SINCE 1997

25 YEAR

# IMPACT REPORT


International Vaccine Institute

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# FOREWORD

**If ever there was a time in human history to celebrate the importance of vaccines, it is now. In one year, the COVID-19 virus emerged and became a pandemic, wrecking lives and the global economy—and then, vaccines were developed that limited the explosive growth of the contagion.**

We have seen, however, that having an available vaccine is different than immunizing the world, and we remain mindful of the severe disparities the pandemic revealed, but that we already knew existed.

At the International Vaccine Institute (IVI), we understand our mission—to continue tackling these disparities, not just for COVID-19, but for the diseases that impact the less wealthy parts of the world. As we celebrate our 25th anniversary and our many accomplishments so far, we keep our mission firmly in mind: contributing to a healthier, safer world, by discovering, developing and delivering vaccines to shield the most vulnerable populations from endemic and emerging infectious diseases.

Millions of children still die every year from diseases for which no vaccine is available, infections like chikungunya, shigella and schistosomiasis. Most of these diseases disproportionately affect impoverished communities in low- and middle-income countries. Besides death and immense suffering, these diseases trap people, communities and economies in a cycle of poverty and disease.

Vaccines keep individuals and their families healthier, helping to lift them up out of poverty and improving local and regional economies. Our endeavors are driven by a desire to save lives, not by profits.

We could never have achieved so much without the tremendous support of our partners, allies and donors. As we prepare an ambitious agenda for the next 25 years, we take a moment to thank everyone for sharing in our critically important mission.

**DR. JEROME KIM**

**IVI Director General**

# IVI AT A GLANCE

**Hosted by the Korean government, IVI officially opened its headquarters in Seoul in 1997 with a mission focused on safeguarding the health of people living in low- and middle-income countries (LMICs). Launched by the United Nations Development Programme, our work supports the entire spectrum of vaccine discovery, development and delivery for poverty-associated infectious diseases, and more recently for emerging diseases.**

We are an international organization, with 39 countries and the World Health Organization (WHO) as our members, who inform every aspect of our work and help us stay focused on our mission. With their support, we now have three offices that coordinate our global operations—headquarters in Seoul, a Europe Regional Office in Stockholm and a country office in Austria (opening in November 2022)—and three Collaborating Centers, research hubs where we have partnered with local institutions on the ground in Ethiopia, Ghana and Madagascar.

We are also a product development partnership, a unique type of international organization that builds collaborations between governments, private sector entities, research institutions and the philanthropic community.

Vaccine research and development is an expensive and time-consuming process: on average, it takes 5-10 years and upwards of US$500 million to move a vaccine from the laboratory to delivery, and many vaccine candidates fail in the clinical trial process. That's why we step in and tackle diseases when pharmaceutical companies will not, when the profit motive is missing because the people who suffer from these diseases come from impoverished regions of the world.

In our work, we carry out epidemiology and surveillance studies to determine which diseases carry the largest burden and use those studies to inform every stage of vaccine discovery, development and delivery. We identify which of these diseases could be tackled through immunization, find promising vaccines languishing—for lack of adequate science budgets—in the research pipelines of pharmaceutical companies, and then plot out how these vaccines could travel through clinical trials and regulatory pathways. Our epidemiological as well as health economics studies also contribute to data on the need, and demand for vaccines, the use of vaccines, as well as on the emergency and spread of antimicrobial resistance.

We know that it is not enough to put the blinders on and narrowly develop and test potential vaccines. Instead, we need to know the environments that vaccines will be used in and develop solutions that work in context, not just in laboratories. We work with research institutions and vaccine manufacturing networks in low- and middle-income countries to test these vaccines—developing these institutions' capabilities in the process—and then see the products through from regulatory approval through distribution and use. We have done this, start to finish, with cholera and—soon—typhoid.

We are motivated to save lives through vaccines and the power of science, and we are also motivated by a desire to share our technological expertise and enhance the scientific and manufacturing capabilities of all our partners so that the global pace of science—and its delivery—can accelerate.

# OUR IMPACT

## OVER THE PAST 25 YEARS

**39**
countries and WHO as member states.

Research collaborations in

**44**
countries across six continents

Biosafety level 3 enhanced (BSL3+) lab at IVI headquarters.


