Vaccine Market

Independent Market Research Report

Confidential For

中慧生物
Ab&B Bio-Tech

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For and on behalf of
Frost & Sullivan (Beijing) Inc., Shanghai Branch Co.

Frost & Sullivan
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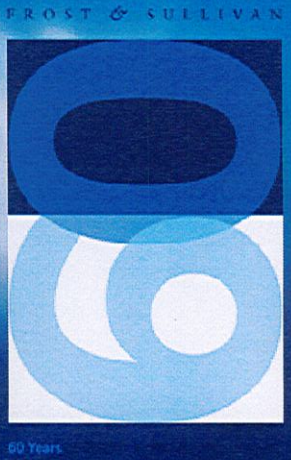

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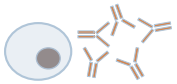
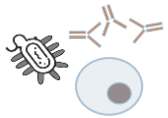
Introduction to the definition and mechanism of action of vaccines

- Vaccines contain agents that resemble a disease-causing microorganism, and work by mimicking disease agents and stimulating the immune system to produce specific humoral immunity and (or) cellular immune response.
- The vaccine agents triggering the immune system represent antigen and lead to production of T-lymphocytes and antibodies. Antibodies bind to corresponding antigens and induced cell destruction by other immune cells.
- Vaccination is to artificially input immunogens or immune effector substances into the body, so that the body can acquire the ability to prevent certain infectious diseases through artificial automatic immunity or artificial passive immunity, which belongs to primary prevention.
- Vaccination can prevent related diseases, which is an important ways of prevention.

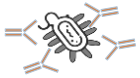
Vaccine Delivery



Production of Antibodies



Pathogen Exposure



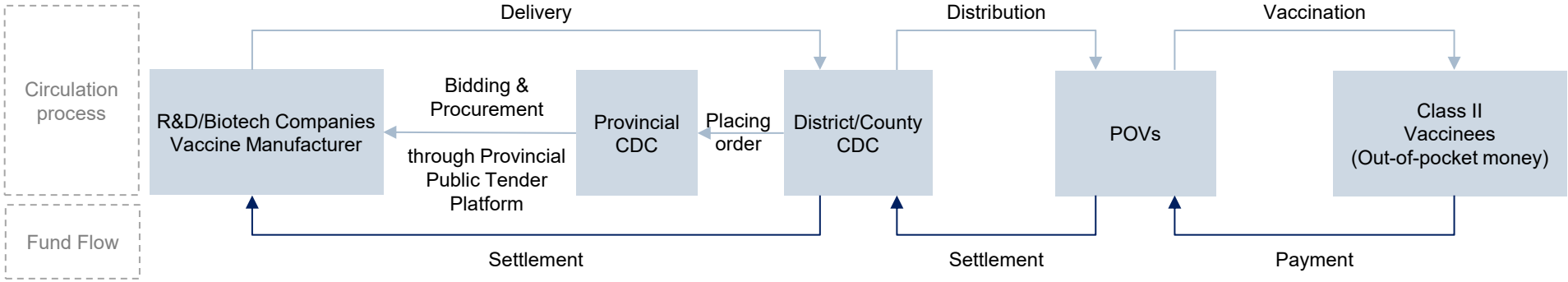
Protection

Description

- Inactivated influenza virus often enters human body through injections. Other methods such as skin patches, aerosols via inhalation devices, and eating genetically engineered plants are also being developed.
- Vaccines use weakened or killed forms pathogens to ensure that pathogens don't develop into the full blown disease, but just like a disease, they trigger an immune response that creates antibodies.
- The goal of immunization is to produce memory of the vaccine antigen via a large population of memory cells. If the real pathogen enters the body in the future, memory cells will recognize it.
- When the familiar antigens are detected, the immune system will produce antibodies to attack them. Antibodies produced after immunization with viral vaccines are effective at preventing viral disease.

Source: WHO, Frost & Sullivan analysis

Overview of the Circulation of Class II Vaccines in China



Source: Frost & Sullivan Analysis

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Introduction to vaccine types and design principles

- Vaccine is a biological preparation that provides active acquired immunity against one or several diseases. A vaccine typically contains a substance that resembles a disease-causing microorganism and is often made from weakened or killed forms of the microbe, its toxins, or one of its surface proteins.
- The substance stimulates the production of antibodies to recognize and destroy any of the microorganisms associated with that substance that it may encounter in the future.
- Currently, vaccines can be divided into preventive vaccines and therapeutic vaccines. Therapeutic vaccines are still in the stage of research, since there is no commercial product approved.

	Category	Design Principle	Main Vaccine Types
	**Inactivated Vaccine**	• Inactivated vaccines are vaccines that use heat or chemical reagents to kill pathogenic microorganisms, causing them to lose their pathogenic ability but retain their antigenic properties. They typically require large doses and multiple doses of vaccination.	• Whole virion inactivated vaccine • Split vaccine • Inactivated subunit vaccine
	**Viral vector Vaccine**	• Constructing genes encoding antigen proteins onto harmless viral vectors, stably expressing antigen substances in the human body and inducing specific immune responses	• Adenovirus vector vaccine • Slow virus vector vaccine • Adeno associated virus vector vaccine
	**Live attenuated Vaccine**	• Attenuated live vaccines contain pathogens that have been artificially screened for virulence and have reduced virulence. They do not have pathogenicity, but still retain immunogenicity and proliferation ability	• Influenza attenuated live vaccine • Measles attenuated live vaccine • Varicella Vaccine
	**Recombinant protein Vaccine**	• Introduce the target antigen gene into an expression vector, and then transfect it into insect cells, bacteria, yeast, or mammalian cells to express a large amount of antigen protein under certain induction conditions.	• Recombinant subunit vaccine • Virus particle like vaccine • Nanoparticle vaccine
	**Nucleic acid Vaccine**	• Nucleic acid vaccines involve directly introducing exogenous genes (DNA or RNA) encoding a certain antigen protein into animal cells, and synthesizing the antigen protein through the host cell expression system.	• DNA vaccine • mRNA vaccine • Circular RNA vaccine

Source: Frost & Sullivan

Definition and Classification of Inactivated Subunit Vaccines

- Though both inactivated and recombinant subunit vaccines contain only pathogen-specific antigens, their production differs significantly. Inactivated subunit vaccines purify antigens directly from live pathogens, while recombinant subunit vaccines obtain them via genetic engineering and expression systems.
- Unlike whole-pathogen vaccines, inactivated subunit vaccines contain only specific components from harmful bacteria, parasites, or viruses. These purified components, called antigens, are proteins or synthetic peptides and are classified as protein, polysaccharide, or conjugate subunit vaccines, based on the antigen type.
- In 1981, Heptavax-B, developed by Hilleman, became the first FDA-approved inactivated subunit vaccine for hepatitis B. It was derived from human blood and contained the hepatitis B virus surface antigen, HBsAg.

Classification of Inactivated Subunit Vaccine

Vaccine type	Protein Subunit Vaccine	Polysaccharide Subunit Vaccine	Subunit Conjugate Vaccine
Technique	The pathogen is cultured and the target antigenic protein is obtained by inactivation, lysis and purification.	Fermentation culture in a bioreactor, followed by bacterial lysis to extract and purify cell wall polysaccharides.	Cultivation of pathogenic bacteria, extraction and purification of polysaccharides and proteins, chemical activation, and in vitro cross-linking.
Ingredients	Contains specific isolated proteins from viral or bacterial pathogens.	Contains polysaccharide components found in the cell walls of some bacteria.	Contains polysaccharide chains conjugated to carrier proteins
Relevant Products	**Influenza virus subunit vaccine** contains haemagglutinin and neuraminidase	**Pneumococcal polysaccharide vaccine** contains podocarbophilic polysaccharide	**Meningococcal ACWY conjugate vaccine** contains polysaccharide conjugated to diphtheria or tetanus toxoid

Sources: GAVI, Frost & Sullivan

Comparison Between Inactivated Subunit Vaccines and Split Vaccines and Analysis of Technical Difficulties

- Inactivated subunit vaccines have the advantage of being technically mature, safe and with few side effects. In order to improve immunogenicity, possible methods include the addition of suitable adjuvants and the optimisation of the vaccine process to improve antigen purity.

Inactivated Subunit Vaccine Versus Split Vaccine

Inactivated subunit and split virion vaccines are both derived from inactivated pathogens, such as influenza virus lysed and subunit vaccines, but differences in their components lead to distinct characteristics.

Type	Influenza Virus Split Vaccine	Influenza Virus sSubunit Vaccine
Technical Principle	Addition of a lysing agent to the inactivated virus to cleave the viral envelope and release the outer envelope proteins as well as the inner nuclear and matrix proteins.	Further purification based on lysed vaccine, including only the main targets of anti-influenza neutralising antibodies, haemagglutinin and neuraminidase.
Immunogenicity	No authoritative or definitive comparative conclusion	
Safety	The safety is inferior to that of inactivated subunit vaccines	Single component, high safety

Technical Challenges of Inactivated Subunit Vaccines

Enhancing the immunogenicity

- Adjuvants non-specifically enhance or modify the immune response to a specific antigen, boosting its immunogenicity or altering the response type without being immunogenic themselves. Due to the weak immunogenicity of inactivated subunit vaccines, adjuvants are often added to improve efficacy.
- Optimizing the vaccine production process to remove lysing agents, ovalbumin, and inactivators enhances antigen purity, boosting both immunogenicity and safety.

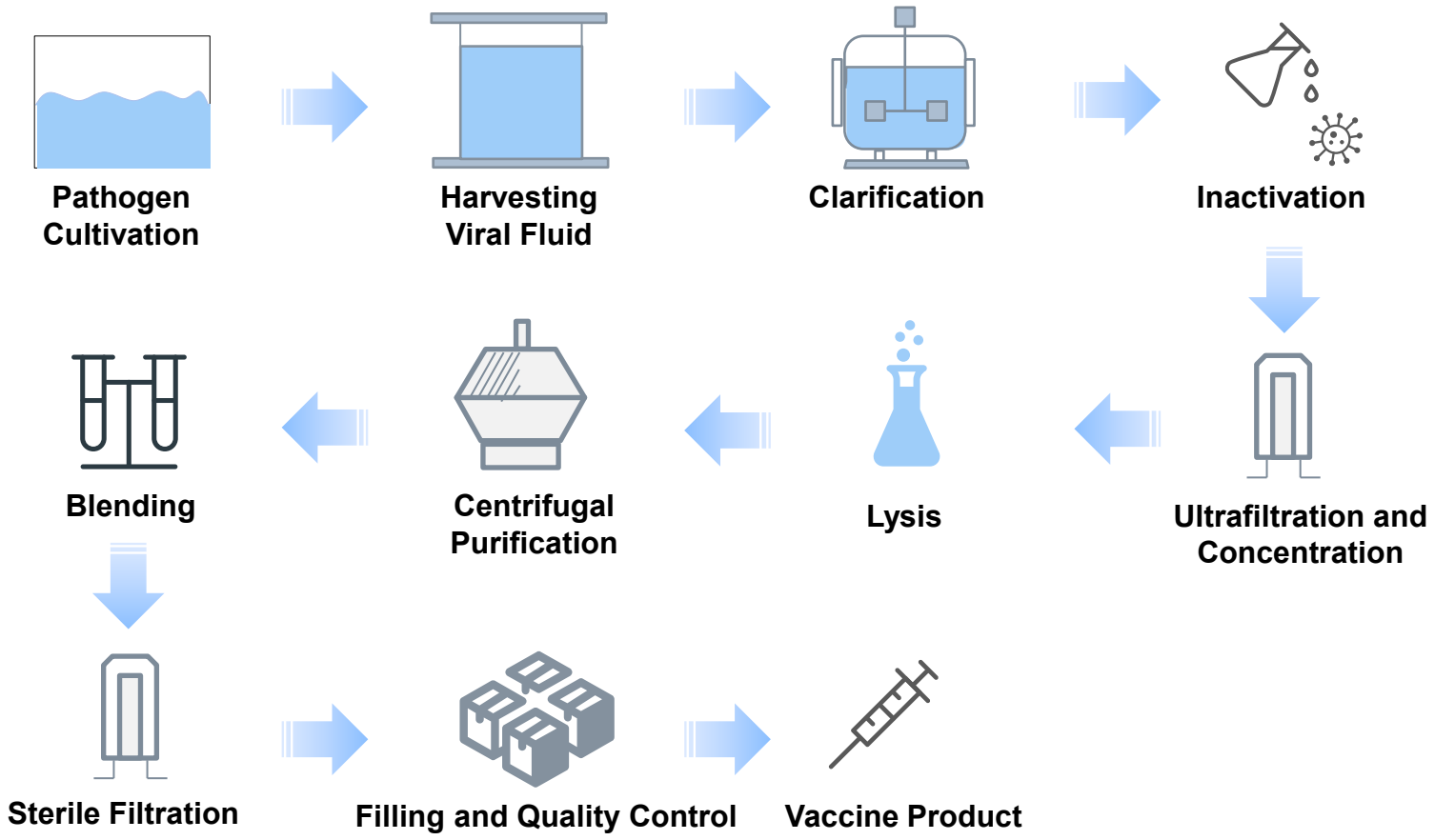
Selecting Combinations

- Inactivated subunit vaccines contain only pathogen-specific components as antigens, so choosing suitable antigens and ensuring they can induce a sufficient immune response are key challenges in inactivated subunit vaccine development.

Source: Frost & Sullivan

Production Process of Inactivated Subunit Vaccines

- An inactivated subunit vaccine contains only specific antigens derived from inactivated pathogens through processes like lysis and purification. Key production steps include pathogen cultivation, clarification, inactivation, concentration, lysis, centrifugal purification, blending, sterile filtration, filling, and quality control.



Source: Frost & Sullivan

Applications and Classification of mRNA Vaccines

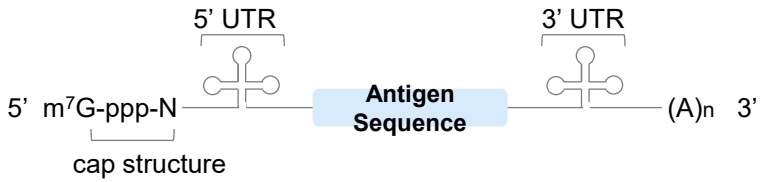
- The mRNA vaccine is a new type that uses mRNA sequences encoding specific antigens, which enter host cells to express these antigens, providing prevention or treatment.
- Its main applications include preventing infectious diseases and treating tumors, with current research focusing on COVID-19, influenza, RSV, melanoma, prostate cancer, and colorectal cancer.
- mRNA vaccines are classified as non-replicating or self-amplifying based on the mRNA type.
- In August 2021, Pfizer and BioNTech's BNT162b2 became the world's first approved mRNA vaccine.

Application Areas of mRNA Vaccines

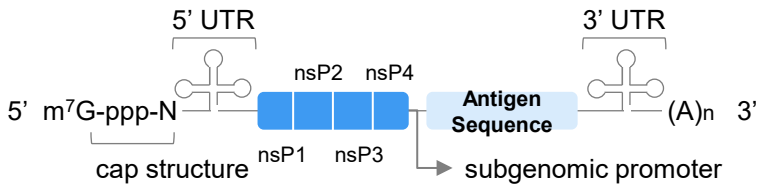
	Infectious Diseases	Tumor
Principle	mRNA vaccines for infectious diseases encode pathogen antigens, which, once expressed in the body, induce cellular and humoral immunity, stimulating antibodies and immune cells to prevent the pathogen.	mRNA encoding tumor-specific antigens is delivered into the body, where these antigens are translated and presented on cell surfaces, activating the immune system to specifically recognize and kill tumor cells.
Focus	Including COVID-19, influenza, respiratory syncytial virus (RSV) infection, HIV, and others.	Including melanoma, prostate cancer, lung cancer, colorectal cancer, and others.

Classification of mRNA Vaccines

Non-replicating mRNA Vaccine



Self-amplifying mRN Vaccine



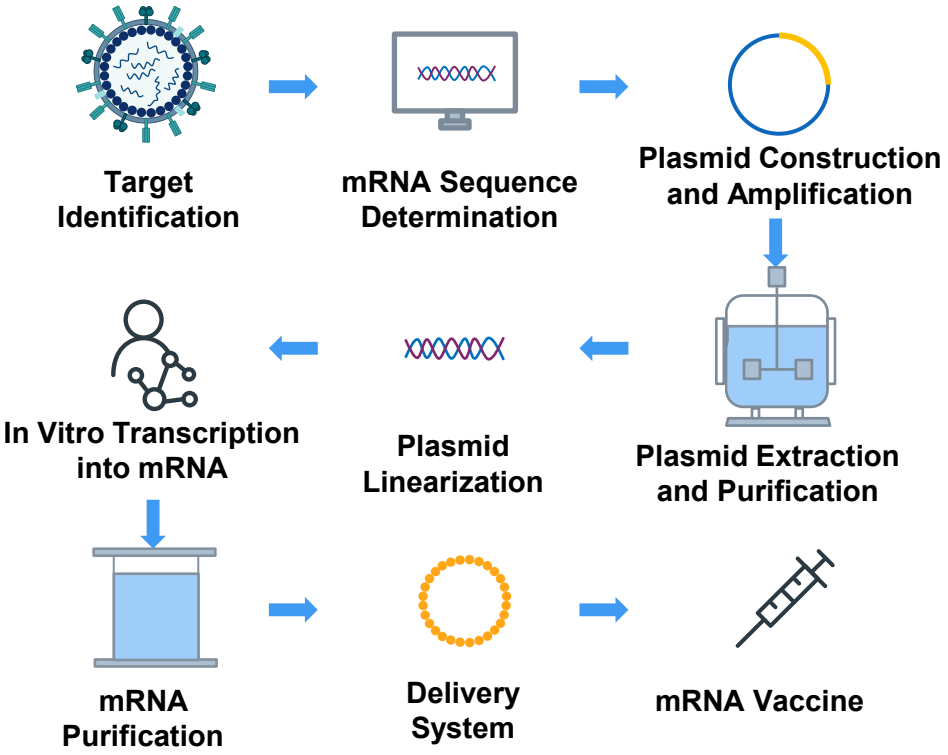
Self-amplifying mRNA is longer than non-amplifying mRNA. In addition to the basic elements of mRNA, it includes an open reading frame at the 5′ end that encodes four nonstructural proteins (nsP1-4) and a subgenomic promoter. Self-amplifying mRNA can replicate within the body, producing high levels of antigen and inducing a stronger immune response.

Source: Literature Review, Frost & Sullivan

Analysis of the mRNA Vaccine Production Process, Advantages, and Challenges

- Due to differences in mechanisms and design, mRNA vaccines offer many advantages over traditional vaccines, including high safety, effectiveness, production efficiency, and rapid response capability.
- The COVID-19 pandemic accelerated the clinical use of mRNA vaccines. However, despite these advantages, the short usage history means that further research is needed to assess the long-term safety and efficacy of mRNA vaccines, and challenges remain in the design of effective delivery systems.

mRNA Vaccine Production Process



The Advantages of mRNA Vaccines

- **Safety:** mRNA is a non-infectious, non-integrating platform, eliminating infection and mutagenesis risks. It is biodegradable, and its half-life can be adjusted through modi-fications and delivery methods.
- **Efficacy:** Modifications improve mRNA stability and translation. Encapsulation in carrier molecules enables rapid uptake and expression in the cytoplasm, enhancing in vivo delivery. Co-administration with adjuvants boosts immunogenicity.
- **High Production Efficiency:** mRNA is produced via in vitro transcription, allowing faster production with a relatively simple process compared to traditional live-attenuated or inactivated virus vaccines.
- **Rapid Response:** mRNA vaccines have short development cycles, with easily modifiable sequences, enabling quick responses to emerging infectious diseases.

Challenges to mRNA Vaccines

- mRNA vaccines are less stable, easily degraded, and have a large molecular mass and negative charge, making cell entry difficult and requiring delivery systems.
- mRNA vaccines have a short history of application and lack long-term safety and efficacy data.

Source: Literature Review, Frost & Sullivan

Delivery Strategy for mRNA Vaccines

- Effective delivery methods remain a major challenge for mRNA vaccines. Current delivery approaches include carrier-based delivery, naked mRNA injection, and dendritic cell (DC) delivery, with naked mRNA injection and DC delivery primarily used in tumor mRNA vaccine development.
- Among carrier delivery systems, lipid nanoparticles (LNPs) are the most widely used tool for in vivo mRNA delivery.

Delivery System	Delivery Mechanism	Advantages	Limitations
Lipid Carrier	• Lipid mixtures with cationic or ionizable lipids form positively charged vesicles that encapsulate negatively charged mRNA. Once inside the cell, the lipid carrier enters an acidic endosome, where the lipids interact with the endosomal membrane, disrupting it and releasing mRNA into the cytoplasm for ribosomal translation.	• Biocompatible • Low immunogenicity • Low toxicity	• The molecular shape of lipids may affect mRNA expression efficiency. • The weakly acidic head of ionizable lipids can lead to LNP instability.
Polymer Carriers	• Positively charged cationic polymers can form complexes with mRNA vaccines through charge interactions. After cellular uptake, they enter acidic endosomes, where the positively charged polymers interact with negatively charged phospholipids on the endosomal membrane, disrupting it, inducing membrane fusion, and releasing the mRNA.	• Good stability	• Toxicity • Poor biocompatibility
Peptide Carrier	• Positively charged peptides used for nucleic acid delivery contain lysine and arginine residues, allowing them to form nanocomplexes with negatively charged mRNA via elec-trostatic interactions. These complexes are efficiently taken up by cells and enter endosomes. The peptides then interact with negatively charged phospholipids on the endosomal membrane, disrupting it, inducing fusion, and releasing mRNA.	• Relatively stable • Low immunogenicity • Low toxicity	• Some cationic peptides bind too tightly to mRNA, affecting its release.
Virus-like Replication Particle	• Virus-like replicon particles (VRPs) can encapsulate antigen-encoding mRNA and deliver it to the cytosol, mimicking viral infection.	• Ability to maintain self-replication	• Highly immunogenic • Somewhat toxic.

Source: Literature Review, Frost & Sullivan

Overview of Subunit Vaccines

- Subunit vaccines, created using synthetic peptides or recombinant technology, are regarded as a safe and dependable approach. Notable subunit vaccines approved by the FDA include those for human papillomavirus (HPV), hepatitis B, and influenza.
- A subunit vaccine strategy, where only essential microbial components necessary to trigger a suitable immune response (such as protein/peptide and carbohydrate antigens) are administered

Benefit:

- They can greatly enhance vaccine safety.
- This approach may also facilitate the development of vaccines in cases where traditional methods have been unsuccessful, such as HIV vaccines.
- Subunit vaccines can be manufactured in a well-characterized form, improving batch consistency,
- They are designed to direct immune responses toward specific microbial targets (epitopes).
- Additionally, they allow the integration of non-natural components and can be freeze-dried, enabling transport and storage without refrigeration.

Basic Design Process:

1. Immunogenic subunit identification
2. Expression and synthesis of subunit
3. Extraction and purification
4. Adjuvant addition or vector incorporation
5. Formulation and delivery

Type of Subunit vaccine

Recombinant Protein Vaccines

Recombinant vaccines are produced by inserting viral or bacterial DNA into bacterial or yeast cells, which then manufacture specific proteins from the pathogen. These proteins are purified and used as the vaccine's active ingredient, like in hepatitis B vaccine.

Toxoid Vaccines

Toxoid vaccines use inactivated bacterial toxins, resembling toxins but non-poisonous. They stimulate the immune system to recognize and respond to toxins, providing protection against bacteria that release harmful proteins.

