SPIKY'MUNE

BUSINESS PLAN

Cholera remains one of the most persistent global health challenges of the 21st century. Despite significant medical advances, current vaccination strategies face critical limitations in reaching the world's most vulnerable populations, particularly in regions with inadequate healthcare infrastructure and compromised cold chain systems. The seventh cholera pandemic, ongoing since 1961, continues to disproportionately affect Sub-Saharan Africa, which accounts for approximately 60% of global cases (Vax-Before-Travel, 2025).

This business plan presents Spiky'Mune, a biotechnology innovation that addresses these fundamental challenges through the development of an edible cholera vaccine produced in genetically modified *Opuntia ficus-indica* cactus plants. By leveraging plant-based molecular farming technology, Spiky'Mune eliminates the need for cold chain storage and complex distribution networks, offering a thermostable, locally producible vaccine solution specifically designed for resource-limited settings.

The global cholera vaccine market, valued at $104 million in 2025 with 10% projected growth (Pandey, 2025b), reveals significant supply-demand imbalance. Annual demand exceeds 100 million doses while production capacity remains at 37-50 million doses (WHO, 2024). This gap becomes more pronounced considering the near-monopolistic position of existing suppliers and the logistical complexities associated with traditional vaccine deployment in endemic regions.

Spiky'Mune's innovative approach addresses multiple market failures simultaneously. The cactus-based delivery system requires no refrigeration, dramatically reducing distribution costs. Local cultivation capabilities enable decentralized production, reducing dependency on international supply chains while creating sustainable economic opportunities in target regions.

Our target market spans three key segments: government health ministries seeking cost-effective solutions, international organizations (WHO, UNICEF, GAVI) influencing global vaccination policies, and humanitarian NGOs requiring rapid emergency deployment. The Total Addressable Market reaches $3.744 billion globally, with a Serviceable Available Market of $1.595 billion across Sub-Saharan Africa.

This business plan demonstrates the commercial viability and social impact potential of the Spiky'Mune innovation. The convergence of increasing climate-driven cholera outbreaks, expanding vaccine market demand, and technological advances in plant-based therapeutics creates an unprecedented opportunity for transformative impact. Spiky'Mune represents not merely a product innovation, but a paradigm shift toward decentralized, sustainable healthcare solutions that can reach the world's most underserved populations.

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List of abbreviations

AWD - Acute Watery Diarrhoea

CAGR - Compound Annual Growth Rate

CAM - Crassulacean Acid Metabolism

CDC - Centers for Disease Control and Prevention

CEBS - Community Event-Based Surveillance

CHW - Community Health Workers

COGS - Cost of Goods Sold

CTxB - Cholera Toxin B subunit

DRC - Democratic Republic of Congo

EBITDA - Earnings Before Interest, Taxes, Depreciation, and Amortization

EU - European Union

GAVI - Global Alliance for Vaccines and Immunisation

GMO - Genetically Modified Organism

GMP - Good Manufacturing Practices

GNI - Gross National Income

GTFCC - Global Task Force on Cholera Control

IAR - Intra Action Review

ICG - International Coordinating Group on Vaccine Provision

ICH - International Council for Harmonisation

IFRC - International Federation of Red Cross and Red Crescent Societies

IMS - Incident Management System

IP - Intellectual Property

IPC - Infection Prevention and Control

MSF - Médecins Sans Frontières

NBMA - National Biosafety Management Agency

NGO - Non-Governmental Organization

NPV - Net Present Value

NRA - National Regulatory Authority

OCV - Oral Cholera Vaccine

OGM - Organisme Génétiquement Modifié

ORS - Oral Rehydration Solution

PAHO - Pan American Health Organization

PESTEL - Political, Economic, Social, Technological, Environmental, Legal

PHEOC - Public Health Emergency Operations Center

R&D - Research and Development

RCCE - Risk Communication and Community Engagement

RDC - République Démocratique du Congo

RDT - Rapid Diagnostic Test

ROI - Return on Investment

SAM - Serviceable Available Market

SOM - Serviceable Obtainable Market

TAM - Total Addressable Market

UN - United Nations

UNICEF - United Nations Children's Fund

WASH - Water, Sanitation and Hygiene

WHO - World Health Organization

1. Market and competitive environment analysis

This section establishes the strategic foundations of the Spiky'Mune project through comprehensive analysis of three critical dimensions: the global epidemiological landscape, existing vaccine market dynamics, and our solution's competitive positioning. The analysis reveals both the urgent public health need and significant market opportunity that justify this innovative approach to cholera prevention.

1.1. Market analysis

1.1.1. Global epidemiological context

1.1.1.1. Current global cholera situation

Cholera remains a major global health threat with a resurgence observed in recent years. The World Health Organization (WHO) has recorded seven cholera pandemics over the past two centuries. The current cholera epidemic is considered to have started in 1961 (Vax-Before-Travel, 2025). In July 2025, over 355,800 cholera cases and nearly 4,000 deaths were reported from 30 countries across Africa and South-East Asia regions (WHO Global Cholera and AWD dashboard public, July 2025).

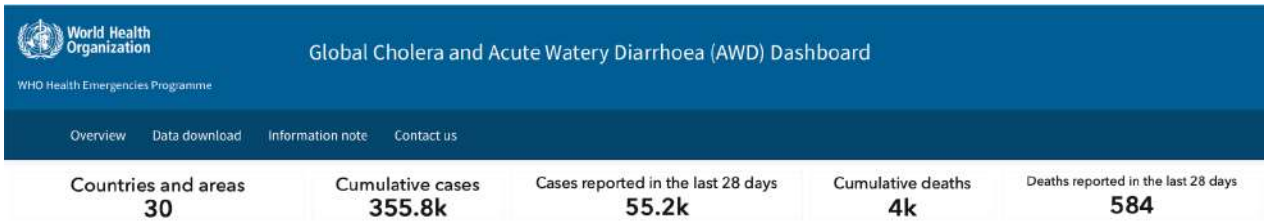

Figure 1: The WHO's Global Cholera and Acute Watery Diarrhoea Dashboard was updated in June 2025

Africa accounts for the majority of cases, about 60% in 2025, making it the most affected continent. Despite previous progress, recent years have seen increases in outbreaks due to multiple compounding factors, with the WHO classifying the resurgence as a grade 3 emergency (Vax-Before-Travel, 2025).

1.1.1.2. Exacerbating factors

Several factors exacerbate the cholera burden globally (Figure 2). These include poor sanitation and hygiene, unsafe water sources, ongoing conflicts and political instability that weaken health infrastructure, mass displacements, and low public awareness. Overcrowding and forced migrations create environments conducive to cholera transmission. Individual factors, including poor hygiene, cultural practices, and low education levels, further increase risk (Cholera: a public health threat that still causes devastating outbreaks, 2019), (Dureab et al., 2019).

Criteria	Risk factors
Epidemiology	• In an endemic area: ▫ annual cholera outbreak or cholera outbreak in at least 3 out of the last 5 years (with incidence of at least 1 case/1000 in each year that cholera occurred) ▫ no cholera outbreak within the 5 previous years [(c)] • In the event of population movements: ▫ people from an endemic area move to a non-endemic area (risk of introduction) ▫ people from a non-endemic area move to an endemic area (no natural immunity) • Uncontrolled outbreak in a neighbouring country
Water **Sanitation** **Hygiene**	• Unprotected water sources; unchlorinated or contaminated water • Water quantity/person/day < 15-20 litres • Ongoing water-borne outbreak (e.g. hepatitis E) • Lack of adequate equipment for transporting, storing and handling water at home • Open defecation in water or other open spaces • Insufficient number of latrines (> 20 persons/latrine) or unused latrines due to poor construction, poor maintenance, any reason • Lack of adequate hygiene facilities and equipment
Demography	• Overcrowding (refugee population beyond the camp's intended capacity, high urbanization, detention centre, etc.)
Other	• Specific characteristics that increase the probability of cholera outbreak: climatic (floods or droughts), socio-economic, cultural, etc.

Figure 2 : Risk factors for cholera outbreak in a humanitarian emergency *(4.7 Vaccination strategies | MSF Medical Guidelines, no date)*

Climate change, with its associated extreme weather events such as floods, droughts, and heatwaves, exacerbates cholera transmission by damaging water and sanitation infrastructure and increasing exposure to contaminated water sources (Médecine / Science, 2025). These climate-driven factors intensify outbreaks, particularly in vulnerable communities with poor health systems, propelling an increasing need for both reactive and preventive vaccination campaigns. The rapidly changing climate context places cholera firmly in the category of climate crisis-related health threats,

necessitating urgent expansion of vaccine coverage (Davisweddi, 2025), (The Global Alliance Against Cholera (G.A.A.C), 2025).

Beyond these, significant challenges related to cholera vaccination further worsen the situation. The global emergency stockpile of oral cholera vaccines managed by the International Coordinating Group on Vaccine Provision (ICG) is often insufficient, leading to shortages where vulnerable populations cannot receive vaccines promptly during outbreaks. This depletion of the stockpile leaves inadequate supply for preventive vaccination campaigns, limiting the ability to forestall future epidemics.

1.1.1.3. Geographical distribution of cholera worldwide

Cholera is predominantly found in regions with inadequate water, sanitation, and hygiene (WASH) infrastructure. Africa remains the primary hotspot, with persistent outbreaks in multiple countries including Democratic Republic of Congo, Ethiopia, Nigeria, and others. Asia and parts of the Eastern Mediterranean region also experience outbreaks but with varying intensity. Climate and conflict dynamics influence geographical distribution, contributing to cross-border spread and epidemic persistence (Assistweb, 2022), (Vax-Before-Travel, 2023), (Cholera worldwide overview, 2025).

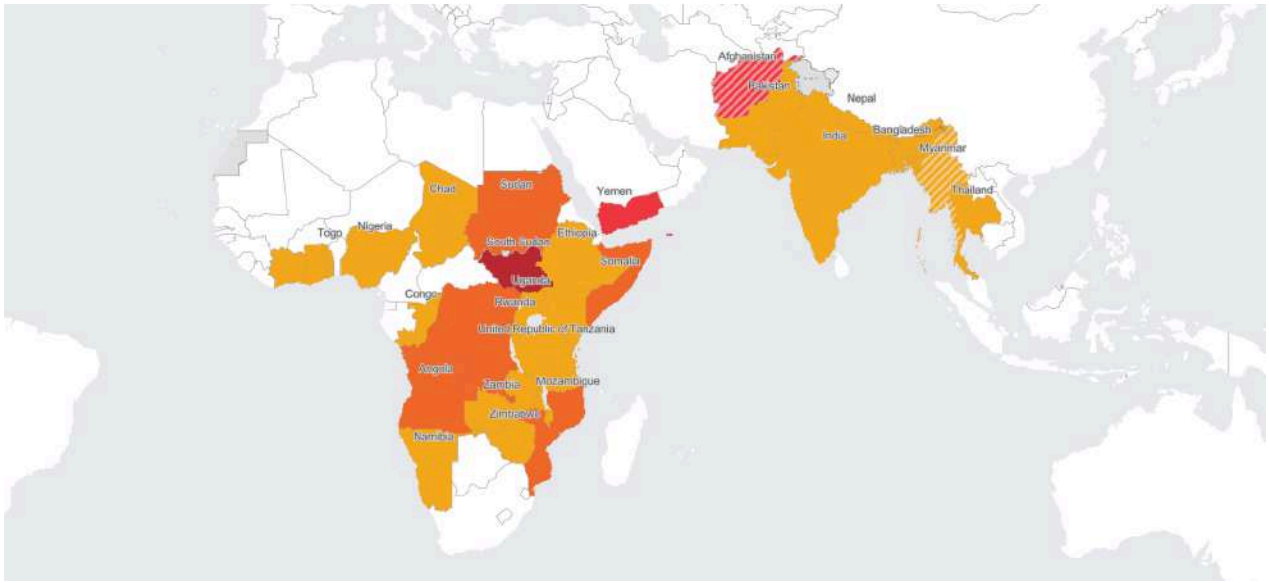

Figure 3 : Cholera and acute watery diarrhoea (AWD) cases per 100 000 *(WHO Global Cholera and AWD dashboard public, July 2025)*

1.1.2. Vaccine market analysis

1.1.2.1. Traditional cholera vaccine market

First of all, cholera vaccines, specifically oral cholera vaccines (OCVs), are the main tool for prevention in endemic and outbreak settings. Leading licensed vaccines such as Dukoral, Shanchol and Euvichol have WHO prequalification, enabling their use in mass vaccination campaigns led by governments and NGOs (Pandey, 2025b).

The global cholera vaccine market has grown significantly, valued at about USD 104 million in 2025 and projected to reach around USD 246 million by 2034, with a compound annual growth rate (CAGR) of approximately 10% (Figure 5).

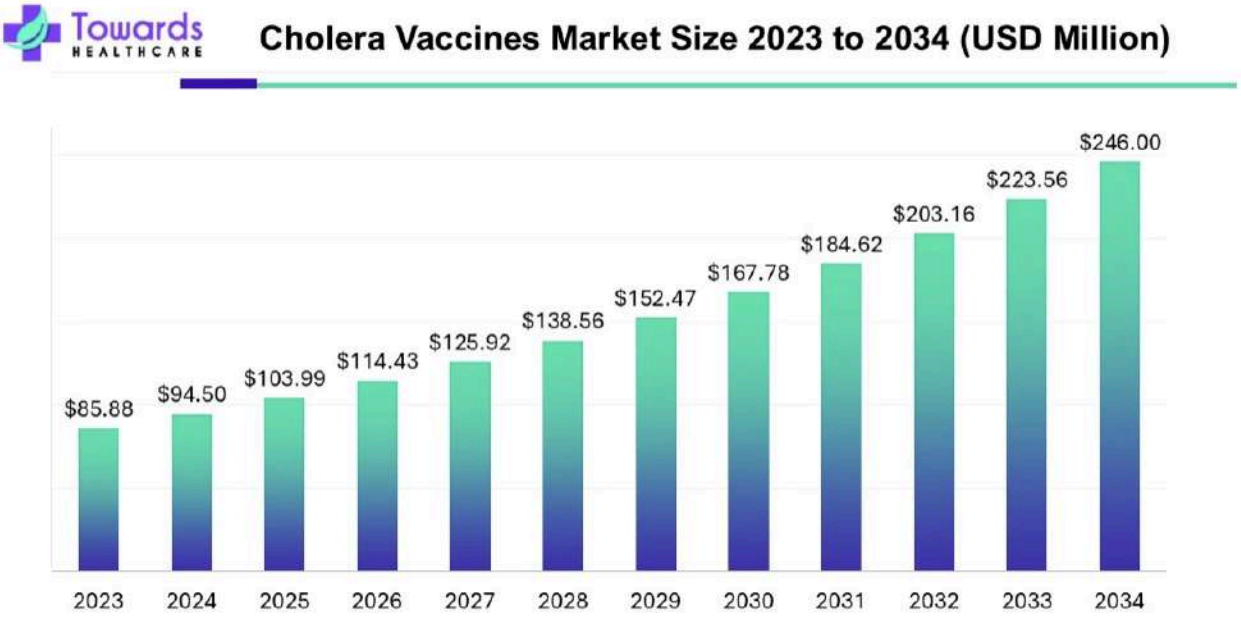

Figure 4: Cholera vaccines market size 2023 to 2034 *(Pandey, 2025b)*

In conclusion, the global cholera vaccine market is experiencing sustained growth driven by the urgent need to contain outbreaks in high-risk regions, with significant potential for expansion in emerging markets across Africa and Asia.

1.1.2.2. Demand analysis

Globally, there is a significant gap between cholera vaccine demand and supply (WHO, 2024 ; Gavi, 2023). Estimates indicate an annual requirement exceeding 100 million doses for effective preventive immunization against cholera, while current production remains around 37 to 50 million doses (WHO, 2024). This shortfall means many at-risk populations remain unvaccinated, intensifying susceptibility to outbreaks. Moreover, since January 2025, the ICG has received 38 requests from 12 countries, triple the number compared to the same period last year, in July. Already this year, over 40 million doses have been allocated by the ICG, compared to 35 million doses allocated in all of 2024 (Vax-Before-Travel, 2025). As demand continues to grow, the shortage of emergency vaccine stocks is worsening and further exacerbating this gap. Consequently, many countries struggle to conduct large-scale preventive campaigns, compromising long-term cholera control efforts.

Due to the shortage of doses for emergency protection, a single-dose vaccination strategy has been temporarily adopted, deviating from the standard two-dose regimen. This approach aims to maximize the number of individuals vaccinated at high risk with the available doses, thereby providing broader population-level protection despite the limited supply. Studies suggest one dose offers good initial short-term protection against cholera outbreaks, making it the most practical strategy under current constraints (MSF Medical Guidelines, 2025). However, a return to the two-dose schedule and expansion of preventive vaccination campaigns are recommended as vaccine availability improves.