*IVI state parties and signatories:*

**2**
**VACCINES DEVELOPED:**

Oral Cholera Vaccine
**$28M**

Lower vaccine development costs
**LAB TO LICENSURE**

Vi-DT typhoid conjugate vaccine
**$29M**

Developing COVID-19 vaccines in partnership with over 20 companies that have committed a combined 1 billion doses to COVAX.

VACCINES FOR
**9 INFECTIOUS DISEASES**
of global health importance in clinical trials.

MORE THAN
**1 MILLION**
people vaccinated through IVI campaigns across Africa and Asia.

MORE THAN
**1,300**
journal articles published.

MORE THAN
**40**
clinical trials sponsored by IVI since 2005.

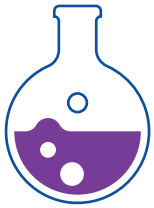
**3,000+**
vaccine professionals from LMICs trained through IVI's annual International Vaccinology Course.

# VACCINE DEVELOPMENT

**IVI has the skills, knowledge and resources to work along the entire vaccine value chain: from epidemiological studies establishing the burden of an infectious disease to the discovery of new vaccines in the laboratory through the delivery and impact of the vaccine in real-world settings.**

## DISCOVER

At our laboratories in Seoul, we have microbiological, immunological, genomic containment, as well as animal facilities and teams with expertise in molecular biology, microbial genetics, bioinformatics, and immunology. Through our laboratory capacity, we can improve existing vaccines and identify new candidates for research.



## DEVELOP

We partner with qualified vaccine manufacturers from low- and middle-income countries, and transfer our know-how to our partners so they can lead the vaccine development process. We also help manufacturers and sponsors of new vaccines navigate the path to regulatory approval.

## DELIVER

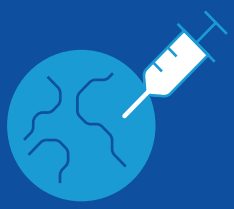
We facilitate the introduction of new licensed vaccines in countries where they are needed, including by carrying out vaccination campaigns and by generating scientific data on the need for vaccines and the impact of vaccination.

## IVI VACCINES ARE:

**Low Cost**

**Easy to administer in resource-limited settings.**

**Easily produced by manufacturers in developing countries.**



**Protective against diseases of global public health importance.**

# FINDING A TYPHOID VACCINE FOR CHILDREN

**IVI's work on typhoid began when our work on cholera began—with the Diseases of the Most Impoverished (DOMI) grant, in 2000. This grant provided the resources to examine the burden of typhoid in six Asian countries, and additional funding allowed us to closely examine the epidemiology of the disease in sub-Saharan Africa.**

The disease is most often contracted through contaminated food and water. An estimated 11-20 million people contract typhoid infections every year, with children hit particularly hard—which means that new vaccines must work well with younger populations. Yet, the two vaccines currently available work better with adults than children and are also too expensive. As with cholera, travelers heading to typhoid-endemic regions can access the vaccines more easily than those living in the endemic regions.

IVI adopted a two-prong approach. First, we launched a vaccine acceptance project to increase immunization acceptance. More than a half million people in Nepal and Pakistan were vaccinated through this initiative. Second, we began work developing a new vaccine that was easier to use in the field and provided more protection for children.

IVI partnered with Shanta Biotech of India, the company that brought the oral cholera vaccine over the finish line, but a corporate merger resulted in the typhoid work losing steam; the new parent company did not appreciate the market for a new typhoid vaccine. IVI then partnered with three companies and transferred the nascent vaccine technology to all three: SK bioscience of South Korea, Bio Farma of Indonesia and Incepta of Bangladesh.

With funding from the Bill & Melinda Gates Foundation, SK bioscience conducted Phase I and Phase II trials in the Philippines, while Bio Farma conducted trials on a related vaccine candidate in Indonesia. SK bioscience then launched a Phase III trial in the Philippines and Nepal, with IVI providing critical support that built the capacity in Nepal to run such a trial. The medical staff and scientists of research institutions were trained at home, and in India, even the medical offices were redesigned so that the layout facilitated research.

