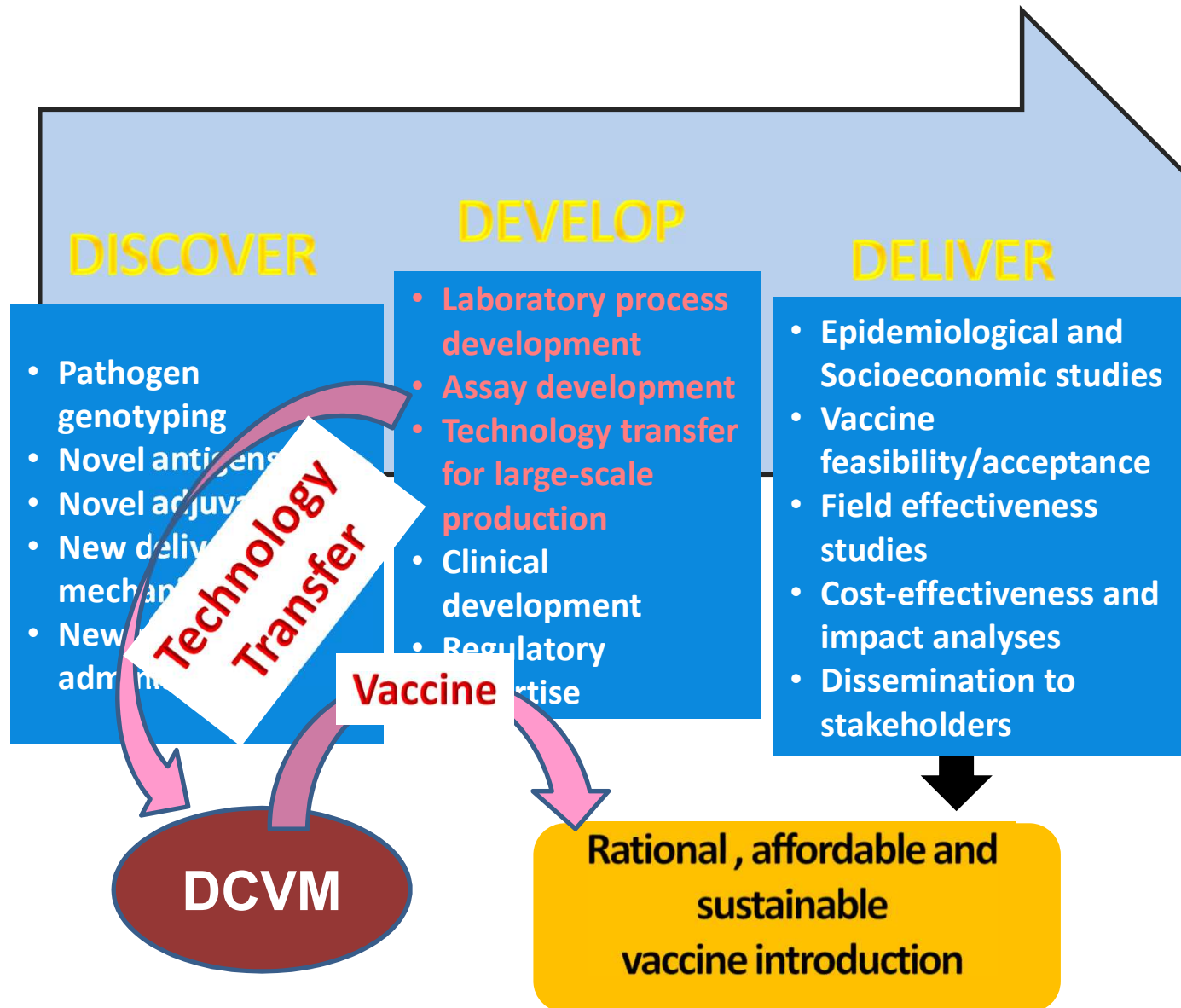
IVI Full Spectrum: Bench to Delivery



IVI Full Spectrum: Bench to Delivery



IVI Full Spectrum: Bench to Delivery



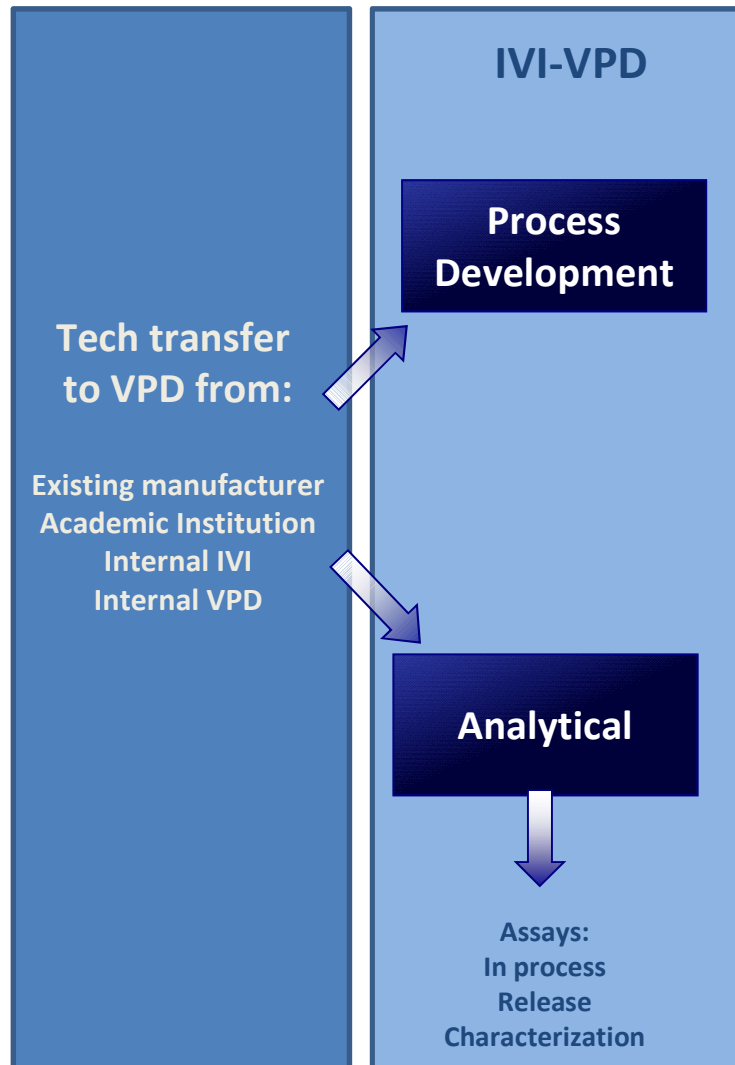
Vaccine Development and TT Process at IVI