Compounding these supply challenges is the near-monopolistic position held by EuBiologics as the principal supplier of WHO-prequalified cholera vaccines (WHO, 2024). Despite the company's scale-up efforts, with a production expected to reach over 70 million doses by 2025, the monopoly limits market competition, which affects pricing, innovation speed, and supply resilience (Gavi, 2024). Even EuBiologics, in an interview with Gavi, has advocated for fostering competition, recognizing that diversity among manufacturers is crucial to meeting global demand and reducing vulnerabilities associated with single-supplier dependence. Encouraging entry of new producers and alternative vaccine technologies is therefore essential to alleviate supply constraints and improve vaccine accessibility (Gavi, 2024).

Additionally, logistical barriers such as the requirement for strict cold chain maintenance, complex importation procedures, and the lack of local vaccine production infrastructure severely hinder timely vaccine distribution and access, especially in remote and resource-limited settings. These vaccination supply and delivery constraints critically impair cholera control efforts worldwide.

1.1.2.3. Emerging edible vaccine market

Edible vaccines represent an innovative and emerging segment within the vaccine market, projected to grow from approximately $8.8 billion in 2024 to $9.6 billion in 2025 globally, with a CAGR near 9-10% . And a strong projected CAGR of around 8.8% , expected to reach over USD 13.3 billion by 2034 (Figure 6). This surge is driven by advancements in genetic engineering and biopharming, rising demand for pandemic preparedness, growing public acceptance of genetically modified foods, and efforts to address critical challenges in traditional vaccination such as cold chain dependency and complex logistics.

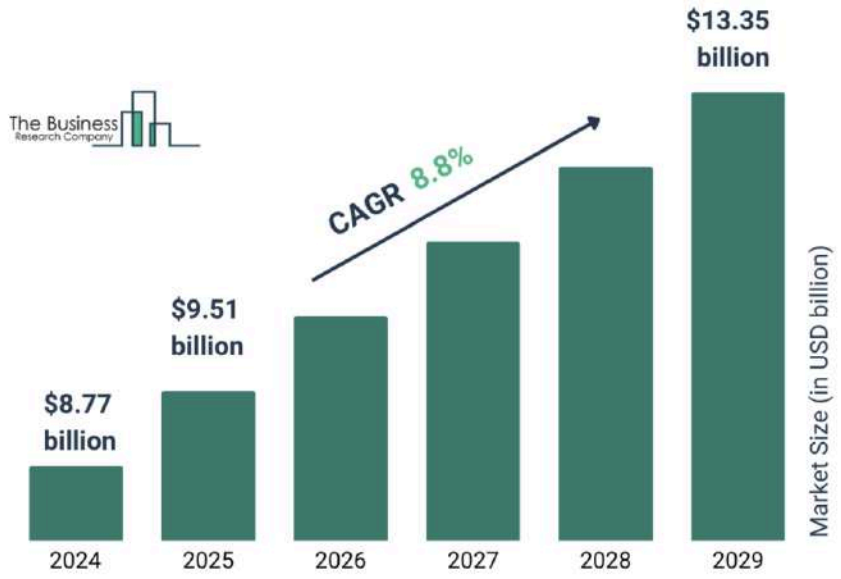

Figure 5 : Edible vaccine market growth forecast *(Edible Vaccine Global Market Report, 2025).*

This emerging market's applicability is particularly significant in low-resource and climate-vulnerable regions, where edible vaccines offer promising solutions to logistical hurdles by bypassing cold chain requirements and minimizing healthcare infrastructure demands. These features align closely with the objectives of sustainable and eco-friendly healthcare innovations, making edible vaccines a critical component of global immunization expansion strategies in the context of growing infectious disease threats exacerbated by climate change (*Edible Vaccine Global Market Report*, 2025).

Nevertheless, challenges remain in regulatory approval pathways, manufacturing scale-up, consistency of immune response, and addressing public concerns regarding genetic modification. Continued research investment, strategic partnerships among biotech firms, governments, and NGOs, and robust community engagement are essential to realize the market's full potential and integrate edible vaccines into mainstream healthcare frameworks (*Edible Vaccine Global Market Report*, 2025).

1.1.2.4. Geographical market segmentation

As previously noted, the two primary regions affected by cholera are South Asia and Africa, a pattern clearly illustrated in the map below:

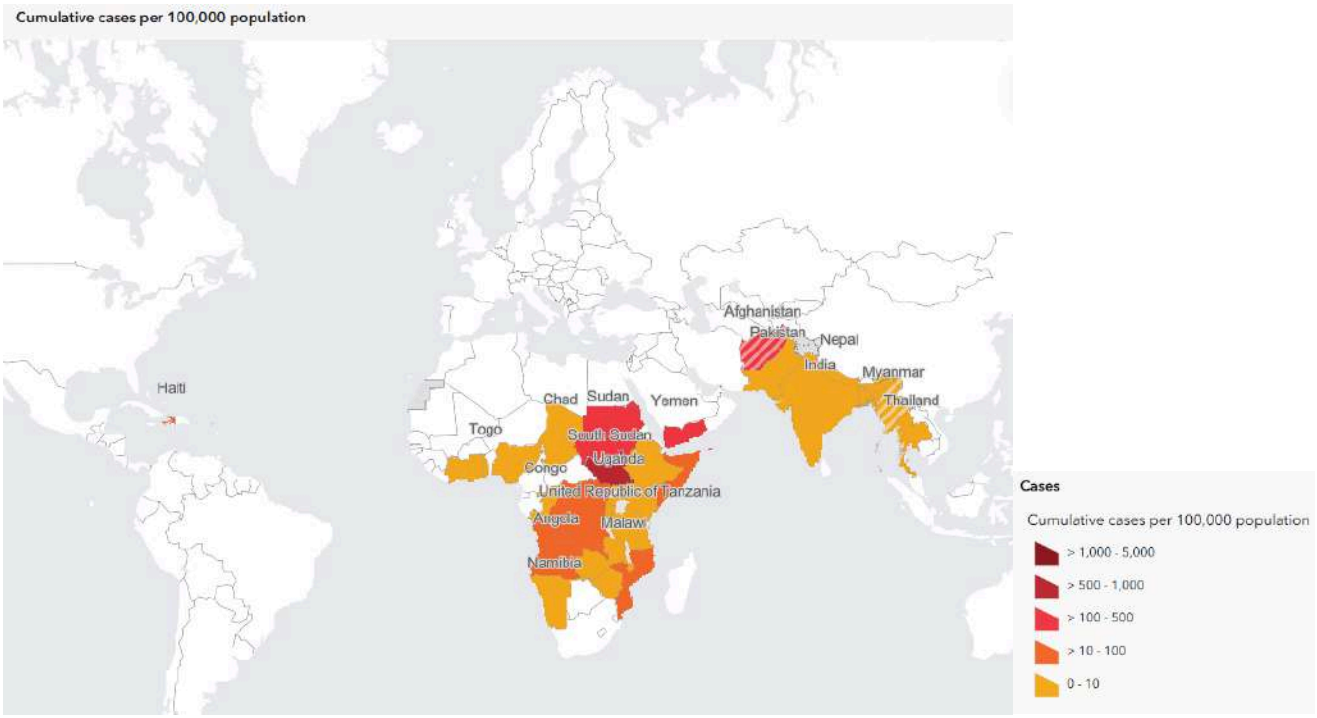

Figure 6: Global repartition of cholera cumulative cases reported from January 1st to August 28th, 2025 *(WHO global cholera and AWD dashboard)*

With Africa accounting for approximately 60% of the total cholera cases worldwide, our focus is directed toward this region (Vax-Before-Travel, 2025). However, it is important to note that not all African countries permit the use of genetically modified organisms (GMOs), which impacts vaccine strategies and implementation.

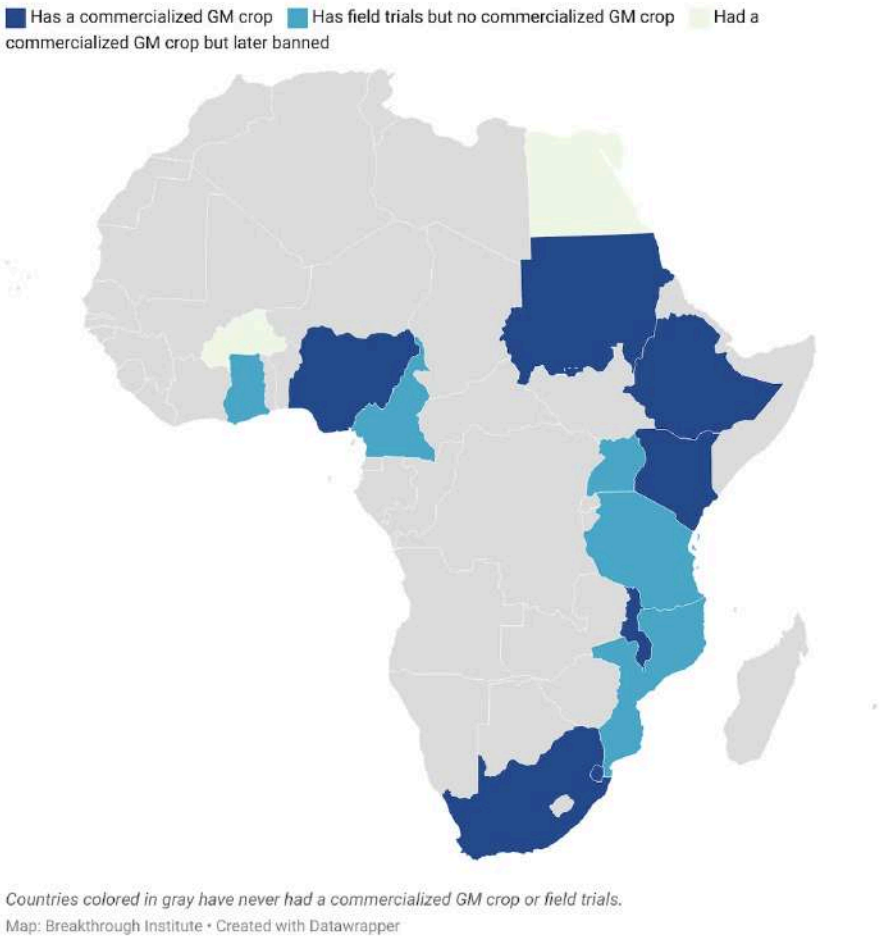

Figure 7 : Global map of the regulations about GMO cultivation in 2023 *(Genetic Literacy Project, 2023)*

Gavi, the Vaccine Alliance, is a global partnership that funds vaccination campaigns in countries whose gross national income (GNI) per capita falls below a defined threshold, currently set at US$ 1,820 as of 2025 (Gavi, 2023). The program's approach prioritizes countries that are least able to finance immunization programmes independently, directing resources where the impact will be greatest. The following map (Figure 9) illustrates the global distribution of nations currently eligible for Gavi support:

Figure 8 : Global map of the Gavi eligible's countries *(Gavi, the Vaccine Alliance)*

Eligibility for Gavi support is determined by national income status and is overseen by the ICG, which comprises the WHO, UNICEF, the International Red Cross (IRC), and Médecins Sans Frontières (MSF).

For the purposes of this analysis, we selected three countries with recent cholera pandemic outbreaks, where GMOs are authorized and which currently meet Gavi criteria: Ethiopia, Nigeria, and the Democratic Republic of Congo (DRC). During the week of July 21, 2025, Ethiopia reported nearly 6,000 cumulative cases of cholera, Nigeria 5,000 cases, knowing that it is the second most under-vaccinated country according to John Johnson, and the DRC 187 cases, according to the WHO global cholera and acute watery diarrhea dashboard (WHO global cholera and AWD dashboard, 2025).

1.1.2.5. PESTEL

PESTELs were thus drawn up for each of these three countries (Ethiopia, Nigeria and DRC). It evaluates the political, economic, sociocultural, technological, environmental, and legal dimensions that may affect the feasibility and success of the project. This macro-environmental analysis is useful to understand those countries' situations for a better implementation of our solution.

1.1.2.5.1. Political Factors

The countries under consideration maintain regional cooperation frameworks, with strong diplomatic and developmental ties involving France and the European Union (EU). The political environment in these three countries significantly impacts the adoption of novel biotechnologies. In the DRC, international cooperation is crucial: France has committed €500 million in aid for 2022–2025, while the EU continues its engagement through the European Union Training Mission (EUTM) until 2026 (Banque mondiale, 2025; Direction générale du Trésor, s.d.; Ministère de l'Europe et des Affaires étrangères, 2024; African Risk Capacity, 2021).

Nigeria, France's primary trading partner in Sub-Saharan Africa (accounting for 20% of French trade in the region), has established a cooperative framework with the EU since 2020, including joint ministerial dialogues. The principal objective of this partnership is to relaunch a strategic, balanced, and mutually beneficial political cooperation between the EU and Nigeria, fostering high-level dialogue and collaboration across governance, security, sustainable development, trade, health, and global challenges such as climate change and pandemics. (Anadolu Agency, 2024;European External Action Service, 2020).

Ethiopia displays a particularly dynamic profile, characterized by an active foreign policy. It is a BRICS membership since 2024, and has strong bilateral relations with both the EU and France, iIllustrated by high-level visits and sustained cooperation in the political, cultural heritage, humanitarian, and economic fields, notably through reconstruction and restoration projects and close collaboration for peace and development (Ministère de l'Europe et des Affaires étrangères, n.d.).

1.1.2.5.2. Economic Factors

The target countries are economically challenged or face significant inequalities. Although this presents obstacles, they remain eligible to seek financial support from Gavi to implement vaccination campaigns. Moreover, Gavi's backing facilitates their progress towards financial autonomy in immunization funding.

Ethiopia is notably investing heavily in its healthcare sector, with a $5 billion budget allocated for 2024–2025, 30% of which targets general and specialized hospitals (Ethiopian Investment Commission, 2023). Vaccine imports are projected to increase from $179 million in 2023 to $214 million by 2028, reflecting an annual growth rate of 2.7% (ReportLinker, n.d.). This growth underscores Ethiopia's commitment to innovative health interventions, including the adoption of edible vaccines.

1.1.2.5.3. Sociocultural Factors

Sociocultural dynamics play a decisive role in the acceptance of GMO-based vaccines. In the DRC, public trust in vaccines remains limited, with only 43.8% of the population expressing a favorable opinion. There is also strong caution toward genetically modified organisms and a preference for traditional remedies (WHO, 2023; UNICEF, 2012). Nevertheless, the population has experience with oral vaccination, especially for polio, which demonstrates the feasibility of oral vaccine strategies if accompanied by strong communication. During an interview, Dr. Traoré - logistic vaccine expert in DRC, emphasizes the importance of involving community and religious leaders to build trust. This aspect will be more detailed in the communication plan presented in the following sections.

In Nigeria, cholera is a well-known threat, and NGOs already play a central role in prevention through water treatment, sanitation, and hygiene education (IOM, 2024; Solidarités International, 2024). This shows the potential for integrating edible vaccines into existing community-based strategies, particularly if backed by trusted social and religious leaders.

In Ethiopia, stigma surrounding cholera remains high, as the disease is often officially labeled “acute watery diarrhea” to avoid political and economic fallout (Social Science in Humanitarian Action Platform, 2025). Nevertheless, the Ethiopian government has adopted a National Cholera Elimination Plan (2022–2028) with the goal of achieving zero transmission in hotspot areas by 2028 (Hussen et al., 2024). Despite the people wanting to eradicate the disease, concerns about GMOs are widespread, rooted in fears of biodiversity loss, dependence on multinational seed companies, and threats to agricultural exports (The Issue of Genetically Modified Organism and Access to Food in Ethiopia, n.d.).

To face mistrust in vaccines in those countries, anthropological studies would need to be conducted. However, since this is a lengthy process and is not feasible by the Spiky'mune team, we must rely on studies that have already been conducted. This approach has been detailed in the communication plan in part 4.4 of this business plan.

1.1.2.5.4. Environmental Factors

From an ecological perspective, the use of *Opuntia ficus-indica* presents significant advantages. The cactus grows naturally in Ethiopia, Nigeria, and the DRC without disturbing local ecosystems, and it thrives under the meteorological conditions of these countries. This makes it an environmentally sustainable platform for vaccine production, with minimal ecological risks according to Dr. Traoré. More information is available in part 2.2 of this business plan.

1.1.2.5.5. Legal Factors

Legal frameworks on GMOs are one of the most decisive factors. In the DRC, commercial GMO cultivation is prohibited unless special exemptions are granted, and confined trials are mandatory. Strict biosafety controls and compliance with EU traceability standards apply, which complicates the approval of an edible vaccine project.