Building in-country capacity to run the clinical trial took 9 months, while the trial itself lasted 15 months. As a result, Nepal can now host additional clinical trials, including another IVI-run evaluation of a COVID-19 vaccine candidate and the evaluation of a new, simplified oral cholera vaccine.

The typhoid vaccine candidate tested in Nepal and the Philippines obtained an export license from the Korean Ministry of Food and Drug Safety in May 2022 and is now undergoing regulatory approval with WHO, with the decision expected by early 2023. Manufacturing preparations are expected to finish by mid-2024. In Indonesia, Bio Farma's candidate is also in the regulatory review process.

The end result of this work is that at least two new vaccines, approved and more effective with children, will soon be available. The competition between the two vaccines will help ensure lower prices and a more plentiful supply. And, most importantly, the increased supply at lower prices will decrease both the caseload and the mortality rate from typhoid. Put simply, more lives will be saved.

- **An estimated 11-20 million people contract typhoid infections every year, with children hit particularly hard**
- **Building in-country capacity to run the clinical trial took 18 months, while the trial itself only lasted 15 months.**
- **At least two new vaccines typhoid conjugate vaccines, that are more effective with children will soon be available.**
- **Competition between two vaccines will help ensure lower prices and a more plentiful supply.**

## BUILDING A GLOBAL STOCKPILE OF

# AFFORDABLE CHOLERA VACCINES

**Cholera is a disease associated with locations torn apart by war or natural disasters, or the camps of displaced persons and families fleeing these catastrophes. Cholera can also be found in most places where poverty is entrenched, and safe food and water are not easy to come by.**

An expensive cholera vaccine was developed for people who were traveling to places where cholera was endemic—but that vaccine never sold at a price that was accessible in areas where burden is high, safe water and sanitation deficient, and where the risk of death from cholera is greatest. And, because of the poverty of the people who needed the vaccine the most, there was no profit motive for pharmaceutical companies to develop a less expensive product – a situation known as "market failure."

The first grant that IVI received, in 2000, established a program tasked with understanding the true burden of cholera in six Asian countries, along with the economics and realities that confront the development of a less expensive cholera vaccine.

Next, IVI established a partnership with VaBiotech, a Vietnamese company that produced a separate cholera vaccine. Since the country's regulatory authority did not meet WHO's standards, VaBiotech's vaccine was not used widely outside of the country. IVI worked with VaBiotech to reformulate the vaccine with production standards that met all international guidelines, and then evaluate the vaccine through clinical trials in Vietnam and India.

Once the trials demonstrated the vaccine's safety and effectiveness, in 2005 IVI initiated a transfer of the vaccine technology to Shantha Biotechnics, an Indian company, and launched a new clinical trial that showed the version produced in India had an efficacy rate of 65% for at least five years. In 2009, the vaccine was licensed in Vietnam and India and, in 2011, it was prequalified by WHO.

The story of cholera vaccines does not end there, however. The one manufacturer, Shantha, had limited production capacity and more products were needed to meet the ever-escalating global needs, a point underscored by a massive cholera outbreak in Haiti in 2010. That year—in between the initial licenses and WHO prequalification—IVI began to look for another private sector partner. But this second search was much more difficult, as too many companies declined the opportunity to produce an inexpensive product for impoverished regions.


IVI eventually partnered with EuBiologics, a small South Korean Company that had no vaccine production experience. But along with the transfer of vaccine technology, IVI provided training of all aspects of production. In return, EuBiologics created its own vaccine candidate and completed the initial safety trials in 2013, when WHO established a global stockpile of cholera vaccines. In 2014, a Phase III clinical trial showed that the new vaccine was just as safe and efficacious as IVI's first cholera vaccine. In 2015 the South Korea Ministry of Food and Drug Safety approved the vaccine, Euvichol®, with WHO prequalification taking place at the end of that year.

Today, IVI's cholera vaccines comprise 90% of WHO's stockpile, which it distributes to countries as well as relief efforts when needed. IVI continues to work with new partners to improve the current vaccine options, transferring OCV technology to Incepta in Bangladesh and to Bharat Immunologicals and Biologicals Corporation Limited (BIBCOL) in India in 2021. In 2020, Incepta's Cholvax OCV was licensed for national use. This work will continue until cholera is no longer a current threat.