**Tech transfer
to VPD from:**

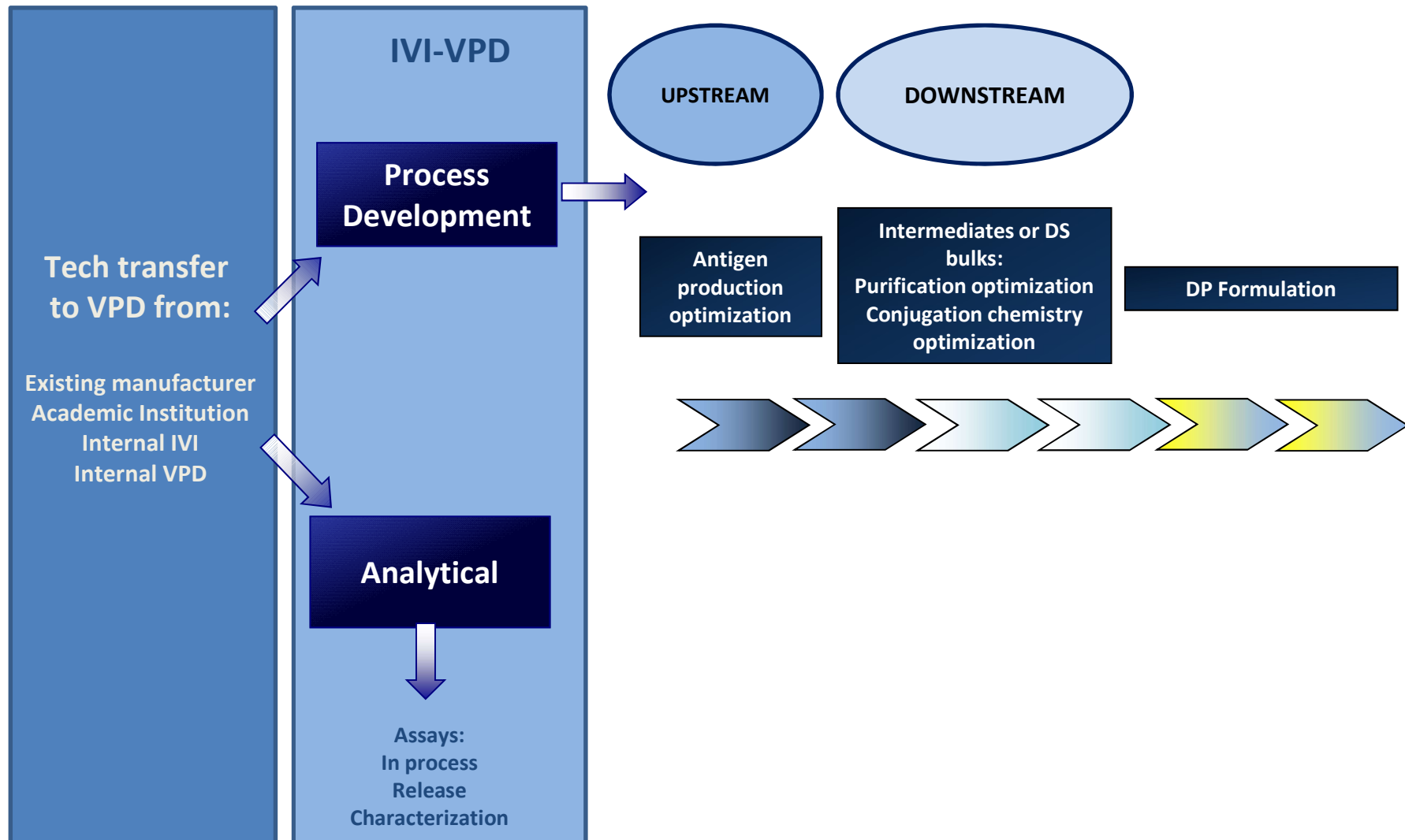
Existing manufacturer
Academic Institution
Internal IVI
Internal VPD