Conjugate Vaccines

Conjugate vaccines enhance immune response by attaching polysaccharides from bacterial surfaces to a protein, usually diphtheria or tetanus toxoid, which helps train the immune system, especially in infants and young children.

Virus Like Particles

Virus-like particles (VLPs) mimic viruses without being infectious, lacking genetic material. They self-assemble from viral proteins and effectively stimulate immune responses by presenting multiple antigens, sometimes acting as adjuvants to enhance immunity.

OMV Vaccines

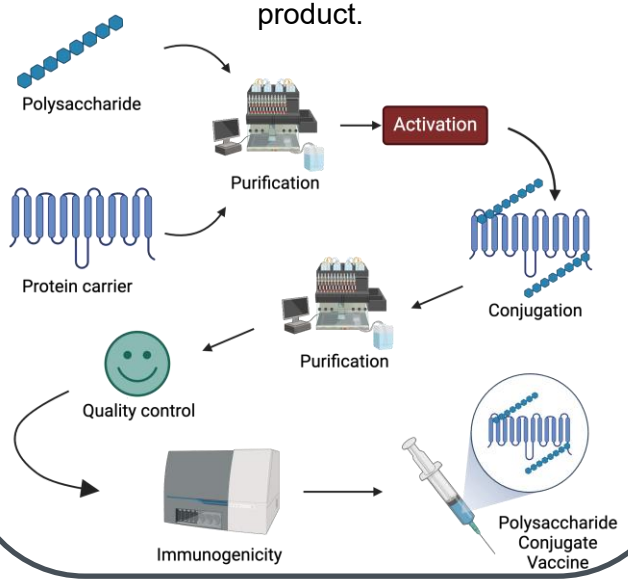
Outer Membrane Vesicles (OMVs) are non-infectious particles derived from bacterial outer membranes, containing membrane antigens. In vaccines, OMVs can be modified to remove toxins, retain immunogenic antigens, and naturally act as adjuvants.

Overview of Polysaccharide Conjugate Vaccines

- Chemical conjugation with a carrier protein significantly enhances the immunogenicity of weakly immunogenic antigens and is effectively used in polysaccharide conjugate vaccine development against infectious diseases.
- This approach covalently binds polysaccharide and protein, enhancing the polysaccharide's immunogenic properties by incorporating the protein's beneficial characteristics. It also provides an epitope for CD4+ T cells, supporting a memory response to polysaccharides and improving overall immune response durability

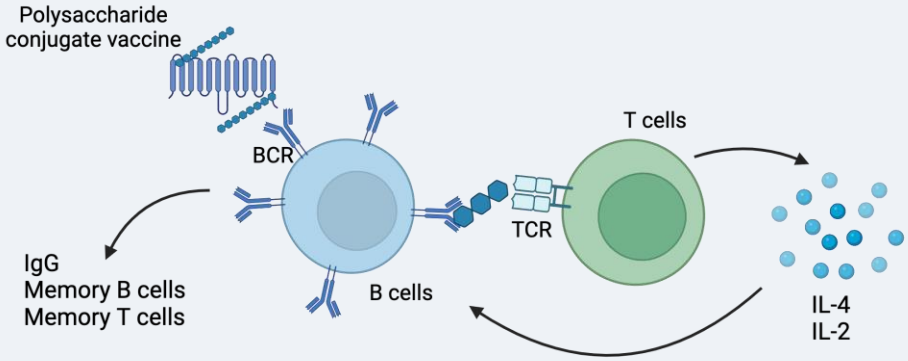
Manufacture process

To prepare a polysaccharide conjugate vaccine, the polysaccharide and carrier protein are purified, coupled chemically, then purified again, quality-checked, and tested for immunogenicity, resulting in the final vaccine product.



Mechanism of Action

The polysaccharide conjugate vaccine is processed by antigen-presenting cells, presenting glycan-peptides on MHC II, triggering IL-4 and IL-2 release, which matures B cells into memory cells producing IgG antibodies.



Benefit

- More effective and long-lasting.
- The conjugate vaccine provide **long-term immunity** and **long-lived T-cell memory**, which helps in recognizing and responding to future infections.
- The conjugate vaccine can generate a **strong booster response** upon re-exposure to the antigen.

Production Complexity of Polysaccharide Conjugate Vaccines

- The complexity of polysaccharide-conjugated vaccine production arises from challenges related to antigen selection, carrier protein interference, precise antigen ratios, serotype compatibility, and quality control during manufacturing. Overcoming these challenges requires careful process design and optimization, such as the use of Quality-by-Design (QbD) methods, to ensure the efficient, safe, and stable production of the vaccine.

1. Antigen Selection and Serotype Integration

- A major challenge is incorporating additional serotypes into the vaccine without compromising safety, efficacy, and manufacturability. Key considerations include:
  - **Antigen Selection:** The right serotypes must be chosen based on global prevalence and disease burden.
  - **Optimal Conjugation Chemistry:** Ensuring efficient conjugation of the polysaccharides while maintaining their stability.
  - **Carrier Protein Selection:** The choice of carrier protein must be carefully considered to avoid interfering with the immune response to the polysaccharide antigens, especially when multiple serotype-specific polysaccharides are conjugated to the same carrier protein.

2. Carrier Protein Interference with Immune Response

- Carrier proteins can interfere with the immune system's response to polysaccharide antigens. This is especially problematic when multiple polysaccharides from different serotypes are conjugated to the same carrier protein, potentially leading to reduced vaccine efficacy and diminished serotype-specific immunity

3. Challenges with Multivalent Vaccines

- Compared to traditional monovalent vaccines, higher-valent PCVs (those with multiple serotypes) face additional complexities, such as:
  - **Precise Antigen Ratios:** High-valent vaccines require precise antigen ratios to ensure the correct immune response.
  - **Serotype Compatibility Issues:** Compatibility between different serotypes may cause challenges in scaling up production and optimizing yields, which in turn affects cost-effectiveness and global availability.

4. Quality Control and Process Optimization

- To address the process-related challenges, the Quality-by-Design (QbD) approach must be implemented to ensure that quality is built into the process design. This approach, as suggested by ICH-Q8 guidelines, includes:
  - Identifying Critical Quality Attributes (CQA), Critical Materials Attributes (CMA), and Critical Process Parameters (CPP).
  - Developing a control strategy and optimizing the production process through Design of Experiments (DoE), followed by data analysis to refine the process.

Overview of recombinant vaccines

- Recombinant vaccines are usually produced by benefiting from bacteria, yeast, mammalian, and insect cells. It involves the recombinant expression of proteins and viral vectors. This technology provides the possibility of developing vaccines against difficult-to-culture or non-culturable viruses and eliminates safety risks by using bioprocesses that are more controlled with defined process components and a shorter process of production, which is very important in terms of responding to a pandemic

Subtypes of Recombinant Vaccine

Recombinant Protein Vaccines

- Most of the recombinant vaccines developed in the recent decays are classified as recombinant protein vaccines. including hepatitis B and, more recently, HPV

DNA Vaccines

- DNA vaccines involve the administration of a naked DNA plasmid directly into the muscle, which has the capability to provoke an immune response and provide protection against pathogens after challenge.
- There is no risk of infection, contrary to attenuated vaccines; they elicit both humoral and cell-mediated immunity, and they are capable of inducing long-lived immune responses and increased cytotoxic T-cell responses.

Live Recombinant Vaccines using bacterial or viral vectors

- This approach uses the capacity of infection and the immunological properties of the live vector to elicit an immune response against its own proteins, as well as towards the heterologous protein being presented. A number of bacteria (such as Salmonella typhi and bacille Calmette-Guérin (BCG)) and viruses (such as vaccinia and adenovirus) have been investigated as live recombinant vector vaccines.
- Effectively stimulate the immune system as in natural infections and have intrinsic adjuvant properties.

Benefits of recombinant vaccines:

- Recombinant vaccines are safe, effective, and the upstream process in recombinant vaccine technology is fast compared to cell culture and in egg production and does not require the handling of live virus and the accompanying expensive Biosafety containment equipment.
- It is likely that more recombinant vaccines will be developed in the future, providing protection against even more diseases. In addition, advances in genetic engineering techniques and the use of novel vectors, such as viral vectors and nanoparticles, may further enhance the effectiveness of recombinant vaccines and expand their potential applications. These developments could lead to the development of vaccines for diseases that have been difficult to target with traditional vaccine approaches, such as cancer and autoimmune diseases.

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Global Development History of the Vaccine

- The past decades have seen the application of molecular genetics and its increased insights into immunology, microbiology and genomics applied to vaccines. Current progress comprises the development of recombinant meningococcal B vaccine and new techniques for seasonal influenza vaccines manufacturing. Molecular genetics sets the scene for a bright future for vaccines, including the development of new vaccine delivery systems (e.g. DNA vaccines) and new adjuvants , including the development of effective tuberculosis vaccines, ebola vaccines, HIV, etc.

1700s	**1798:** Development of first smallpox vaccine
1800s	**1885: First live-attenuated vaccine** – live-attenuated rabies **1886: First inactivated vaccine** – cholera, plague, typhoid
1900s	**1900s**: **Toxoid vaccines** – diphtheria and tetanus toxoids **1927**: BCG **1936**: Influenza vaccine **1948**: **First combination vaccines** – diphtheria, tetanus and pertussis **1955**: **Subunit vaccines** – Polio (injected, inactivated) vaccine **1970s**: **First polysaccharide vaccine** - Meningococcal (meningococcal polysaccharides) vaccine - Pneumococcal (pneumococcal polysaccharides) vaccine **1981**: **First recombinant antigen vaccine** - HBV **1999**: Meningococcal (group C) vaccine
	Boom of New Vaccines
2000-2010	**2000**: Meningococcal (group C) vaccine **2000**: Pneumococcal (heptavalent pneumococcal conjugate) vaccine **2005**: Meningococcal (quadrivakent meningococcal conjugate) vaccine **2006:** Combined Hib vaccine **2008:** HPV **2010:** PCV13 (13-valent pneumococcal conjugate) **2010: First therapeutic vaccine** – Provenge for prostate cancer
2013	Shingles: Children's Influenza Rotavirus
2015	Meningococcal B: Meningococcal ACWY
2017	Hexavalent: DTaP/IPV/Hib/HepB
2020	**First mRNA vaccine** - COVID-19 vaccines, e.g. Pfizer, Moderna

Key takeaways

- The first smallpox vaccine was developed in 1798. It opened the door for the development of vaccines. In 18th century, Louis Pasteur's experiments spearheaded the development of live attenuated cholera vaccine and inactivated anthrax vaccines.
- From 1890 to 1950, bacterial vaccine development proliferated, including the Bacillis-Calmette-Guerin (BCG) vaccination, which is still in use today.
- In 1972, recombinant DNA technology was established at Stanford University, and subsequently applied to vaccine development. Among genetic engineering vaccines, the recombinant hepatitis B vaccine is more successful, which has a better immune effect.
- In the late 1980s and early 1990s, nucleic acids expressing gene products were used for gene therapy experiments, and they could induce an immune response in the body, which set off a research boom in nucleic acid vaccines.
- In 2020, the world's first mRNA vaccine has begun its rollout after being produced at unprecedented speed as part of the global effort to end the Covid-19 pandemic. The two mRNA Covid-19 vaccines – one made by Pfizer/BioNTech and the other by Moderna – mark the first time mRNA vaccine technology has been approved for use.

Source: Frost & Sullivan

Vaccines Approved by FDA in 2019-2024

Year	Number of Vaccines Approved	Trade Name	Indications	Company Name
2019	 3	DENGVAXIA	Dengue fever	Sanofi
		JYNNEOS	Smallpox, monkeypox	Bavarian Nordic
		ERVEBO	Ebola	MSD
2020	 2	AUDENZ	Influenza	Seqirus
		MenQuadfi	Meningococcal disease	Sanofi
2021	 3	PREHEVBRIO*	Hepatitis B	VBI Vaccines
		VAXNEUVANCE	Pneumococcal	MSD
		TICOVAC	Tick-borne encephalitis	Pfizer
2022	 2	IPOL	Poliomyelitis	Sanofi
		PRIORIX	MMR	GSK
2023	 5	CYFENDUS	Anthrax	Emergent BioSolutions
		Abrysyo	RSV	Pfizer
		Arexvy	RSV	GSK
		Penbraya	Meningococcal disease	Pfizer
		Ixchiq	Chikungunya virus	Valneva
2024	 2	MRESVIA	RSV	Moderna
		CAPVAXIVE	Pneumococcal 21-valent Conjugate virus	Merck

**Note: has been voluntarily withdrawn from the market by the company*
COVID-19 vaccines are not included in the chart

Source: FDA, Frost & Sullivan

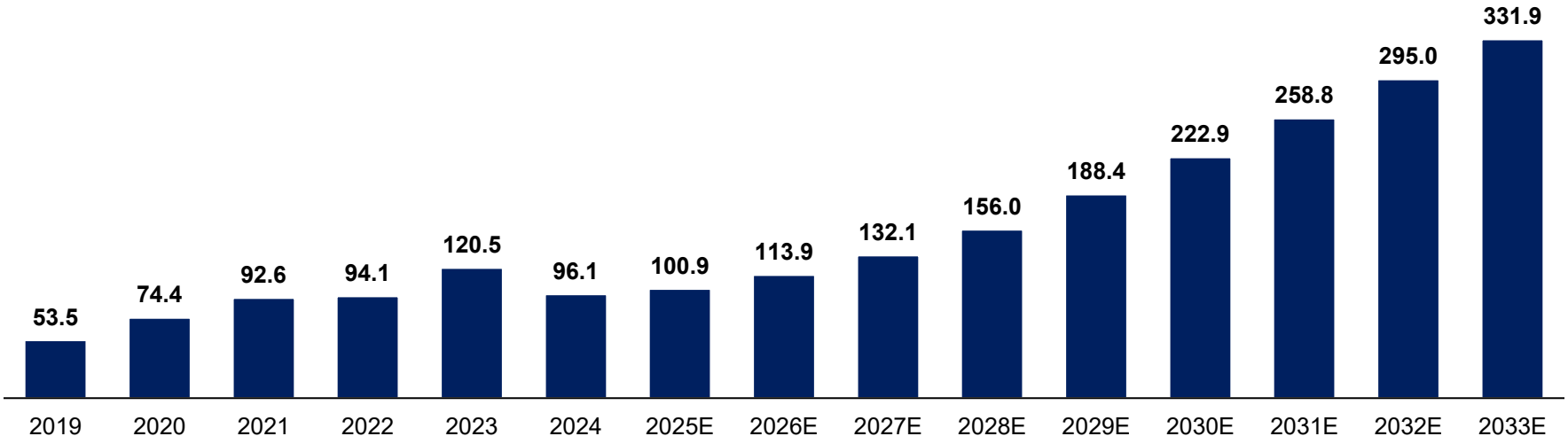
China Human Vaccine Market Size by Production Value, 2019-2033E

- From the perspective of the vaccine industry as a whole, there is not much difference in market size between the production value and sales dimensions
- COVID-19 vaccines, grew from RMB53.5 billion in 2019 to RMB96.1 billion in 2024, at a CAGR of 12.4%. Driven by the expected continuous launch of innovative vaccines, the vaccine market in China is expected to further grow to RMB331.9 billion in 2033, at a CAGR of 14.8% from 2024 to 2033.

China Human Vaccine Market Size, 2019-2033E

Period	CAGR
2019-2024	12.4%
2024-2033E	14.8%

Unit: Billion RMB



Note: The COVID-19 vaccine market has not been considered.

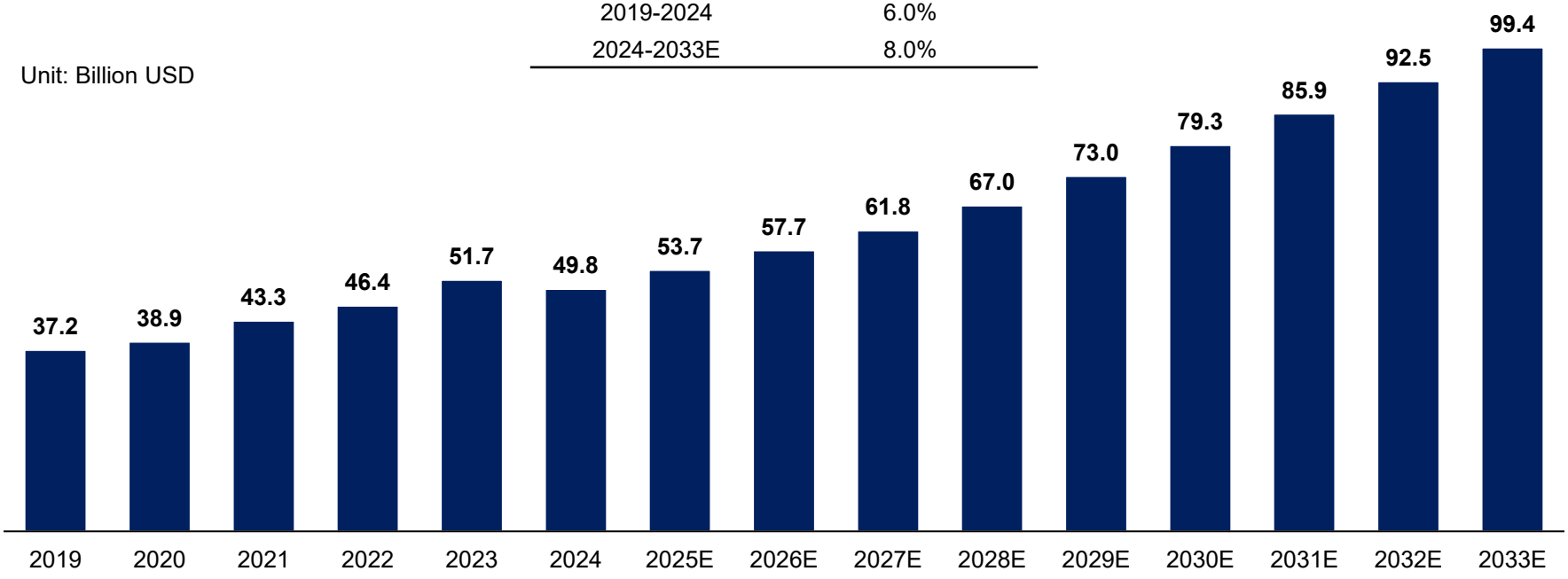
Source: Annual Repot, Frost & Sullivan

Global Human Vaccine Market Size, 2019-2033E

- The global vaccine market, in terms of sales revenue and without considering COVID-19 vaccines, increased from US$37.2 billion in 2019 to US$49.8 billion in 2024, at a CAGR of 6.0%. Driven by the continuous commercialization of innovative vaccines and market growth in emerging countries, such as China, the global vaccine market is expected to reach US$99.4 billion in 2033 at a CAGR of 8.0% from 2024 to 2033.

Global Human Vaccine Market Size, 2019-2033E

Period	CAGR
2019-2024	6.0%
2024-2033E	8.0%



Note: The COVID-19 vaccine market has not been considered.

Source: Annual Repot, Frost & Sullivan

Global Vaccination Situation, Challenges and Needs

- In April 2021, the World Health Organization (WHO), the United Nations Children's Fund (UNICEF) and the Global Alliance for Vaccines and Immunization (GAVI), among other organizations, announced the Immunization Agenda 2030, which seeks to promote vaccination to protect people of all ages from disease. At the same time, the Agenda for Immunization calls on the pharmaceutical industry and researchers to strengthen collaboration with governments and funders to accelerate vaccine research and development and ensure a sustained supply of affordable vaccines.

Major Developments and Challenges

Wide Variation in Vaccination Rates

- The reasons for the wide variation in vaccination rates among GAVI are highly correlated with national economies.
- In Ethiopia, where less than 40% of children have received basic vaccinations, vaccination rates are relatively low.

High Price of Vaccines

- Countries not covered by GAVI pay high prices for vaccines.
- Unaffordable vaccine prices not only limit a country's ability to expand vaccine coverage, but also discourage the introduction of new vaccines, which can further reduce vaccination rates.

Low Vaccine Accessibility

- Developing countries have limited medical resources compared to developed regions.
- Developing countries have low vaccine accessibility due to insufficient capacity of vaccine resources, dependence on a few manufacturers, and safety lapses in the production process.

Needs of Developing Countries

- Increase vaccine coverage: direct more GAVI funds to regions with low coverage (e.g., Asia, Africa, Latin America).
- Save on vaccine costs: control prices through centralized purchasing and pricing agreements.
- Improve accessibility: developing countries adopt collaborative vaccination models to speed introductions, ensure quality, and expand the Vaccine Assistance Program (VAP) for stronger national immunization programs.