## IVI'S ORAL CHOLERA VACCINE:

Oral cholera vaccines (OCV) developed by IVI make up **90%** of the global OCV stockpile.

IVI aims to vaccinate an additional

**1 MILLION**

**people by 2024.**

**100 MILLION**

doses used in public vaccinations across 20 countries.

# STRENGTHENING RESEARCH CAPACITY

## IN LOW- & MIDDLE-INCOME COUNTRIES

**One of the most important aspects of IVI's work is in building the capacity for institutions in low- and middle-income countries to discover, develop and deliver vaccines themselves. IVI provides training and technical assistance to our collaborating research partners in areas ranging from good clinical practice to infectious disease surveillance and reporting. We also provide technology transfer to vaccine manufacturers and technical assistance to national regulatory authorities (NRAs) in developing countries.**

Our capacity-building activities are exemplified in our work with local partners in clinical trials, where we help build human and physical capacity to handle the demands of clinical trials.

The recent Phase III clinical trial testing of our typhoid conjugate vaccine in Nepal provides a perfect case study for how we embrace this work, where the payoff stretches well beyond the one clinical trial. An improved science infrastructure can handle additional clinical trials and is also better prepared to handle advanced medical problems. And the entire country benefits in a virtuous cycle; as it grows its scientific expertise, it becomes known for research capacity and then draws in more scientific investment.

We selected Nepal due to its high, endemic burden of typhoid, even though it lacked a research infrastructure and had hosted few clinical trials. With a target sample size of 1,800 participants, IVI staff had a goal of finding four trial sites.

We first met with health officials, respected doctors and community leaders to develop an initial list of 20 potential sites. We then spoke with potential site investigators and senior leadership at each facility to gauge their interest in not just participating in the trial but working to upgrade their facilities.

We visited 13 sites to determine their potential to conduct safe and accurate research that respected the rights and needs of participants. Staff training needs as well as technology and infrastructure needs were recorded. Eventually, we identified four sites, with two as alternates.

For each site, medical and research staff were selected to form a team of about 30 people. Extensive trainings covered everything from the scientific processes of collecting data to protocols in working with trial participants that showed respect and care. Site leadership attended additional trainings in Nepal's capital, Kathmandu. Mock drills and roleplaying helped the teams prepare for many of the scenarios that research trials could confront, from the mundane to the emergencies.

The infrastructure needs of the trial resulted in some construction projects, as the facilities needed appropriate space to administer and work with participants and to collect samples and analyze data. Floorplans were modified so that enough indoor area could be allotted to this research. Technology was procured to collect and process patient data and ensure that Wi-Fi and internet access could facilitate communication between trial sites and IVI staff.

IVI staff and research teams also spent considerable time conducting community engagement, so that parents and children considering whether to participate understood the goals of the trial—to see whether our typhoid conjugate vaccine candidate could be more effective and easier to administer than what is currently available. The outreach effort helped ensure that trial participants had the support of their neighbors moving forward.

Participant recruitment plans were drawn up to ensure that each site met its goal, and then a quality assurance plan was developed that

included an initial monitoring visit after the first several participants were recruited—so that mistakes in procedures could be quickly rectified. The last step was a site readiness evaluation, in which all this work was examined by an outside consultant.

The end result was not only a crucial step in the evaluation of a new typhoid conjugate vaccine with long lasting immunogenicity, but also in the development of research infrastructure in four new locations that can be used in evaluating how other vaccines and technologies can improve the well-being of the Nepalese people. IVI, for example, recently used the same four sites in testing a COVID-19 vaccine candidate—and the site preparation work proceeded at a much quicker pace. These research trials will bring more medical breakthroughs to Nepal and help everyone live a healthier life.