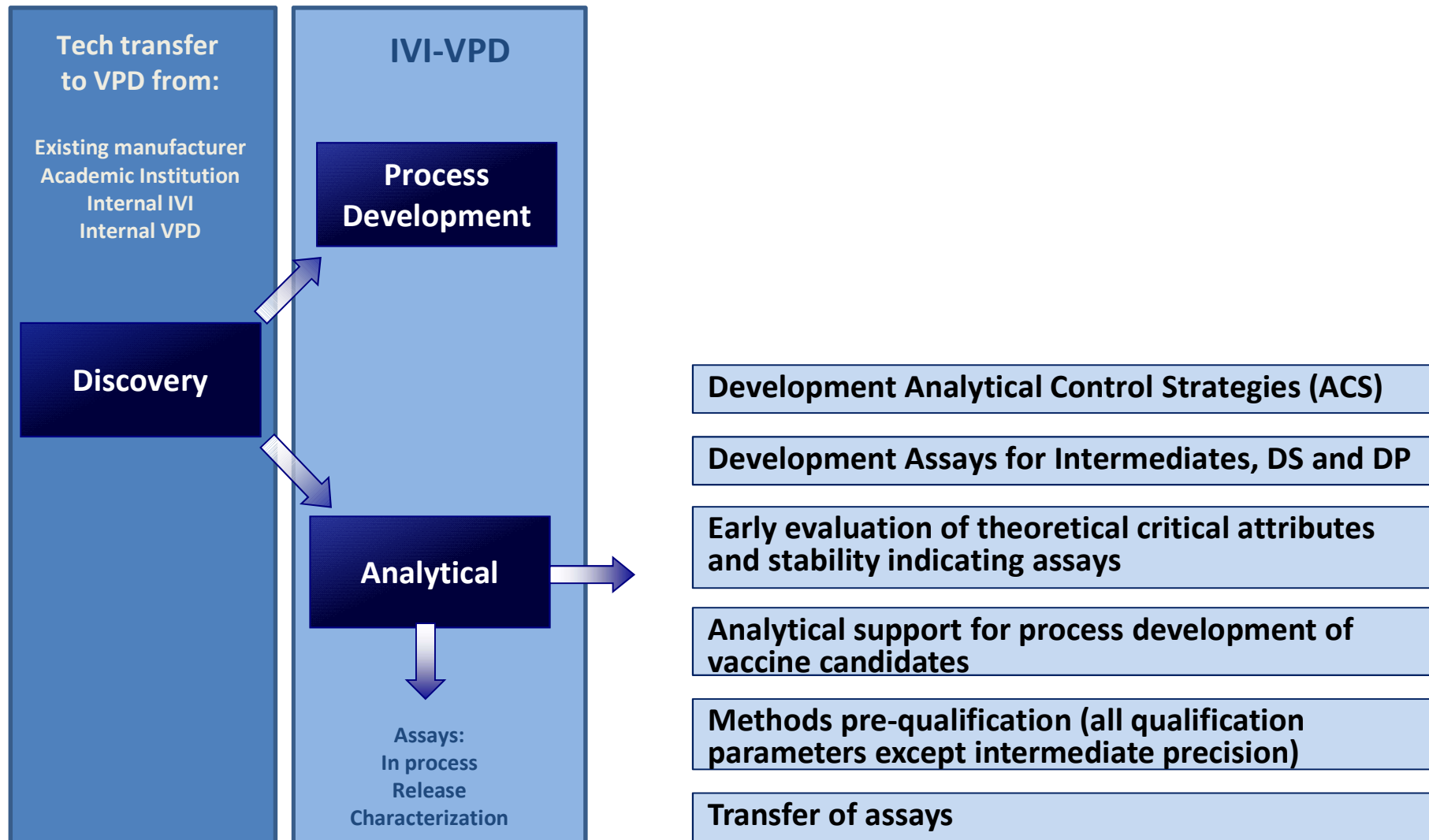
Vaccine Development and TT Process at IVI



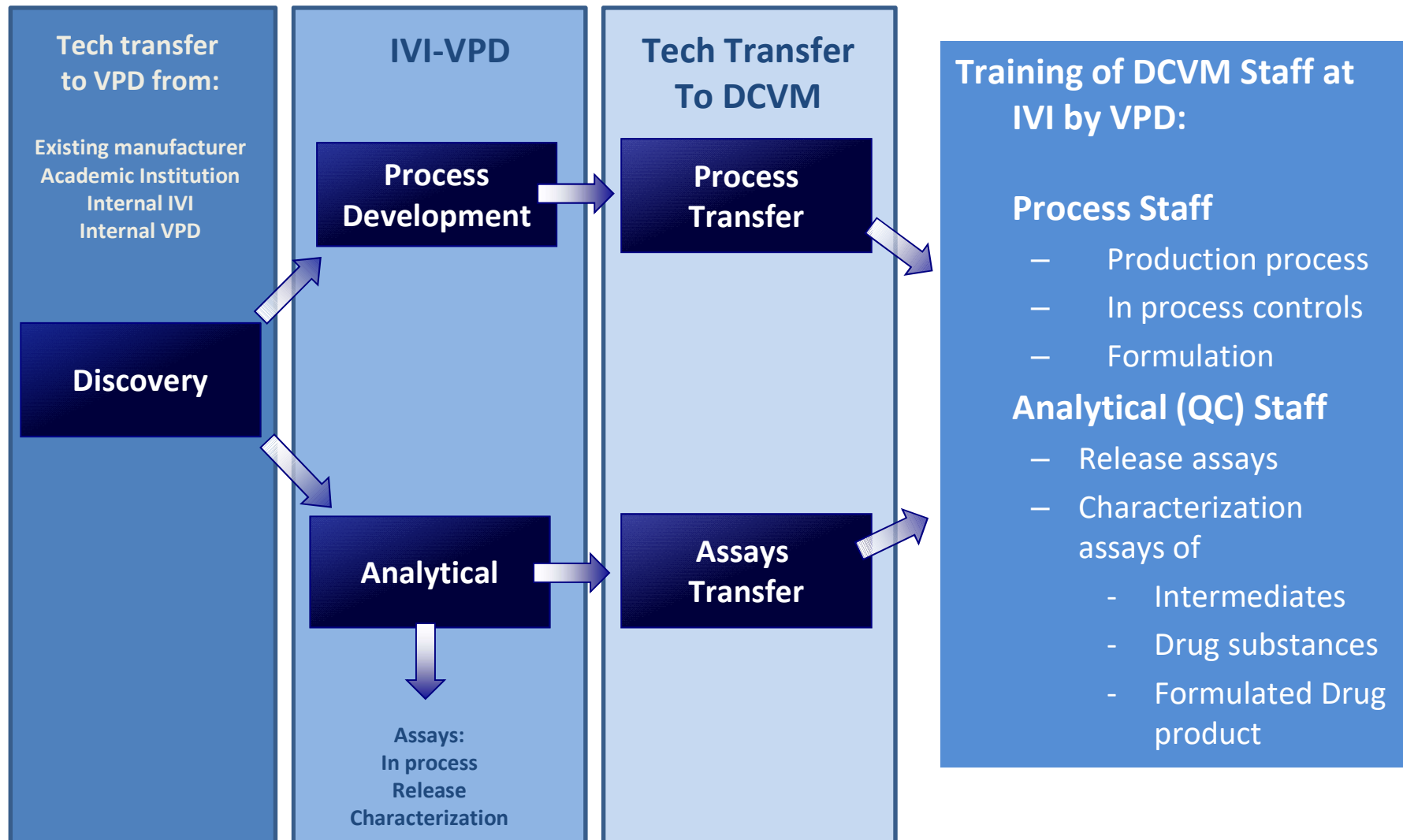
Vaccine Development and TT Process at IVI