Source: Literature Review, Frost & Sullivan

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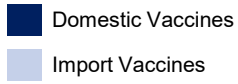
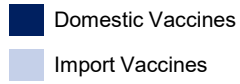
Vaccines Approved by NMPA in 2019-2024



Year	Number of Vaccines Approved	Trade Name	Indications	Company Name
2019	4 domestic, 1 import, 5 total	Quadrivalent influenza virus split vaccine	Influenza	GDK（金迪克生物）
		SHINGRIX	Herpes zoster	GSK
		Varicella vaccine	Varicella	SINOVAC（科兴生物）
		WEUPHORIA（沃安欣）	Pneumonia	WALVAX（沃森生物）
		Cecolin（馨可宁）	Cervical carcinoma	Wantai BioPharm（万泰生物）
2020	5 domestic, 5 total	Wugan（雾感）	Influenza	BCHT（百克生物）
		Diphtheria,Tetanus and Acellular Pertussis Combined Vaccine， Adsorbed	Diphtheria, Tetanus and Acellular Pertussis	Minhai（民海生物）
		Group A and Group C Meningococcal Conjugate Vaccine	Cerebrospinal meningitis	OLYMVAX（欧林生物）
		Influenza Vaccine (Split Virion), Inactivated, Quadrivalent	Influenza	SINOVAC（科兴生物）
		23-valent Pneumococcal Polysaccharide Vaccine	Pneumonia	SINOVAC（科兴生物）

Source: NMPA, Frost & Sullivan analysis

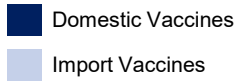
Vaccines Approved by NMPA in 2019-2024



Year	Number of Vaccines Approved	Trade Name	Indications	Company Name
2021	8	Menphecia （美奈喜）	Cerebrospinal meningitis, pneumonia	CanSinoBIO （康希诺生物）
		Menhycia （曼海欣）	Cerebrospinal meningitis, pneumonia	CanSinoBIO （康希诺生物）
		Rabies Vaccine (Vero Cell), Freeze-dried	Rabies	YIDU Biotechnology （亦度生物）
		Weiminfeibao （维民菲宝）	Pneumonia	Minhai （民海生物）
		Haemophilus Influenza Type b Conjugate Vaccine	Cerebrospinal meningitis, pneumonia	Minhai （民海生物）
		Poliomyelitis Vaccine (Vero Cell), Inactivated, Sabin Strains	Poliomyelitis	SINOVAC （科兴生物）
		Influenza Vaccine (Split Virion), Inactivated, Quadrivalent	Influenza	Shanghai institute of biological products （上海生物制品研究所）
		Rabies Vaccine (Vero Cell), Freeze-dried	Rabies	Changchun institute of biological products （长春生物制品研究所）
2022	3	AdimFlu-S （安定伏）	Influenza	ADIMMUNE （国光生物）
		Walrinvax （沃泽惠）	HPV	WALVAX （沃森生物）
		Group ACYW135 Meningococcal polysaccharide vaccine	Cerebrospinal meningitis	Beijing institute of biological products （北京生物制品研究所）

Source: NMPA, Frost & Sullivan analysis

Vaccines Approved by NMPA in 2019-2024

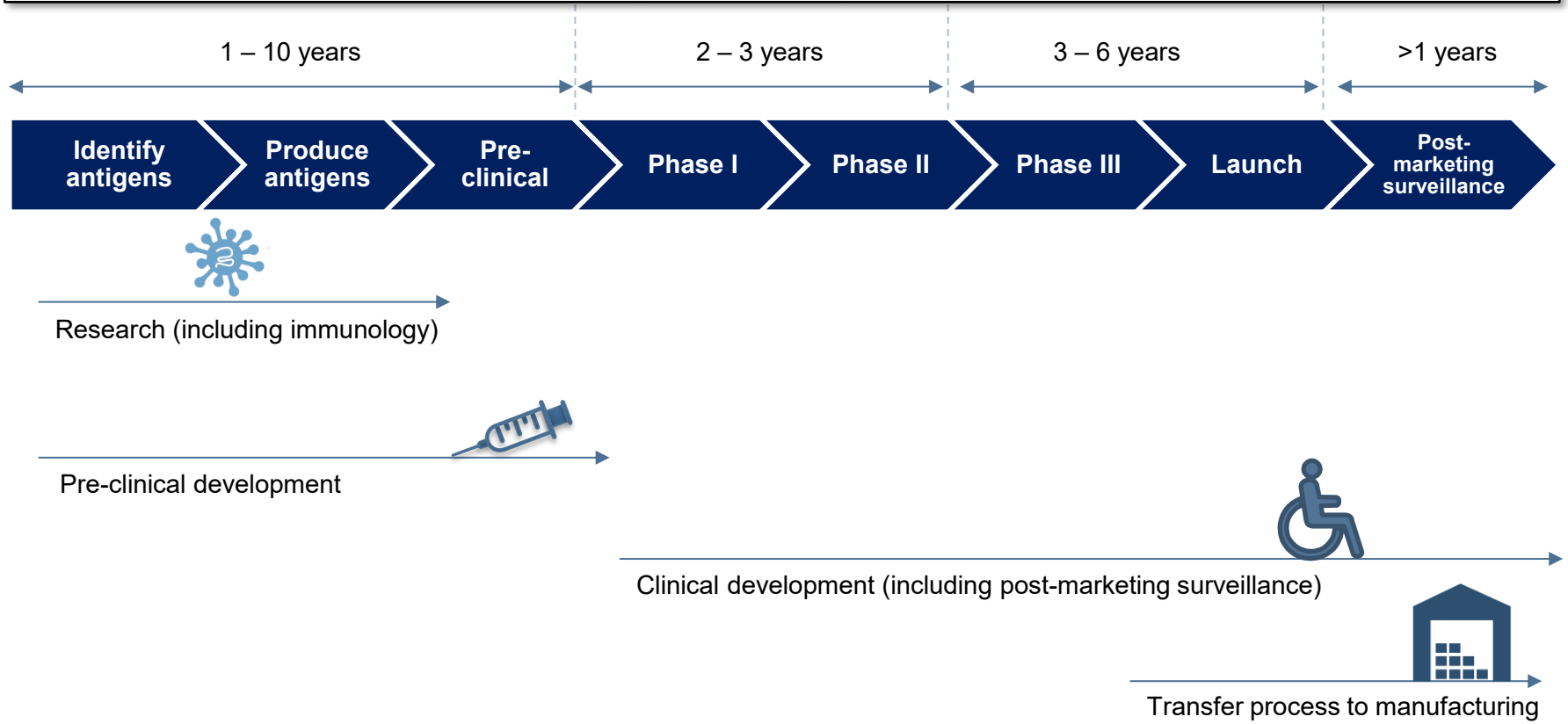


Year	Number of Vaccines Approved	Trade Name	Indications	Company Name
2023	8 domestic, 1 import, 9 total	live attenuated zoster vaccine (感维)	Herpes Zoster	BCHT (百克生物)
		freeze-dried rabies vaccine, vero cell	Rabies	Hualan Biological Bacterin (华兰生物)
		Tetanus Vaccine, Adsorbed	Tetanus	Hualan Biological Bacterin (华兰生物)
		VaxigripTetra (凡尔佳)	Influenza	Sanofi
		ROTALAN (瑞特威)	Rotavirus gastroenteritis	Lanzhou institute of biological products (兰州生物制品研究所)
		Quadrivalent Subunit Influenza Vaccine (慧尔康欣)	Influenza	Ab&b Bio-Tech (中慧元通)
		23-Valent Pneumococcal Polysaccharide Vaccine	Pneumonia	ZFSW (智飞生物)
		freeze-dried rabies vaccine	Rabies	MINHAI (民海生物)
		freeze-dried rabies vaccine, vero cell	Rabies	CuroVax (康润生物)
2024	2 domestic, 2 total	Freeze-dried Rabies Vaccine (Vero Cell) for Human use	Rabies	Aleph (复星雅立峰)
		Varicella Vaccine, Live	Varicella	MINHAI (民海生物)

Source: NMPA, Frost & Sullivan analysis

Introduction to the full lifecycle process of Chinese vaccines and average years of research and development

- The development of a new vaccine can be divided into research, pre-clinical testing, clinical testing, and post-marketing surveillance. It usually takes more than 15 years from identifying the antigens to come to the market.
- During the clinical trials of vaccines, the purpose of phase I is to test the safety of the vaccines on healthy adults. After the phase I is completed, phase II is conducted to evaluate whether the vaccines can meet the expected effects (immunogenicity) and obtain the safety information. The goal of phase III is to evaluate the efficacy and safety of the vaccine, which is a essential phase for obtaining approval for registration.



Source: Frost & Sullivan

Comparison of Vaccination Coverage in China, United States and GAVI Countries

- The vaccination rate of common vaccines available in the market is exhibited as below. For Category I like DTaP, the vaccination rate in China almost verges on the level in U.S. meanwhile GAVI countries also exhibits considerable vaccination rate with aids of charitable funds over the recent years. Rather, the vaccination rate of Category II in China is highly limited by now when compared with the vaccination level in the U.S. as indicated below. Above 90% of people in the U.S. has been vaccinated with pneumococcal vaccines while merely 9% of people in China received such vaccine. Furthermore, less than 1% of people in China has been vaccinated with HPV. Such difference unveils a great market potential in vaccine industry in China, especially for Category II vaccines.

Country	Pneumococcal Vaccines	Hib Vaccines	HPV	Influenza Vaccines	DTaP	Covid 19	Shingles
	>90%	92%	57%	30-40%	95%	58%	35%
	9%	44%	<1%	2-3%	93%	71%	<1%

% of Children Immunized in 73 GAVI Countries (Mostly Consists of Category I Vaccine)	
80%	81%

Note:
- *Due to different immunization programs in China and U.S., the vaccination rate of Category I and Category II vaccines is not applicable above.*
- *The vaccination coverage of pneumococcal vaccines shown above refer to the sum coverage of PCV7 and PCV13 vaccination among children in the U.S. and PPSV23 coverage among children and elderly (>65 years) in China, respectively.*
- *The HPV coverage shown is the vaccination coverage in female at the age of 13-17 years in the U.S. and that in female at the age of 9-15 years in China.*

Source: Frost & Sullivan

Regulations in Vaccine Value Chain in China

- China has imposed stricter rules over the entire value chain of the vaccine industry. Tighter regulation from R&D to inoculation promises higher quality of vaccines and help stamp out illegal behaviors in the vaccine industry. China's state council has officially amended rules for vaccine circulation and vaccination by banning wholesalers from direct sales to clinics at the provincial and country levers where purchase is centralized. Great efforts has been invested to strengthen the cold chain storage, transportation, traceability management system throughout the vaccine distribution process. Revised regulatory requirements such as better record keeping for the production, storing and transport of vaccines and tougher punishment for the lawbreakers is beneficial for public heath.

	Regulators	Documents	Main Content
R&D	CFDA	Technical Guidelines for Preclinical Research on Preventive Vaccines *《预防用疫苗临床前研究技术指导》(2010)*	• Implementation of the Marketing Authorization Holder (MAH) system. • To establish a prioritized review and approval system, and implementation of data protection towards data submitted by applicants for innovative drugs, orphan drugs, and child-specific drugs.
Registration	SAMR, CFDA	Provisions for Drug Registration (2020) *《药品注册管理办法》(2020)*	• To accelerate the process of drug reviews and approval, the State Drug Administration is required to conduct a formal review of the application materials within 5 working days.
Manufacturing	CFDA, MOEP	GMP, Emission standard of water pollutants for pharmaceutical industry *《制药工业水污染物排放标准》*	• To determine the focus of supervision and clear person responsible.. • To optimize the risk management process, material reviewing, and specifying the timeframe for the lot release and reinforce administration.
Sales	CFDA	GSP, Measures for the supervision and administration of circulation of pharmaceuticals *《药品流通监督管理办法》(2016)*	• To reform the distribution of class II vaccine and eliminate the multiple intermediate wholesalers in the vaccine industry. • To increase penalties and accountability to further punish the illegal conduct and ineffective supervision during vaccine distribution.
Distribution	NIFDC	Administrative Measures for Batch Release of Biological Products (2020) *《生物制品批签发管理办法》(2020)*	• To determine the focus of supervision and clear person responsible. • Vaccine products should be completed within 60 days of Lot Release.
Vaccination	SCPC	Vaccine Administration Law of the People's Republic of China *《中华人民共和国疫苗管理法》(2016)*	• Supervise the whole process of vaccine development, production, distribution and vaccination. Ensure the quality and supply of vaccines and standardize vaccination

Source: Government Announcement, Frost & Sullivan analysis

Entry Barriers of Human Vaccines Market in China(1/2)

Market Access Barriers	• High industry entry barriers: In terms of vaccine production management, the state implements a strict access system for vaccine production and strictly controls the establishment of new vaccine production enterprises. There is strict supervision in all aspects of vaccine production, circulation and supervision in China. • High capital needs: Companies need to invest heavily in developing new vaccines. The construction of R&D facilities, manufacturing facilities, testing, and clinical trials all require significant capital expenditures. • High production costs: The vaccine industry has low capacity utilization, and a production line can usually only produce one vaccine, resulting in high production fixed costs. • Fierce competition: The competition pressure of vaccine varieties is high, and the profit margin of enterprises is compressed. Developing core technologies independently is the key to sustainable and healthy development.
Sales Channel Barriers	• Strict management of vaccine circulation: vaccine manufacturers need to entrust enterprises with cold chain storage and transportation conditions for distribution or entrust themselves with cold chain storage and transportation conditions. • From the vaccine manufactures to end users, the vaccine distribution channel involves multiple parties. CDCs and the government plays a very important role in the vaccine bidding, purchase and distribution process. The vaccine manufacturers should build a solid relationship with different parties and expand their sales channels. Through the long-term efforts of developing and maintaining distribution channels, vaccine manufacturers distribute safe and qualitative vaccines to end users. • Industry leaders have a high market share with high brand maturity, causing fierce competition.

Source: Frost & Sullivan Analysis

Entry Barriers Human Vaccines Market in China(2/2)

Technology and Talent Barriers	• The vaccine development process is very complex. Key R&D capabilities include platform technology and advanced, adequate R&D facilities and equipment. • New entrants lack experienced talent with specialized knowledge. • The vaccine development process is complex with a long timeline, requiring experienced technicians. China's vaccine industry lack of senior and middle management personnel. At the same time, the training of personnel requires time and expenditure. • Due to the difficulty of new vaccine research and development, some enterprises have licensed-in the technology from a company with mature production technology. However, the production technology and industrialization of new vaccines are still difficult, especially for enterprises lacking corresponding technical capabilities, forming high vaccine technical barriers.
Production Quality Management Barriers	• China implements a strict access system for vaccine production and strictly controls the establishment of new vaccine manufacturers. In addition to meeting the requirements for the establishment of vaccine manufacturers, newly established vaccine manufacturers shall also comply with the relevant policies of the national vaccine industry authorities. • Biological products, including vaccines, are distinguished from chemical pharmaceuticals by being derived from living organisms with a molecular composition too complex to be defined by physical or chemical means. In addition, the inherent variability of living organisms, and the potential for contamination of materials with agents coming from starting materials or the environment, require special quality control and quality assurance mechanisms.
Regulatory Barriers	• The vaccine industry is a highly administratively supervised industry, which is strictly supervised and controlled by the competent government authorities from research and development, production, circulation, sales and after-sales safety

Source: Frost & Sullivan Analysis

Regulations of Vaccine Market in China - I

Date	Government	Policies	Comments
Feb 2006	State Council	Notice of the State Council on Issuing the "the National Outlines for Medium and Long-term Planning for Scientific and Technological Development (2006-2020)" (*《国务院关于印发《国家中长期科学和技术发展规划纲要(2006-2020年)》的通知》*)	Create an incentive environment for independent innovations. The endeavor will construct a innovation-oriented state, establish an accreditation system for national independent innovation products and regulate the accreditation of independent innovation products.
Dec 2007	Ministry of Health	Notice of the Ministry of Health on Issuing the "Expanded National Immunization Program Implementation Plans" (*《卫生部关于印发《扩大国家免疫规划实施方案》的通知》*)	The national immunization plan will be upgraded from 6 vaccines that can prevent 7 types of diseases to 14 vaccines that can prevent 15 types of diseases, including hepatitis A and meningitis.
June 2009	State Council	Notice of the State Council on Issuing the "Several Policies to Promote the Accelerated Development of the Biological Industry" (*《促进生物产业加快发展的若干政策》*)	Promote the industrialization of biotechnology R&D and innovation, build major biotechnology infrastructures, and make further breakthroughs in key technologies such as therapeutic vaccines and antibodies, cell therapy, genetically modified crop breeding, and bioenergy crop cultivation. Innovative products such as influenza vaccine, molecular diagnostic reagents, super rice, and polylactic acid should be promote and applied.
Oct 2010	State Council	Decision of the State Council on Accelerating the Fostering and Development of Strategic Emerging Industries (*《国务院关于加快培育和发展战略性新兴产业的决定》*)	Promote biotechnological medicine, novel vaccine and diagnostic agents, chemical drugs, modern traditional Chinese medicine, and related types of innovative drugs in the treatment and prevention of major diseases. Elevate the level of the Chinese biopharmaceutical industry.
Dec 2011	State Council	The State Council on forwarding the Development and Reform Commission and other departments Notice of the Vaccine Supply System Construction Plan (*《国务院办公厅关于转发发展改革委等部门疫苗供应体系建设规划的通知》*)	Construct the vaccine supply system to fit the demand of the Chinese societal and economic advancement by 2015. By 2020, the goal is to further complete the system to prepare for major emergency response through promoting legal infrastructure and standard systems, furthering financial supportive policies, expanding the R&D budget, investing in human resources, and strengthening the coordination among the vaccine supply system.

Source: Government Announcement, Frost & Sullivan analysis

Regulations of Vaccine Market in China - II

Date	Government	Policies	Comments
Dec 2012	State Council	Notice of the State Council on Issuing the Bio-Industry Development Plan（*《国务院关于印发生物产业发展规划的通知》*）	Improve the pharmaceutical management system and mechanisms, comprehensively enhance the innovation capabilities and product quality management capabilities of biomedical companies. Also accelerate the development and industrialization of new products and new processes such as biotechnology drugs, chemical drugs, and traditional Chinese medicines, enhance regional supporting capabilities, and actively promote the industry structural adjustments will make the biomedical industry bigger and stronger. The policy also emphasize the development and industrialization of novel vaccine, including the ones for therapeutic purposes.
May 2015	State Council	Notice of the State Council on Issuing the "Made in China (2025)" (*《国务院关于印发《中国制造2025》的通知》*)	Encourage R&D of new biotech drugs for major diseases, focusing on novel vaccines.
April 2016	State Council	Decision of the State Council on Amending the Regulation on the Administration of Circulation and Vaccination of Vaccines (*《国务院关于修改《疫苗流通和预防接种管理条例》的决定》*)	Vaccine production enterprises shall distribute Category-II vaccines directly to county disease prevention or authorize enterprises with cold chain storage transport conditions. Vaccines should be stored and transported in the environment with the prescribed temperature during entire distribution process. Information of vaccine manufacturing, storage, transport and uses should has track record.
Dec 2016	State Council	Notice of the State Council on Issuing the “National strategic emerging industry plan during 13th Five-Year Plan Period” (*《国务院关于印发“十三五”国家战略性新兴产业发展规划的通知》*)	The policy aims to build a new system in in biopharmaceutical industry. It pushes for the development of novel drugs and innovative biopharmaceutical products. Also promote and spread green, smart drug manufacturing technology. Strengthen efficient management and policy support for more industry globalization.
Dec 2016	Development and Reform Commission	Notice of Development and Reform Commission on issuing “The biological industry development plan during 13th Five-Year Plan Period” *《发展改革委印发“十三五”生物产业发展规划的通知》*)	The goal to promote the scale of the Chinese biopharmaceutical industry and to help advance the industry to become the leader of the national economy. The policy also encourages the development of therapeutic vaccine, innovating safe and effective Live vector genetic engineering multivalent vaccine.

Source: Government Announcement, Frost & Sullivan analysis

Regulations of Vaccine Market in China – III

Date	Government	Policies	Comments
Jan 2017	State Council	Notice of the State Council on Issuing the Plan for Medicine and Health during 13th Five-Year Plan Period (《国务院关于印发“十三五”卫生与健康规划的通知》)	Improve centralized purchasing of vaccine for hospitals, cold chain management. Standardize regulations to manage vaccination of vaccines in clinics. Aim to establish vaccination abnormal response compensation insurance mechanism. Sales of unapproved vaccine are strictly forbidden.
Feb 2017	State Council	Opinion of the State Council on further enhancing Management of Vaccine and Immunization (《国务院办公厅关于进一步加强疫苗流通和预防接种管理工作的意见》)	All regions should enhance vaccine inspection capabilities. Establish professional drug inspectors team and promote standardized training. Gradually improve capabilities of provincial Food and Drug Administration on vaccine testing.
Feb 2017	State Council	Notice of the State Council on Issuing the Plan for National Drug Safety during 13th Five-Year Plan *“Period*（《国务院关于印发“十三五”国家药品安全规划的通知》）	Improve national vaccine approval system thereby enhance vaccine quality evaluation. In line with international standards, establish cell source database, stem cell database. Establish and improve the standard of biological products research and supply platform, quality evaluation criteria and technology platform.
Sep 2017	Beijing Health Committee	Measures of Beijing Municipality on the Administration of Vaccination Outpatients (2017) (《北京市预防接种门诊管理办法》(2017版))	Setting up vaccination clinics must meet the following conditions at the same time:1. Have the medical institution practice license 2. Vaccination staff shall have the qualification of licensed physician, licensed assistant physician or nurse, regularly participate in the professional training of vaccination organized by the District Health and Family Planning Commission and pass the examination 3. It conforms to the setting standards of vaccination clinics in Beijing, and has passed the on-site acceptance and regular assessment organized by the District Health and Family Planning Commission. 4. Establish and earnestly implement various vaccination management systems to ensure the standardization and safety of vaccine and cold chain use and management, vaccination services.

Source: Government Announcement, Frost & Sullivan analysis

Regulations of Vaccine Market in China – Ⅳ

Date	Government	Policies	Comments
Jun 2019	National People's Congress	Vaccine Administration Law of the People's Republic of China（《中华人民共和国疫苗管理法》）	Units and individuals engaged in vaccine development, production, distribution and vaccination activities shall abide by laws, regulations, rules, standards and norms, ensure the authenticity, accuracy, integrity and traceability of information throughout the process, assume responsibilities according to law and accept social supervision. Disease prevention and control institutions and vaccination units shall truthfully record the circulation of vaccines, vaccination and other information according to law, and provide traceability information to the national vaccine electronic traceability collaboration platform according to regulations. Disease prevention and control institutions, vaccination units, vaccine marketing license holders, and vaccine distribution units shall abide by the vaccine storage and transportation management specifications to ensure the vaccine quality. In addition to the vaccine fee, the vaccination unit may also charge the vaccination service fee for the vaccination of non immunization planned vaccines. The charging standards for vaccination service fees shall be formulated by the competent pricing departments of the people's governments of provinces, autonomous regions and municipalities directly under the Central Government in conjunction with the financial departments.
Oct 2019	Development and Reform Commission	Decision of the National Development and Reform Commission on Amending the Relevant Entries under the Catalogue for Guiding Industrial Restructuring （Version 2019）（发展改革委修订发布《产业结构调整指导目录（2019年本）》）	Listing major disease prevention and treatment vaccines, antibody drugs, gene medicine therapy, cell medicine therapy, recombinant protein drugs, and other modern biotechnology reformed drugs as encouraged industries with supportive policies.
Jul 2022	State Food and Drug Administration	《Regulations on the Administration of Vaccine Production and Distribution》(No. 55 in 2022)（《疫苗生产流通管理规定》（2022年 第55号））	Further refine the relevant regulations that enterprises and regulatory authorities need to comply with in all aspects of vaccine production, circulation and supervision. The holder is responsible for the whole process of vaccine. In terms of commissioned production, it is required to meet strict conditions before commissioned production, and all vaccine production processes must be commissioned. During the circulation of vaccine, the holder shall be responsible for the vaccine quality and must comply with the requirements of the whole process electronic traceability system.

Source: Government Announcement, Frost & Sullivan analysis

Overview of Class II Vaccines in China

- According to the Regulations on the Administration of Vaccine Circulation and Vaccination, Chinese vaccines can be divided into immunization plan vaccines and non immunization plan vaccines based on the payment subject of vaccination fees. Immunization vaccines and non immunization vaccines are relative, not absolute constants. As conditions mature, many non immunization program vaccines will also be included in the national immunization program.