**BUILDING RESEARCH CAPACITY IN NEPAL:**

## 9 MONTHS THAT PAID OFF

**Phase III clinical trial for Vi-DT typhoid conjugate vaccine**

- 20 sites examined; four sites selected.
- Identified and trained young investigators who could take a leadership role at each site.
- At each site, research teams were recruited and trained—almost all had not worked in a clinical trial previously.
- At each site, a minimum of four rooms were allocated for the trial, and necessary equipment was procured.
- Community outreach/ stakeholder engagement to alleviate mistrust.
- All sites were then evaluated by an independent consultant to ensure readiness.
- Only then could the study recruit 1,800 participants.
- Vi-DT was shown to be safe, with a single dose providing long-term protection, including in infants under age 2.
- Vi-DT licensed for export by the Korean Ministry of Food and Drug Safety.
- Three of the 4 trial sites participated in a separate trial, testing a COVID-19 vaccine candidate, and all four are ready for the next challenges.

| | Annual Deaths | Geographic distribution |
|---|---|---|
| **Cholera** | **95,000** | **Sub-Saharan Africa, India, Bangladesh, Yemen** |
| **WHAT IS IT:** Cholera is a diarrheal infection that strikes in crowded settings with limited access to safe water and sanitation. Deadly outbreaks occur in vulnerable populations after natural disasters and other humanitarian crises, including forced displacement. | | |
| **WHAT HAS IVI ACCOMPLISHED:** IVI developed the world's first affordable oral cholera vaccines, transferred the technology to manufacturers in low- and middle-income countries, and helped them obtain regulatory approval by the WHO. The vaccines have immunized more than 70 million people across 20 countries. IVI aims to vaccinate an additional 1 million people through its own campaigns by 2024. | | |
| **Typhoid** | **65,000-187,000** | **Mainly South Asia** |
| **WHAT IS IT:** Typhoid fever is a bacterial disease, spread through poor water, sanitation and hygiene. The disease has few symptoms that reliably distinguish it from other infections, making it difficult to diagnose and treat. | | |
| **WHAT HAS IVI ACCOMPLISHED:** IVI has worked with two vaccine manufacturers to develop new typhoid conjugate vaccines that can protect infants under two years of age, as well as young children, against typhoid fever, and provide a longer duration of protection than existing vaccines. Vi-DT, manufactured by SK bioscience, has been licensed for export by the Korean Ministry of Food and Drug Safety, and is currently being evaluated by WHO. IVI has also launched typhoid surveillance and vaccination programs in several African and Pacific Island countries. | | |
| **COVID-19** | **6.5 million since 2020** | **Global** |
| **WHAT IS IT:** The COVID-19 virus swiftly became a global pandemic after it emerged, bringing the global economy to a screeching halt in March 2020. Recovery efforts have revolved around vaccines that limit the worst impacts of the disease. | | |
| **WHAT HAS IVI ACCOMPLISHED:** IVI contributed to the pre-clinical and clinical development of COVID-19 vaccine candidates in partnership with over 20 companies that have committed a combined 1 billion doses to COVAX (~20% of the total). IVI is also partnering with the Coalition for Epidemic Preparedness Innovations (CEPI) to carry out clinical trials of Sinopharm's BBIBP-CorV vaccine to support expanded access to COVID-19 vaccines in Africa. | | |
| **Chikungunya** | **Long-term debilitation** | **Africa, Asia, the Americas** |
| **WHAT IS IT:** Chikungunya is a viral disease spread by Aedes mosquitoes that, while not often fatal, causes debilitating joint pain that can last for years.<br>**WHAT HAS IVI ACCOMPLISHED:** IVI has launched a Phase II/III clinical trial to evaluate a two-dose regimen of a vaccine candidate in five countries in Asia and Latin America. | | |
| **Shigella** | **>212,000** | **Sub-Saharan Africa, India, Pakistan** |
| **WHAT IS IT:** Shigella is a bacterial infection that causes severe dysentery, long-term health and cognitive defects, bloodstream infections and death. Shigella is linked with poverty, malnutrition, poor sanitation and the lack of safe drinking water. | | |
| **WHAT HAS IVI ACCOMPLISHED:** IVI is working on a universal Shigella vaccine candidate, potentially effective against several strains, and then conducted the groundwork for clinical evaluations of the technology. | | |