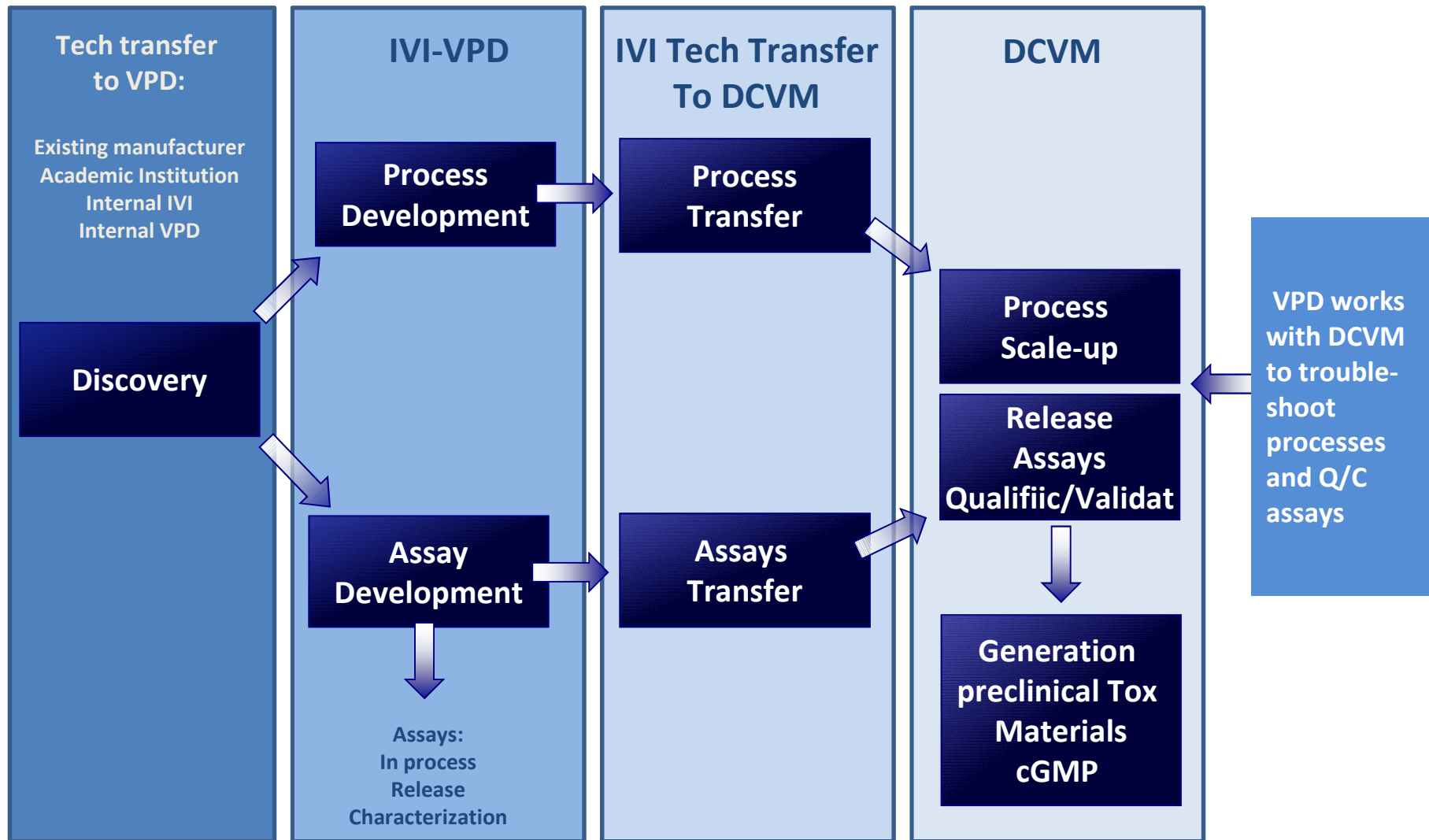
Vaccine Development and TT Process at IVI