Class II Vaccine

Introduction

- Class II vaccines are paid by the recipient or insurance company; With the improvement of China's disposable income level and health awareness, more and more residents have the ability to choose class II vaccines as their health investment to prevent certain diseases

Price

The price of class II vaccines is relatively high

Manufacturer

- Through the provincial centralized bidding platform, production enterprises are responsible for directly connecting and delivering vaccines to vaccination sites, and recipients need to pay for them themselves

Population

Targeting a wider age group

Approved Class II Vaccines Classified by indications

Hepatitis B vaccine[1]	Varicella vaccine[2]	Tick-borne encephalitis vaccine
Rabies vaccine	Influenza vaccine[3]	Enterovirus vaccine
Brucella vaccine	Pneumococcal vaccine[4]	Yellow fever vaccine
JE vaccine [1]	Cholera vaccine	Plague vaccine
meningitis [1]	Rotavirus vaccine	Hepatitis E vaccine
Typhoid vaccine	HPV vaccine	……

Note:
1. There are JE, meningitis and hepatitis B vaccines in botn the immunization planning vaccines and non immunization planning vaccines;
2. Freeze dried varicella attenuated live vaccine is managed as an immunization plan vaccine in emergency vaccination in Beijing, Tianjin and other areas;
3. Influenza virus split vaccine is administered as an immunization program vaccine for the elderly and students in Beijing;
4. The 23 valent pneumococcal polysaccharide vaccine is administered as an immunization program vaccine for elderly people aged 60 and above in Shanghai;
5. The above classification has not been included in the COVID-19 vaccine. At present, the cost of COVID-19 vaccine and vaccination is shared by the medical insurance fund and financial funds

Source: Frost & Sullivan

Growth Drivers of Class II Vaccine Market in China

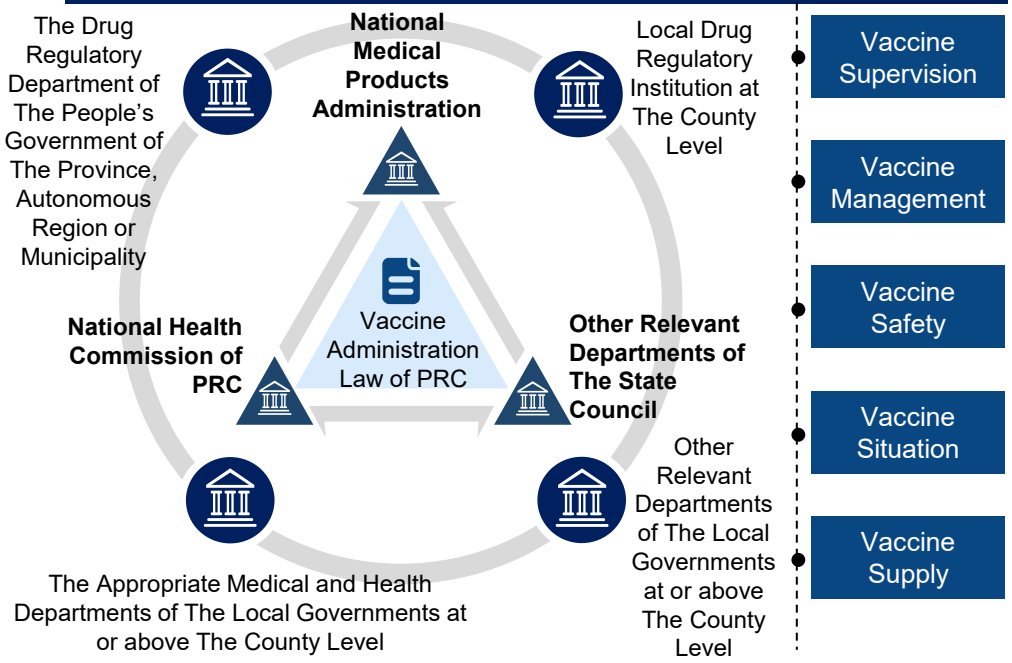
Increasing Affordability and Willingness to Pay	• The steady economic growth in China has improved Chinese citizens' affordability and increased healthcare spending on vaccination as well as provided more accesses to vaccination services. The healthcare expenditure per capita in China was about RMB2,460 in 2023, and there is a potential to further increase in the future. Moreover, the Chinese disposable income per capita has grown rapidly, increasing from RMB28,228.0 in 2018 to RMB39,218.0 in 2023, and this trend is expected to continue, enhancing the willingness and ability to pay for vaccines.
Increasing Awareness of Vaccination	• Chinese residents have paid more attention on the disease prevention and have more knowledge about different types of vaccination, such as HPV vaccines. Increasing awareness of both pediatric and adult vaccination, created by direct marketing efforts, promotional activities by the companies and increasing education level, is driving the market growth. Currently, companies are promoting vaccination through marketing activities and providing vaccine education through online education and consultation, literature and documentaries. All these activities have led to an increase of demand in China vaccine market.
Rapid Development of Technology	• Along with the improvement of technology in the vaccine development, such as transfer from traditional cell-culture technology to the application of bioreactor technology, the quality and efficacy of vaccine are significantly improved. With the upgrading technology, vaccine manufactures can provide new types of vaccines to meet customers' demand.

Source: Frost & Sullivan analysis

Analysis of Regulations on Vaccine Administration in China

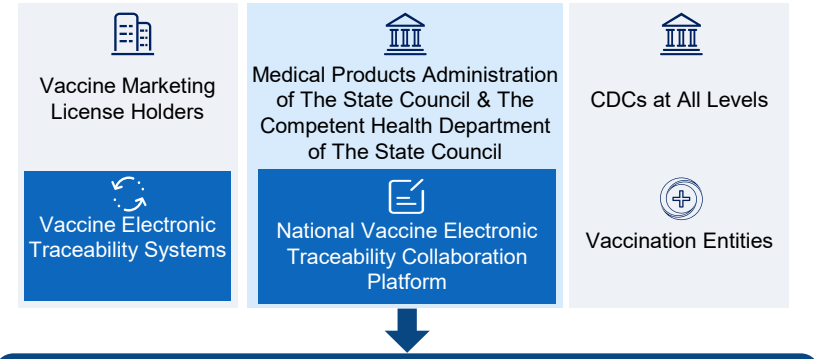
- The promulgation of the **Vaccine Administration Law of the People's Republic of China** aims to establish a coordination mechanism and achieve full electronic traceability. The preventive vaccine industry has entered an era of strong supervision.

Establish a Coordinative Mechanism for Vaccine Supervision



- The medical products administration of the State Council shall be responsible for the supervision and administration of vaccines nationwide. The competent health department of the State Council shall be responsible for the supervision and administration of vaccination nationwide. Other relevant departments of the State Council shall be responsible for supervision and administration relating to vaccines within the scope of their respective functions.

Achieve Whole Process Electronic Traceability



Vaccine Traceability

- **The medical products administration of the State Council** shall, in conjunction with the competent health department of the State Council, formulate uniform vaccine traceability standards and rules, establish a national vaccine electronic traceability collaboration platform, and integrate whole process traceability information on vaccine production, circulation and vaccination so as to realize the traceability of vaccines.
- **Vaccine marketing license holders** shall establish vaccine electronic traceability systems, and link them with the national vaccine electronic traceability collaboration platform so as to realize traceable and verifiable vaccines of the minimum packaging unit in the whole process of production, circulation and vaccination.
- **Disease prevention and control institutions and inoculation entities** shall truthfully record vaccine circulation, vaccination and other circumstances in accordance with the law, and provide traceability information to the national vaccine electronic traceability collaboration platform as required.

Source: Government documents, Frost & Sullivan analysis

Administration of Vaccine Lot Release in China

- Lot release of biological products in these Provisions refers to the process of reviewing and testing for vaccine products, blood products, in vitro diagnostic reagents for blood screening obtained marketing authorization and other biological products specified by National Medical Products Administration (NMPA), prior to marketing or importation, and issuing the lot release certification by designated lot release institutions.
- Products failing to pass lot release shall not be marketed or imported. Products exempted from lot release as approved by the NMPA in accordance with the law shall be excluded.

Provisions for the Lot Release of Biological Products

Approval to manufacturing and selling

↓

Lot release application

↓

Centralized purchasing at provincial level

Authority

- **NMPA:** The NMPA shall be in charge of lot release of biological products nationwide, specifies the scope of product varieties subject to lot release, designates lot release institutions, clarifies the requirements for lot release and guides the implementation of lot release.
- **Drug regulatory departments of provinces, autonomous regions or municipalities**：responsible for the supervision and administration of lot release applicants within their own administrative regions and for organizing on-site inspection of products subject to lot release within their own administrative regions; shall assist lot release institutions to carry out on-site inspection, organize on-site sampling of products for lot release and disposal of non-conforming products in lot release

Coverage

- Lot release of biological products in these Provisions refers to the process of reviewing and testing for vaccine products, blood products, in vitro diagnostic reagents for blood screening obtained marketing authorization and other biological products specified by NMPA, prior to marketing or importation, and issuing the lot release certification by designated lot release institutions.

Standards

- Lot release products shall be manufactured in accordance with the approved process and shall conform to the national drug standards and drug registration standards.

Key points

- Since the implementation of lot release of biological products in 2002, NMPA has gradually expanded the scope of the vaccine batch release system.
- By 2016, lot release management of all marketed vaccines were realized.
- In December 2020, NMPA issued a new version of *Provisions for the Lot Release of Biological Products*: For the lot release of vaccines, dossier review and sample testing shall be conducted lot by lot; In the process of the lot release of specific variety, the lot release institution may make a comprehensive evaluation according to the process and quality control maturity of the variety and previous lot release and dynamically adjust the testing items and testing frequency of the variety.

Source: Government Announcement, Frost & Sullivan Analysis

Growth Drivers and Future Trends of China Vaccine Market

Technical development and availability of new vaccines	• China's vaccine industry has advanced significantly, covering both Class I vaccines and Class II vaccines. Continuous R&D efforts focus on improving existing vaccines and developing next-generation vaccines for diseases such as rabies, malaria, HPV and tuberculosis. Innovations like launch of EV71 vaccine for HFMD, COVID-19 vaccines and domestic PCV13 vaccines, highlight the strong R&D capabilities of domestic companies. These efforts are enhancing vaccine attributes, including acceptability, cost-effectiveness and protection. Companies with robust technical platforms are well-positioned to optimize the design of new vaccines, aligning with market needs and expanding production to meet regional demand. Advances in biotechnology, such as the shift to bioreactor technology, have also improved vaccine quality and efficacy. This technological progress allows manufacturers to offer new vaccine products that better meet consumer demands. Such focus on technological development and innovation is poised to drive significant growth in the Chinese vaccine market.
Favorable policies	• The Chinese government has introduced several policies to stimulate the vaccine market. Initiatives such as the Guidelines of the Plan for Development of the Pharmaceutical Industry (《醫藥工業發展規劃指南》) and the Health and Wellness Plan in the Thirteenth Five-Year Plan (《"十三五" 衛生與健康 規劃》) focus on promoting R&D for multivalent vaccines and expanding national immunization programs. These policies underline the strategic priority on disease prevention, thereby driving market expansion. In addition, policies such as the "Opinions on Further Strengthening Vaccine Circulation and Vaccination Management" (《關於進一步加強疫苗流通和預防接種管理工作的意見》) promote large-scale production of domestic vaccines and industrialization of new vaccines, particularly for combination vaccines and multivalent vaccines. As a result, domestic vaccine manufacturers are expected to gain significant market share in the • Class II vaccine market..
Increasing Affordability and Awareness of Vaccines	• Economic growth in China has improved affordability and healthcare spending on vaccines. Increased health awareness, especially after COVID-19, is boosting vaccination rates. Rising disposable income has further enhanced the ability and willingness of citizens to pay for vaccines.
Resistance to therapeutic drugs and lack of effective treatments	• Drug resistance and the absence of effective treatments for infectious diseases like rabies underscore the importance of vaccination. This realization has prompted greater promotion and adoption of vaccines, thus fueling market growth.
Being geared to international standards	• China's alignment with international standards, evidenced by WHO pre-certification eligibility and International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) membership, positions domestic manufacturers to expand globally. This commitment to meeting global benchmarks is likely to open new international markets..

Source: Frost & Sullivan Analysis

Growth Drivers and Future Trends of China Vaccine Market

Developing multivalent and combination vaccines

- The demand for multivalent and combination vaccines is rising, driven by their effectiveness in preventing multiple diseases. While global companies currently dominate, several Chinese firms are working on developing new multivalent vaccines to meet growing demand.

Source: Frost & Sullivan analysis

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Overview of Influenza (Flu) Viruses

Types of Influenza Viruses

- There are four types of influenza viruses: **A, B, C and D**.
- **Human influenza A and B viruses** cause seasonal epidemics of disease (known as the flu season) almost every winter in the United States.
- Influenza A viruses are the **only** influenza viruses known to cause flu pandemics, i.e., global epidemics of flu disease. A pandemic can occur when **a new and very different influenza A virus emerges** that both infects people and has the ability to spread efficiently between people.
- Influenza A viruses are divided into subtypes based on two proteins on the surface of the virus: **hemagglutinin (H) and neuraminidase (N)**.Of all the influenza viruses that routinely circulate and cause illness in people**, influenza A(H3N2) viruses** tend to change more rapidly, both genetically and antigenically. Influenza A(H3N2) viruses have formed many separate, genetically different clades in recent years that continue to co-circulate.
- Influenza type C infections generally cause **mild illness** and are not thought to cause human flu epidemics.
- Influenza D viruses primarily affect **cattle** and are not known to infect or cause illness in people.

Transmission

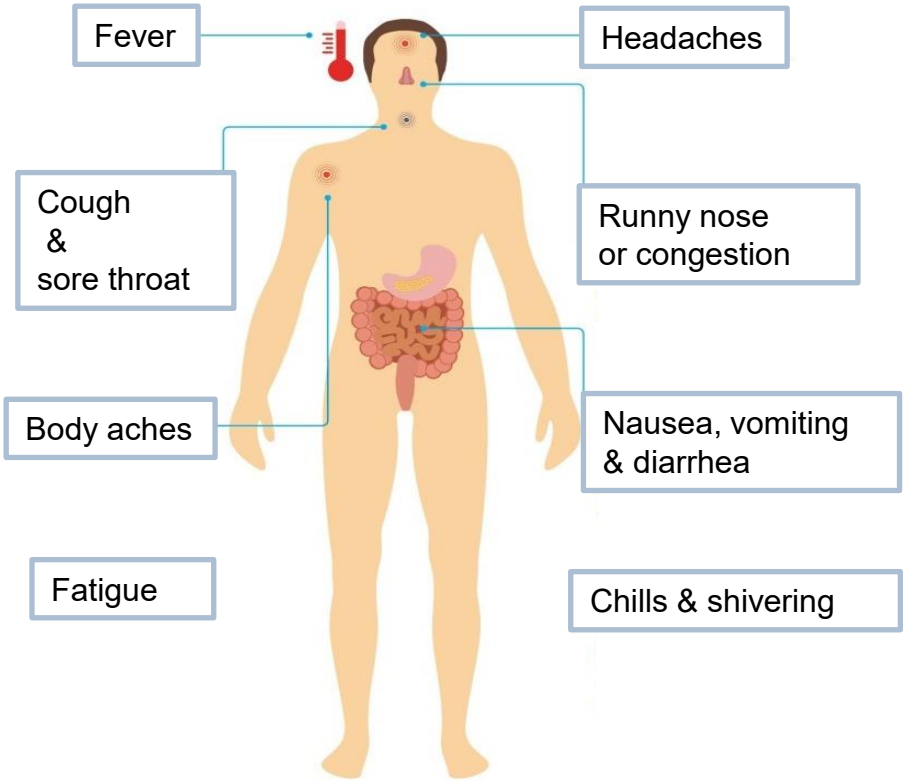
- Most experts believe that flu viruses spread mainly by **tiny droplets** made when people with flu **cough, sneeze or talk.** These droplets can land in the **mouths or noses** of people who are nearby. Less often, a person might get flu by touching a **surface or object** that has flu virus on it and then touching their own **mouth, nose or possibly their eyes.**

Source: Literature research, Frost & Sullivan analysis

Overview of Influenza (Flu)

- Flu is a **contagious respiratory illness** caused by **influenza viruses** that infect the **nose, throat, and sometimes the lungs**. It can cause mild to severe illness, and at times can lead to death. The best way to prevent flu is by getting a **flu vaccine** each year.

Symptoms



Complications

- Complications of flu can include bacterial pneumonia, ear infections, sinus infections and worsening of chronic medical conditions, such as congestive heart failure, asthma, or diabetes.

Risk Factors

- Anyone can get flu (even healthy people), and serious problems related to flu can happen at any age, but some people are at high risk of developing **serious flu-related complications** if they get sick.
- This includes people **65 years and older**, people of any age with **certain chronic medical conditions** (such as asthma, diabetes, or heart disease), pregnant women, and children younger than 5 years.

Source: Literature research, Frost & Sullivan analysis

WHO and CDC Recommendations for Influenza Vaccination

WHO

Recommended Priority Groups for Vaccination

Pregnant women at any stage of pregnancy: there is evidence of a high risk of other serious illnesses associated with influenza in pregnant women.

Children aged 6 months to 5 years: the burden of serious illness is high for children aged 6-23 months, and similarly high for children aged 2-5 years, but lower than the burden of illness for children under 2 years of age.

Elderly (65+): there is growing evidence that vaccines are not as effective in older age groups as they are in younger age groups

Individuals with chronic diseases: Individuals with specific chronic diseases are often also at high risk for severe influenza-associated illnesses, and this group is often the primary target for vaccination

Health care workers: for this population, vaccination protects not only themselves from the influenza virus, but also vulnerable patients

CDC

In principle, vaccination units should provide immunization services to all persons ≥6 months of age who are willing to be vaccinated and have no contraindications.

Recommended Priority Groups for Vaccination

Medical personnel: including clinical care personnel, public health personnel, sanitary and quarantine personnel, etc.

Mega-event participants and support staff

Vulnerable people and employees in places where people gather, such as nursing homes, long-term care facilities, welfare homes, etc.

Key populations: teachers and students in childcare institutions, primary and secondary schools, and detainees and staff of penal institutions.

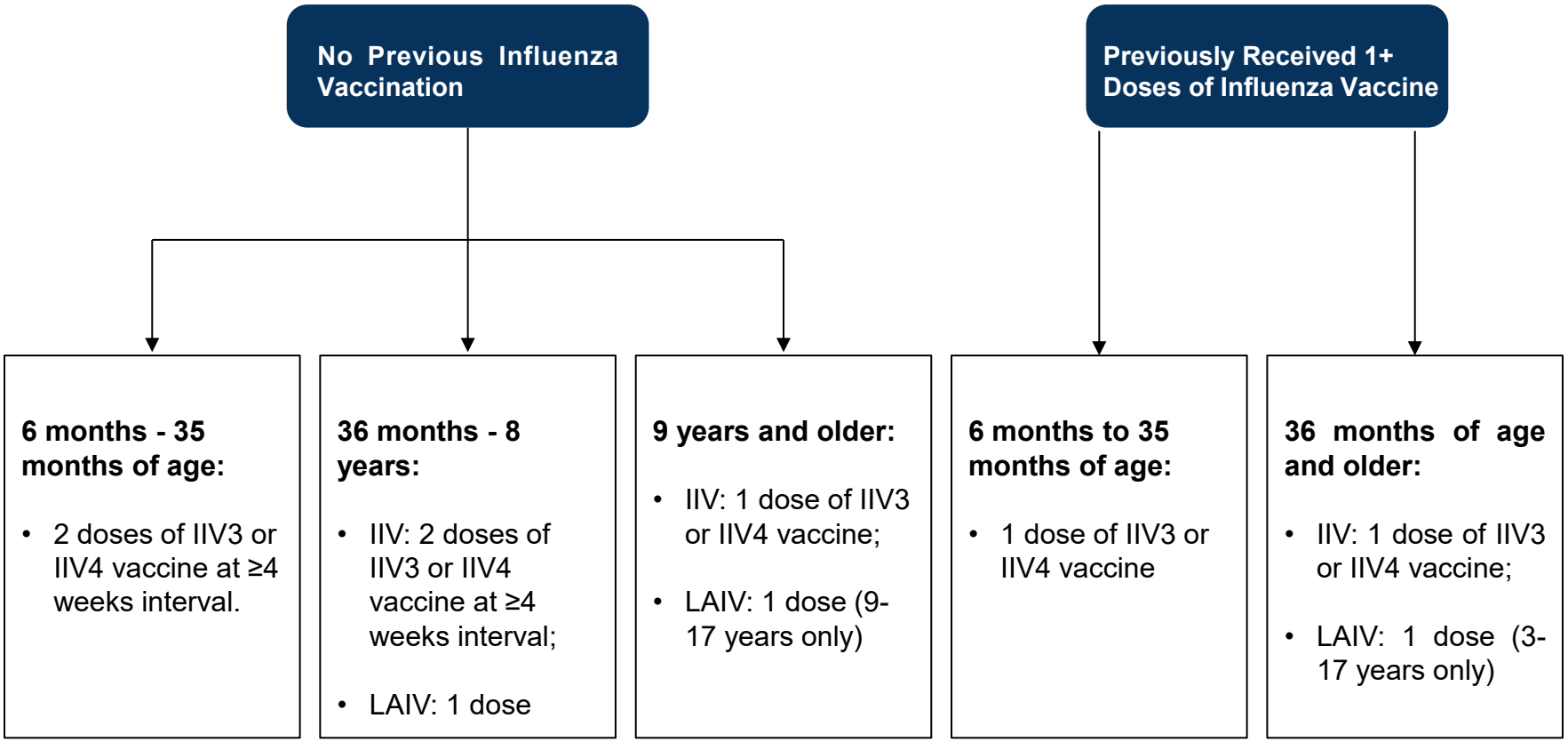
Other populations at high risk for influenza:

- ✓ Homebound seniors age 60+
- ✓ Infants 6-23 months of age
- ✓ Children 2-5 years of age
- ✓ Chronically ill
- ✓ Family members and caregivers of infants younger than 6 months of age
- ✓ Pregnant women or women planning to become pregnant during the influenza season

Resources: WHO, CDC, Frost & Sullivan Analysis

CDC Recommends Influenza Vaccination Doses

- In order to better guide the work of influenza prevention and control and vaccine application, the CDC prepared and issued the "China Influenza Vaccine Preventive Vaccination Technical Guidelines (2023-2024)", in which relevant provisions were made for the number of doses of influenza vaccine to be administered.



Note: (1) IIV: Inactivated vaccine, including spilt virion vaccine and subunit vaccine; (2) LAIV: Live-attenuated vaccine

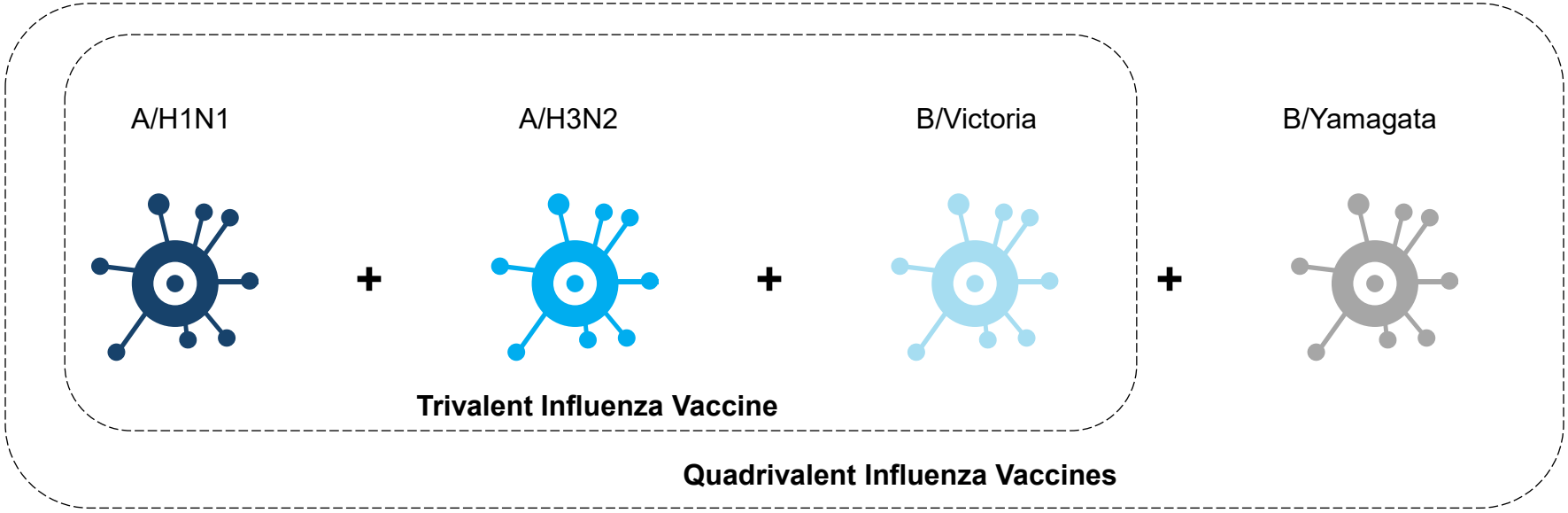
Resources: CDC, Frost & Sullivan Analysis

Influenza Vaccine Classification

Based on Valence

- In February 2012, the WHO recommended that seasonal influenza vaccines include two B lineage strains, and from the 2013-2014 Northern Hemisphere flu season, it advised adding a fourth component (B Yamagata lineage) to support the development of quadrivalent vaccines.
- Influenza vaccines are classified by the range of serotype coverage into trivalent vaccines (including A/H1N1, A/H3N2, and either B/Victoria or B/Yamagata lineages) and quadrivalent vaccines (including A/H1N1, A/H3N2, B/Victoria, and B/Yamagata lineages). Quadrivalent vaccines offer broader protection against B influenza viruses compared to trivalent vaccines.