Ethiopia, on the other hand, has established the Biosafety Proclamation No. 896/2015, which authorizes GMO research and production under strict permitting conditions. Labeling, import/export declarations, and public access to biosafety data are mandatory (Alemayehu, 2021).

In Nigeria, although less detailed in the source document, the National Biosafety Management Agency (NBMA) regulates GMO introduction, and any edible vaccine project would require close collaboration with this authority.

1.2. Competitive Analysis

Direct Competitor	Manufacturer	Location	Type of vaccine	Key features	Target	Last financing amount
Euvichol-Plus / Euvichol-S	EuBiologics	South-Korean	Bivalent inactivated whole-cell vaccines, innactivated	Three different anticholeric vaccines (Euvichol, Euvichol-Plus, Euvichol-S : smaller dose volume) cover serogroups O1 and O139 of Vibrio cholerae. Required a cold chain, but can be stored at temperatures up to 40°C for up to 14 days	Mass campaign and epidemics	$28.1M
Shanchol	Shantha Biotechnics	India	Bivalent inactivated whole-cell vaccines, innactivated	Cover serogroups O1 and O139 of Vibrio cholerae. Administered in a two-dose regimen with a 14-day interval and is suitable for individuals aged one year and above. Required a cold chain. Production discontinued in 2024, replaced by Euvichol-S.	Mass campaing and epidemics	$122M
Dukoral	Valneva	Sweden	Monovalent inactivated oral cholera vaccine	Contains killed whole cells of Vibrio cholerae O1 and a recombinant B subunit of cholera toxin (rCTB). Suspension and effervescent powder for oral suspension. Suitable for adults and children aged 2 years and older.	Travelers and endemic areas	$102M
Vaxchora	Bavarian Nordic	Denmark	Monovalent live-attenuated oral vaccine	Cover serogroups O1 of Vibrio cholerae. Single-dose vaccine, rapid onset of action, effervescent powder and need for a tampon. Suitable for adults and children aged 2 years and older.	Travelers and endemic areas	$183M
MucoRice-CTB	University of Tokyo	Japan	Edible oral vaccine based on genetically modified rice	Under development. GMO producing the cholera toxin B subunit. Thermostable and easily administrable vaccine for developing countries. No cold chain required.	/	/
Spiky'mune	iGEM IONIS team	France	Edible oral vaccine based on genetically modified cactus	Under development. GMO producing the cholera toxin B subunit. Thermostable and easily administrable vaccine for developing countries. No cold chain required. Local production. Cacti do not require many resources (water, fertiliser, etc.).	Mass campaing and epidemics	10.00K€

Figure 9 : Comparative overview of direct competitors differentiated by manufacturer, location, vaccine type, key features, target populations, and recent financing amounts.

The visual overview above (Figure 9) highlights key players in the market, showcasing how our unique advantages set us apart and deliver greater value compared to others.

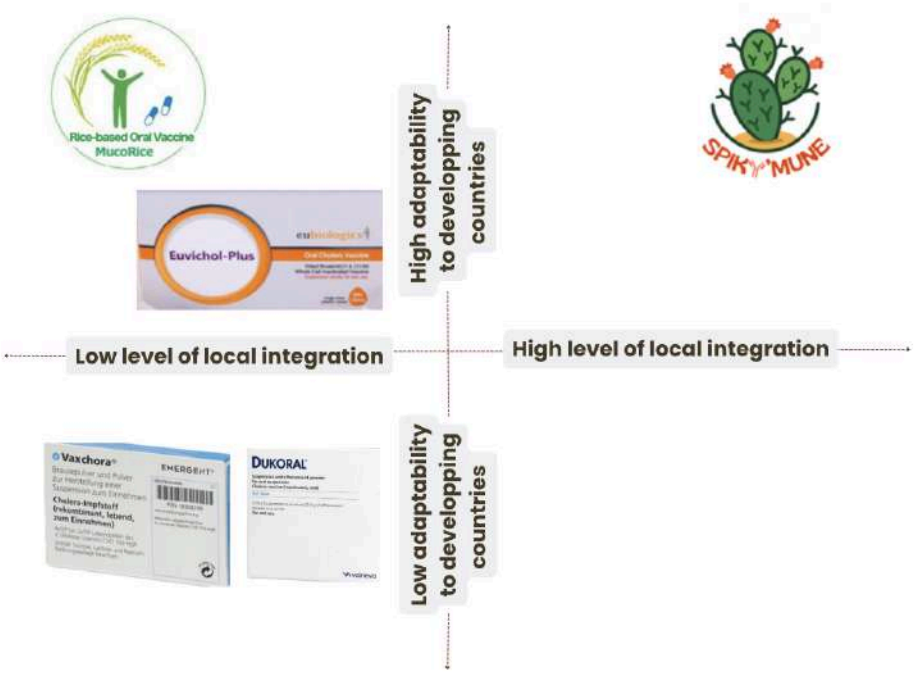

Figure 10 : Visual overview of the key players in the market : Euvichol-Plus, Dukoral, Vaxchora, MucoRice, Spiky'Mune

In the cholera vaccine market, Spiky'Mune revolutionizes the traditional approach by offering the first solution truly designed for developing countries. Where our competitors have difficulties to address the complex challenges of these markets, we provide a comprehensive and innovative response.

Unlike Vaxchora and Dukoral, whose prohibitive costs make them inaccessible to the most vulnerable populations, Spiky'Mune democratizes access to vaccination through an economic model adapted to the budgetary realities of public health programs.

Compared to Euvichol, while competitively priced, we eliminate the major obstacles of cold chain requirements and import dependency. Our local production transforms these constraints into strategic advantages: drastic reduction in logistics costs, enhanced health autonomy, and resilience against supply crises.

Even compared to Mucorice, which shares our vision of a cold chain-free format, Spiky'Mune goes further by integrating the crucial dimension of health sovereignty. Our local production guarantees not only accessibility, but also supply sustainability and the development of the local health ecosystem.

Spiky'Mune embodies a new generation of public health solutions: economically viable, socially responsible, and environmentally sustainable. By producing locally, we create added value within the territory, develop local technical skills, and significantly reduce the carbon footprint associated with transportation.

While Spiky'Mune positions itself favorably against other cholera vaccines, it's essential to recognize that our innovation operates within a broader ecosystem of cholera prevention strategies. To fully demonstrate our value proposition, we must also consider indirect competitors who approach cholera prevention through alternative methodologies.

Indirect Competitor	Manufacturer	Description	Advantages	Limitations
Water Purification Technologies	LifeStraw, PUR, SODIS	Reduce cholera transmission by providing safe drinking water.	High effectiveness in eliminating pathogens Portable and easy to use Supported by NGOs and international agencies Scalable in emergencies Can stop cholera epidemic	Dependence on user compliance and proper usage Limited by water availability Requires training Durability and replacement issues
Hygiene and Sanitation Campaigns	International organizations (Supported by WHO, UNICEF, NGOs)	Prevent disease spread through behavioral change and education	Promote sustainable long-term health improvements Community-driven Free access Effective in reducing transmission	Impact depends on continuous community engagement and infrastructure

Figure 11 : Comparative overview of indirect competitors differentiated by manufacturer, description, advantages, limitations.

These indirect solutions, while addressing the same public health challenge, reveal critical gaps that further validate Spiky'Mune's strategic positioning. By examining water purification technologies and hygiene campaigns, we can better understand why a targeted vaccination approach represents the most comprehensive and sustainable solution for developing countries.

This comparative analysis illustrates how Spiky'Mune not only outperforms direct vaccine competitors but also addresses the fundamental limitations that plague alternative prevention approaches:

2. Technology innovation

Having established the comprehensive market landscape and identified the significant gaps in current cholera vaccination solutions, we now turn our attention to the technological foundation that positions Spiky'Mune as a transformative solution. Our analysis of the epidemiological context, competitive environment, and regulatory framework provides the strategic foundation for understanding how our innovative GMO cactus-based vaccine platform addresses these critical market needs through breakthrough biotechnology.

2.1. Technical overview of Spiky'Mune innovation

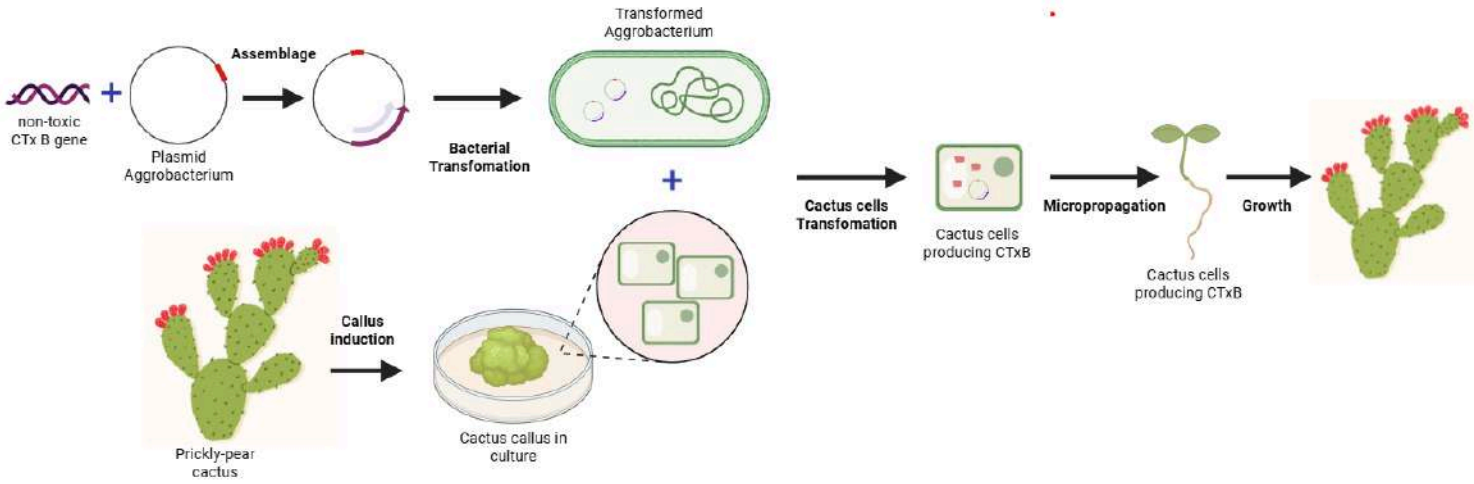

Figure 12 : Overview of the experiments realized to create a genetically modified cactus

The aim is to create a cactus capable of producing the non-toxic protein of the *Vibrio Cholerae*, CTxB. This protein CTxB replaces the use of attenuated or inactivated bacteria of the actual cholera vaccines. Thanks to this, there is no risk of accidentally causing the disease, or bacteria infection. Once in the body, it enables the activation of the body's immune response against cholera, like any other vaccine.

Once transformed, the cactus plants are fully capable of producing the CTxB protein within their edible tissues. And because the protein is produced inside the cactus cells and not secreted, it remains protected and bioavailable when the cactus is consumed. It avoids the gastric enzymes, acids and other degradation factors within the digestive tract. Moreover, being stored inside cells, keeps the CTxB stable

at ambient temperatures and does not require refrigeration, which is a major advantage in remote or resource-limited areas where cold-chain infrastructure is unavailable or unreliable. This simplifies transportation, storage, and administration.

Moreover, by choosing the cactus plant as our vaccine vector, this approach not only targets cholera but can also be adapted to produce other vaccines through the simple replacement of the gene of interest, enabling rapid responses to various waterborne diseases impacting vulnerable populations.

2.2. Why a cactus?

The prickly pear cactus (*Opuntia ficus-indica*), often called the paddle cactus, stands out as an ideal plant for arid and semi-arid countries due to its unique adaptive abilities and great versatility.

A widespread and culturally integrated plant

Opuntia ficus-indica is already present in many countries, sometimes growing wild and other times cultivated for its fruits, young pads (nopalitos), or as fodder. This global distribution, particularly in Africa, Latin America, the Mediterranean, and Asia, makes it easier to gain acceptance and reduces the challenges of introducing a new species. Infrastructure, agricultural know-how, and distribution networks already exist, which makes our project's implementation less complex and faster (Naorem and al., 2024).

Exceptional adaptation to harsh conditions

This cactus is a model of water efficiency thanks to its CAM (Crassulacean Acid Metabolism) process, which allows it to open its stomata at night to absorb CO_2. This minimizes water loss from transpiration (Varela Pérez et al.). It can survive on less than 200 mm of rain per year, provided the soil is well-drained. Its root system and pads give it exceptional resistance to drought (Inglese et al., 2017). It also tolerates extreme temperatures: populations thrive in regions where highs exceed 50°C, and tests show that, once acclimated, it can survive spikes of 69°C for one hour (Nobel, 1994, Le Houérou, 1996).

High and sustainable yield, even in arid environments

Despite its low input requirements, *Opuntia ficus-indica* can provide an impressive biomass. In arid areas (<300 mm/year), mature plantations can produce 50 tons of fresh matter per acre per year (Homer et al., 2020). The thick pads store water, allowing for continuous production even during periods of water stress.

Complementary ecological and socio-economic benefits (Mondragón-Jacobo et al., 2001; Le Houérou, 1996)

Beyond its productive value, this cactus:

1. Stabilizes soil, fights erosion, and improves the structure of marginal lands.
2. Promotes local biodiversity by providing habitat and food for wildlife.
3. Provides a resource for food, fodder, energy, and industry (mucilages, biofuels, etc.).

2.3. Economic yield per plant

For this step, we needed to approximate our yield in order to determine the number of doses we could make per acre per year.

Studies showed that the CTB production yield in transgene tobacco leaves is about 2.4 µg / mg of total soluble protein (TSP) (Walmsley et al., 2006). Let's estimate its production for one kilogram of cladode. Crude protein represents 7.32% of the cladode, so 73.2 g per kilogram, and 10% of it is soluble, so 7.32 g of TSP per kilogram of cactus (Hernández-Urbiola et al., 2014). These calculations let us think that our production yield of our protein of interest might be about 17.6 mg per kilogram of cactus.

The mean yield of Opuntia ficus-indica is around 50 tons per acre per year (Inglese et al., 2011), meaning that the average production of our protein is about 880 g (880,000 mg).

The amount of protein per dose is also controversial, as recombinant proteins elicit very different immune responses. But in this case, we decided to approximate our quantity per dose using the amount Dukoral uses for its vaccine (Clemens et al., 2013). Using 1 mg per dose lets us think that the average quantity of production per acre and per year would be 880,000 doses.

Another crucial step of our project is to transform our cactus into an edible form. Our idea was, after peeling the cactus and removing the spikes, to mix it into a paste. This recipe normally uses different types of flour to harden it and make it easier to eat. This is the main reason why we planned on mixing seeds, for their high concentration and stability of our protein, and adding this powder to our first mixture, improving the concentration of immunogenic residues for a smaller dose and/or a more efficient vaccination.

2.4. Intellectual Property (IP) and Protection

2.4.1. The strategic importance of intellectual property in biotechnology

Intellectual property (IP) ensures the successful development and commercialization of biotechnology innovations. It is necessary due to the considerable economic stakes in the market and regulatory challenges.

IP allows biotechnology companies to protect their research and development investments and protect technological innovation by granting temporary exclusivity. For the Spiky'Mune project, an IP strategy would enable us to secure the methods of genetic transformation of the cactus and the expression of the CtxB protein (Kashyap, 2024). This IP reassures investors by providing strong protection for intellectual assets and partnerships during strategic negotiations. Finally, it creates value for innovation and ensures freedom of exploitation by avoiding conflicts with existing patents. To develop an effective IP strategy, we need to analyze the existing patent landscape to identify opportunities for innovation and ensure freedom to operate in this competitive field.

2.4.2. Patents on edible cholera vaccines

First, US patent US20130149328 described a “Plant-derived vaccine against cholera and malaria, conjugated protein containing CTB-AMA1 or CTB-MSP1, protecting the user against cholera and malaria.” This invention involved expressing the protein in *Lactuca sativa* (lettuce), but its abandonment means that it is now part of the prior art, creating room for our approach using cactus. (Daniell, 2013) Next, researchers developed a cholera vaccine in rice called MucoRice-CTB, which remains stable in powder form for dilution. This development does not focus on plants adapted to arid climates (Su, 2023). There are more recent patents such as

US10030250B2: Edible soy-based vaccine or KR20230008350: *Lactuca sativa* plant capable of producing an edible vaccine protein.