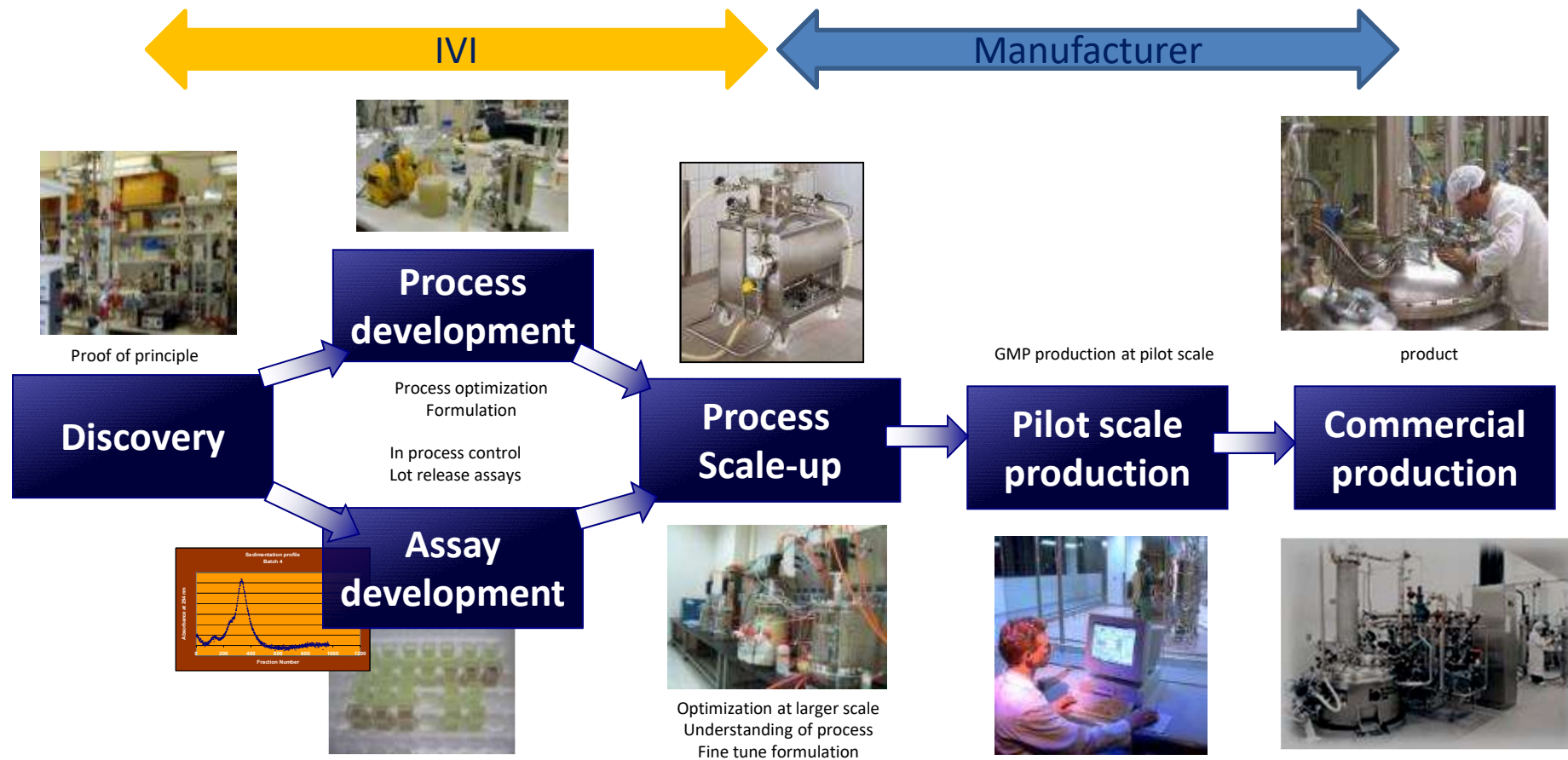
Vaccine Development and TT Process at IVI



Vaccine Development and TT Process at IVI



Vaccine Development Process



Successfully Transferred Vaccine Technologies by IVI

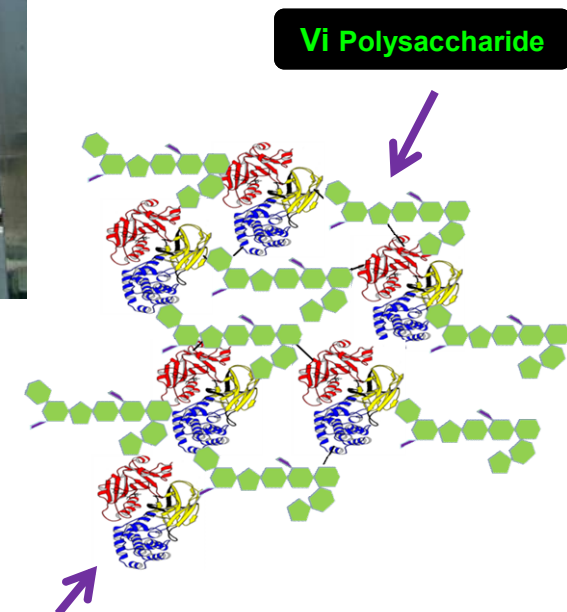
Oral Cholera Vaccine

OCV Formulation:

Strain	LEU/mL
Formalin inactivated EI Tor Inaba (Phil 6973)	600
Heat inactivated Classical Inaba (Cairo 48)	300
Heat inactivated Classical Ogawa (Cairo 50)	300
Formalin inactivated Classical Ogawa (Cairo 50)	300
Formalin inactivated 0139 (4260B)	600



Typhoid Conjugate Vaccine



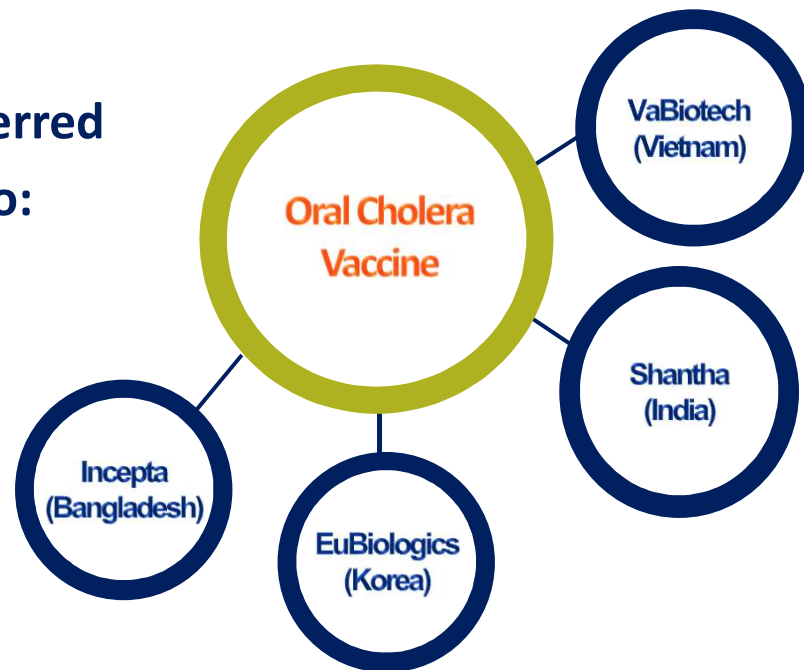
DT

Oral Cholera Vaccine



ORCVAX (VaBiotech, Vietnam)
reformulated in collaboration with
VaBiotech in 2004 to mORCVAX