| | Annual Deaths | Geographic distribution |
|---|---|---|
| **Invasive Non-Typhoidal Salmonella (iNTS)** | **70,000-680,000** | **Sub-Saharan Africa and Eastern Europe** |
| **WHAT IS IT:** Invasive Non-Typhoidal Salmonella, an invasive bacterial infection, is one of the top four global causes of diarrheal diseases. It is linked with poverty, malnutrition, poor sanitation and the lack of safe drinking water. | | |
| What has IVI accomplished: IVI established a proof of concept for a vaccine candidate, conducted laboratory preparations for evaluation, and established a partnership with a private sector manufacturer. IVI also launched a landscape analysis of iNTS that will include a vaccine R&D roadmap, a clinical development plan and regulatory pathway, as well as a business case and investment case. | | |
| **Hepatitis E Virus (HEV)** | **70,000** | **Asia and Eastern Africa** |
| **WHAT IS IT:** Hepatitis E Virus (HEV) is an emerging cause of acute viral hepatitis, primarily spread through contaminated water. Pregnant women are at highest risk of severe disease and death, and the virus can be transmitted at birth from mother to child, as well as from infected blood transfusions and through the consumption of infected animal products. Outbreaks have been documented in refugee settings where water and sanitation are poor. Although a safe and highly effective vaccine has been approved in China and Pakistan, it is not yet readily available for global public use. | | |
| **WHAT HAS IVI ACCOMPLISHED:** IVI has launched HEV surveillance efforts in Africa and Nepal. IVI is also preparing to conduct a Phase II clinical trial of Hecolin® hepatitis E vaccine in pregnant women with partners in Pakistan while developing a roadmap for its widespread use. | | |
| **AMR** | **700,000** | **Global** |
| **WHAT IS IT:** AMR is caused by the overuse of antimicrobial medicines, such as antibiotics, antivirals and antifungals used to prevent and treat infections. The pathogens that cause infections can evolve over time and become resistant to medicines. Consequently, infections and illnesses can become untreatable, disease risk increases, and medical procedures such as routine surgery can become riskier. | | |
| **WHAT HAS IVI ACCOMPLISHED:** IVI has launched extensive surveillance programs in Asia, capturing data on antimicrobial use and AMR infections throughout the continent. IVI has also launched an initiative to improve quality assurance of antimicrobials to ensure their potency meets accepted standards, as well as a project in Asia and Africa to improve data-sharing and use to improve AMR policy, planning and advocacy. IVI's Vi-DT typhoid conjugate vaccine (TCV) will also help curb outbreaks of extensively drug-resistant typhoid fever (XDR-TF), such as the outbreak in Pakistan that began in 2016 and has been spreading since. TCV was shown to be highly effective against XDR-TF in an outbreak setting. | | |
| **Human Papilloma Virus (HPV)** | **250,000** | **Global** |
| **WHAT IS IT:** HPV is a common viral infection that causes skin or mucous membrane growth. Some types of HPV cause cervical cancer—in fact, nearly all cases of cervical cancer are caused by HPV infection. Since 2006, a two-dose HPV vaccine has been available, but the uptake in LMICs has been limited. | | |
| **WHAT HAS IVI ACCOMPLISHED:** In 2018, IVI launched a study to demonstrate the effectiveness of a single-dose HPV vaccine administered to young women in Thailand and generate data to inform global public health policy. A single dose vaccine could allow countries to substantially expand coverage by lowering costs and simplifying delivery. | | |
| **Schistosomiasis** | **200,000** | **Global** |
| **WHAT IS IT:** Schistosomiasis is a parasitic disease that can damage the bladder, kidneys and liver. It has been identified in 79 countries, with the highest disease burden in sub-Saharan Africa, and especially in poor and rural communities with agricultural, domestic, and recreational practices that routinely take place in waters infested with the parasitic worms. More than 200 million people around the world require treatment for schistosomiasis. There is currently no vaccine. | | |
| **WHAT HAS IVI ACCOMPLISHED:** In Burkina Faso and Madagascar, IVI is carrying out a seroprevalence and disease burden study, as well as a study to estimate the disease's financial burden on communities. IVI is also carrying out a Phase I clinical trial to assess the safety and immunogenicity of SchistoShield®, one of the leading schistosomiasis vaccine candidates. | | |

International Vaccine Institute

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