The Current Serotype Voverage of Trivalent and Quadrivalent Influenza Vaccines

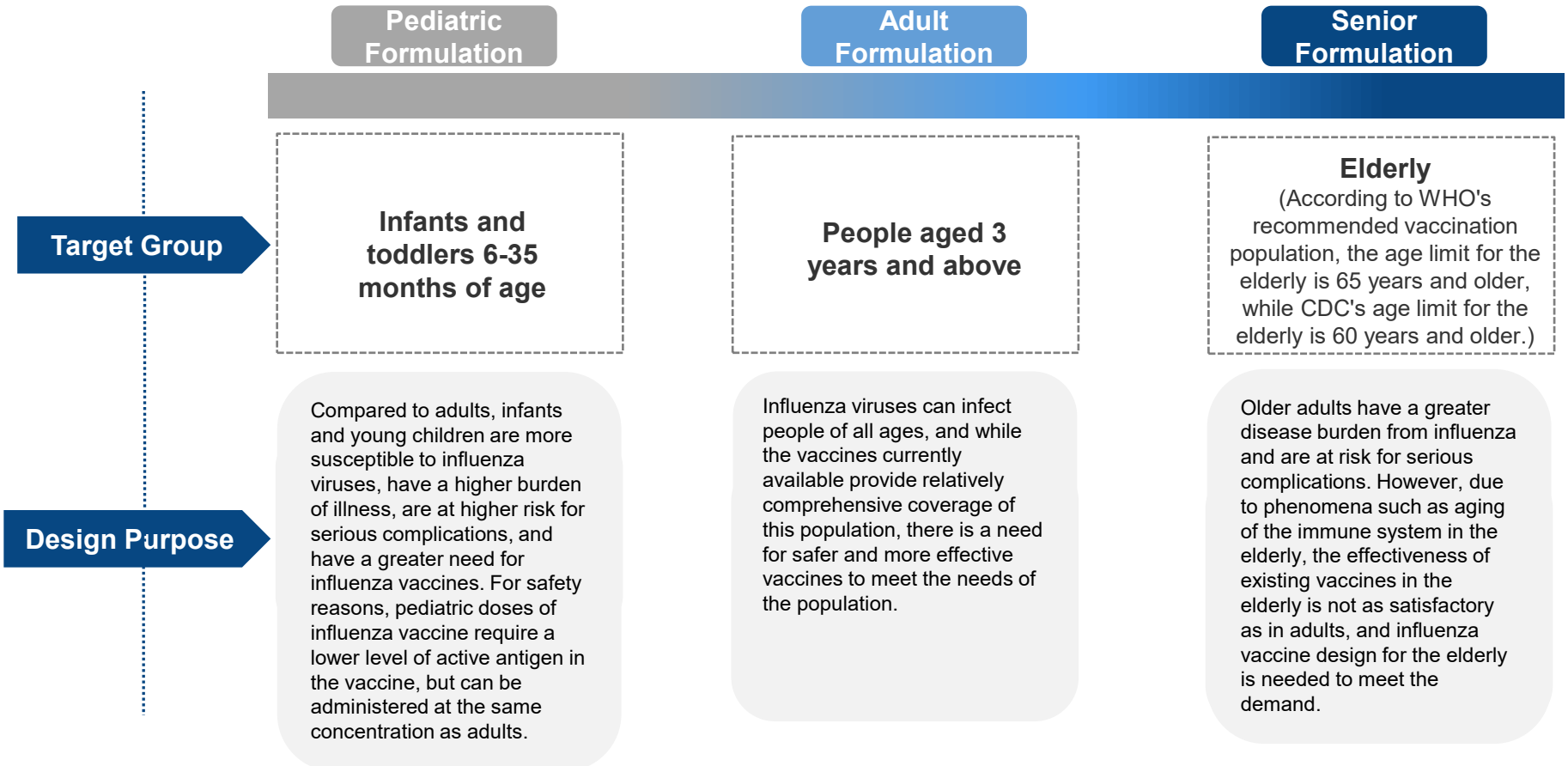


Resources: WHO, Frost & Sullivan Analysis

Influenza Vaccine Classification

Based on Vaccination Population

- According to WHO and CDC recommendations, the influenza vaccine should be administered to people over 6 months of age, which can be subdivided into 6-35 months of age, 3 years of age and older, and the elderly for safety and effectiveness reasons, and the corresponding vaccines will have some differences in dosage.



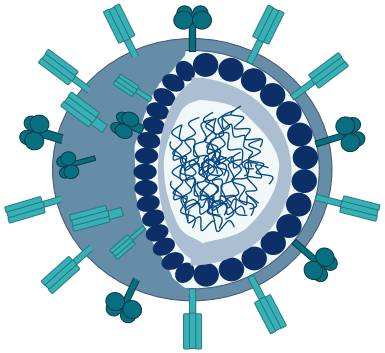
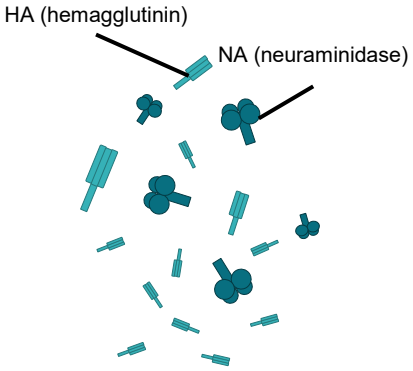
Note: According to the "Influenza Vaccines: WHO Position Paper" (May 2022), current quadrivalent and trivalent inactivated influenza vaccines for individuals aged ≥3 years contain 15 micrograms of each HA subtype per dose. For children aged 6-36 months, the HA concentration is 7.5 micrograms or 15 micrograms per dose.

Resources: Frost & Sullivan Analysis

Influenza Vaccine Classification and Characterization

Besed on Technology Type

- Influenza is a popular field of vaccine research, with nearly a century of study on influenza vaccines. They can be primarily categorized into whole-virus inactivated influenza vaccines, split-virus influenza vaccines, and subunit influenza vaccines.

	Whole-virus Inactivated Influenza Vaccines	Split-virus Influenza Vaccines	Inactivated subunit vaccine
Vaccine Description	A whole-virus inactivated vaccine involves culturing the virus and then inactivating it using heat or chemicals. This type of vaccine contains complete virus particles.	A split-virus vaccine involves inactivating the virus and then adding a lytic agent to disrupt its lipid membrane. It contains influenza virus nucleoprotein, matrix protein, and other internal proteins, along with surface antigens.	An inactivated subunit vaccine is based on a split-virus vaccine, with membrane proteins HA (hemagglutinin) and NA (neuraminidase) isolated and purified to obtain HA and NA proteins.
Vaccine structure			

Resources: Frost & Sullivan Analysis

Influenza Vaccine Classification and Characterization

Besed on Technology Type

- Influenza is a popular field of vaccine research, with nearly a century of study on influenza vaccines. They can be primarily categorized into whole-virus inactivated influenza vaccines, split-virus influenza vaccines, and subunit influenza vaccines.

	Vaccine Description	Vaccine Characteristics
Whole-virus Inactivated Vaccine	• A whole-virus inactivated vaccine involves culturing the virus and then inactivating it with heat or chemicals. This type of vaccine contains various antigenic proteins of the virus.	• Simple and fast preparation method, high safety, long history of application • High inoculation dose, multiple inoculations required, long production time
Split-virus Vaccine	• A split-virus vaccine involves inactivating the virus and then adding a lytic agent to disrupt the viral lipid membrane, allowing for better purification of viral antigens.	• Simple preparation method • Antigenic composition not as simple as inactivated subunit vaccines, less safe than inactivated subunit vaccines
Inactivated Subunit Vaccine	• An inactivated subunit vaccine is based on a split-virus vaccine, with membrane proteins HA and NA isolated and purified using suitable methods to obtain HA and NA proteins for vaccine preparation.	• Contains a single antigenic component, good safety, few side effects • Weak immunogenicity, need to ensure the purity of the antigen, need to cooperate with the appropriate adjuvant
Live Attenuated Vaccine	• A live attenuated vaccine is produced using attenuated strains obtained through virulence variation or artificial selection, allowing it to mimic viral infection without causing disease.	• Activates the immune system like a natural infection, triggering a strong and long-lasting immune response • Not suitable for people with weakened immune systems
Recombinant Vaccine	• A recombinant vaccine uses genetic engineering to insert DNA sequences for viral antigens into host cells via plasmids. The antigens are then expressed, purified, and made into a vaccine, often using the baculovirus-insect cell system.	• High antigen purity, good safety • Weak immunogenicity, need to cooperate with corresponding adjuvant, need to consider the composition of the formulation
mRNA Vaccine	• An mRNA vaccine contains mRNA encoding antigen proteins. In the body, it directly translates into the corresponding antigen protein, bypassing replication and transcription, to stimulate an immune response.	• Rapid and low-cost production, high safety and rapid response to infectious disease pandemics • Lack of long-term safety and efficacy studies, need to address delivery issues

Resources: Frost & Sullivan Analysis

Influenza Vaccine Safety and Efficacy Indicators

- To ensure the quality of influenza vaccines, both the WHO and the Chinese Pharmacopoeia set standards for safety and efficacy indicators in finished product testing. The WHO has established guidelines for inactivated influenza vaccines, including whole-virus inactivated, split-virus, and inactivated subunit vaccines. In contrast, the Chinese Pharmacopoeia includes only whole-virus inactivated influenza vaccines and split-virus influenza vaccines.

Key Indicators	Explanation of Key Indicators	WHO including inactivated influenza vaccines (whole-virus inactivated influenza vaccine, split-virus influenza vaccine, and subunit influenza vaccine)	Chinese Pharmacopoei including whole-virus inactivated influenza vaccine and split-virus influenza vaccine
Hemagglutinin Content	Key antigenic substances in influenza vaccines	• Each dose contains at least 15 μg hemagglutinin of each influenza virus • In some countries, lower lower limits may be set based on clinical experience	• Whole-virus inactivated influenza vaccine: Each human dose is 0.5ml or 1.0ml, containing 15μg of HA from each influenza virus strain. • Split-virus influenza vaccine: Each human dose is 0.25ml, containing 7.5μg of HA from each influenza virus strain; or 0.5ml, containing 15μg of HA from each strain. • The HA content of each strain per dose should be no less than 80% of the labeled amount.
Endotoxin Content	A component of the cell wall of gram-negative bacteria that can cause a range of toxic reactions when it enters the body	• Allowable endotoxin levels are determined by individual state regulatory agencies	• Whole-virus inactivated influenza vaccine: Should not exceed 10 EU per dose. • Split-virus influenza vaccine: Should be less than 20 EU per ml.
Protein Content	In addition to specific antigenic proteins, host cell proteins, protein A and other impurities may be present in the vaccine	• The total protein content shall not exceed six times the total hemagglutinin content of the vaccine as determined in the hemagglutinin content test. However, in no case shall the per person dose exceed 100 μg of protein per virus strain and the total protein content exceed 300 μg of protein per person dose	• Whole-virus inactivated influenza vaccine: Should not exceed 400μg/ml and must not be more than 4.5 times the total HA content in the vaccine. • Split-virus influenza vaccine: Should not exceed 400μg/ml and must not be more than 4.5 times the total HA content in the vaccine.
Ovalbumin Content	Vaccines produced using chicken embryos may contain ovalbumin, an impurity in vaccine production	• Should be no higher than 5 μg per person.	• Whole-virus inactivated influenza vaccine: Should not exceed 250 ng/ml. • Split-virus influenza vaccine: Should not exceed 200 ng/ml.

Resources: Literature Review, Frost & Sullivan Analysis

Influenza Vaccine Safety and Efficacy Indicators

- To ensure the quality of influenza vaccines, both the WHO and the Chinese Pharmacopoeia set standards for safety and efficacy indicators in finished product testing. The WHO has established guidelines for inactivated influenza vaccines, including whole-virus inactivated, split-virus, and inactivated subunit vaccines. In contrast, the Chinese Pharmacopoeia includes only whole-virus inactivated influenza vaccines and split-virus influenza vaccines.

Key Indicators	Explanation of Key Indicators	WHO	Chinese Pharmacopoei
		including inactivated influenza vaccines (whole-virus inactivated influenza vaccine, split-virus influenza vaccine, and subunit influenza vaccine)	including whole-virus inactivated influenza vaccine and split-virus influenza vaccine
Other Residues Content	Includes free methanol, antibiotics and thiomersal used in vaccine production.	• Not specified	• Antibiotics: The whole-virus inactivated influenza vaccine and split-virus influenza vaccine should not exceed 50 ng per dose. • Thimerosal: Should not exceed 50 μg per dose in the whole-virus inactivated influenza vaccine, and 100 μg/ml in the split-virus influenza vaccine. • Free methanol: Should not exceed 50 μg/ml in the split-virus influenza vaccine.

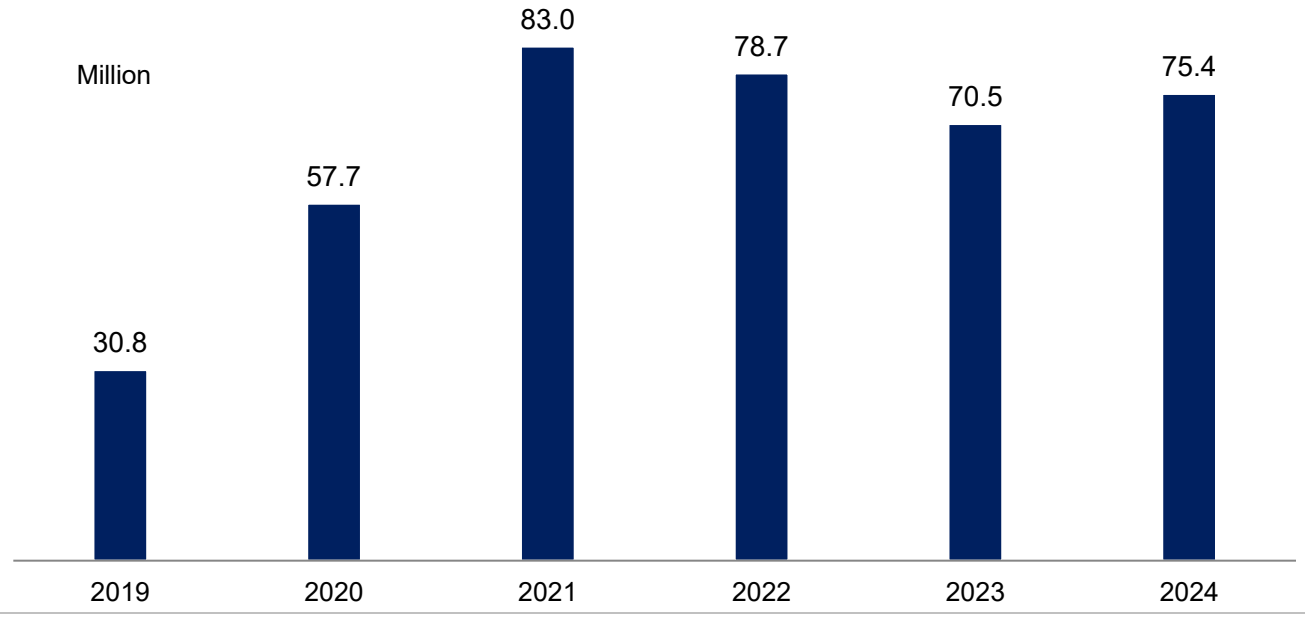
Resources: Literature Review, Frost & Sullivan Analysis

Lot Release of Influenza Vaccine in China, 2019-2024

- The influenza vaccine market in China has grown significantly from 2019 to 2021, and decreased in next two years. The total number of lot release increased from 30.8 million in 2019 to 83.0 million in 2021, and slightly decreased to 70.5 million in 2023. And in 2024 it rose again to 75.4 million. The CAGR from 2019 to 2024 is 19.6%.
- China's quadrivalent influenza vaccine market has grown significantly. The total number of lot release increased from 9.7 million in 2019 to 46.6 million in 2024, at a CAGR of 36.8%.

Lot Release of Influenza Vaccine in China , 2019-2024

Period	CAGR
2019-2024	19.6%



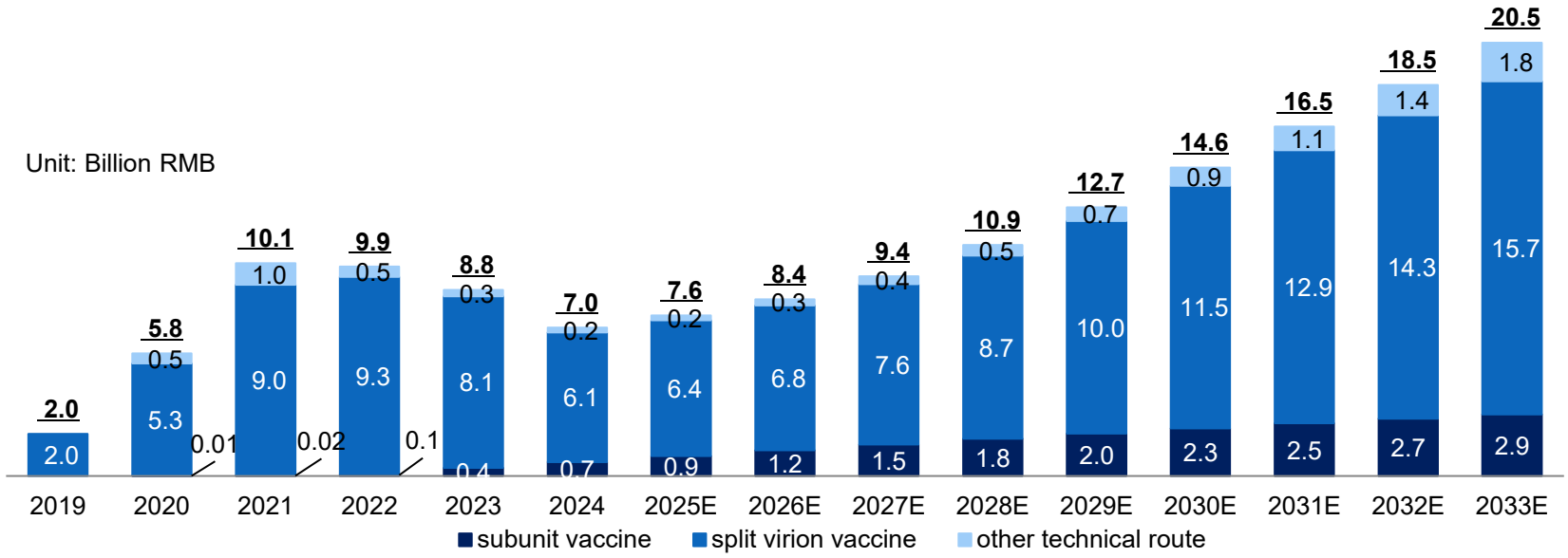
Source: Expert interview, NIFDC, Frost & Sullivan analysis

China Influenza Vaccine Market Production Value, Separated by Technical Route, 2019-2033E

- The influenza vaccine market in China has also grown significantly from RMB2.0 billion in 2019 to RMB7.0 billion in 2024, at a CAGR of 28.7%. The influenza vaccine market in China is estimated to further increase to RMB20.5 billion in 2033, at a CAGR of 12.6% from 2024 to 2033.

China Influenza Vaccine Market Production Value, 2019-2033E

Period	CAGR			
	Subunit vaccine	Split virion vaccine	Other technical routes	Total
2019-2024	-	25.3%	-	28.7%
2024-2033E	18.0%	11.0%	26.3%	12.6%



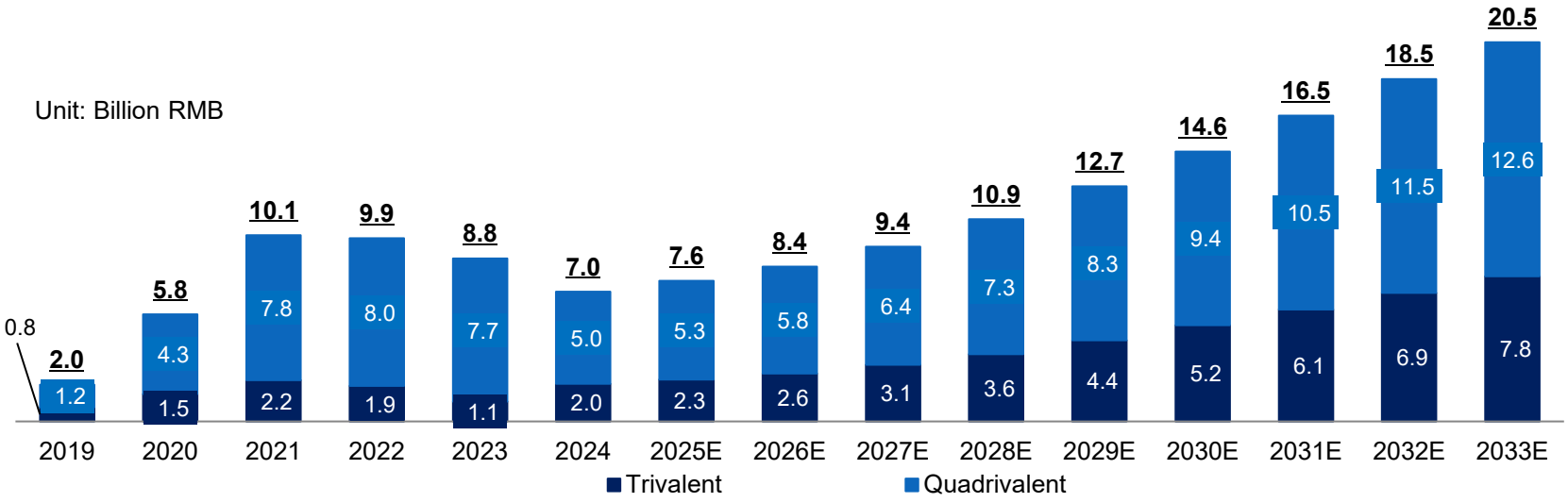
Source: Expert interview, NIFDC, Frost & Sullivan analysis

China Influenza Vaccine Market Production Value, Separated by Tri- and Quadri-valent, 2019-2033E

- The influenza vaccine market in China has grown to RMB7,007 million in 2024, and it will be reach to RMB20,468.4 million in 2033, with a CAGR of 12.6% from 2024 to 2033.