To meet the projected demand for OCV
vaccination in the public market, IVI transferred
the mORCVAX manufacturing technology to:



Cholera Vaccine : IVI Manufacturers Support

Company	Collaboration	Stage of Development
Vabiotech (Vietnam)	IVI re-formulated, redeveloped process to meet WHO standards Tech Transfer in 2007	<ul style="list-style-type: none"> • Re-licensed in Vietnam
Shantha (India)	Tech Transfer May 2008	<ul style="list-style-type: none"> • Licensed in India (Feb 2009). • WHO prequalified Sep 2011
EuBiologics (Korea)	Tech Transfer 2010 - 2011	<ul style="list-style-type: none"> • Korean export license 2015 • WHO PQ Dec 2015 • WHO PQ 2016 New formulation (600L, no thimerosal)
Incepta (Bangladesh)	Tech Transfer 2014	<ul style="list-style-type: none"> • Clinical trial for licensure completed in 2017, license expected in 2017

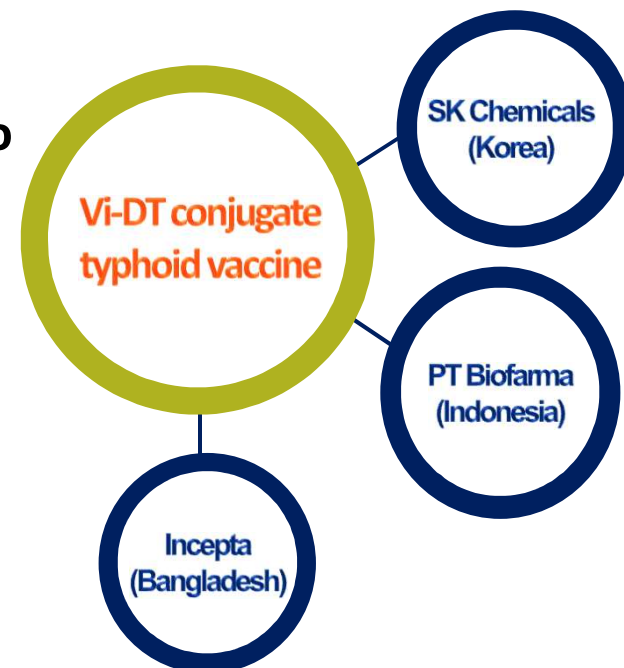
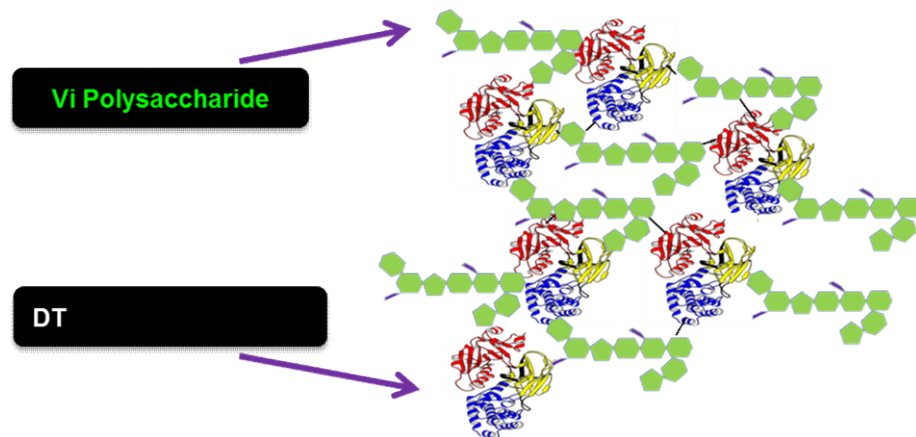


Typhoid Conjugate Vaccine

Conjugation technology for Vi was originally developed at US NIH (Vi-rEPA)

Vi conjugation technology transferred from US NIH to IVI
Vi-DT developed at IVI

- IVI Vi-DT technology was transferred to



- IVI will continue working with these partners on vaccine development and WHO prequalification

Typhoid Conjugate Vaccine (TCV) Program

Manufacturing Partners	Partnership	Stage of development	Likely start of first clinical trial
Shantha (India)	Tech transfer 2010	Produced clinical lots Have now decided to discontinued development	Partnership discontinued
BioFarma (Indonesia)	Tech transfer 2013	Phase 1 (First in Human)	March 2017
SK Chemicals (Korea)	Tech transfer 2013	Phase 1 (First in Human)	Sept 2016
Incepta (Bangladesh)	Tech transfer 2014	Preclinical studies	



Vaccine Technology Transfer (TT)



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Vaccine Technology Transfer (TT)

Objective:

Transfer Vaccine production processes and analytical controls from Originating laboratory (IVI) to Receiving laboratory (DCVM)

Deliverable:

The successful execution of a demonstration batches

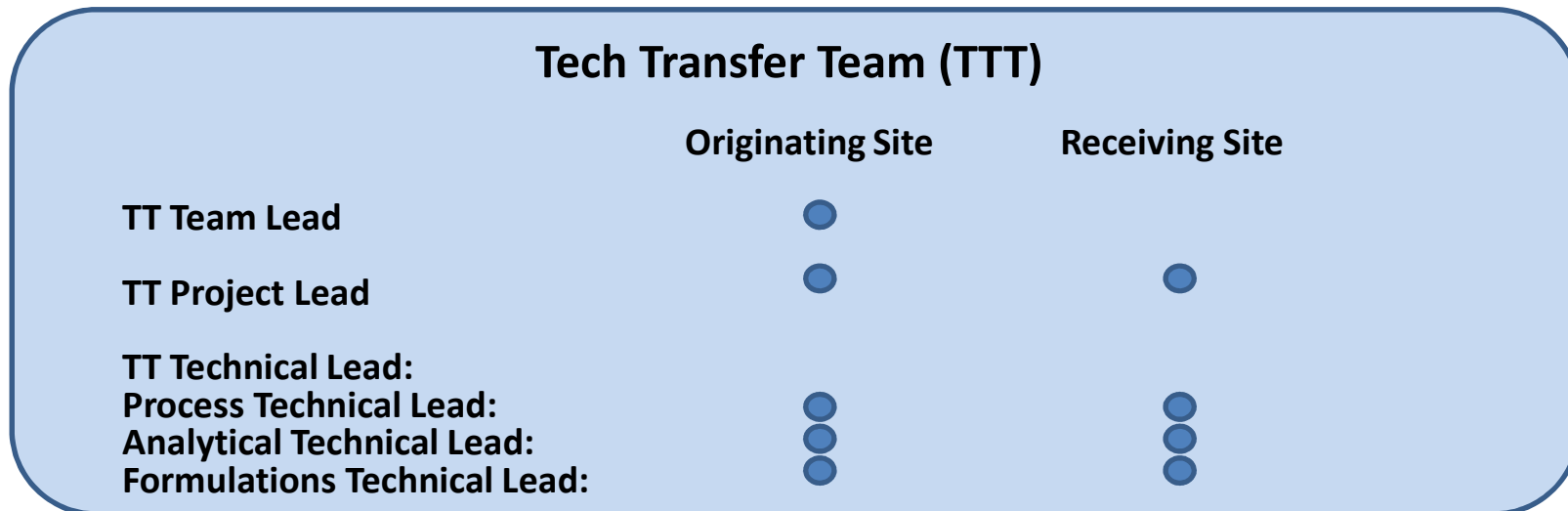
Prior Initiation of Technology Transfer:

- **Tech Transfer Team (TTT) Formed**
- **Draft Technical Transfer Protocol (TTP)**
 - **Agree on Success Criteria**
- **Write checklist for TT and each area**

Note: TTP is drafted and agreed upon by both the Receiving manufacturing partner and IVI as the Originating laboratory.

Technical Transfer Team (TTT)

Responsible for receiving and implementing processes and analytical methods to the manufacturer's Receiving laboratory site



TT Team Leadership:

- TT Project Lead is from Originating lab until the processes and assays has successfully been demonstrated at the Receiving lab.

Technical Transfer Protocol (TTP)

1.0 PURPOSE

2.0 SCOPE

3.0 ADDRESS OF ORIGINATING AND RECEIVING FACILITIES

4.0 TECHNOLOGY TRANSFER TEAM MEMBERS

5.0 ROLES AND RESPONSIBILITIES

6.0 COMMUNICATION PLAN AND ESCALATION PROCESS

7.0 VACCINE AND ITS INTERMEDIATES

8.0 DELIVERABLES

8.1 IVI - Originating lab

8.2 Manufacturer - Receiving lab

9.0 SUCCESS CRITERIA

9.1 Cell Banking

9.2 Cell Culture/Fermentation

9.3 Purification

9.3.1 Batch Records

9.3.2 Target Quality Attributes

9.3.3 Reports

9.4 Analytical

9.4.1 Release Tests

9.4.2 Characterization Tests

9.4.3 In Process Control Tests

9.5 Formulation

10.0 TECH TRANSFER SCHEDULE

11.0 REPORTS



TTP DELIVERABLEs

by Originating Laboratories

General

- **Structure and physical properties of the product and intermediates**
- **Any special concerns related to safety or toxicological hazards**
- **List of all raw materials**
- **Research reference materials**
 - **DS intermediates – e.g. polysaccharides, proteins, conjugates; formulated DP**
 - **negative controls - placebos, matrixes**
 - **positive controls**
- **Any development associated documentation - process, assays, and formulation (presentations, reports)**
- **Stability, storage conditions, etc**

Production Process

- **Process flow diagrams showing the sequence of operations**
- **A step-by-step written procedure for each processing operation**
- **The rationale for the process design, defining the envelope of acceptable processing parameters and equipment choice**
- **Batch records for each processing operation**
- **Known Critical process steps indicated**
- **Data concerning hold points**
- **API storage conditions**
- **The rationale for the process design**
- **Equipment requirements**

Analytical

- **Analytical control strategy (ACS)**
- **List of test methods (in-process, release and characterization) + SOPs,**
- **Specifications for in-process and release tests**
- **Assays research reference materials**
 - **DS intermediates – e.g. polysaccharides, proteins, conjugates; formulated DP**
 - **negative controls - placebos, matrixes**
 - **positive controls**
- **Critical reagents - antisera, Mabs**
- **Equipment requirements**
- **Any development documentation associated with the assay (presentations, reports)**
- **Known Critical Quality Attributes (CQAs)**

TTP DELIVERABLEs

by Receiving Laboratories listed in TTP

- Produce at least two demonstration batches
- Write Batch records (BPRs)
 - BPRs are reviewed and approved by Originating lab (IVI) and Receiving lab (Purification Technical leads) prior to execution of the demonstration batches
- Scale - Laboratory and pilot (a scale similar to that practiced in IVI) scales
- Write detailed process description of the demonstration batches
- Outline all changes required to successfully implement the process at the Receiving lab
- Write a brief summary of the demonstration batches to document the successful execution of the process at the site
- Record investigations of deviations, potential impact, corrective actions
- It is expected that batches produced by the Receiving lab will meet specifications for all quality attributes and critical quality attributes
- Changes to the quality attributes need to be approved by the TTT.

Note: It is important that any changes required to accommodate the process at the Receiving site must be approved through the TT Team and TT Team leader before the initiation of lab/pilot work.