2.4.3. Patents on plant transformation and potential obstacles

The Korean patent KR100850525B1 entitled “Method for transforming cactus using *Agrobacterium* and transformed cactus prepared by this method” is the main obstacle identified for our project. This patent describes two methods of transformation (Lee & Kim, 2008) :

- Puncture method: wounds made on the surface of the cactus with fine tungsten needles and inoculation with *Agrobacterium*
- Vacuum infiltration: *Agrobacterium* forced into the cactus tissue under vacuum pressure

Our project presents different workaround strategy approaches to minimize the risk of infringement. First, *Opuntia ficus-indica* belongs to a different genus than *Notocactus Scopa*, and our genetic construct implemented in this cactus has a CtxB-His expression cassette with different plant promoters. We also use alternative transformation techniques (electroporation, biolistics). Discussions with the patent holders could lead to the negotiation of an operating license.

2.4.4. Spiky'Mune intellectual property

Our innovation offers four areas of IP protection: our genetic construction with the CtxB-His sequence and cactus-specific promoters, our transformation methods, formulations including active ingredient stability and optimal dosage, and therapeutic use according to dosage. Until we have IP and have sufficiently developed our technology, we can protect our innovation through trade secrets and study the associated legal framework.

The recommended legal structure is the SAS (Société par Actions Simplifiée, or simplified joint-stock company) for biotechnology fundraising, which allows intellectual property to be contributed as share capital. It is necessary to obtain Novel Food authorization from the EFSA, which can take 3 to 5 years and cost several hundred thousand euros, as well as phase I to III clinical trials spanning 8 to 15 years and costing several million euros. To reconcile profitability and social mission, we plan to offer differentiated licenses based on economic development level, partnerships with NGOs, and local technology transfers in target regions.

In conclusion, despite the constraints imposed by existing patents, our approach using *Opuntia ficus-indica* offers clear differentiation, enabling robust IP protection.

2.4.5. Counterfeit Prevention and Black Market Control

The unique nature of Spiky'Mune as a productive GMO vaccine producing plant requires preventive measures against unauthorized reproduction, illicit trade and quality control circumvention. Our strategy first relies on genetic authentication markers integrated during plant transformation. The natural genetic stability of *Opuntia ficus indica*, characterized by a low spontaneous mutation rate, makes it an ideal platform for incorporating unique identification sequences. Alongside the CTxB gene insertion, we integrate proprietary genetic markers constituting a molecular "fingerprint" specific to Spiky'Mune. These markers, strategically positioned to avoid interfering with target gene expression or disrupting normal plant development, allow differentiation of our modified cacti from wild plants or any unauthorized reproduction. To strengthen control, our genetic construct includes an inducible promoter activated only in the presence of a specific molecule, enabling regulation of CTxB expression. In the absence of this inducer, the promoter remains inactive, a characteristic that can be exploited to phenotypically differentiate authentic plants cultivated according to our protocols from potential illegal copies. We avoid adding permanent repressor sequences that could complicate large-scale production. We have also decided to conduct an annual audit to test the cacti and verify our authentication genes.

Beyond technical barriers, our strategy relies on the existing legal framework in our target countries. In the DRC, the Environmental Code (2023) prohibits commercial GMO cultivation without exemption like our project and provides for sanctions of up to 20 years imprisonment. In Nigeria, the NBMA Act (2015) imposes severe penalties for any illegal GMO manipulation (NBMA, 2015; DRC Environmental Code, 2023). We will work closely with these national biosafety authorities to report any suspicious activity, with our genetic markers facilitating forensic identification of counterfeit plants. Training programs for healthcare professionals will enable identification of authentic plants through batch traceability documentation and certificates of origin. Finally, our partnerships with international organizations (WHO, UNICEF, Gavi) will create a trust and control ecosystem limiting opportunities for counterfeit.

3. Our value chain

3.1. Competitive advantages

Competitive Advantages
Spiky'mune Edible Cactus OGM Vaccine vs Traditional Cholera Vaccines

Differentiating Factor	Spiky'mune (Edible Cactus OGM)	MucoRICE CTB	Euvichol Plus/S	Vaxchora	Dukoral	Advantage Type
BUSINESS MODEL	Durable vaccine infrastructure (6 years) - Decentralized B2B model	Academic research model	Recurring unit dose sales	Premium traveler B2C model	Premium traveler B2C model	DISRUPTION
COST PER DOSE	$0.96/dose after infrastructure setup	Unknown research phase	€2.60/dose (Shanchol/Euvichol)	$80/dose	$60/dose	ECONOMIC
INFRASTRUCTURE NEEDS	Total operational autonomy - No cold chain required	Research infrastructure only	15 logistics centers + cold chain	Standard pharmaceutical supply chain	Complex buffer preparation required	DISRUPTION
PRODUCTION CAPACITY	115 million doses/year	Laboratory scale only	Industrial manufacturing 70M doses/year	Pharmaceutical manufacturing	Pharmaceutical manufacturing	INNOVATION
CO2 ENVIRONMENTAL IMPACT	95% reduction in emissions vs cold chain	Unknown impact	Intensive cold chain required	Standard pharmaceutical footprint	Standard pharmaceutical footprint	SUSTAINABILITY
GEOGRAPHIC ACCESSIBILITY	Isolated areas accessible - Desert climate adapted	Unknown	Urban areas + logistics infrastructure	Developed markets only	Developed markets only	ACCESSIBILITY
ADMINISTRATION METHOD	Edible cactus format - simplified administration	Edible rice format	Oral liquid requiring medical administration	Single oral dose in clinical setting	Oral with buffer preparation required	INNOVATION
DEPLOYMENT STRATEGY	Permanent infrastructure - Continuous prevention	Unknown	Punctual mass campaigns	Individual traveler vaccination	Individual traveler vaccination	DISRUPTION
SCALABILITY	Multi-pathogen portfolio potential	Unknown	Cholera-specific product	Cholera-specific product	Cholera + limited ETEC	INNOVATION
TOTAL DIFFERENTIATION	Paradigm revolution: From product to infrastructure	Incremental innovation	Vaccine commodity	Premium vaccine commodity	Premium vaccine commodity	DISRUPTION

Figure 13 : Spiky'Mune's competitive advantages

3.2. Customer segmentation

Our analysis of the vaccine market and our exploratory qualitative study reveal three distinct customer segments, each operating with specific purchasing rationales and decision-making criteria. This segmentation allows us to tailor our commercial strategy and value proposition to each customer type.

Customer segmentation

Type of Organization	Role	Decision-making	Priorities	Segment
Governments	Direct buyers	High	Sovereignty, price, policy	*Strategic buyers*
International organizations	Prescribers / influencers	Medium	Scientific standards	*Institutional influencers*
Humanitarian NGOs	Operational buyers	Medium-High	Logistics, speed	*Operational buyers*

Figure 14: Table showing the customer segmentation of Spiky'Mune

Strategic Buyers include governments and ministries of health, which have high decision-making power and significant national budgets. Their priorities are focused on health sovereignty, cost optimization, and political considerations. These clients favor solutions that strengthen national autonomy and offer optimal long-term value for money.

Institutional Influencers comprise international organizations like the WHO, UNICEF, and GAVI - the Vaccine Alliance. While their direct purchasing power is limited, they exert a decisive influence on the entire ecosystem. Their scientific validation, recommendations and funding facilitate adoption by the other segments. These organizations prioritize compliance with international standards and excellence in clinical data.

Operational Buyers consist of humanitarian NGOs and field organizations that have high purchasing autonomy for their interventions. Faced with urgent situations and tight budgetary constraints, they primarily seek logistical efficiency, rapid deployment, and optimized operational costs.

3.3. Creating customer value

Strategic buyers' perspective (Governments)

Their goal: Government health ministries seek to ensure national health security while optimizing public spending, strengthening healthcare sovereignty, and demonstrating effective policy implementation.

Our response: For government health authorities in developing countries, our edible cholera vaccine addresses critical sovereignty and economic challenges. By enabling local cultivation and production, we reduce dependency on foreign pharmaceutical companies and create domestic value chains. The elimination of cold storage requirements dramatically cuts national healthcare infrastructure costs and enables deployment in remote areas previously unreachable. Our transparent technology transfer approach allows governments to build internal capabilities and potentially adapt the platform for other endemic diseases. The simplified distribution model enhances vaccination coverage rates, providing measurable public health outcomes that strengthen political credibility.

Value generated: Economic (reduced healthcare costs), Political (health sovereignty), Functional (expanded coverage), and Social (improved population health outcomes).

Institutional influencers' perspective (International Organizations)

Their goal: WHO, UNICEF, and GAVI aim to establish evidence-based global health standards, ensure equitable vaccine access worldwide, and validate innovative solutions that can scale across multiple contexts.

Our response: For international health organizations, our vaccine represents a paradigm shift toward sustainable and scalable global health solutions. Our rigorous clinical data and safety profiles will meet the highest international standards, supporting evidence-based recommendations. The technology's adaptability across different geographical and cultural contexts aligns with their mandate for universal health coverage. By eliminating cold chain dependency, we enable vaccination in crisis situations and remote areas where traditional vaccines fail. Our open-source approach to technology transfer supports their mission of health equity and capacity building in low-resource settings. The platform's potential for multi-disease applications offers unprecedented opportunities for preventive health interventions.

Value generated: Scientific (robust evidence base), Operational (crisis response capability), Strategic (scalable innovation platform), and Ethical (equitable access advancement).

Operational buyers' perspective (Humanitarian NGOs)

Their goal: Humanitarian organizations need rapid-deployment, cost-effective solutions that work in challenging field conditions while maximizing the number of lives protected per dollar spent.

Our response: For humanitarian NGOs operating in crisis zones and resource-constrained environments, our edible vaccine transforms operational capabilities. The elimination of cold chain requirements enables immediate deployment in disaster zones, refugee camps, and conflict areas where infrastructure is compromised. Our simplified administration protocol reduces training needs and deployment time, allowing faster response to cholera outbreaks. The significantly lower per-dose cost multiplies vaccination coverage within existing budgets. Local cultivation capabilities create sustainable intervention models that continue protecting communities even after emergency teams withdraw. The culturally acceptable format increases community uptake rates, maximizing the effectiveness of limited intervention windows.

Value generated: Operational (rapid deployment capability), Economic (cost efficiency and budget optimization), Functional (infrastructure independence), and Impact (sustained community protection).

4. Product strategy

4.1. Product roadmap

Spiky'Mune's journey from innovative concept to global health solution is mapped across a comprehensive 20-year timeline starting in 2026. This roadmap outlines our strategic phases from initial R&D through full-scale commercialization, ensuring we maintain scientific rigor while accelerating access to life-saving vaccination for vulnerable populations worldwide.

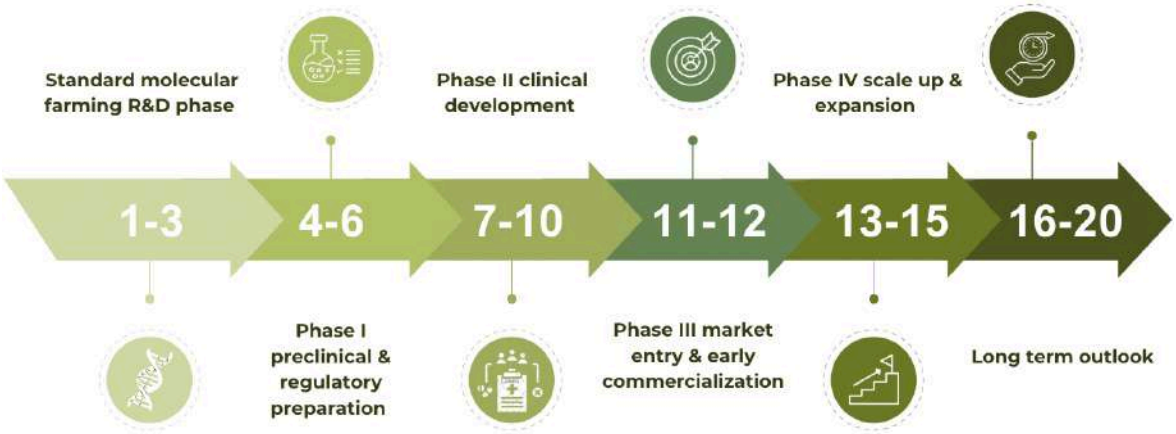

Figure 15: 20 years Roadmap of Spiky'Mune

4.2. Keys and allied partners

Allied collaborators	Nature of partner's contribution	Envisioned actions	Justification
Expert Researchers in GMO Plants	Intellectual	Advice/exchanges	Support on proof of concept
Expert Researchers in Edible Vaccines	Intellectual	Advice/exchanges	Support on proof of concept in laboratory
Médecins / chercheurs experts en immunologie	Intellectual	Advice/exchanges	To get feedback on our edible vaccine project and advice around vaccination (side effects, duration of effects, etc.)
International vaccination partnership and network	Intellectual	Expertise and partnerships	Expertise, advocacy, distribution support, integration into existing vaccination programs
CEPI (Coalition for Epidemic Preparedness Innovations)	Funding	Apply to CEPI calls for proposals, pitch the oral delivery platform	CEPI supports early-stage biotech projects with pandemic potential.
Institut Pasteur / Institut Mérieux	Intellectual	Explore co-publication or advisory collaboration	Scientific credibility, joint research publications, access to virology expertise
Bioclusters / Incubators (e.g. Paris Biotech Santé, Genopole, etc.)	Intellectual and funding	Apply for incubation or acceleration programs	These structures provide resources and networks critical to early-stage biotech startups

Figure 16 : Spiky'Mune's allied partners

Key partners	Nature of partner's contribution	Envisioned actions	Justification
Thermo Fisher Scientific (or equivalent)	Material	Collaboration to obtain R&D materials Contact sales team, set up professional account, negotiate procurement terms	Lab activities (R&D, prototyping) are impossible without reliable access to high-quality biological materials and instruments
Bpifrance / Health VC Funds	Financial	Apply to public funding programs, pitch to VC investors	High development costs require solid financial partners early on Need funding for preclinical and clinical development
WHO (World Health Organization)	Regulatory support, participation in the WHO Pandemic Treaty, access to global health infrastructure and certified lab networks	Engage with WHO treaty task force, request inclusion as an industrial stakeholder, map access mechanisms	Certified lab networks (equity-based, across signatory countries) Distribution of our vaccin: allocation systems (10% free, 10% reduced price) A dedicated fund (financed by WHO Member States) Partnerships with LMICs (Brazil, Malaysia for local industry; Ethiopia for aid access) Global visibility and legitimacy for commercial deployment of the oral vaccine
CRO (Contract Research Organization)	Operational (Conducting preclinical and clinical trials, regulatory and methodological expertise)	Identify CROs specialized in oral vaccines, request proposals, negotiate contracts	Clinical trials are mandatory for market approval and are rarely handled internally by early-stage startups
CDMO (Contract Development and Manufacturing Organization)	Industrial-scale production, compliance with GMP (Good Manufacturing Practices)	Identify CDMOs with biologics/oral vaccine experience, arrange meetings	Large-scale, certified manufacturing is critical and typically cannot be done internally
Regulatory Affairs Consultant / Expert	Strategy for regulatory filings, market authorization (EMA, FDA, ANSM), dossier preparation	Find expert consultants, hold meetings, contract services	Market authorization is complex and requires deep regulatory expertise
IP Law Firm / Patent Attorney	Regulatory	Drafting and filing patents, IP protection strategy Hire a patent attorney, build IP roadmap, secure licenses if needed	Strong IP protection is crucial for future valuation and competitive edge
Government partners (EMA, FDA, USAID)	Commercial, financial, and politic	Informations, meeting and negotiations	Regulatory rejection or political resistance at the national level = project shutdown.
National biosafety agency	GMO safety assessment, environmental risk evaluation, biosafety compliance	Meeting and negotiations for biosafety protocols, environmental impact studies, GMO approval processes	Securing approval to cultivate our GMO cacti in target countries requires compliance with national biosafety regulations, environmental risk assessments, and official government authorization.
Agricultural and environmental partners (FAO, CGIAR, UNEP)	Agricultural expertise, sustainability frameworks, climate adaptation	Meeting and negotiations for agricultural partnership	To enable local production, we need to identify local farmers for the cultivation, maintenance, and harvesting of genetically modified cacti.
Academic Research Center (University, Inserm...)	Proof of concept (Access to scientific expertise, oral formulation support, preclinical platforms)	Develop collaborations, propose co-development or research service agreements	Startups often lack internal capabilities in immunology, oral formulation, or delivery systems

Figure 17: Spiky'Mune's keys partners

4.3. Go-to-market

4.3.1. State of the art : case study of the Euvichol's vaccine

To gain a comprehensive understanding of the entire process involved in bringing a cholera vaccine to market for the most vulnerable populations, we conducted a case study on Euvichol, which currently holds a monopoly in the market (refer to the interview with EuBiologics, appendix 1).

This case study traces the vaccine's journey from production, through the necessary regulatory approvals for market authorization, inclusion in the global stockpile, and finally the deployment process leading to vaccination of individuals. The study also highlights the key stakeholders involved at each stage of this complex pathway. Please, refer to the appendix 2.