China Influenza Vaccine Market Production Value, 2019-2033E

Period	CAGR		
	Trivalent	Quadrivalent	Total
2019-2024	21.5%	32.6%	28.7%
2024-2033E	16.1%	10.9%	12.6%



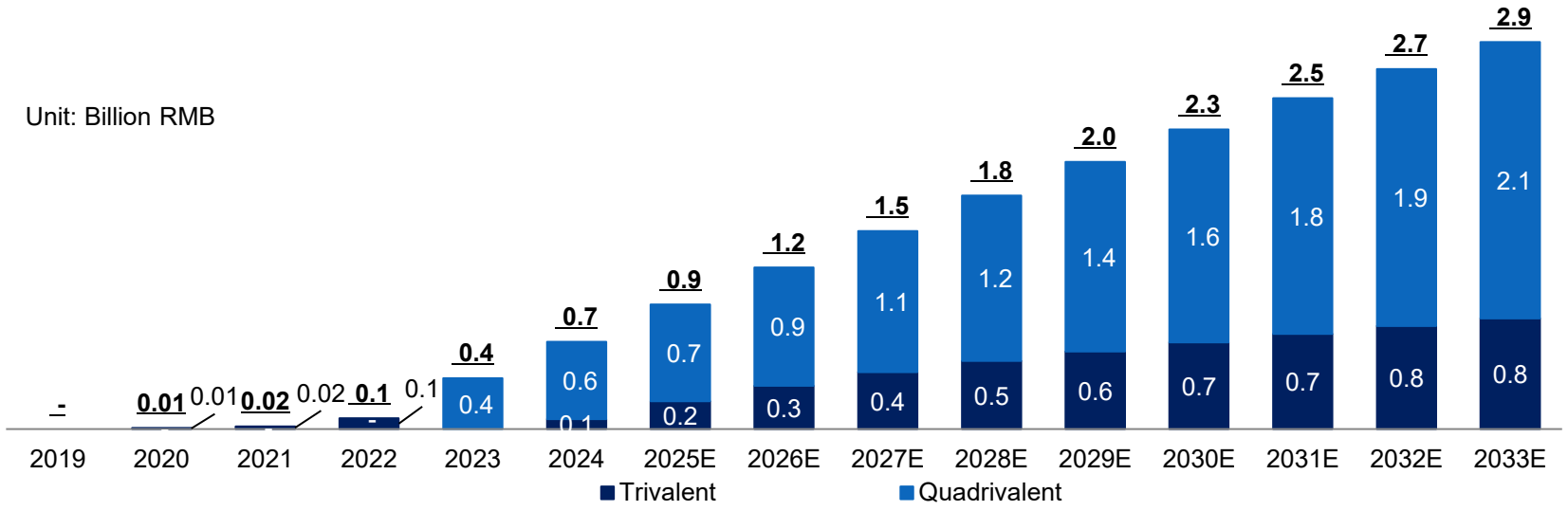
Source: Expert interview, NIFDC, Frost & Sullivan analysis

China Subunit Influenza Vaccine Market Production Value, Separated by Tri- and Quadri-valent, 2019-2033E

- The subunit influenza vaccine market in China has grown to RMB 0.7 billion in 2024. With the approval of more subunit influenza vaccine products in the future, it will be able to drive market to RMB 2.9 billion in 2033, with a CAGR of 18.0% from 2024 to 2033.

China Subunit Influenza Vaccine Market Production Value, 2019-2033E

Period	CAGR		
	Trivalent	Quadrivalent	Total
2019-2024	-	-	-
2024-2033E	30.9%	15.2%	18.0%



Source: Expert interview, NIFDC, Frost & Sullivan analysis

Marketed Influenza Vaccines in global market (1)

Type	Brand Name (Generic Name)	Technical Route	Company	FDA approval date*	Age Coverage
Trivalent	FLUVIRIN	Inactivated, subunit	Seqirus	1988	4 years of age and older
	AFLURIA	Split Virion		2007/09	6 month of age and older
	Agriflu	Inactivated, subunit		2009/11	18 years of age and older
	Flucelvax	Inactivated, subunit		2012/11	6 month of age and older
	FLUAD	Inactivated, subunit		2015/11	65 years of age and older
	Fluzone	Split Virion	Sanofi	1980	6 month of age and older
	Fluzone High-Dose	Split Virion		2009/12	65 years of age and older
	Fluzone Intradermal	Split Virion		2011/05	18-64 years of age
	Flublok	Recombinant, subunit		2013/01	18 years of age and older
	Fluarix	Split Virion	GSK	2005/08	6 month of age and older
	FluLaval	Split Virion		2006/10	6 month of age and older
	FluMist	Live Attenuated	AZ	2003/06	2-49 years of age

Note: The approval date is the time when the vaccine was first approved, without considering the expansion of the age group of the vaccinated population
By end of July 21st, 2025

Source : FDA, Frost & Sullivan

Marketed Influenza Vaccines in global market (2)

Type	Brand Name (Generic Name)	Technical Route	Company	FDA approval date*	Age Coverage
Quadrivalent	Flucelvax Quadrivalent	Inactivated, subunit	Seqirus	2016/05	6 month of age and older
	Afluria Quadrivalent	Split Virion		2017/07	6 month of age and older
	Fluad Quadrivalent	Inactivated, subunit		2020/02	65 years of age and older
	Fluzone Quadrivalent	Split Virion	Sanofi	2013/6	6 month of age and older
	Fluzone Intradermal Quadrivalent	Split Virion		2014/12	18-64 years of age
	Flublok Quadrivalent	Recombinant, subunit		2016/10	18 years of age and older
	Fluzone High-Dose Quadrivalent	Split Virion		2019/11	65 years of age and older
	Fluarix Quadrivalent	Split Virion	GSK	2012/11	6 month of age and older
	Flulaval Quadrivalent	Split Virion		2013/08	6 month of age and older
	FluMist Quadrivalent	Live Attenuated	AZ	2003/07	2-49 years of age

Note: The approval date is the time when the vaccine was first approved, without considering the expansion of the age group of the vaccinated population
By end of July 21st, 2025

Source : FDA, Frost & Sullivan

Competitive landscape of Influenza Vaccines in global market

Type	Generic Name	Technical Route	Company	Clinical Stage	FPD	Age Coverage	Location
Trivalent	GSK4382276A	mRNA	GSK	II	2024/05/28	Adults 18 Years of Age and Older	US
	PF-07845104	mRNA	Pfizer	I/II (completed)	2024/05/31	Adults 18 Years of Age and Older	US
Quadrivalent	mRNA-1010	mRNA	Moderna	III	2024/09/19	Adults ≥50 Years of Age	Global
	mRNA-1020			I/II (completed)	2022/04/18	Adults 18 Years of Age and Older	US
	mRNA-1030			I/II (completed)	2022/04/18	Adults 18 Years of Age and Older	US
	SP0237	mRNA	Sanofi	II	2024/04/12	Adults 18 Years of Age and Older	US, Puerto Rico, Honduras
	OVX836	Non-VLP nanoparticles	Osivax	II (completed)	2024/09/03	Adults 20 to 69 Years of Age	Belgium
	KBP-V001	Recombinant	KBio	I (completed)	2020/06/19	Adults 18 to 49 Years of Age	US
Pentavalent	mRNA-1011	mRNA	Moderna	I/II (completed)	2023/04/24	Adults 50 to 75 Years of Age	US
Hexavalent	mRNA-1012	mRNA	Moderna	I/II (completed)	2023/04/24	Adults 50 to 75 Years of Age	US
	-	mRNA	Sanofi	I/II	2024/12/20	Adults 50 Years of Age and Older	US, Australia
Not Disclose	UFluA	Non-VLP nanoparticles	Emergent BioSolutions	I (completed)	2021/12/13	Adults 18 to 45 Years of Age	Australia

By end of July 21st, 2025

Source: CclinicalTrials.gov, Frost & Sullivan

Marketed Influenza Vaccines in China(1)

Type	Brand Name (Generic Name)	Technical Route	Company	NMPA approval date[1]	Age Coverage	End-user Price[2]	Market Share[3] (2024)
unknown	-	Whole Virion Inactivated	Lanzhou institute of biological products（兰州生物制品研究所）	2000	NA	NA	-
Trivalent	英扶宁	Split Virion		2005/02	6 months of age and older	NA	-
	-	Split Virion	CuroVax（康润生物）	2005/03	3 years of age and older	NA	-
	Anflu (安尔来福)	Split Virion	Sinovac（科兴）	2007/01	6 months of age and older	52.5 (0.25ml) 80 (0.5ml)	10.0%
	Influenza vaccine	Split Virion	Shanghai institute of biological products（上海生物制品研究所）	2007/05	6 months of age and older	31 (0.25ml) 58 (0.5ml)	2.5%
	YUGANNING (御感宁)	Split Virion	TOYOUVAX（天元生物）	2007/06	6 months of age and older	68 (0.25ml) 88 (0.5ml)	1.8%
	适普利尔	Split Virion	Changchun institute of biological products（长春生物制品研究所）	2004/09	6 months of age and older	31 (0.25ml) 50 (0.5ml)	6.8%
	Influenza vaccine	Split Virion	Hualan Biological Bacterin（华兰生物）	2008/04	6 months of age and older	31 (0.25ml) 53 (0.5ml)	3.8%
	Influenza vaccine	Split Virion	Fosun Apexvac（复星雅立峰）	2009/06	6 months of age and older	60.5 (0.25ml) 80.5 (0.5ml)	7.0%
	FLU-K (孚洛克)	Subunit	ZHONGYIANKE biotech（中逸安科）	2010/04	3 years of age and older	168 (0.5ml)	0.5%
	-	Split Virion	AIM（艾美疫苗）	2012/11	3 years of age and older	NA	-
	VAXIGRIP (凡尔灵)	Split Virion	Sanofi Pasteur Biological Products	2013/06	6 months of age and older	55 (0.25ml) 70 (0.5ml)	4.8%
	Influenza vaccine	Split Virion	Adimmune（国光生物）	2015/10	3 years of age and older	135.5 (0.5ml)	-
	感雾	live attenuated	BCHT（百克生物）	2020/02	3-17 years of age	298 (0.2ml)	0.9%

Source： NMPA, Frost & Sullivan

Marketed Influenza Vaccines in China(2)

Type	Brand Name (Generic Name)	Technical Route	Company	NMPA approval date*	Age Coverage	End-user Price*	Market Share (2024)
Quadrivalent	Influenza vaccine, quadrivalent	Split Virion	Hualan Biological Bacterin (华兰生物)	2018/06	6 months of age and older	128 (0.25ml) 88 (0.5ml)	20.1%
	迪福赛尔	Split Virion	GDK biological technology (金迪克生物)	2019/05	3 years of age and older	88 (0.5ml)	3.5%
	Influenza vaccine, quadrivalent	Split Virion	Changchun institute of biological products (长春生物制品研究所)	2020/03	3 years of age and older	95 (0.5ml)	2.9%
	Influenza vaccine, quadrivalent	Split Virion	Wuhan institute of biological products (武汉生物制品研究所)	2020/04	3 years of age and older	88 (0.5ml)	4.8%
	Influenza vaccine, quadrivalent	Split Virion	Sinovac (科兴)	2020/06	3 years of age and older	88 (0.5ml)	13.8%
	Influenza vaccine, quadrivalent	Split Virion	Shanghai institute of biological products (上海生物制品研究所)	2021/03	6 months of age and older	91.5 (0.5ml)	9.5%
	安定伏	Split Virion	Adimmune (国光生物)	2022/02	3 years of age and older	205.5 (0.5ml)	0.5%
	VaxigripTetra (凡尔佳)	Split Virion	Sanofi Pasteur Biological Products	2023/02	6 months of age and older	128 (0.5ml)	4.3%
	Influenza vaccine, quadrivalent	Split Virion	ZFSW (智飞生物)	2025/03	3 years of age and older	NA	-
	Influenza vaccine, quadrivalent	Split Virion	Fosun Apexvac (复星雅立峰)	2025/06	3 years of age and older	NA	-
	Influenza vaccine, quadrivalent	Split Virion	TOYOUVAX (天元生物药业)	2025/07	NA	NA	-
	慧尔康欣	Subunit	Ab&b Biotechnology (中慧元通)	2023/05	3 years of age and older	319 (0.5ml)	2.4%

Note:

1. *The approval date is the time when the vaccine was first approved, without considering the expansion of the age group of the vaccinated population;*
2. *The end-user price is determined by the median of winning bid prices in provinces with publicly disclosed data in 2024;*
3. *The market share was calculated by Production volume;*
4. *By end of July 21st, 2025*

Source: NMPA, Frost & Sullivan

Competitive Landscape of Influenza Vaccines in China

Type	Technical Route	Company	Clinical Stage	FPD*	Age Coverage
Trivalent	Subunit	Ab&b Biotechnology（中慧生物）	NDA	2024/9/19	3 years of age and older
			NDA	2024/10/1	6-35 months of age
	Live attenuated	BCHT（百克生物）	NDA	2024/4/24	3-59 years of age
	Split Virion	ZFSW（智飞生物）	NDA	2024/10/24	3 years of age and older
			NDA	2024/11/2	6-35 months of age;
	Split Virion	Chengda biotechnology（成大生物）	NDA	2025/3/21	NA
	Split Virion	Olymvax（欧林生物）	I	2025/1/23	6 months of age and older
	Split Virion	Peisen Biotechnology（培森生物）	I (completed)	2022/3/29	3 years of age and older
Quadrivalent	Subunit	Ab&b Biotechnology（中慧生物）	NDA	2024/6/28	6-35 months of age
	Subunit	Changchun institute of biological products（长春生物制品研究所）	I	2024/04/28	3 years of age and older
	Split Virion	CuroVax（康润生物）	NDA	2024/3/22	3 years of age and older
			I	2024/4/3	6-35 months of age
	Split Virion	ZFSW（智飞生物）	NDA	2024/9/30	6-35 months of age
	Split Virion	Wuhan institute of biological products（武汉生物制品研究所）	NDA	2024/11/14	3 years of age and older
	Split Virion	BioKangtai（康泰生物）	NDA	2024/11/22	3 years of age and older
	Split Virion	Chengda biotechnology（成大生物）	NDA	2025/1/24	3 years of age and older

**Note: The dates for products in NDA stage are the dates handled by CDE*
By end of July 21st , 2025

Source: CDE, Frost & Sullivan

Competitive Landscape of Influenza Vaccines in China

Type	Technical Route	Company	Clinical Stage	FPD*	Age Coverage
Quadrivalent	Split Virion	Sinovac （科兴）	III(completed)	2023/9	6-35 months of age
	Split Virion	WALVAX （沃森生物）	III	2024/10	3 years of age and older
	Split Virion	ZFSW （智飞生物）	I/II	2025/1	Adults 18 Years of Age and Older
	Split Virion	Olymvax （欧林生物）	I	2025/1	6 months of age and older
	Split Virion	Hygiea Biotech （海基亚生物）	I	2020/10	6-35 months of age; 3 years of age and older
			III	2025/4	3 years of age and older
	Split Virion	GDK biological technology （金迪克）	NDA	2025/7	6-35 months of age

**Note: The dates for products in NDA stage are the dates handled by CDE*
By end of July 21st , 2025

Source: CDE, Frost & Sullivan

Growth Drivers and Future Trends of the Chinese Influenza Vaccine Market

Increased market demand	• Influenza affects individuals of all ages, especially infants, children and the elderly, necessitating widespread immunization. The China CDC advises annual vaccinations for all individuals aged six months and above who are willing and have no contraindications. The target population for influenza vaccines is huge and the market demand is high. As the immune protection generated by influenza decrease over time and the frequent emergence of influenza virus mutations may result in mismatch between the vaccine strain and the prevalent virus strain, it is necessary to receive annual vaccination for best protection. China CDC also recommends vaccination of one to two doses to generate a sufficient amount of antibodies. The annual and multi dose vaccination of influenza vaccines has expanded market demand for vaccines and driven market development.
Favorable policies	• Though influenza vaccines are not included in China's national immunization program, several regions have initiated free vaccination schemes for certain demographics, boosting public vaccination rates. For instance, Beijing offers free vaccines to residents over 60, students and other key groups, while Zhejiang and Shenzhen have similar initiatives that offer free vaccines to the elderly. These policies increase public willingness to vaccinate, promoting market growth. • In recent years, in order to improve the vaccination rate, the country has introduced various policies to promote the popularization of influenza vaccines. The "14th Five Year Plan for National Health （《"十四五"国民健康规划》）" released by the State Council in April 2022 and the "Notice on Doing a Good Job in the Prevention and Control of Influenza in the 2021-2022 Epidemic Season（《关于做好2021-2022年六星级流感防控工作的通知》）" issued by the Comprehensive Group of the State Council Joint Prevention and Control Mechanism in October 2021 clearly state that: ① Encourage places with conditions to implement free vaccination, improve the vaccination rate of influenza vaccines, and reduce the occurrence of clustered influenza epidemics; ② Reasonably plan or add an influenza vaccination unit, and make overall arrangements for the vaccination of COVID-19 vaccine, influenza vaccine and other routine vaccines; ③ Information management of vaccination data.

Source: Frost & Sullivan

Growth Drivers and Future Trends of the Chinese Influenza Vaccine Market

The number of players is increasing, production capacity is expanding, and new vaccines are gradually emerging	• The approval of the Company's quadrivalent subunit influenza vaccine, which is the first marketed quadrivalent subunit influenza vaccine in China, in May 2023 represents a significant advancement, addressing a domestic gap with its high safety and targeted protection. Inspired by mRNA COVID-19 vaccine successes, there has been a notable increase in investment in developing mRNA vaccines and other diverse vaccine types, providing more choices, better protection with enhanced safety to target populations, and thus boosting market adoption.
The epidemic drives the recovery of demand for influenza vaccines	• Due to the impact of the COVID-19, the number of influenza cases in 2020 and 2021 is low, resulting in a low demand for influenza vaccination. However, the COVID-19 has greatly strengthened the residents' awareness of influenza prevention and control and their willingness to vaccinate. At the same time, in September 2023, the Chinese CDC released the "Technical Guidelines for Influenza Vaccination in China (2023-2024)（《中国流感疫苗预防接种技术指南（2023—2024）》）", which pointed out that annual influenza vaccination is the most economical and effective measure to prevent influenza. Require all disease control centers to actively organize scientific popularization, health education, risk communication, etc., guide the public to scientifically understand and prevent influenza, enhance protection awareness and health literacy, and gradually improve vaccine coverage for key populations

Source: Frost & Sullivan

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Overview of Pneumococcal Disease（PD）

- **Pneumococcal disease（PD）** including a wide range of diseases caused by Streptococcus pneumoniae (Spn). Spn infections range from ear and sinus infections to pneumonia and bloodstream infections.

PD

Non-invasive Pneumococcal Disease (NIPD)

NIPD occur outside the major organs or bloodstream. Streptococcus pneumoniae can spread from the nose and throat to the upper and lower respiratory tracts. The bacteria can cause:

- Otitis media
- Bronchitis
- Nasosinusitis

Invasive Pneumococcal Disease (IPD)

IPD is more severe than NIPD and occur in major organs or in a person's bloodstream. Including：

- Bacteremia
- Sepsis
- Meningitis
- Pneumonia
- Osteomyelitis
- Septic arthritis

Symptoms

Middle Ear Effusion; Ear Pain

Chest Pain, Accelerated Heartbeat

Fever

Cough

Pain，Swelling around The Cheeks

.....

Risk Factors

Children（under 5）

Age

Diabetes Mellitus

Cardiovas Cular Disease

Hypertension

Nephropa -thy

Smoking

.....

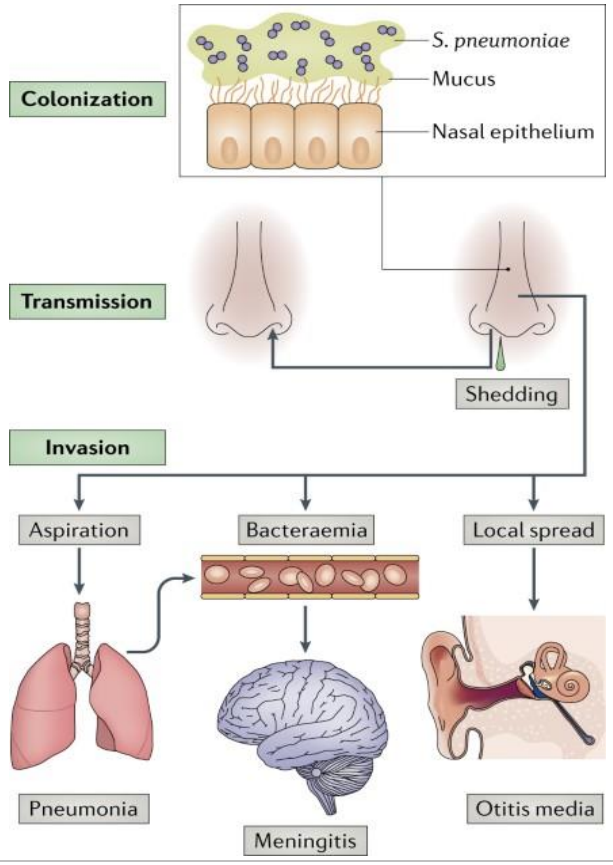
Source: Frost & Sullivan Analysis

Overview of Streptococcus Pneumoniae（Spn）

- **Streptococcus pneumoniae**（Spn）is the leading cause of community-acquired pneumonia.The incidence of pneumococcal pneumonia is highest in individuals of extreme age and with comorbid .
- There are more than 90 known serotypes of Streptococcus pneumoniae. Distribution of serotypes causing disease varies with time and age, disease syndrome, disease severity, geographic region, and presence of antimicrobial genes. Prior to the introduction of Streptococcus pneumoniae conjugate vaccine (PCV) by WHO in different regions, 6-11 serotypes accounted for more than 70% of all invasive pneumococcal diseases (IPD).

Mechanism of infection

- Streptococcus pneumoniae often colonizes the nasopharynx, and from the nasopharynx, pneumococci can spread directly through the airway to the lower respiratory tract, causing pneumonia, or to the sinuses or middle ear, causing disease.
- Bacteria may also penetrate the epithelial cell surface, leading to localized infection or bacteremia. Pleura and meninges can be infected through local transmission of infection or bacteraemia.
- Invasive Pneumococcal Disease is an infection evidenced by the isolation of bacteria from a normally sterile site (e.g., blood, cerebrospinal fluid, or pleural cavity), which is caused by invasion of respiratory epithelium.



（Streptococcus pneumoniae）

Infection

- Infection is primarily through Streptococcus pneumoniae in respiratory droplets. There are many healthy, asymptomatic carriers of the bacteria, but no animal hosts or insect vectors.
- Bacteria can be spread by airborne droplets, for example, when an infected person coughs or sneezes. Bacteria are not spread through contaminated food or water.

Source: Frost & Sullivan Analysis

Pneumococcal Disease Treatment and Prevention

- In the clinical treatment of pneumococcal disease, the primary consideration is the selection of a sensitive antibiotic. However, Streptococcus pneumoniae (Spn) can develop resistance to commonly used antibiotics, significantly increasing the difficulty of treatment.
- With the growing issue of pneumococcal antibiotic resistance and the increasing prevalence of pneumococcal disease complications, the use of pneumococcal vaccines to prevent pneumococcal disease has become increasingly necessary and urgent.

Disease treatment

- Currently, in the clinical treatment of pneumococcal disease (PD), antibiotic therapy is the first choice. However, Streptococcus pneumoniae (Spn) has developed significant resistance to commonly used antibiotics, such as penicillins, macrolides, quinolones, cephalosporins, and TMP-SMX, which has become a serious global issue.