TTP SUCCESS CRITERIA

- **Success criteria (SC) need to be listed for each process step**
 - **Cell Banking**
 - **Cell Culture/Fermentation**
 - **Purification**
 - **Conjugation**
 - **Formulation**
- **SC need to be achieved to consider the technology transfer complete**
- **Changes to the SC must be approved by the TT Team leads.**

Tech Transfer Checklist

Process (Fermentation, Purification, Conjugation, Formulation)

Item	Responsible person	Expected date of completion	Actual date of completion	Comments
Bill of Materials				
Process Description				
In-Process Samples				
Reference Std				
In-Process Assays				
Process Consistency at Originating Lab				
Success Criteria				
Process Lab Demo at Receiving lab				
Process Pilot Demo at Receiving lab				
Process Successfully Transferred				

TTP Analytical

Analytical Assays

Release Tests
Characterization Tests
In Process Control Tests

- Assays already being performed by Receiving lab are verified under **Analytical Bridging Protocol**
- Assays “Novel” to Receiving **are transferred** to Receiving lab under a separate **Analytical Tech Transfer Protocol**
- TT and Bridging results for each method are summarized in separate **Analytical TT or Bridging Report**
- Analytical TT Reports are **referenced** in **Tech Transfer Report**

Assays Transfer Protocol

- **Single protocol for each "Novel" assay at the Receiving lab**
- **Includes copy of SOP number at the Originating lab**
- **Reference materials (Research reference materials) and Critical reagents provided by Originating lab**
- **Success criteria for assay transfer**
- **Indication if assay measures Critical Quality Attribute (COA) or Critical Process step**

Assay Bridging Protocol

- **For assays already run at the Receiving lab**
- **Can be combined for all assays**
- **Success criteria for assay bridging**

TTP: Tech Transfer Schedule and Reports

TECH TRANSFER SCHEDULE

- Anticipated TT schedules/timelines for each area (process, analytical and formulation) are outlined in this section.

REPORTS

A table containing the list of projected reports to be written for technology transfer activities:

- Upstream process
- Downstream process
- Conjugation process
- Analytical TT reports
- Formulation TT reports

Tech Transfer Report

written by Receiving lab

Content:

- Flow chart
- Structure and pertinent physical properties of the product and intermediates
- A detailed process description of the demonstration batch(es)
- A brief summary of the demonstration batches (to document the successful execution of the process at the Receiving site)
- A table containing the list of reports related to all technology transfer activities – Process (Upstream, Downstream, Conjugation, and Formulation)
- A Table with the list of analytical methods used during production process and release of Vaccine candidate after TT. It should contain
 - Attribute measured by each method
 - Purpose of the assay (Release, In process or Characterization)
 - SOP numbers from both laboratories (Originating and Receiving)
 - Indication if method was transferred or verified/bridged
 - The status of the assay qualification/validation
- List of changes required to successfully implement the process at the Receiving site
- Investigation of deviations, potential impact, corrective actions

Thanks to...

IVI VPD Group, IVI D&D group, IVI leadership, IVI Epidemiology/ Surveillance

IVI Donors: BMGF, Gov. Korea and Sweden

VaBiotech, Shantha, EuBiologics, Incepta, SK Chemicals, BT Biofarma

IVI Collaborators

Academy of Medical Sciences, North Korea
Aga Khan University, Pakistan
Agence de Medcine Preventive, France
Armauer Hansen Research Institute (AHRI), Ethiopia
Bernhard Nocht Institute for Tropical Medicine, Germany
Biofarma, Indonesia
BMBF, Government of Germany
Catholic University, South Korea
Celltrion, South Korea
Coalition against Typhoid
Directorate of Health Services, Department of Health and Family Welfare, State Government of Orissa, India
Ethiopian Health and Nutrition Research Institute, Ethiopia
EuBiologics, South Korea
Fred Hutchinson Cancer Research Center, USA
Gavi, the Vaccine Alliance, Switzerland
Green Cross, South Korea
Group for Technical Assistance, Nepal
icddr, Bangladesh
Incepta Pharmaceuticals, Bangladesh
Indian Council of Medical Research, India
Institut Pasteur, Senegal
Institut Supérieur des Sciences de la Population, Burkina Faso
Instituto Butantan, Brazil
Johns Hopkins University, International Vaccine Access Center (IVAC), USA
Kenya Medical Research Institute, Kenya
Kilimanjaro Christian Medical Centre, Tanzania
Korea Center for Disease Control, South Korea
Korea National Institute of Health (KNIH), South Korea
Korea Research Institute of Bioscience and Biotechnology (KRIBB), South Korea
Kumasi Centre for Collaborative Research in Tropical Medicine, Ghana

Mahidol University, Thailand
Ministries of Health (Ethiopia, Kazakhstan, Kyrgyzstan, Mongolia, Sudan)
Ministries of Public Health (Brazil, Colombia, Thailand)
National Institute of Cholera and Enteric Diseases (NICED), India
National Institute of Hygiene and Epidemiology (NIHE), Vietnam
National Institutes of Health (NIH), USA
PATH, USA
Pohang University of Science and Technology (POSTECH), South Korea
Regional Medical Research Centre, Bhubaneswar, Orissa, India
Sabin Vaccine Institute, USA
Sanofi Pasteur, France
Seoul National University, South Korea
Shantha Biotechnics, India
SK Chemicals, South Korea
University of Alabama at Birmingham, USA
University of Florida, USA
University of Gothenburg, Sweden
University of Queensland, Australia
University of Vermont, USA
University of Virginia, USA
VaBiotech, Vietnam
Wellcome Trust Sanger Institute, UK
WHO Initiative for Vaccine Research (IVR), Switzerland
WHO Regional Office for South-East Asia (SEARO), India
WHO Regional Office for the Western Pacific (WPRO), Philippines
World Health Organization, Switzerland
Yonsei University, South Korea

Thank you



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Thank you



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Questions?