4.3.2. Our go-to-market strategy

Our go-to-market strategy is designed to guide Spiky'Mune's successful introduction and growth in the global vaccine market through a structured, phased approach. It focuses on four key segments that together address regulatory entry, market validation, expansion, and long-term diversification. This strategic framework ensures a clear pathway from initial WHO prequalification to broad international adoption and technological innovation, positioning Spiky'Mune to effectively meet public health needs while building a sustainable business (Figure 18).

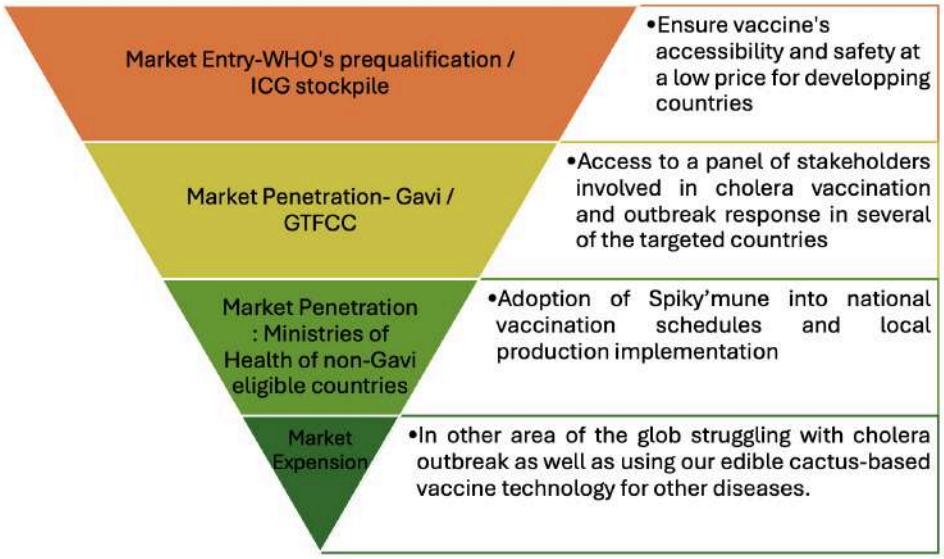

Figure 18: Market expansion strategy of Spiky'Mune

4.3.2.1. Market entry segment : WHO's prequalification and entry in the ICG stockpile

Our market entry strategy is anchored on achieving WHO prequalification, which is essential for accessing the international vaccine market. This regulatory milestone is not merely a certification requirement but rather a strategic enabler that simultaneously unlocks three following market access pathways essential for our international expansion.

WHO prequalification provides access to the international vaccine market by establishing global recognition of our product's quality, safety, and efficacy standards (WHO, 2024; WHO, 2023). This certification is mandatory for integration into the global vaccine stockpile, a crucial repository that ensures rapid deployment

capabilities during cholera epidemic responses (WHO, 2023). Furthermore, major humanitarian organizations including UNICEF, MSF, and other NGOs conducting vaccination campaigns can only procure vaccines that have achieved WHO prequalification status, making this certification essential for accessing the humanitarian market segment.

The prequalification also enables access to Gavi funding mechanisms, which provide financing for vaccination programs in low-income countries. This represents a significant strategic advantage as it removes cost barriers for our target markets, allowing eligible countries to access our vaccines at no direct expense through Gavi's subsidy programs. Additionally, WHO prequalification serves as a regulatory catalyst that enhances confidence among national regulatory authorities, facilitating faster approval and distribution processes at the country level.

Following successful prequalification, our immediate strategic objective focuses on integration into the international vaccine stockpile managed by the ICG. This inclusion guarantees global visibility among international decision-makers and ensures rapid deployment capabilities during cholera epidemics. The stockpile integration also provides logistical support from established international partners while creating market stability through advance purchase commitments.

4.3.2.2. Market penetration segment : Strategic validation and systematic deployment in Africa

Our market penetration strategy is designed as a two-phase approach that begins with rigorous field validation through carefully selected pilot programs, followed by systematic expansion across Gavi-eligible countries in Sub-Saharan Africa.

<u>Phase 1:</u> Pilot program implementation and operational validation

Our penetration strategy rests on implementing pilot programs in three strategically selected countries: Ethiopia, the DRC, and Nigeria. These countries were chosen based on multiple strategic criteria that make them ideal testing grounds for our technology. All three nations are Gavi-eligible, ensuring guaranteed financing without placing cost burdens on their governments (WHO, 2025). They also represent regions with endemic cholera presence, providing substantial target populations and recurring vaccination needs. The geographic diversity across these countries offers varied climatic and logistical conditions that will thoroughly test our product's

adaptability, while existing relationships with WHO, UNICEF, and GTFCC (Global Task Force on Cholera Control) partners facilitate smoother implementation processes.

The financing mechanism for these pilot programs operates through a well-established international framework. Local governments submit funding applications to Gavi for cholera vaccination campaigns, which Gavi then approves and finances (Gavi, 2025). UNICEF subsequently procures our vaccine doses from the international stockpile using Gavi-provided funds, with final deployment handled by locally trained teams. This mechanism ensures cost-free access for recipient countries while maintaining quality standards through international oversight.

Our pilot program objectives are designed to demonstrate both clinical effectiveness and operational feasibility. We target vaccinating 50,000 people across the three pilot countries, with field efficacy validation demonstrating greater than 85% protection rates. Community acceptance metrics aim for over 90% user satisfaction, while logistical optimization targets achieving a 40% reduction in distribution costs compared to traditional vaccine approaches. These measurable outcomes will provide compelling evidence for subsequent expansion phases.

Phase 2: Systematic expansion across Gavi-Eligible Africa

Building upon demonstrated pilot success, Phase 2 involves systematic expansion to Gavi-eligible Sub-Saharan African countries with documented cholera prevalence. This expansion follows a tiered approach that prioritizes countries based on strategic considerations including geographic proximity, logistical infrastructure, and market potential.

Our penetration strategy leverages the GTFCC partnership network, which includes 48 institutions comprising international organizations, academic and research institutions, UN agencies, foundations, and government agencies (GTFCC, 2025). This extensive network provides established relationships and operational frameworks that accelerate market entry processes. Local technical support includes comprehensive training programs for national teams and technology transfer initiatives that build local capacity and ensure sustainable implementation. The goal will be the adoption of Spiky'mune into national vaccination schedules.

The financing continues to operate through systematic Gavi mechanisms, maintaining zero direct costs for recipient governments while ensuring sustainable funding models.

4.3.2.3. Market expansion segment

Then, our market expansion strategy encompasses three distinct but complementary approaches: geographic expansion to non-Gavi eligible African countries, international diversification to at-risk markets worldwide, and technological diversification through platform extension to additional diseases.

4.3.2.3.1. Geographic expansion: non-gavi eligible african countries

The first expansion vector targets emerging African economies with sufficient economic development to finance vaccination programs directly. These markets include higher middle-income countries which possess developed health systems and government budgets capable of direct vaccine procurement. Additionally, we target transitioning economies where health investment represents a policy priority and economic growth supports increased healthcare spending.

4.3.2.3.2. International market diversification

International expansion targets countries with cholera prevalence outside Africa, focusing initially on regions where humanitarian contexts create urgent needs and established international funding mechanisms. Asian markets present significant opportunities driven by humanitarian crises and international NGO operations. Latin American countries face recurrent health crises that create sustained demand for accessible vaccination solutions. Middle Eastern conflict zones require vaccination programs for displaced populations and areas with compromised healthcare infrastructure.

Our entry strategy for international markets emphasizes partnerships with established international NGOs including MSF, Oxfam, and Save the Children, organizations that possess operational expertise and funding access in challenging environments. UN agency support through WHO and UNICEF provides additional pathways for reaching refugee populations and managing complex logistics in unstable regions. Regulatory adaptation ensures compliance with diverse national authority requirements while maintaining our core product advantages.

4.3.2.3.3. Technological platform diversification

The most significant long-term expansion opportunity lies in extending our OGM cactus technology to address additional diseases, leveraging our established technology, regulatory expertise, and production infrastructure. The first phase of technological diversification targets endemic African diseases where our cost advantages and distribution capabilities provide maximum impact.

Typhoid fever represents an immediate opportunity with an addressable market of approximately 15 million doses annually and the potential for 40% price premiums over our cholera vaccine. Hepatitis A presents a larger market opportunity of 25 million doses annually with potential for 60% price premiums due to the vaccine's application in both endemic regions and travel medicine.

The second phase of technological diversification focuses on diseases with global market potential. Multi-strain cholera vaccines extending our current efficacy profile can command 25% price premiums while expanding market applicability. Combination vaccines pairing cholera with typhoid or other diseases provide cost reduction opportunities of approximately 30% while simplifying vaccination programs.

4.3.3. TAM (Total addressable market), SAM (Serviceable Available Market), SOM (Serviceable Obtainable Market)

To accurately quantify the market potential for Spiky'Mune, we performed a TAM, SAM, and SOM analysis. This approach allowed us to define our Total Addressable Market (TAM), the overall revenue opportunity for our product regardless of geographic, economic, regulatory or logistical barriers, which corresponds to the worldwide cholera vaccine market. The Serviceable Available Market (SAM), the segment of the TAM that our innovation could realistically serve taking into account target areas, which corresponds to the Sub-Saharan Africa cholera market. Finally, the Serviceable Obtainable Market (SOM), the portion of the SAM that we can capture in the short term, corresponds to the cholera market in DRC, Ethiopia and Nigeria. In practice, this means we segmented our market into three clear categories, following our go-to-market strategy. Each segment reflects a different level of accessibility and impact, and together they provide a realistic projection of the financial opportunity.

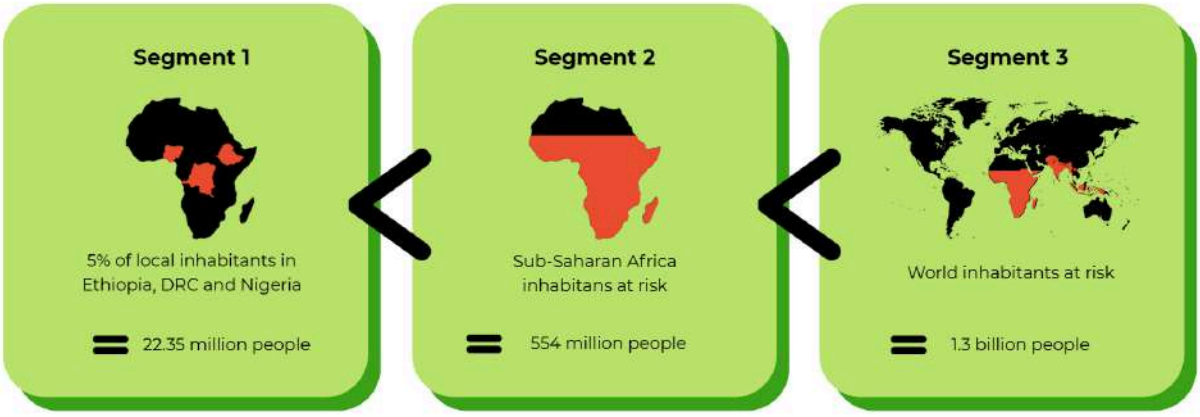

Figure 19: SPIKY'MUNE's customer segments

This segmentation is not just theoretical as it translates directly into market value. Let us look at the revenue potential for each segment and see how Spiky'Mune can realistically grow from the short term to the global scale.

SOM: Segment 1

It targets populations in cholera-endemic areas of Sub-Saharan Africa, where health infrastructure is limited and cholera outbreaks are recurrent, particularly in Ethiopia, Nigeria and the RDC, three Gavi-eligible countries (World Population Review, 2025). Based on demographic and water access data, an estimated 22 million individuals in these regions lack access to clean water and could immediately benefit from a low-cost, refrigeration-free oral vaccine. Assuming a pilot deployment thanks to the Gabi support, and a price at $0.96 per dose that needs to be taken at 3 different times, this represents a Serviceable Obtainable Market of approximately $64.4 million in potential annual revenue.

Figure 20: The expected TAM, SAM and SOM for SPIKY'MUNE

SAM: Segment 2

The SAM corresponds to a regional deployment across Sub-Saharan Africa, targeting populations in cholera-endemic rural areas with limited access to clean water and health infrastructure. This segment focuses on the 554 million people at risk identified by studies (Lessler and al., 2018; Ali and al., 2015) as exposed to cholera or lacking safe water. Considering that this vaccine needs to be taken at 3 different times, and costs $0.96 per dose, this segment represents a Serviceable Available Market of $1.595 billion.

TAM: Segment 3

The TAM includes all individuals at risk of cholera worldwide, regardless of infrastructure, geography, or local partnerships. According to WHO and the Global Task Force on Cholera Control (World Population Review, 2025; GTFCC), 1.3 billion people live in cholera-endemic countries and are potentially exposed to outbreaks due to poor sanitation and lack of safe drinking water. If SPIKY'MUNE were deployed at a global scale, supported by governments and international organizations, the Total Addressable Market would reach $3.744 billion, based on a unit price of $0.96 per dose (taken 3 times) and full population coverage.

4.4. Communication plan

GENERAL OBJECTIVE : **IMPLEMENT THE SOLUTION ON THE MARKET**						
	TITLE OF ACTION: **Clinical trials validation**					
OBJECTIVES	Demonstrate to researchers and decision-makers, through validated testing, that the solution is safe, effective, and valuable.					
COMMUNICATION PLAN						
STAGES OF IMPLEMENTATION OF THE ACTION	TARGET AUDIENCE	WHAT SHOULD THE TARGET THINK OR REMEMBER?	WHICH IDEAS SHOULD BE HIGHLIGHTED?	COMMUNICATION METHODS AND MEDIA		
Stage 1: Convince the researchers of the viability of the project to have their support in clinical trials validation	Researchers	The project is viable, they can support us without any fear	Reliable results Security and safety of the solution It is useful and unique	ACTION : Participation in scientific conferences, meetings with researchers, summits on the climate crisis, epidemics, immunology, etc.	SUPPORTS : scientific poster with results	LANGUAGE : Scientific, precise, professional
Stage 2: Convince the decision makers of the viability of the project, its safety and the fact that it respects the regulation	Decision-makers	The project is viable, the results are convincing and the lethods used respect the reglementation, The project can pass the clinical trials validation	Reliable results Security and safety of the methods used impact on our solution on the problem we want to solve	ACTION : Strong presentation of our R and D approach with the results and methods Communicate on our social media taht our resuts are viable	SUPPORTS : scientific poster with results and methods Social media posts showing good results	LANGUAGE : Scientific, precise, professional
	TITLE OF ACTION: **Validation by global health organizations**					
OBJECTIVES	Obtain OMS prequalification and enter on GAVI stockpile					
COMMUNICATION PLAN						
STAGES OF IMPLEMENTATION OF THE ACTION	TARGET AUDIENCE	WHAT SHOULD THE TARGET THINK OR REMEMBER?	WHICH IDEAS SHOULD BE HIGHLIGHTED?	COMMUNICATION METHODS AND MEDIA		
Stage 1: Those prequalifiactions require money and fund that will be needed	Investors	They should invest on our project	Reliable results Security and safety of the solution It is useful and unique	ACTION: Participating in forums, conferences, meetings, to meet investors. Present the marketing poster to show the interest of the solution and its inovative aspect Show the scientific results to prove the viability of the project Posts on social media to showcase investors and partnerships and attract new ones Frenquent newsletters to keep investors informed so that they can see what their investment is being used for and that it is being used for a project that is moving forward and that makes sense	SUPPORT: newsletters, pubications on social media mentionning them, publications with partnerships, marketing poster, simplified and visual business plan	LANGUAGE: professional, diplomatic, and precise language
Stage 2: Prove that the project respects the reglementations and show our clinical trials results	Decision-makers from global health organization	The project respects the reglementation, it answers to a real need and can be put in the stockpile and obtain the OMS prequalification	Respect of the reglementation The project is solving a real need : lack of cholera vaccine, added-value of our solution	ACTION: Submit the project to the global health organizations responsible for bringing new vaccines or medical devices to market and provide the documentation they request, highlighting the reliability of the results, the importance of the issue the project is attempting to address, and compliance with regulations.	SUPPORT: Scienitific poster or brochure with the methods and results highlighting that reglementations have been respected and that results are viable	LANGUAGE:professional, diplomatic, sientific and very precise language
	TITLE OF ACTION: **Validation by the target governments (of the countries where the vaccine will be distributed)**					