Antimicrobial Drug Resistance

- With the introduction of widespread pneumococcal vaccination, resistant Streptococcus pneumoniae (Spn) strains have decreased in some developed regions. However, in many Asian countries where antibiotics are widely used, resistant clones spread extensively, and vaccine coverage is low, the issue of Spn resistance remains severe.
- Furthermore, in China, the incidence of cross-resistance and multidrug resistance in Spn to commonly used antibiotics is high. Data from the Asia-Pacific region's Pathogen Resistance Monitoring Network in 2012 showed that the overall multidrug resistance rate of Spn in Asia was 59.3%, while in China, this rate was as high as 83.3%.

Morbidity and Mortality

- The mortality rate of invasive pneumococcal disease in children is very high. In low- and middle-income countries, sepsis can have a mortality rate of up to 20%, while meningitis can reach as high as 50%.

Aftereffects

- Among children who survive pneumococcal meningitis, 24.7% experience long-term neurological sequelae, such as hearing loss, intellectual disability, motor abnormalities, and seizures.

Vaccine Applications

- The use of pneumococcal vaccines effectively reduces bacterial resistance and prevents S. pneumoniae-related diseases. Particularly, the application of conjugate vaccines has shown significant and consistent effectiveness in preventing pneumococcal disease in children, with the safety of the vaccines also being further confirmed.

Resources: WHO, Literature Review, Frost & Sullivan Analysis

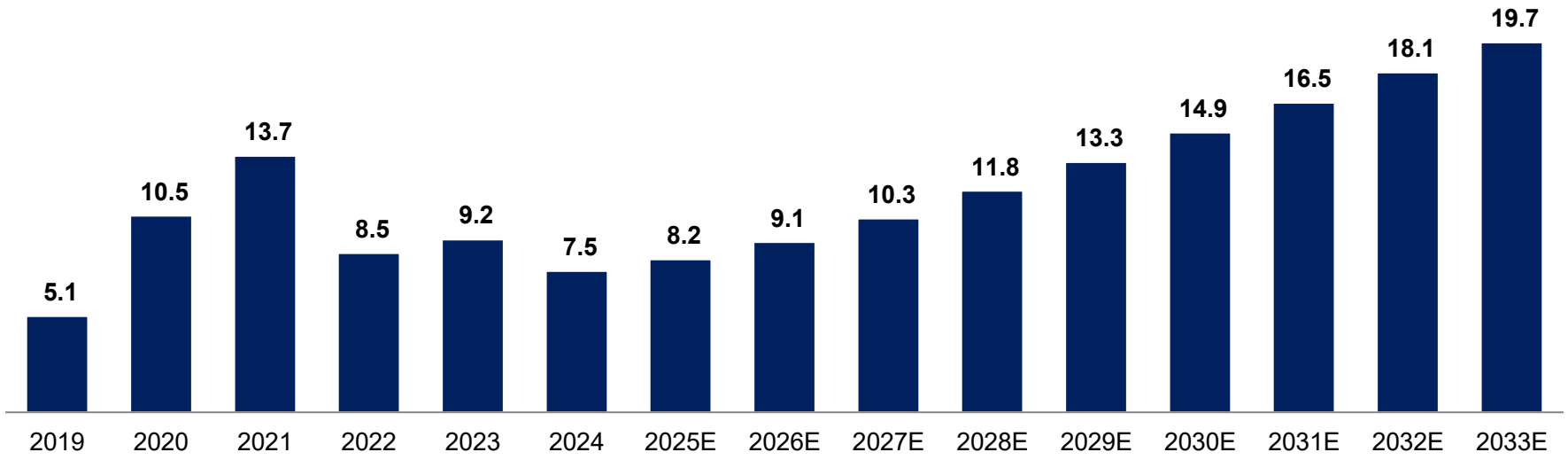
China Pneumococcal Vaccine Market Production Value, 2019-2033E

- The pneumococcal vaccine market in China, in terms of production value increased from RMB5.1 billion in 2019 to RMB7.5 billion in 2024, at a CAGR of 8.0%. The total number of lot release increased from 14.2 million in 2019 to 16.6 million in 2024. It is expected to further increase to RMB19.7 billion in 2033, at a CAGR of 11.3% from 2024 to 2033.

China Pneumococcal Vaccine Market Production Value, 2019-2033E

Period	CAGR
2019-2024	8.0%
2024-2033E	11.3%

Unit: Billion RMB



Source: Expert interview, NIFDC, Frost & Sullivan analysis

Marketed Pneumococcal Vaccines in China

Type	Brand Name (Generic Name)	Technical Route	Company	NMPA approval date*	Age Coverage
23-valent	PNEUMOVAX（纽莫法）	Polysaccharide	MSD	2010/02	50 years of age and older; ≥2 years who are at increased risk
	沃朵菲		WALVAX（沃森生物）	2017/03	≥2 years who are at increased risk
	维民菲乐		MINHAI（民海生物）	2018/08	≥2 years who are at increased risk
	惠益康		Chengdu institute of biological products（成都生物制品研究所）	2020/07	≥2 years who are at increased risk
	23-valent Pneumococcal Polysaccharide Vaccine		Sinovac（科兴）	2020/12	≥2 years who are at increased risk
	优威克		ZFSW（智飞生物）	2023/08	≥2 years who are at increased risk
13-valent	Prevnar 13	Polysaccharide conjugate	Pfizer	2016/10	6 weeks through 5 years of age
	维民菲宝		MINHAI（民海生物）	2021/09	6 weeks through 5 years of age
	Weuphoria（沃安心13）		WALVAX（沃森生物）	2019/12	6 weeks through 5 years of age
	优佩欣		Cansino（康希诺）	2025/06	6 weeks through 5 years of age

Note: The approval date is the time when the vaccine was first approved, without considering the expansion of the age group of the vaccinated population
By end of July 21st, 2025

Source： NMPA, Frost & Sullivan

Competitive Landscape of Pneumococcal Vaccines in China

Type	Technical Route	Company	Clinical Stage	FPD	Age Coverage
13-valent	Polysaccharide conjugate	Lanzhou Institute of Biological Products（兰州生物制品研究所）	NDA	2023/3/16	2 months through 5 years of age (at least 6 weeks of age)
			I (completed)	2016/7/4	2 months through 59 years of age (at least 6 weeks of age)
		AIM（艾美疫苗）	NDA	2024/11/15	2 months through 5 years of age (at least 6 weeks of age)
		Fosum Adgenvax（复星安特金）	III	2022/5/7	2-3 months of age (at least 6 weeks of age)
			I	2020/4/21	2 months of age and older (at least 6 weeks of age)
		SinoVac（科兴）	III	2023/10/19	2 months through 5 years of age (at least 6 weeks of age)
			I	2022/8/30	2 months of age and older (at least 6 weeks of age)
		Kunli Biopharmaceutical（坤力生物）	I	2021/7/27	2 months through 59 years of age (at least 6 weeks of age)
		Microvac Biotech（微超生物）	I	2022/3/24	2 months through 49 years of age (at least 6 weeks of age)
		BravoVax, chengda（博沃生物/辽宁成大）	I	2022/10/28	2 months of age and older (at least 6 weeks of age)
		Chengdu Institute of Biological Products（成都生物制品研究所）	I	2023/3/23	2 months through 59 years of age (at least 6 weeks of age)

By end of July 21st, 2025

Source: CDE, Frost & Sullivan

Competitive Landscape of Pneumococcal Vaccines in China

Type	Technical Route	Company	Clinical Stage	FPD	Age Coverage
23-valent	Polysaccharide	Lanzhou Institute of Biological Products（兰州生物制品研究所）	III (completed)	2015/12/24	2 years of age and older
		Aimei Vacin BioPharm（艾美卫信）	III	2023/8/1	2 years of age and older
		Ab&b Biotechnology（中慧元通生物）	I (completed)	2020/9/8	2 years of age and older
20-valent	Polysaccharide conjugate	MINHAI（民海生物）	II	2025/3/21	2 months through 5 years of age
			I	2024/11/20	2 months through 59 years of age
		Innovax Biotech（万泰沧海生物）	I	2023/3/13	6 weeks of age and older
		Microvac Biotech/JUWEI BIO（微超生物/聚微生物）	I	2023/4/3	2 months through 55 years of age (at least 6 weeks of age)
		Pfizer（辉瑞）	I	2025/5/7	6 weeks through 49 years of age
			I	2025/6/18	50 years of age and older
15-valent	Polysaccharide conjugate	ZFSW（智飞生物）	NDA	2025/6/5	3 months through 5 years of age
			I (completed)	2019/6/4	6 weeks of age and older
26-valent	Polysaccharide conjugate	ZFSW（智飞生物）	I/II	2024/8/20	2 months of age and older (at least 6 weeks of age)
Not Applicable	Protein-based pneumococcal vaccine	Cansino（康希诺）	I (completed)	2019/9/6	18-49 years of age
			I	2022/11/9	50 years of age and older

By end of July 21st, 2025

Source: CDE, Frost & Sullivan

Competitive Landscape of Pneumococcal Vaccines in China

Type	Technical Route	Company	Clinical Stage	FPD	Age Coverage
24-valent	Polysaccharide conjugate	Reinovax (瑞宙生物)	II	2024/4/15	18 years of age and older
			I	2024/4/15	2 months through 17 years of age (at least 6 weeks of age)
		Kunli Biopharmaceutical (坤力生物)	I/II (completed)	2022/2/18	18 years of age and older
		Fosum Adgenvax (复兴安特金)	I	2025/5/28	2 months of age and older (at least 6 weeks of age)
		SinoVac (科兴)	I	2024/8/13	2-17 years of age
			I	2025/1/23	2-23 months of age
			Ib/II	2025/6/13	18 years of age and older

By end of July 21st, 2025

Source: CDE, Frost & Sullivan

Growth Drivers and Future Trends of the Chinese Pneumococcal Vaccines market

Increased risk among the elderly	• As age increases, the risk of pneumococcal disease also increases among the elderly population aged 65 and above. In 2023, By 2023, the population aged 65 and above in China has reached 216.8 million, and is expected to grow to 286.0 million by 2032. With the development of the aging trend of China's population and the continuous improvement of per capita disposable income, the demand for pneumococcal vaccine (especially 23 valent pneumococcal polysaccharide vaccine) will gradually increase, and the market scale of pneumococcal vaccine is expected to continue to expand.
The vaccination rate of pneumococcal vaccine has increased	• In many regions of China, pneumococcal vaccines are still not covered by immunization program and with relatively low vaccination rates. Due to the serious illness caused by Spn, the WHO recommends that all countries include PCV in their immunization schedules, and the US CDC also recommends that the public receive vaccines. Based on the increasing health awareness of the Chinese people, the demand for preventive medical care will also increase. The vaccination rate of pneumococcal vaccine in China will gradually increase, thus the market size is expected to expand.
Expansion of serotype coverage	• Multivalent pneumococcal vaccines address a broader array of pneumococcal serotypes and higher valent vaccines can prevent more pneumococcal serotypes and thus have better preventive effects. PCV7 has been gradually replaced by PCV13. Meanwhile, PCV24 is being developed and some PCV24 candidates have entered the clinical stage. The serotype coverage will likely expand further with the continuous development of new pneumococcal vaccines.

Source: Frost & Sullivan

Future Trends of Chinese Pneumococcal Vaccines Market

An increase in domestically produced pneumonia vaccines	• Prior to 2019, Pfizer's Prevnar 13 was the only 13-valent PCV approved and currently on sale worldwide. At the end of 2019, the domestically produced 13-valent PCV broke Pfizer's import monopoly and was launched in the Chinese market in 2020. With the support of national policies and the influx of a large number of overseas returnees with cutting-edge technology, domestic manufacturers have begun to gradually break the monopoly of multinational companies. At present, China has two domestically produced 13-valent PCVs on the market, five domestically produced 23-valent PPSVs. The number of domestically produced vaccines will gradually increase in the future.
The scope of application for pneumococcal vaccine expands	• At present, the 13 valent PCVs currently under development in China has expanded its scope of application to a wider population. Some clinical trials have studied healthy individuals aged 2 months (minimum 6 weeks) to 59 years old, while the two 24 valent pneumococcal polysaccharide conjugate vaccines currently under development are applicable to individuals aged 18 years and above. With the accumulation of rich experience in the experimental population, the scope of application of pneumococcal polysaccharide conjugate vaccine will continue to expand.

Source: Frost & Sullivan

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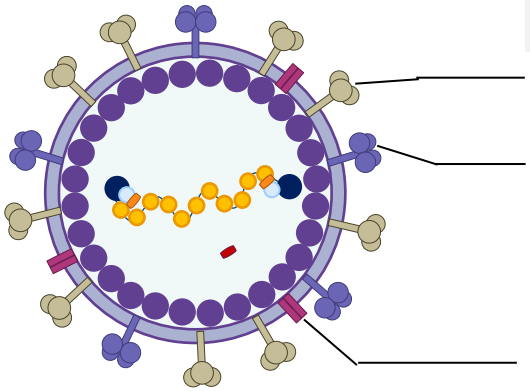
Morphology and Structure of RSV and Key Timeline of Virus Research

- Respiratory Syncytial Virus(RSV) belongs to the *Pneumovirus* genus of the *Paramyxoviridae* family. Based on viral strain differences, human RSV has two primary antigenic subtypes (A and B), mainly determined by antigenic drift and duplications in the RSV-G sequence, along with whole-genome sequence variations, including differences within the RSV-F sequence.
- Although RSV was discovered as early as 1955, its structure has only been elucidated in the past decade.

The morphology and structure of RSV



The whole genome of RSV is segmented into 10 genes, encoding 3 non-structural proteins and 8 structural proteins. Among the structural proteins, three are located on the virus surface:

- ✓ **Attachment glycoprotein(G):** Primarily functions to bind the viral particle to the cell surface by interacting with adhesion molecules on the host cell.
- ✓ **Fusion glycoprotein(F):** It anchored to the RSV membrane surface through its transmembrane domain. Intercellular Adhesion Molecule-1 (ICAM-1), a type I glycoprotein in the immunoglobulin superfamily, facilitates RSV entry and infection in human epithelial cells by binding to the F glycoprotein. The F protein exists in two conformations: prefusion F and postfusion F. When the virus fuses with the cell via the F protein, the unstable prefusion F undergoes a conformational change into the stable postfusion F.
- ✓ **Small hydrophobic protein (SH):** Forming a pentameric ion channel and is thought to be associated with delayed apoptosis of infected cells.

Key Timeline in Respiratory Syncytial Virus Research

1955
First discovered in chimpanzees.

1957
First discovered in human

1966
The first formalin-inactivated RSV vaccine

1998
The first palivizumab approved in the U.S. for the treatment of RSV infection

2008
ALN-RSV01 became the first siRNA therapy approved for clinical trials.

2011
The structure of the prefusion F protein of RSV has been elucidated.

2013
The structure of the postfusion F protein and polymerase complex of RSV has been elucidated.

2017
The RSV vaccine has been designated by the WHO as one of the highest priority vaccines for global development.

2020
Moderna's mRNA vaccine entered Phase I clinical trials.

2020
IGF1R was identified as a receptor for RSV entry into the host.

资料来源：WHO，CDC，弗若斯特沙利文分析

RSV-Related Diseases, Transmission Characteristics, and High-Risk Populations

- RSV is one of the common viruses that infect the respiratory tract. Infections of the upper respiratory tract typically present with cold-like symptoms, which are usually mild and self-limiting. In some cases, however, RSV infection can progress to a lower respiratory tract infection, primarily manifesting as bronchiolitis or pneumonia.
- The severity of RSV infection is age-dependent, with infants, the elderly, and adults with chronic illnesses being considered high-risk populations.

RSV-Related Diseases

- Upper respiratory tract infection: Clinically presents with symptoms of upper respiratory irritation, such as nasal congestion, runny nose, cough, and hoarseness. Congestion and edema may be observed in areas such as the nasal mucosa, pharynx, bulbar conjunctiva, and tympanic membrane. Fever is also commonly associated.

- Lower respiratory tract infection: Children infected with RSV may develop lower respiratory tract infections, primarily presenting as bronchiolitis or pneumonia.

RSV Transmission

- RSV is transmitted through droplets and the secretions of infected individuals. The virus can survive on surfaces for approximately 4 to 7 hours.
- Individuals infected with RSV are usually contagious for 3 to 8 days. However, some infants and people with weakened immune systems can continue to spread the virus for up to 4 weeks, even after their symptoms have stopped.

High-Risk Populations

Infants

- High-risk populations for severe RSV infection include:
  - ✓ Premature infants
  - ✓ Infants aged 6 months or younger
  - ✓ Children under 2 years old with chronic lung disease or congenital heart disease
  - ✓ Children with weakened immune systems
  - ✓ Children with neuromuscular disorders, including those who have difficulty swallowing or clearing mucus secretions

Elderly individuals & Adults with chronic illnesses

- High-risk populations for severe RSV infection include:
  - ✓ Elderly individuals, especially those aged 65 and older
  - ✓ Adults with chronic heart or lung diseases
  - ✓ Adults with weakened immune systems

资料来源：WHO，CDC，弗若斯特沙利文分析

Marketed RSV Vaccines in global market

Brand Name (Generic Name)	Technical Route	Manufacturer	FDA approval date*	Age Coverage
ABRYSVO	recombinant	Pfizer	2023/05	32-36 weeks gestational age; 60 years of age and older; 18-59 years of age who are at increased risk
AREXVY	recombinant	GSK	2023/05	60 years of age and older; 50-59 years of age who are at increased risk
mRESVIA	mRNA	Moderna	2024/05	60 years of age and older

Note: The approval date is the time when the vaccine was first approved, without considering the expansion of the age group of the vaccinated population
By end of July 21st, 2025

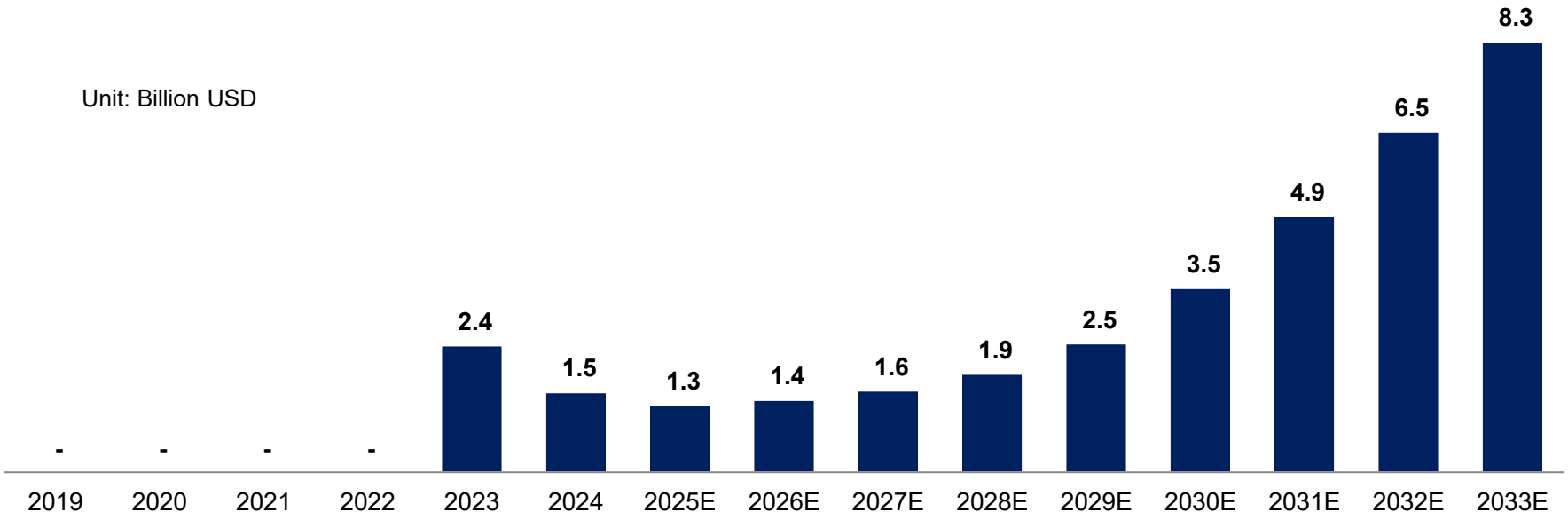
Source : FDA, Frost & Sullivan

Global RSV Vaccine Market Size and Forecasted, 2019-2033E

- Since the 1960s, the development of RSV vaccines has been a priority for the WHO. In May 2023, Arexvy became the world's first approved RSV vaccine, followed closely by Pfizer's Abrysvo, which also received FDA approval. On May 31st of this year, mResvia developed by Moderna became the third RSV vaccine approved by the FDA. As of now, there are no relevant vaccine products approved in China.
- The global market size for RSV vaccines is expected to reach 1.5 billion USD in 2024. From 2024 to 2033, RSV product sales are expected to grow at CAGR of 20.6%, with market size reaching 8.3 billion USD in 2033.

Global RSV Vaccine Market Size and Forecasted, 2019-2033E

Period	CAGR
2019-2024	-
2024-2033E	20.6%



Source: Expert interview, Annual Report, Frost & Sullivan analysis

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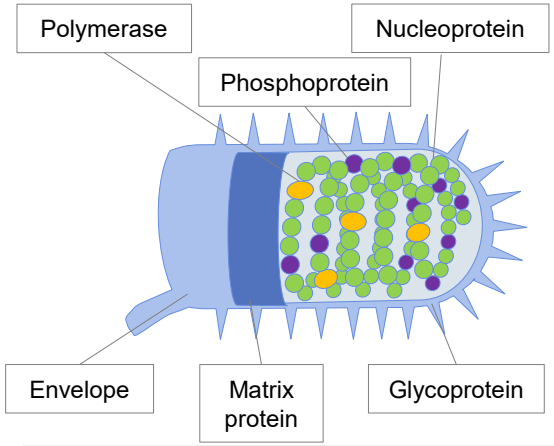
Overview of Rabies

- Rabies is a vaccine-preventable zoonotic viral disease that occurs in over 150 countries and regions. Once clinical symptoms appear, rabies is nearly 100% fatal. Rabies vaccine is an active immunizing agent used to prevent infection caused by the rabies virus. The vaccine works by causing your body to produce its own protection (antibodies) against the rabies virus.

Rabies virus



- The rabies virus belongs to the *Mononegavirales* order, Rhabdoviridae family, and *Lyssavirus* genus.
- The virus particles are bullet-shaped, measuring 100-300 nm in length and approximately 75 nm in diameter.
- The viral genome is about 12 kb in length and sequentially encodes five structural proteins: nucleoprotein, phosphoprotein, matrix protein, glycoprotein, and RNA-dependent RNA polymerase.

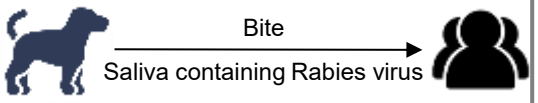
Symptoms

Rabies → **Furious**: Furious rabies is primarily characterized by confusion, phobic spasms, and autonomic dysfunction, such as pupil dilation and excessive salivation.

Rabies → **Paralytic**: In paralytic rabies, patients remain conscious but exhibit neurological symptoms similar to Guillain-Barré syndrome, including progressive, ascending, symmetrical paralysis, flaccid limb weakness, and varying degrees of sensory impairment.

Transmission routes

- The rabies virus is transmitted through direct contact with the saliva or brain/nervous system tissue of an infected animal (for example, through broken skin or mucous membranes in the eyes, nose, or mouth).
- In addition to bites and scratches, other modes of transmission are rare, such as rabies aerosol exposure or organ transplants from rabies-infected donors.