OBJECTIVES	Government accept to distribute the solution in their countries					
COMMUNICATION PLAN						
STAGES OF IMPLEMENTATION OF THE ACTION	TARGET AUDIENCE	WHAT SHOULD THE TARGET THINK OR REMEMBER?	WHICH IDEAS SHOULD BE HIGHLIGHTED?	COMMUNICATION METHODS AND MEDIA		
Stage 1: Once a vaccine or a medical dispositive is validated by the global health organizations, it has to be accepted by the local governments and for this the project must be presented as essential, beneficial for the country, non-threatening	Governments, political leaders, national decision-makers, Ministry of Health	The project answers a real need, It is beneficial for the country to implement it and distribute it	It is really useful and can have a real impact It answers a global public health issue We must be perceived as allies	ACTION: Find a way to contact governments to support the request for implementation of the solution in target countries, provide a clear and professional explanatory brochure Show how it could benefically affect the image of the country	SUPPORT: Project brochure with the goal, the problem statement, the action plan, and the simplified scientific aspect	LANGUAGE: Diplomatic and professional language

GENERAL OBJECTIVE : **DISTRIBUTE THE SOLUTION IN THE TARGET ZONES AND REACH AS MANY PEOPLE AS POSSIBLE**						
	TITLE OF ACTION: **Encourage all levels of authority to distribute the vaccine**					
OBJECTIVES	Shows to all the authority levels that the solution is really helpful and can change the quality of life of their people and that it answes a real need and challenge					
COMMUNICATION PLAN						
STAGES OF IMPLEMENTATION OF THE ACTION	TARGET AUDIENCE	WHAT SHOULD THE TARGET THINK OR REMEMBER?	WHICH IDEAS SHOULD BE HIGHLIGHTED?	COMMUNICATION METHODS AND MEDIA		
Stage 1: Convince the sanitary authorities to distribute the vaccine	Sanitary authorities	They should distribute the vaccine It is a good solution	help to sole a public health issue really useful reliable and efficient	ACTION: Call them to explain the goal of the project, why it is important, why it concerns them and what is our action plan Send by email a brochure for a more visual communication media	SUPPORT: Email project brochure with the goal, the problem statement with key numbers and datas for more credibility , the action plan, and the simplified scientific aspect	LANGUAGE: local or english language Use a diplomatic and professional language
Stage 2: Convince the administrative authorities to distribute the vaccine	Administrative authorities	They should distribute the vaccine It is a good solution	reduce the number of cholera cases better for the country's image	ACTION: call them to explain the goal of the project, why it is important, why it concerns them and what is our action plan and to show how it could benefically affect the image of the country Send by email a brochure for a more visual communication media	SUPPORT: Email project brochure with the goal, the problem statement with key numbers and datas for more credibility , the action plan, and the simplified scientific aspect	LANGUAGE: local or english language Use a diplomatic and professional language
Stage 3: Convince the traditional authorities to distribute the vaccine	Traditional authorities: village chiefs, clan chiefs, chieftains, dignitaries, or elders	They should distribute the vaccine It is a good solution	Will improve the quality life of their region and people is not harmful they can be reassured about the risks They can trust the process, the team and he product	ACTION: Go directly talk with them and present the project or ask partneers humanitarian teams to do that Give a brochure so they can keep it and it is more visual, easier to understand, more attractive	SUPPORT: Project brochure with the goal, the problem statement, the action plan, and the simplified scientific aspect	LANGUAGE: local language or English use simple language

	TITLE OF ACTION: **Allows the logistical distribution of the vaccine in all the concerned regions**					
OBJECTIVES	All parties involved in vaccine distribution must understand that this is a truly important public health issue and understand the distribution process.					
COMMUNICATION PLAN						
STAGES OF IMPLEMENTATION OF THE ACTION	TARGET AUDIENCE	WHAT SHOULD THE TARGET THINK OR REMEMBER?	WHICH IDEAS SHOULD BE HIGHLIGHTED?	COMMUNICATION METHODS AND MEDIA		
Stage 1: Explain to local relays the importance of our project and what are the practical information to know and to present it to the people that wa aim to reach	Local relays	They know how to distribute the vaccine and present its interest to the people thatbwill receive the vaccines	Practical and logistical informations Goal of the project Importance of the project	ACTION: Call those relays to explain to them the project and the organization needed, insisting on the importance of it Organize the vaccine distribution in health centers with them Send them brochures for the visual aspect	SUPPORT: Project brochure with the goal, action plan, the simplified scientific aspect, the logistical aspect	LANGUAGE: Use local an accessible language
Stage 2: Explain to humanitarian teams the importance of our project and what are the practical information t know and to present it to the people that wa aim to reach	Humanitarian teams	They understad that the distribution of the vaccine is crucial and answers a real need They want to cooperate and include the project in their sanitary campaigns	Goal of the project Importance of the project and its added value Action plan and communication strategy for local population	ACTION: Call those teams to have a direct exchange with them and present to them the project and the organization needed Send them a brochure brief them on their role in informing and training healthcare teams	SUPPORT: Project brochure with the goal, action plan, the simplified scientific aspect, the logistical aspect	LANGUAGE: professional and precise
Stage 3: Explain to local and mobile health teams the importance of our project and what are the practical information to know and to present it to the people that wa aim to reach	Mobile health teams Local health teams	They know how to distribute the vaccine They understand how it works and are able to explain it to the people They understant the importance of vaccination and can transmit the message and sensibilize people about it and about hygien measures	Practical and logistical informations Goal of the project Importance of the project Scientific aspects Action plan and communication strategy for local population	ACTION: Organize meetings between those health teams and the humanitarian ones. The Humanitarian team will explain to them the goal of the project, logistical, practical and scientific aspects through explanatory brochure and presentation	SUPPORT: Logistical brochure Technical and scientific brochure showing how the vaccine works Presentation about how we want to communicate the project to the local population and what is our action plan	LANGUAGE: scientific and technical
GENERAL OBJECTIVE : **ASSURE VACCINE ACCEPTATION BY LOCAL POPULATION**						
OBJECTIVES	Build trust with locals, prevent misunderstandings and the spread of false rumors, remain honest, and convey messages about education and awareness of the disease and hygiene measures.					
COMMUNICATION PLAN						
STAGES OF IMPLEMENTATION OF THE ACTION	TARGET AUDIENCE	WHAT SHOULD THE TARGET THINK OR REMEMBER?	WHICH IDEAS SHOULD BE HIGHLIGHTED?	COMMUNICATION METHODS AND MEDIA		
Stage 1: Spread the message through traditional and informal healers to gain the trust of locals and minimize negative preconceptions, they are lisened and Visiting these healers does not disrupt the local customs	Traditional or informal healers: medicine sellers, healers, herbalists, self-medication	Sanitary measures and vaccination are good for their community	Immediate danger of cholera Sanitary practices to prevent its transmission Vaccination is a good solution, which should not be feared	ACTION: Go talk to them and explain the threat of the epidemics and show them it is important to sread awareness messages to protect their communities	SUPPORT: informational flyers	LANGUAGE: vulgarized terms and local language

Stage 2: Gain the trust of religious leaders, as they are highly respected and influential, and their trust is necessary to gain that of the local population	Religious leaders	Sanitary measures and vaccination are good for their community	Immediate danger of cholera Sanitary practices to prevent its transmission Vaccination is a good solution, which should not be feared	ACTION: Go talk to them and explain the threat of the epidemics and show them it is important to sread awareness messages to protect their communities	SUPPORT: informational flyers	LANGUAGE: vulgarized terms and local language
Stage 3: Raise awareness among a larger number of people, including those who are most isolated	Geographically less accessible populations	They should remember the important of the threat of cholera epidemics and thusvthe importance to adopt sanitary measures and get vaccinated	Immediate danger of cholera Sanitary practices to prevent its transmission Vaccination is a good solution, which should not be feared	ACTION: Use meeting points or places where many people gather, such as markets, to spread messages and even set up vaccination booths there Convey messages and testimonials from locals (for the trusting) during radio interviews to reach isolated people	SUPPORT: Radio report and testimony Printed or handmade posters explaining: - what cholera is - how it is transmitted and the hygiene measures to prevent it - vaccination and its role	LANGUAGE: vulgarized terms and local language
Stage 4: Young people have access to social media and are highly influential among their peers, so they can be effective vehicles for educational and awareness messages	Youth	They should remember the importance of the threat of cholera epidemics and thusvthe importance to adopt sanitary measures and get vaccinated They want to spread what they learnt	Immediate danger of cholera Sanitary practices to prevent its transmission Vaccination is a good solution, which should not be feared	ACTION: Include health education, peer education, and co-creation activities in vaccination campaigns so that young people who attend can pass on what they have learned to their friends and family and on social media. Also use social media to convey educational and awareness messages that are accessible to all	SUPPORT: Printed or handmade posters explaining: - what cholera is - how it is transmitted and the hygiene measures to prevent it - vaccination and its role Social media publications about those subjects, explained in a dynamique and attractive way	LANGUAGE: vulgarized terms and local language / English
Stage 5: Children are particularly vulnerable to cholera. It is therefore important that they too understand the importance of sanitary measures and vaccination	Children	They shoud understand what is cholera, how it is transmitted and how to avoid its propagation through sanitary measures and vaccination and why it is important	Immediate danger of cholera Sanitary practices to prevent its transmission Vaccination is a good solution, which should not be feared	ACTION: Incorporate activities such as storytelling, theater, art, and simple messages during vaccination campaigns Provide educational activities in schools	SUPPORT: Printed or handmade posters explaining: - what cholera is - how it is transmitted and the hygiene measures to prevent it - vaccination and its role Materials for making educational games	LANGUAGE: vulgarized terms adapted to children with a lot of metaphores, images and comparisons with things they know Local language

Figure 21: Detailed communication plan covering our three objectives: implement the solution on the market, distribute the solution in the target area, ensure vaccine acceptance.

5. Regulatory compliance strategy

5.1. International regulatory framework

5.1.1. WHO prequalification

5.1.1.1. Objective of WHO prequalification

The prequalification of vaccines by the WHO is a rigorous evaluation process designed to ensure that vaccines intended for immunization programs meet international standards of quality, safety, and efficacy.

This process provides assurance to international procurement agencies (such as UNICEF and Gavi) as well as developing countries that only reliable vaccines, adapted to the specific needs of national programs and the conditions of low-resource settings, are used (Vaccines | WHO - Prequalification of medical products (IVDs, medicines, vaccines and immunization devices, vector control), no date).

5.1.1.2. Main steps of the prequalification process

Figure 22: Main steps of the prequalification process (Lee, 2025), (Lauren Goodwin et al., 2024), (How can I apply to have a vaccine prequalified? | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control), no date)

Step 1- Pre-submission (Letter of intent) - response within 30 days

The manufacturer informs WHO of its intention to submit a vaccine for evaluation.

Step 2- Prequalification application: submission of the complete dossier

The manufacturer submits a comprehensive file in line with international standard formats (ICH Common Technical Document), including:

- Detailed description of the vaccine and its manufacturing process (Product Dossier)
- Clinical trial data on efficacy and safety (Clinical Trial Report)
- Manufacturing site information (Site Master File) including manufacturing site, its layout, equipment and personnel.
- Quality control procedures

Step 3- Dossier evaluation - response within 60 to 90 days

- Documentary Evaluation

WHO thoroughly reviews the quality of the data, compliance with Good Manufacturing Practices (GMP), clinical trial results, and suitability for targeted health contexts (e.g., product thermostability).

- On-site Inspections

  In-person inspections verify compliance with GMP standards.

- Independent Laboratory Testing

  WHO conducts laboratory quality control tests on product samples.

Step 4 - Prequalification Decision

If the product meets all requirements, it is granted the “WHO prequalified” status, which enables procurement by international agencies.

Step 5 - Maintenance and Monitoring

Once prequalified, the vaccine undergoes continuous post-qualification monitoring: periodic reassessments, change management, and prompt handling of complaints.

5.1.1.3. Purpose of the prequalification

- Allows procurement by major international agencies (UNICEF, Gavi), which is essential for financing and market access in developing countries.
- Ensures safety, efficacy, and quality of vaccines used in immunization programs.
- Facilitates regulatory recognition by national authorities, often accelerating local approval processes (via reliance procedures).
- Encourages innovation by supporting vaccines adapted to challenging contexts (e.g., thermostable vaccines).
- Builds trust among countries and donors, ensuring sustainable supply chains.

5.1.1.4. Required documents for a prequalification dossier

The submission must include:

- Full technical dossier of the vaccine (manufacturing process, finished product quality)
- Clinical trial reports demonstrating safety and efficacy
- Quality documentation of the production site (Site Master File)
- Quality control and batch release protocols
- Detailed description of packaging and transport conditions
- Official notification from a functional National Regulatory Authority (NRA) recognized by WHO
- Signed commitments and agreement on WHO terms and conditions

5.1.1.5. Cost and financial aspects

WHO prequalification is subject to fees: payments are required at different stages, including screening, dossier evaluation, site inspections, and laboratory testing (World Health Organization, 2018b), (Fees for prequalification | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control), no date).

Vaccine category	Screening fee US$	Reduced evaluation fee[1] US$	Evaluation fee US$	Site inspection fee US$
Simple / traditional	2,500	25,000	100,000	30,000
Combination / novel	5,000	66,000	232,750	30,000

[1] For products for which there is urgent public health need but no (or a very small) commercial market..

Figure 23 : Comparison of prequalification fees including screening, evaluation, and site inspection across vaccine categories: traditional/simple, combination, and novel platforms (WHO, no date)

Fees vary depending on the vaccine category (simple / traditional or combination / novel) (WHO, no date) as described in the table “Vaccines categorization for fee payment” (WHO, no date) and type of evaluation (approximatively USD 5,000–25,000 or more per product) as we can see in the Figure 20.

Annual maintenance fees also apply. Determination of the annual payable for vaccines is a two-step process (Fees for prequalification | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control), no date) :

1. Vaccine manufacturers are required to submit, by 30th June each year, a declaration of their tier: I, II, III or IV

2. Determination of manufacturer-tier, based on a rolling average of total sales of the prequalified vaccine to UN agencies (including the PAHO Revolving Found) and GAVI, hereinafter referred to as "PQ-enabled sales", over the previous, completed three-year period. The manufacturer tiers, defined according to average yearly total sales value, are given in Table 1 below.

Tier	Average annual PQ-enabled sales over the previous, completed three-year period (US$)
1	US$ 0 to US$ 1 million
2	>US$ 1 million to US$ 20 million
3	>US$ 20 million to US$ 300 million
4	>US$ 300 million

Figure 24: Vaccine manufacturer-tiers for annual fee calculation

Vaccine category	Tier 1 US$	Tier 2 US$	Tier 3 US$	Tier 4 US$
Simple / traditional	4,800	19,200	41,500	140,000
Combination / novel	8,400	33,600	72,500	250,000

Figure 25 : Annual maintenance fees for prequalified vaccines

Payment of these fees does not guarantee prequalification. Payment of the annual fee should be made before 30th November of the calendar year in which the invoice was issued (Fees for prequalification | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control), no date).

5.1.1.6. Benefits of WHO prequalification for manufacturers

1. Facilitated access to international markets in developing countries through procurement agencies (UNICEF, PAHO, Gavi, etc.)
2. International recognition of the product as meeting GMP and clinical standards
3. Contribution to global public health, increasing confidence among end-users and partners
4. Expanded business opportunities in low-resource countries, with priority positioning in international tenders
5. Potential acceleration of regulatory approvals in certain countries via reliance on WHO's evaluation
6. Technical support and continuous follow-up, helping improve manufacturing standards and compliance

5.1.2. ICG stockpile

Once your cholera vaccine is prequalified by the WHO, the process to integrate it into the global stockpile managed by the ICG involves several key steps (*ICG*, no date), (*Gavi*, 2024) .

5.1.2.1. Objectives of stockpile inclusion

- Rapid response to outbreaks: The stockpile ensures ready availability of vaccine doses to be deployed swiftly in cholera outbreaks or high-risk areas, preventing or containing epidemics.
- Equitable access: It guarantees that low- and middle-income countries affected by cholera can receive vaccines at humanitarian prices, overcoming economic barriers.
- Coordinated global management: The ICG consolidates demand from countries, manages allocation, and synchronizes procurement and distribution logistics to optimize vaccine use and prevent shortages.
- Quality assurance: Only WHO-prequalified vaccines that meet strict safety, efficacy, and manufacturing standards can be included, ensuring public health safety.

5.1.2.2. Key steps for stockpile integration

Step 1 - Submission and evaluation by the ICG

A formal application must be submitted to the ICG, which comprises WHO, UNICEF, the International Federation of Red Cross and Red Crescent Societies (IFRC), and MSF. The ICG rigorously reviews all relevant data on the vaccine's safety, efficacy, production quality, and manufacturing capacity to ensure it meets the criteria for inclusion in the stockpile.

Step 2 - Manufacturing capacity and supply assurance

Vaccine producers must demonstrate the ability to supply sufficient doses rapidly to meet urgent epidemic response demands. Flexibility and speed of delivery are critical, as outbreak responses require quick mobilization of vaccines.

Step 3 - Contracts and partnership agreements

Upon positive evaluation, manufacturers negotiate supply agreements with ICG partners, setting terms for procurement quantities, delivery schedules, pricing (often at humanitarian or reduced rates), and responsibilities regarding logistics, storage, and distribution.

Step 4 - Compliance with regulatory and logistical standards

The vaccine and its packaging must comply with regulatory requirements in recipient countries and meet logistical standards of the stockpile—especially concerning cold chain integrity, traceability, and quality controls.

Step 5 - Integration and availability

Once accepted, vaccine doses are stored under controlled conditions, typically managed by UNICEF supply hubs. The vaccines are then mobilized rapidly in response to approved country requests facilitated by the ICG.

Step 6 - Post-integration monitoring

Continuous monitoring is conducted through regular audits, usage reports, and pharmacovigilance activities to ensure the vaccine's ongoing quality, safety, and optimal use within the stockpile.

5.1.2.3. Benefits of stockpile integration

- Priority access during outbreaks: Vaccines in the stockpile can be deployed immediately to respond to emergency outbreaks, reducing disease spread and mortality.
- Financial and logistical support: Member organizations provide funding mechanisms, technical assistance, and logistic expertise supporting vaccine deployment and efficient campaign implementation.
- Global visibility and trust: Inclusion signals compliance with highest international standards and facilitates regulatory acceptance by recipient countries.
- Market stability for manufacturers: Advance purchase commitments and volume guarantees help manufacturers plan production and scale without market uncertainties.
- Equity: Ensures availability of vaccines to vulnerable and underserved populations who might otherwise lack access due to cost or supply constraints.

This structured pathway ensures that only vaccines meeting global safety and efficacy criteria with dependable production capacity are deployed through an efficient, coordinated global mechanism, maximizing public health impact in cholera-prone regions.

5.1.2.4. ICG process to release vaccines from the emergency stockpiles

Once a country facing a cholera outbreak requests vaccine doses from the global emergency stockpile, the ICG evaluates the request based on epidemiological data, vaccination strategy, operational readiness, and current stockpile availability. Upon approval, the UNICEF Supply Division places an order with the vaccine manufacturer, such as EuBiologics, to release the required doses. These doses are usually physically stored at the manufacturer's warehouse or designated cold chain facilities. UNICEF then organizes the shipment, ensuring maintenance of cold chain logistics and coordinating with the recipient country's health authorities. Upon arrival, vaccines are distributed through national vaccination campaigns supported by ministries of health and partner organizations. This process enables rapid mobilization of vaccines to outbreak areas, maximizing timely control and prevention of cholera spread (Figure 21).

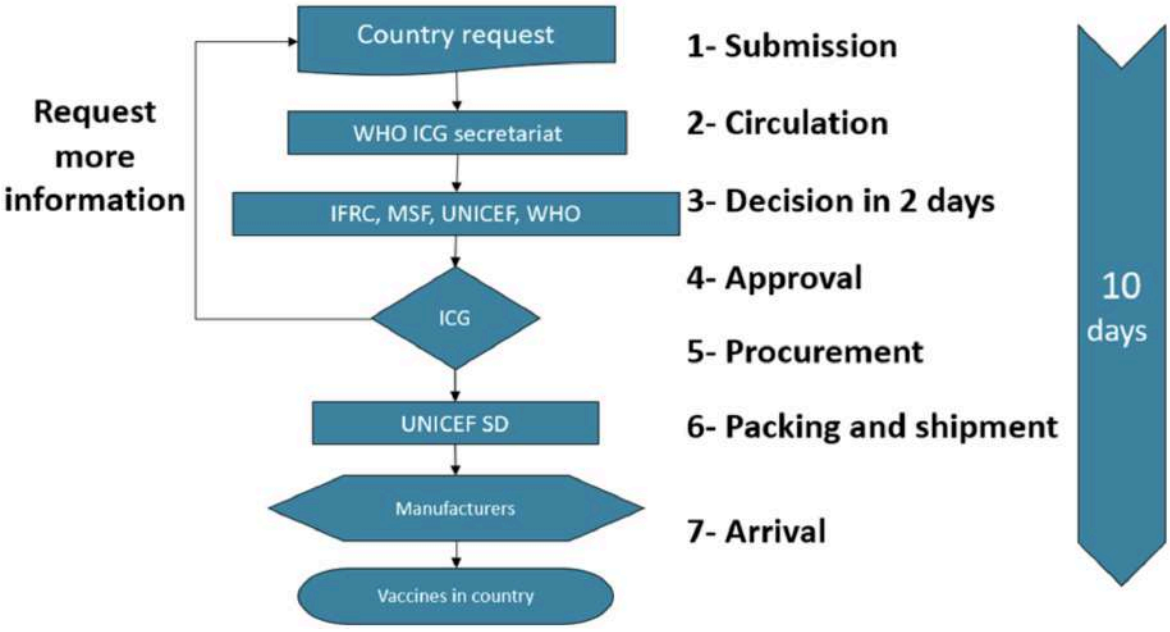

Figure 26 : ICG process to release vaccines from the emergency stockpiles (ICG (no date))

5.1.3. Gavi eligibility

5.1.3.1. Gavi's support for cholera vaccination in developing countries

Gavi, the Vaccine Alliance, provides financial and technical support to developing countries to improve access to vaccines, including cholera vaccines. This support involves subsidizing vaccines, strengthening immunization systems, and assisting in the effective deployment of vaccination campaigns. By doing so, Gavi helps increase vaccination coverage in low-income countries and reduce the burden of vaccine-preventable diseases (Gavi, 2025).

5.1.3.2. Eligibility criteria for countries

Eligibility for Gavi support mainly depends on a country's Gross National Income (GNI) per capita. As of 2025, countries with a GNI per capita of $1,820 or less (based on the World Bank's data) qualify for Gavi's assistance. This threshold is updated annually for inflation.

Eligible countries fall into different categories based on their economic status and transition phases:

- Initial self-financing phase (lowest GNI countries)
- Preparatory transition phase (countries approaching the threshold)
- Accelerated transition phase (countries gradually withdrawing from Gavi support over eight years)

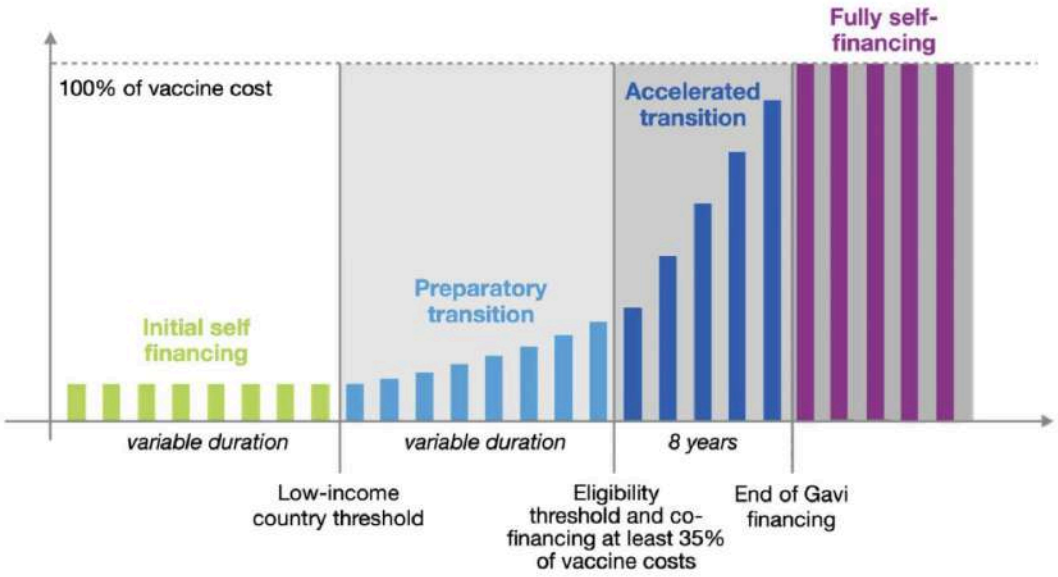

Figure 27: Illustration of transition phases and thresholds (Gavi Eligibility and Transition Policy, 2023)

Countries are also expected to co-finance a share of vaccine costs, typically at least 35% during advanced transition phases. After completing the transition period, countries become fully self-financing and no longer qualify for new Gavi funding (Co-financing policy, 2023).

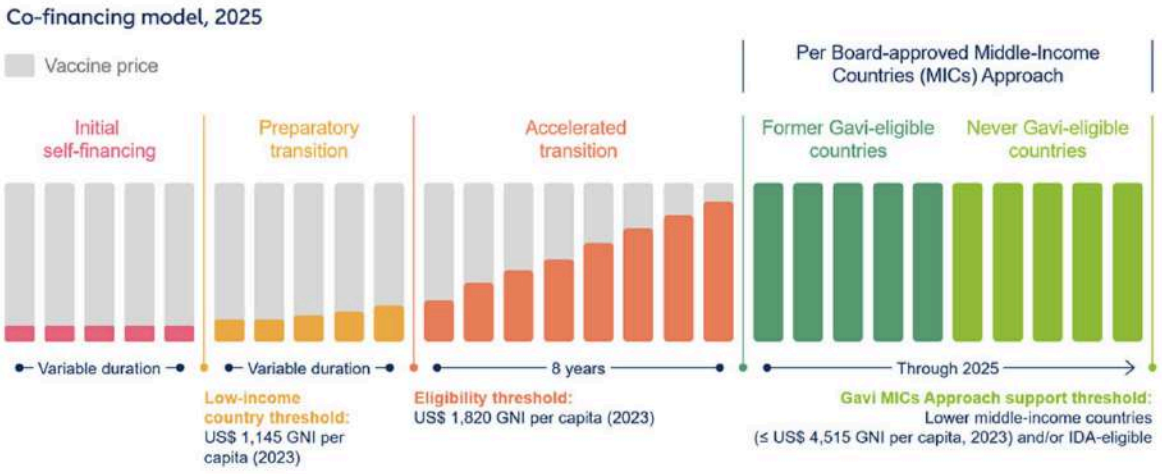

Figure 28: Co-financing model of Gavi (Gavi Eligibility and Transition Policy, 2025)

Gavi provides financial support for preventive cholera vaccine campaigns through Ops. Countries are eligible to apply for up to US$ 0.65/0.55/0.45 per dose based on transition status (*Vaccine Funding Guidelines*, 2023).

5.1.3.3. Steps to apply for gavi support

1. Eligible countries submit an application to introduce a new vaccine or strengthen immunization programs.
2. The application is reviewed by an independent expert panel covering immunization, logistics, finance, equity, and related areas.
3. Upon approval, Gavi finances part of the vaccines and provides technical support for program implementation.
4. Countries contribute co-financing as per policy requirements.
5. Gavi supports monitoring and evaluation to ensure equitable and effective vaccination coverage.

5.2. Multi-Phase Regulatory Deployment Strategy by geographical area

5.2.1. Before transportation

5.2.1.1. European Regulation

The development of Spiky'Mune requires strict compliance with European and international regulations before any transport to target countries. This phase involves three main regulatory authorities.

The European Medicines Agency (EMA) regulates innovative vaccines according to Regulation 726/2004/EC. For Spiky'Mune, a centralized procedure will be mandatory given its hybrid nature combining vaccine, GMO, and food. The Marketing Authorization Application (MAA) dossier must include comprehensive preclinical data on efficacy and safety, Phase I, II, and III clinical studies compliant with Good Clinical Practice (ICH-GCP), a Risk Management Plan (RMP) specific to edible vaccines, and an environmental assessment according to Directive 2001/18/EC on GMOs.

CE marking constitutes a crucial step for commercialization in Europe. Spiky'Mune falls under Class III (high risk) according to Regulation MDR 2017/745, requiring the intervention of a notified body. The triple nature of the product requires evaluation according to Regulation 726/2004/EC for medicines, Directive 2001/18/EC for GMOs, and Regulation 178/2002/EC for food safety.

FDA approval strengthens Spiky'Mune's international credibility and facilitates partnerships with WHO, UNICEF, and Gavi for deployment in developing countries. The "Fast Track" designation applicable to vaccines for developing countries accelerates approval procedures.

5.2.1.2. Transport to Target Countries

The transport of Spiky'Mune to target countries is subject to international conventions. The Cartagena Protocol on Biosafety applies as all target countries are signatories. Transport of living genetically modified organisms requires Advance Informed Agreement (AIA) from each destination country, complete accompanying documentation including identity, characteristics, and emergency contact, as well as

clear labeling "contains GMOs" according to international standards. IATA/ICAO regulations impose classification as "dangerous goods class 6.2" specific to living GMOs, requiring specialized packaging, transport personnel training, and specific declarations.

5.2.2. After transportation

5.2.2.1. Local Regulation: Cultivation and Development

Each target country presents a specific regulatory framework for GMOs. In Ethiopia, Proclamation No. 896/2015 authorizes GMO cultivation under strict permits. For Spiky'Mune, a confined cultivation permit valid for 5 years must be issued by the EFCCC (Ministry of Environment, Forestry and Climate Change), followed by a commercialization permit for 10 years after comprehensive risk assessment. This assessment must cover human and animal health, biodiversity, environment, and socio-cultural factors. Mandatory labeling "contains GMOs" is required, with ambiguous terms prohibited.

In Nigeria, the National Biosafety Management Agency Act (2015) requires risk assessment by the NBMA before any approval, with severe criminal sanctions for illegal cultivation. In the Democratic Republic of Congo, the Environmental Code (2023) currently prohibits commercial GMO cultivation without presidential derogation, imposing confined cultivation under surveillance by the National Biosafety Authority.

5.2.2.2. Vaccine Registration

Each country has a specific authority for vaccine registration. In Ethiopia, the Ethiopian Food and Drug Authority (EFDA) requires a dossier according to WHO standards. In Nigeria, the National Agency for Food and Drug Administration and Control (NAFDAC) supervises registration, while in DRC, the Ministry of Health applies WHO standards with adapted local procedures.

The absence of regulatory precedent for edible vaccines requires adapted evaluation protocols for oral administration, stability studies under tropical conditions reaching up to 50°C, assessment of food and drug interactions, as well as specialized pharmacovigilance procedures. Vaccination protocols must define standardized dosing based on CTxB protein concentration, administration methods as raw food,

juice, or freeze-dried powder, training of healthcare personnel in edible vaccine specificities, and integration into national vaccination programs.

5.2.3. Post Marketing

5.2.3.1. Long-term Surveillance

After market launch, a robust post-marketing surveillance system becomes essential. This system must combine traditional medical surveillance for adverse effects and immunological efficacy, environmental monitoring of impact on pollinators and soil microbiome, complete traceability of GMO seed batches, and periodic reports to EFDA, NAFDAC, and Congolese authorities.

Long-term follow-up includes immunity duration studies on control populations, epidemiological surveillance of cholera in deployment areas, comparative efficacy assessment with traditional vaccines, and monitoring of potential Vibrio cholerae mutations.

5.2.3.2. Biosafety and Insurance

Continuous surveillance according to OECD 2024 protocols includes monitoring genetic dissemination to related wild species, assessment of impact on local biodiversity, surveillance of selection antibiotic resistance, and protocols for recall and secure destruction in case of problems.

The hybrid nature of Spiky'Mune requires specialized insurance covering pharmaceutical liability for patient adverse effects, GMO environmental risks including contamination and biodiversity impact, food liability for contamination and allergies, and international clinical trial insurance according to EU Directive 85/374/EEC. Compensation funds could be established following the WHO emergency vaccine model, with shared responsibilities between manufacturers and local agents including trigger thresholds, agro-medical product recall procedures, and compensation mechanisms for adverse effects.

This multi-scale regulatory approach ensures health and environmental safety while enabling access to this vaccine innovation in regions most affected by cholera.

5.2.4. Democratic Republic of Congo regulations

DRC follows the World Health Organization's guideline for vaccine evaluation, clinical trials, and quality standards . Plus, WHO considers edible vaccines, even those derived from genetically modified organisms (GMOs), as pharmaceutical products. As stated in the *WHO informal consultation on scientific basis for regulatory evaluation of candidate human vaccines from plants*, "Vaccines derived from bioengineered plants and intended for human use are regulated as biologics, and not foods.". Thus, we can conclude for the sake of the following information that the Spiky'mune vaccine will be considered a pharmaceutical product. Still, pharmaceutical regulation will apply to our edible vaccine. Still, since our product is a GMO, looking at the regulatory framework is also a necessity to ensure a law-abiding process of import and usage of our vaccine.

See Appendix 3 for more details.

5.2.5. Nigeria regulations

As an edible vaccine, the regulations surrounding our product are still unclear in this country. But, since Spiky'mune produces a GMO that is also a medical device, we look at the regulations surrounding both those entities, be it biosecurity, GMOs' cultivation rights etc... As well as the regulatory authorities that manage public health, biotechnology development, and pharmaceutical approval processes.

See Appendix 4 for more details.

The regulatory compliance strategy outlined above establishes the legal and institutional framework required to transform Spiky'Mune from innovation to deployed solution. While navigating WHO prequalification, ICG stockpile inclusion, and country-specific GMO regulations demands significant time and resources, these pathways provide the essential validation and partnerships necessary for scaled deployment. This regulatory foundation, combined with the strategic market positioning and technological advantages previously detailed, positions Spiky'Mune to address a critical gap in global cholera prevention.

To conclude, Spiky'Mune represents a transformative approach to cholera prevention that addresses the fundamental barriers preventing effective vaccination coverage in the world's most vulnerable regions. By leveraging the unique properties of Opuntia ficus-indica and plant-based molecular farming technology, this innovation eliminates the cold chain dependency and logistical complexities that have historically limited vaccine accessibility in resource-constrained settings.

The comprehensive business plan demonstrates both the public health imperative and commercial viability of this solution. With a global cholera vaccine market facing a critical supply-demand gap—annual demand exceeding 100 million doses while production remains at 37-50 million—Spiky'Mune offers not merely an alternative product, but a paradigm shift toward decentralized, sustainable healthcare delivery. The Total Addressable Market of €910 million globally, with a Serviceable Available Market of €350 million across Sub-Saharan Africa, underscores the significant economic opportunity aligned with substantial social impact.

The strategic pathway outlined—from WHO prequalification and ICG stockpile inclusion through systematic deployment in Gavi-eligible countries—provides a clear roadmap for market entry and expansion. The multi-phase regulatory strategy addresses the complex legal frameworks across target countries while maintaining rigorous safety and efficacy standards. Partnerships with established organizations including WHO, UNICEF, GAVI, and GTFCC provide the institutional support necessary for successful implementation.

Beyond immediate cholera prevention, Spiky'Mune establishes a scalable technological platform adaptable to other infectious diseases prevalent in developing regions. The capacity for local cultivation not only reduces distribution costs by eliminating cold chain requirements but also creates sustainable economic opportunities and builds healthcare sovereignty in target communities.

The convergence of increasing climate-driven cholera outbreaks, expanding vaccine market demand, and technological advances in plant-based therapeutics creates an unprecedented window of opportunity. Spiky'Mune stands positioned to capture this opportunity while delivering a measurable impact on global health equity.

This business plan demonstrates that innovative biotechnology, when strategically aligned with humanitarian delivery mechanisms and sustainable local production models, can transform global health outcomes for the world's most underserved populations. Spiky'Mune represents more than a product innovation—it embodies a new model for addressing persistent global health challenges through technology, partnership, and community-centered design.

Appendix

Appendix 1 : Retranscription of the interview with EuBiologics

When we entered the market, Shantha Biotechnics (India) was the previous supplier. We took a monopolistic position, and currently we manage by producing at full capacity. Our main challenge is the unpredictability of demand since outbreaks are difficult to predict, and we cannot produce beyond our maximum capacity quickly.

However, in terms of market dominance, we're stable because we supply on time at full capacity.

We are the sole supplier to the WHO global stockpile. Another product, Dukoral, exists but has high cost and requirements unsuitable for outbreak or campaign settings in low-income countries. Dukoral targets Europe and Canada; our market is low-income countries, so they are not direct competitors.

We evolved our vaccine products from an earlier five-component classic formulation to a triple component. Our new process requires only one formalin inactivation step versus two previously this improved manufacturing capacity by 40%, addressing supply shortfalls. Price-wise, Envichol-S is more affordable, keeping our competitive advantage.

Private market demand is small, mostly for travel and military vaccines in middle-income countries. For example, in South Korea, market size is approximately $100,000/year compared to humanitarian demand. About 97% of revenues come from global stockpile sales; only 3% from private markets.

The second part regards the business model and vaccine development history. The company incorporated in 2010, executed licensing for vaccine development with the International Vaccine Institute (IVI), funded partly by the Gates Foundation.

Grants from nonprofits like Gates require signing a global access agreement capping pricing to UNICEF, limiting profit margin between 20–30%. Pricing = cost of goods + allowed profit margin under this agreement.

For private markets, pricing varies based on country income level and policy. Gates Foundation grants helped us double production capacity. Pricing is reviewed by Gates-appointed consultants who analyze costs and margins.

Given the unpredictability of cholera outbreaks, we use volume-based pricing tiers to maintain sustainability by covering fixed costs.

Euvichol vaccine is our only product; contract manufacturing services (CMO) for clinical trial materials also generate revenue.

We have vaccine trials ongoing in Mali and The Gambia, with regulatory qualification in progress.

Clinical trials conducted in South Korea and the Philippines led to WHO prequalification in Dec 2015.

Market entry followed UNICEF tenders; initial funding was limited and required venture capital. Our manufacturing complies with Korean NRA and WHO standards. Export requires NRA approval (3-4 weeks). UNICEF coordinates orders; ICCG (MSF, UNICEF, IRC, etc.) approves outbreak vaccine deployment. After approval, UNICEF informs us of order quantities; we ship within 48 hours. Gavi funds eligible countries, paying us directly. Countries unable to pay get operational costs covered by funding partners.

Pricing increases require Gates Foundation approval and are limited to inflation adjustments under global access agreements.

Transportation terms are FCA to departure airports; distribution managed by UNICEF or country health authorities.

We receive vaccination campaign updates from WHO and related task forces but do not manage coverage follow-up.

Our killed vaccine is very safe, with no reported adverse events.

No intellectual property protects the vaccine. Technology transfers to manufacturers in South Africa and elsewhere are public information.

Challenges :

- Cost of clinical trials and market barriers hinder new suppliers. Market entry requires serious commitment due to costs and timelines.
- Demand unpredictability is a critical challenge.
- UNICEF accounts for 97% of our revenue and controls purchasing decisions.
- External funding fluctuations, e.g., US cuts to Gavi, impact programs starting 2026.

New oral vaccines under development target improved efficacy and durability, e.g., capsule vaccines for children unable to swallow tablets.

Local stockpiles and technology transfer efforts in Africa are underway but challenging to realize.

We view your edible vaccine approach as innovative and promising, but implementation will be complex.

Appendix 2 : State of the art: humanitarian supply and distribution of EuBiologics oral cholera vaccine (based on the interview with the Marketing team of EuBiologics)

A) Introduction to the EuBiologics/Euvichol® case

EuBiologics, a South Korean biotechnology company, has become one of the world's leading producers of OCV through its flagship product Euvichol®. This vaccine has been prequalified by the WHO, a recognized international standard that enables its inclusion in the global vaccine stockpile managed by humanitarian actors such as Gavi and UNICEF (WHO, 2024c). WHO prequalification is an essential prerequisite for large-scale procurement and distribution in low- and middle-income countries, ensuring the vaccine meets strict safety, quality, and efficacy standards required by national and international health agencies (WHO, 2025).

EuBiologics currently produces three WHO-prequalified OCVs : Euvichol, Euvichol-Plus, and the recently approved Euvichol-S. Euvichol-S represents a significant innovation with a simplified, streamlined formulation offering around a

40% increase in production capacity compared with previous versions, addressing global supply shortages (WHO, 2024c; EuBiologics, 2025).

B) Humanitarian distribution and market strategy

EuBiologics' distribution strategy revolves primarily around inclusion in the global oral cholera vaccine stockpile, established in 2013 to enable rapid deployment to cholera outbreaks and endemic regions (Gavi, 2024a). WHO prequalification not only allows access to this stockpile but also expedites national regulatory approvals, critical in countries with complex approval processes.

The stockpile is financially supported mainly by Gavi, the Vaccine Alliance, which pools funds from public sector donors and philanthropic organizations. The stockpile is managed by the International Coordinating Group (ICG), comprising the International Federation of the Red Cross (IFRC), Médecins Sans Frontières (MSF), UNICEF, and WHO (which serves as the Secretariat) (Gavi, 2024a).

EuBiologics currently holds a near-monopoly on the OCV market since Shanta Biotechnics exited in 2022. Its production facilities are based in South Korea, with the entire stockpile physically stored in a warehouse near Seoul. This centralized system facilitates quality control but also implies high dependence on EuBiologics for supply continuity (Gavi, 2024b).

Distribution from the stockpile involves close collaboration between international agencies, local governments, and NGOs for planning and executing vaccination campaigns. The oral administration route taken by Euvichol® greatly simplifies logistics and community acceptance by eliminating needles, needle disposal issues, and the need for highly trained administration personnel (Gavi, 2025).

C) Step-by-Step supply chain workflow from manufacturer to end user

1. WHO Prequalification

EuBiologics develops and submits vaccine dossiers for WHO evaluation. Following successful dossier review, manufacturing site inspections, and compliance inspections, WHO awards prequalification status. This is mandatory for vaccine inclusion in the global stockpile.

2. Stockpile inclusion and financing

After prequalification, EuBiologics coordinates with the ICG and Gavi to include the vaccine in the global stockpile. Gavi provides funding, sourced from governments and donors, which finances bulk vaccine purchases.

UNICEF, as a key partner of ICG, acts as the centralized procurement agent buying vaccine doses from EuBiologics at negotiated humanitarian prices, using the funds supplied by Gavi.

The vaccine doses are physically stockpiled, primarily on-site at EuBiologics' warehouse near Seoul.

3. Country requests and ICG allocation

Countries experiencing outbreaks or requiring preventive campaigns submit formal vaccine requests via national health authorities through ICG channels.

The ICG reviews requests according to epidemiological data, outbreak severity, and country capacity to deliver vaccination campaigns.

4. ICG approval and UNICEF order

Upon ICG approval, UNICEF places an order with EuBiologics to release the necessary quantities from the stockpile, fulfilling the country's demand. UNICEF organizes vaccine shipping, managing cold chain logistics and coordinating with local distribution networks.

5. Vaccine distribution and campaign implementation

Upon arrival in-country, joint efforts by ministries of health, UNICEF, NGOs (e.g., MSF, IFRC), and community health workers implement vaccination campaigns.

The oral vaccine format facilitates rapid community-wide administration, improving coverage with fewer logistical constraints.

6. Post-campaign monitoring and stockpile replenishment

The vaccine stocks in the global stockpile are monitored continuously. Campaign outcomes and pharmacovigilance reports inform ICG and WHO reviews.

UNICEF and Gavi coordinate with EuBiologics to replenish the stockpile as doses are consumed, ensuring readiness for future needs.

D) Economic and logistical dimensions

EuBiologics applies a humanitarian pricing model, selling vaccines at cost or subsidized rates to UNICEF, supported by Gavi's funding. This ensures affordability for low- and middle-income countries despite limited health budgets (Em, A., 2024).

The vaccine design improvements (including shift from glass vials to plastic tubes) facilitate easier transport, lower storage volume, reduced cold chain dependency (especially with the new Euvichol-S aiming for Controlled Temperature Chain compatibility), and simplify administration (EuBiologics, 2018; Gavi, 2025).

To conclude, the EuBiologics/Euvichol® case exemplifies a successful public-private partnership model in deploying a non-profit medical product in resource-limited settings. Critical success factors include WHO prequalification, efficient global stockpile management supported financially by Gavi, centralized procurement and logistics coordination by UNICEF, and innovative product design tailored to field realities. This integrated approach dramatically improves vaccine availability and accelerates responses during epidemic outbreaks.

Appendix 3 : Overview of the Regulations Applicable to the Spiky'mune Project in Nigeria

Theme	Description (Nigeria)
Consumer rights & GMO labelling	GMOs must be clearly identified and labelled according to NBMA guidelines, including traits, characteristics, and unique identifiers. GM content below 4% due to accidental mixture remains unlabelled. (National Biosafety Management Agency [NBMA], 2017)
GMO governance & risk assessment	The NBMA Act (2015) requires mandatory risk assessments before GMO approval. Strict penalties apply for illegal import, export, or release. (National Biosafety Management Agency [NBMA], 2015
Import & export of GMOs	Applications for commercial release or import require socio-economic impact evaluation and full documentation accompanying exports (identity, traits, contact, BCH reference).(NBMA, 2017)
Agricultural labour & GMO use	Court ruling highlights the obligation for actors dealing with GMOs to obtain NBMA approval before handling products. (High Court of Nigeria, 2009)
Vaccine registration & obligations	NAFDAC requires submission of dossiers (safety, efficacy, GMP compliance, clinical data). Post-licensing, every vaccine batch undergoes lot-release testing and oversight. (National Agency for Food and Drug Administration and Control [NAFDAC], n.d.)
GMO social acceptance	Nigerian society is divided: proponents see food security potential; opponents raise safety, health, environmental, and cultural concerns. Awareness levels and policy stance fuel debates. (Oluwadare & Akinola, 2022)
Humanitarian aid & NGOs	NGOs operate under the 1999 Constitution and CAMA (2020), requiring CAC registration. International NGOs must register with NPC. OCHA's HRP (2024) coordinates humanitarian responses with donors.(Amaka Eke & Co., 2020; OCHA, 2024)
Clinical trials & ethics	NAFDAC authorises and monitors clinical trials under the NAFDAC Act (2004). NHREC ensures compliance with ethical standards in line with WHO and the Declaration of Helsinki.(NAFDAC, 2021; NHREC, n.d.)

International framework	Nigeria ratified the Cartagena Protocol (2003). The NBMA Act (2015, amended 2019) enforces CPB commitments, including biosafety and public engagement. (EnviroNews, 2019)
Post-marketing & monitoring	NBMA oversees GMO post-release monitoring (e.g., TELA maize). NAFDAC ensures pharmacovigilance and post-market surveillance of vaccines and medicines.(NBMA, 2025; NAFDAC, n.d.)
Liability	Operators must notify NBMA of damages caused by GMOs, evaluate damage, and take immediate response measures. NBMA determines responsibility and can recover costs. (NBMA, 2017)

Appendix 4 : Overview of the Regulations Applicable to the Spiky'mune Project in Nigeria

Theme	Description (RDC)
Consumer rights & vaccine communication	Consumers entitled to clear, non-misleading information; sellers legally bound to provide full disclosure. Vaccine safety & reporting managed under national health law via SNIS/DHIS2. (Civil Code RDC, 2018; UN Guidelines, 2016; DHIS2, 2013)
GMO governance	Commercial GMO cultivation prohibited without presidential exemption; confined trials mandatory; severe sanctions (up to 20 years prison). Oversight by National Biosafety Authority. (Code de l'Environnement RDC, 2023; Environews RDC, 2023)
Labeling & risk assessment	Draft law requires all GMOs/products to be clearly labeled with traits, traceability code, and safety instructions. (Projet de loi biosécurité RDC, 2023)
Import, export & GMO cultivation	Strict biosafety checks; GMO cross-border movements must include documentation (identity, safety rules, contact details). (Projet de loi biosécurité RDC, 2023)

Agricultural labor & contracts	Agricultural labor law recognizes worker rights, but enforcement is weak in rural areas. (Code du Travail RDC, 2016)
Vaccine registration & obligations	RDC applies WHO standards; campaigns supervised by the Ministry of Health with Gavi, UNICEF, WHO support. (Loi Santé Publique RDC, 2018; WHO, 2024; Gavi, 2024; UNICEF, 2024)
GMO cultivation & social acceptance	Strong public caution toward GMOs; preference for organic farming; mistrust of biotech innovations. (7sur7.cd, 2015)
Humanitarian aid & NGOs	Aid central for health response; simplified procedures but sovereignty emphasized. EU committed €60M (2025); NGOs central in cholera & vaccination campaigns. (EU Civil Protection & Humanitarian Aid, 2025; Oxfam, 2025)
Intellectual property	No specific GMO patent regime; IP laws apply; biosafety restrictions on commercialization. (Code de la Propriété Industrielle RDC, 2002; Code de l'Environnement RDC, 2023)
Clinical trials & ethics	Biosafety law requires confined trials; vaccines must follow WHO norms and national ethical approvals. (ANB RDC, 2023; WHO, 2024)
International framework	RDC ratified Paris Agreement; participates in biosafety collaborations; aligns with WHO vaccine norms.
Post-marketing & environmental monitoring	Surveillance via SNIS/DHIS2; epidemiological monitoring mandatory. (Loi Santé Publique RDC, 2018; DHIS2, 2013)
Waste management & biosafety	GMO waste must be safely contained/disposed of; EIAs required before projects. (Code de l'Environnement RDC, 2023)
Liability & insurance	Illegal GMO dissemination punished with criminal sanctions; sellers liable for unsafe/misleading products. (Code civil RDC, 2018; Code de l'Environnement RDC, 2023)

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