Treatment

Currently, there is no effective medical treatment for rabies; once clinical symptoms appear, the disease is nearly 100% fatal. Treatment for rabies primarily focuses on post-exposure prophylaxis (PEP) to prevent the virus from reaching the central nervous system.

PEP includes:

- Immediate and thorough washing and local treatment of the bite or scratch site after suspected exposure;
- Administration of a WHO-approved rabies vaccine regimen;
- Use of rabies immune globulin (RIG).

Source: WHO, Frost & Sullivan

Rabies Risk Levels in Different Countries and Regions Worldwide

- The UK Department of Public Health has conducted a post-exposure risk assessment for different regions and countries worldwide based on the presence of rabies in livestock and wildlife.
- All regions are considered low-risk for rabies exposure following contact with primates and rodents. However, except for the UK and Ireland, all areas worldwide are considered high-risk for rabies exposure from bats.
- Most regions in Asia, Africa, South America, and Central America are classified as high-risk for rabies exposure from terrestrial animals, including China. The Chinese CDC recommends immediate post-exposure prophylaxis, including rabies vaccination, after any injury from high-risk animals (dogs, cats, stray or wild mammals, and bats). Currently, there is high demand for rabies vaccines in China.

Risk Levels for Rabies Exposure Following Contact with Terrestrial Animals

- High-Risk Regions: Rabies occurs in both wildlife and companion animals.
- Low-Risk Regions: Rabies occurs in wildlife but not in companion animals.
- No-Risk Regions: No indigenous rabies in terrestrial animals.

Source: Public Health England, Frost & Sullivan

Rabies Vaccination Scenarios

Pre-Exposure Prophylaxis

- **Primary Immunization**

It is recommended that all individuals who are continuously or frequently exposed to environments with a risk of rabies receive pre-exposure prophylactic rabies vaccination.

Vaccination Schedule

Three doses are administered on day 0, day 7, and day 21 (or day 28).

- **Booster Immunization**

Regular booster immunization is recommended only for individuals with continuous, frequent, or high-risk exposure to rabies virus due to occupational reasons (e.g., laboratory personnel working with rabies virus and veterinarians).

Immunization Schedule

- Laboratory personnel exposed to rabies virus should monitor their serum neutralizing antibody levels every 6 months.
- Veterinarians and personnel in animal epidemic control departments should monitor their serum neutralizing antibody levels every 2 years.
- A booster dose should be administered if the serum neutralizing antibody level is <0.5 IU/ml.

Post-Exposure Prophylaxis

Exposure Category	Contact Mode	Exposure Level	Post-Exposure Immunoprophylaxis
I	Meets any of the following: • Touching or feeding animals • Intact skin exposed to animal saliva • Intact skin contact with excreta or secretions from healthy animals or confirmed rabies-free animals	None	If the contact method is reliable, no treatment is needed.
II	Meets any of the following: • Minor scratches or abrasions on bare skin without bleeding • Licks on broken skin	Mild	• Wound treatment • Rabies vaccination
III	Meets any of the following: • Single or multiple transdermal bites or scratches • Broken skin exposed to animal saliva • Mucosal contact with saliva (e.g., licks on open wounds) • Exposure to bats	Severe	• Wound treatment • Administration of rabies immunoglobulin (RIG) (anti-rabies serum or rabies immune globulin) • Rabies vaccination

Vaccination Schedules

- 5-Dose Schedule: Administer one dose on days 0, 3, 7, 14, and 28, totaling 5 doses.
- Simplified 4-Dose Schedule: Reduces the final dose from the 5-dose schedule, with doses administered on days 0, 3, 7, and 14-28, totaling 4 doses.
- "2-1-1" Schedule: Administer two doses on day 0 (one in each deltoid muscle of the upper arms), followed by one dose on day 7 and another on day 21, totaling 4 doses. (This schedule is only applicable for rabies vaccines approved for the "2-1-1" schedule in China.)

Source: China CDC, Frost & Sullivan

Comparison of Rabies solutions in Developed and Developing Countries

- According to the Rabies vaccines: WHO position paper – April 2018, Rabies is a viral zoonotic disease responsible for an estimated 59 thousand human deaths in 2015. Most cases occur in Africa and Asia, with approximately 40% of cases in children aged <15 years, which indicates the huge demand in developing countries.
- According to the WHO Zero Human Rabies Deaths from dog-transmitted rabies by 2030 (Zero by 30), each country pays effort to control this disease with different methods.
- Human rabies vaccine is essential for prevention of rabies, especially after exposure to rabies, in which case the mortality rate is nearly 100% without post-exposure prophylaxis.

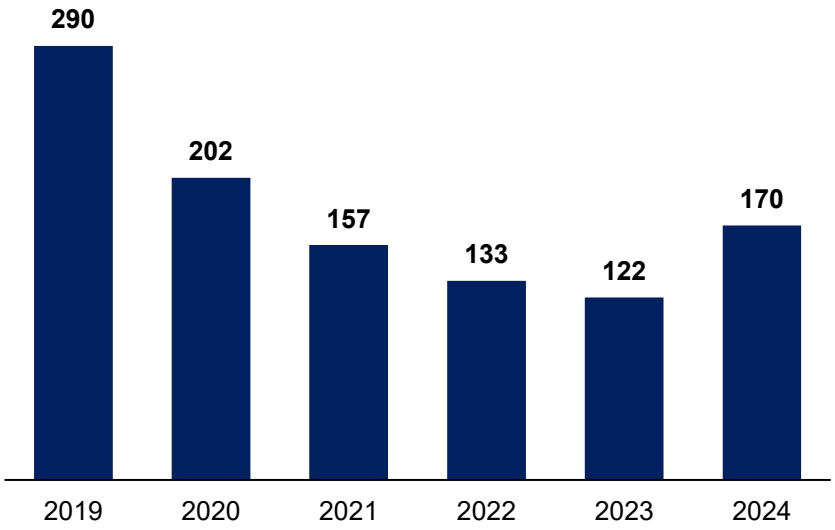
	Typical countries	Type of rabies vaccine	Current situation	Trend
Developing countries	• India • Egypt • Bangladesh • Thailand • Philippines	• Human rabies vaccine for PEP is the majority of rabies vaccine used in developing countries with high incidence and death toll of rabies.	• Over 95% of human deaths with rabies is occurring in developing countries in Asia and Africa regions. • For these countries with high bite incidence and morality, immediate PEP is the most effective way to control the death toll of rabies.	• As the incidence of rabies in these countries is predicted to keep a high level in the next few years, the demand of human rabies vaccine will still keep a high level. • With the growing awareness of prevention of rabies, animal vaccination will also raise the attention. For instance, mass dog vaccination was initiated in Bangladesh in 2011 with the help from WHO.
Developed countries	• U.S. • Japan • Australia • England	• Animal rabies vaccines for pets is the majority of rabies vaccine used in countries with low risk of human rabies.	• In some developed countries with established animal disease control system, such as the US and Japan, rabies is a rare disease and only several new cases are reported each year. • For these countries, the main method to control and prevent rabies is vaccination for pets.	• With the low incidence of rabies in developed countries, prevention vaccination for animals will keep its role as the main method to control rabies.

Source: WHO, Frost & Sullivan

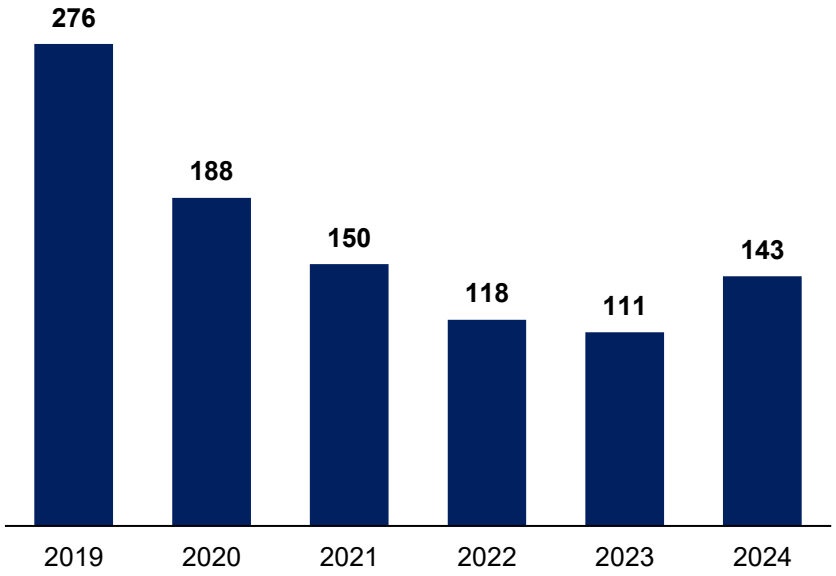
Number of New Cases and Deaths of Rabies in China，2019-2024

- According to the Statistical Report on China's Health Care Development（卫生健康事业发展统计公报）, there were 170 new cases of rabies and 143 deaths from rabies in China in 2024.

New Cases of Rabies in China，2019-2024



Deaths of rabies in China，2019-2024



Source： Statistical Report on China's Health Care Development, Frost & Sullivan

Analysis of Different Cell Lines for Rabies Vaccine

- The production of high-quality rabies vaccines has been made feasible through modern cell cultivation techniques using diploid cell strains for vaccine production. Human diploid cell vaccine (HDCV) is a vaccine cultured and manufactured using healthy human embryonic lung fibroblasts as a matrix. It is often used as a reference vaccine because it has no potential tumor-causing DNA residues or risk of foreign protein allergens, and is theoretically safer.
- The WHO recommends human diploid cells as one of the safest cell culture substrates for the production of viral vaccines. Although there are only two human diploid cell rabies vaccines currently available on the market. In the next 2-3 years, the production of human diploid rabies vaccines is expected to increase, and human diploid rabies vaccines are expected to become one of the main participants in the rabies vaccine market.

		Introduction	Immunogenicity	Safety	Cost & Yield	Challenges
Traditional Cell Line	Primary Cell	• PCEC	• Qualified immunogenicity	• For PCEC, egg ingredients may cause allergic reactions	• Relatively high cost • Rely on the supply of high standard eggs	• Risk of insufficient supply • Time-consuming
		• PHKC	• Qualified immunogenicity	• -	• Low cost • Adherent culture needed, difficulties in scale up	• Easy to be contaminated • Cell preservation is tedious
	Vero Cell	• Isolated from kidney epithelial cells extracted from an African green monkey	• Qualified immunogenicity	• Presence of residual host cell DNA	• Low cost	Potential tumorigenicity of the DNA of high-passage Vero cells
Innovative Cell Line	Human Diploid Cell	• Usually derived from cell lines established from normal human fetal tissue. • Mainly includes MCR-5, 2BS, EI-38 cell line.	• Qualified immunogenicity • Neutralizing antibodies produce faster and better antibody responses	• No residual host cell proteins and foreign DNA in vaccines, can significantly reduce adverse reactions	• High cost • Difficulties in scale up	• Strict requirements for environmental control, medium formulation, and cultivation techniques

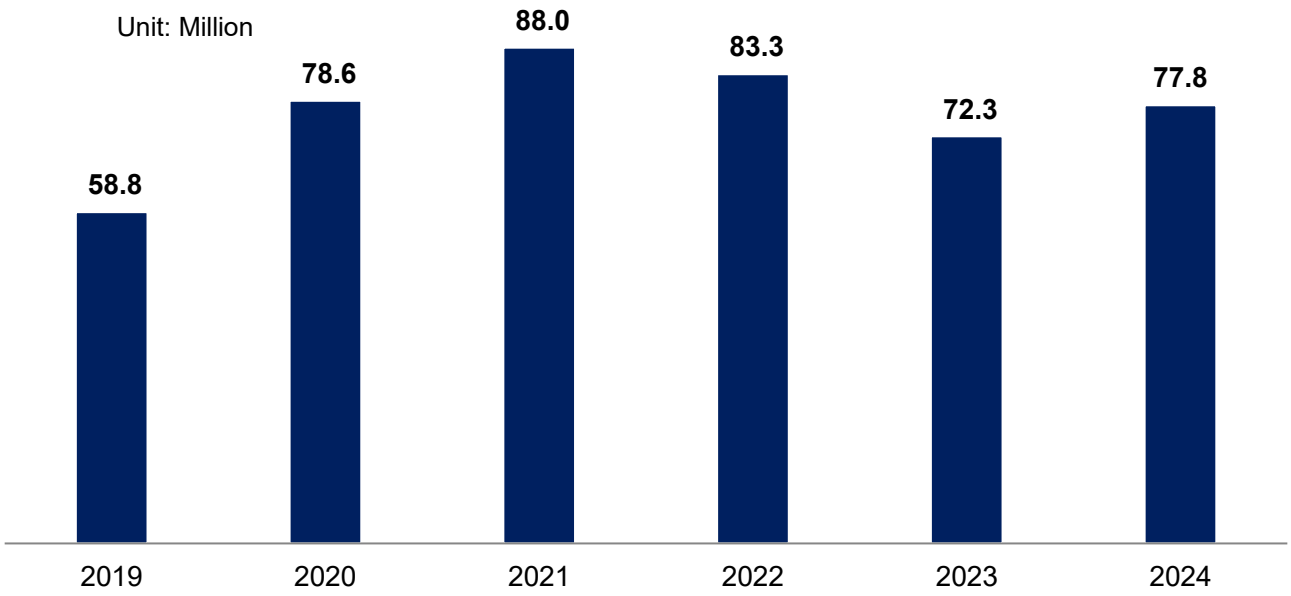
Source: Frost & Sullivan

Lot Release of Rabies Vaccine in China, 2019-2024

- Due to the negative impact of the "Changchun Changsheng Vaccine Event" ("长春长生疫苗事件"), lot release of rabies vaccines has experienced a downward trend in 2018 and 2019. Until 2020, lot release of rabies vaccine returned to original level.
- The lot release of rabies vaccine experienced a fluctuation from 58.8 million in 2019 to 77.8 million in 2024, with a CAGR of 5.8%.

Lot Release of Rabies Vaccine in China , 2019-2024

Period	CAGR
2019-2024	5.8%



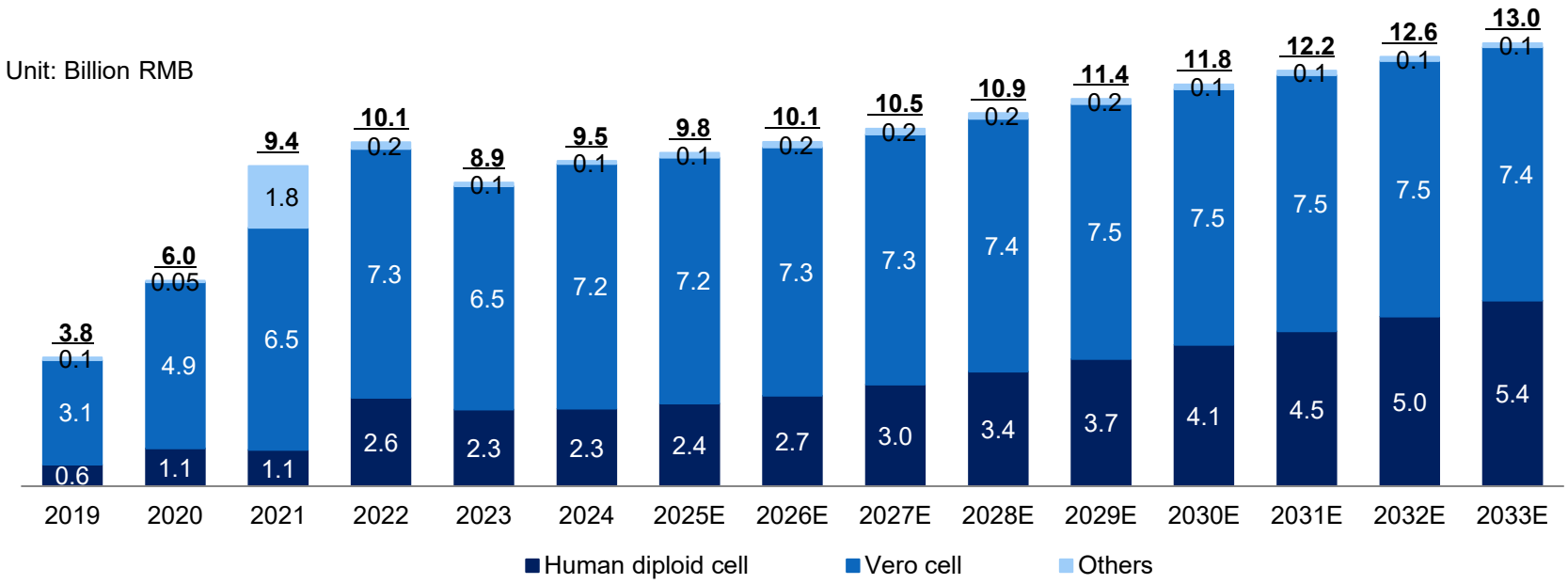
Source: Expert interview, NIFDC, Frost & Sullivan analysis

China Rabies Vaccine Market Production Value, Separated by Cell Lines, 2019-2033E

- The rabies vaccine market in China, in terms of production value, increased from RMB3.8 billion in 2019 to RMB9.5 billion in 2024, at a CAGR of 20.3%. The total number of lot release increased from 58.8 million in 2019 to 77.8 million in 2023. Driven by increase in vaccination rates and the introduction of high-value rabies vaccines, the rabies vaccine market in China is estimated to further increase to RMB13.0 billion in 2033, at a CAGR of 3.5% from 2024 to 2033.

China Rabies Vaccine Market Production Value, 2019-2033E

Period	CAGR			
	Human diploid cell	Vero cell	Others	Total
2019-2024	29.1%	18.5%	2.2%	20.3%
2024-2033E	10.2%	0.4%	3.2%	3.5%



Source: Expert interview, NIFDC, Frost & Sullivan analysis

Marketed Human Rabies Vaccines in China(1)

Cell Line	Brand Name (Generic Name)	Company	NMPA approval date	Immunization Schedule[3]	End-User Price[1]	Market Share[2] (2024)
Human Rabies Vaccine (Vero Cell)	武生旺宁	Wuhan institute of biological products (武汉生物制品研究所)	2004/01	Essen 5 doses	/	-
	成大速达	Chengda Biotechnology (成大生物)	2004/01	Zagreb 4 doses & Essen 5 doses	89.5	-
	-	HK Biotech (惠康生物)	2006/11	Essen 5 doses	80	-
	-	Fosun Apexvac (复星雅立峰)	2016/09	Essen 5 doses	74	2.5%[5]
Human Rabies Vaccine, lyophilized (Vero Cell)	-	Yisheng Biopharma (依生生物)	2003/04	Essen 5 doses	95	18.8%
	-	Chengda Biotechnology (成大生物)	2004/01	Zagreb 4 doses & Essen 5 doses	98	32.3%
	武生欣宁	Wuhan institute of biological products (武汉生物制品研究所)	2005/01	Essen 5 doses	/	-
	-	AIM (艾美疫苗)	2007/09	Essen 5 doses	99	6.1%
	-	PRCMISE Biological (诺诚生物)	2008/01	Essen 5 doses	/	-
	-	Zhuoyi Biological (卓谊生物)	2016/11	Essen 5 doses	118.5	6.7%
	-	Changchun institute of biological products (长春生物制品研究所)	2021/04	Zagreb 4 doses & Essen 5 doses	99	11.7%
	-	Yidu Biotechnology (亦度生物)	2021/07	Zagreb 4 doses & Essen 5 doses	91	10.0%
	-	Hualan Biological Bacterin (华兰生物)	2023/04	Zagreb 4 doses & Essen 5 doses	129	1.2%
	-	CuroVax (康润生物)	2023/09	Zagreb 4 doses & Essen 5 doses	158	-
	-	Fosun Apexvac (复星雅立峰)	2024/03	Essen 5 doses	113	-

Source: NMPA, Frost & Sullivan

Marketed Human Rabies Vaccines in China(2)

Cell Line	Brand Name (Generic Name)	Company	NMPA approval date	Immunization Schedule[3]	End-User Price[1]	Market Share[2] (2024)
Human Rabies Vaccine, lyophilized (Human Diploid Cell)	-	Kanghua Biological Products (康华生物)	2012/01	Essen 5 doses	315	5.0%
	-	MINHAI (民海生物)	2023/09	Zagreb 4 doses & Essen 5 doses	298	4.3%
Human Rabies Vaccine (Hamster Kidney Cell)	-	Yatai biopharmaceuticals (亚泰生物)	1999/01	Essen 5 doses	/	-
	-	CGE Healthcare (远大生物)	2000/01	Essen 5 doses	79	1.4%
	-	Lanzhou institute of biological products (兰州生物制品研究所)	2000/01	Essen 5 doses	/	-
	-	Zhongke Biotic (中科生物/博晖生物)	2000/02	Essen 5 doses	95	-
	-	AIM (艾美疫苗)	2006/01	Essen 5 doses	/	-
Human Rabies Vaccine, lyophilized (Hamster Kidney Cell)	-	Lanzhou institute of biological products (兰州生物制品研究所)	2005/01	Essen 5 doses	/	-

Note:
1.The end-user price is determined by the median of winning bid prices in provinces with publicly disclosed data in 2024;
2. The market share was calculated by Production volume;
3. Post exposure vaccination program, in addition, all approved products can be used for the pre exposure prophylaxis 3-dose immunization program
4. Certain human rabies vaccines are applicable to two immunization schedules, as they have undergone clinical validation and are proven to achieve the desired effects under each schedule. The decision of which schedule to adopt is primarily determined by the vaccine itself, and its administration should follow the instructions provided in the medication guide;
5. Including the lyophilized and non-lyophilized type of the company's human rabies vaccines;
6. By end of July 21st, 2025

Source: NMPA, Frost & Sullivan

Competitive Landscape of Rabies Vaccines in China (1)

Cell Line	Company	Clinical Stage	FPD*	Immunization Schedule
Vero cell	Nuocheng Biological Products (诺辰生物)	NDA	2024/07/26	Zagreb 4 doses & Essen 5 doses
	Sinovac (科兴)	NDA	2025/1/25	1-1-1-1 & Essen 5 doses
	Ronsen (荣盛生物)	NDA	2025/03/13	Essen 5 doses
	AIM (艾美疫苗)	NDA	2025/04/08	Essen 5 doses
	GDK biotechnology (金迪克生物)	III (completed)	2017/12/20	Essen 5 doses
	Maokangyuan Biotechnology (茂康源生物)	III	2019/12/25	Essen 5 doses
	ZFSW (智飞生物)	III	2020/12/10	Zagreb 4 doses & Essen 5 doses
	Chengda Biotechnology (成大生物)	III (completed)	2021/07/28	1-1-1-1
		I	2025/02/24	Essen 5 doses
	RBSPH (银河阳光生物制品)	III	2022/11/04	1-1-1-1 & Essen 5 doses
	Yisheng Biopharmaceutical (依生生物)	III	2024/11/12	1-1-1-1 & Zagreb 4 dose
	Yidu Biotechnology (亦度生物)	III	2025/06/17	1-1-1-1
	Yatai Biological Pharmaceutical (亚泰生物药业)	I (completed)	2021/02/23	Essen 5 doses

Source: CDE, Frost & Sullivan

Competitive Landscape of Rabies Vaccines in China (2)

Cell Line	Company	Clinical Stage	FPD*	Immunization Schedule
Chicken Embryo Cell	King-cell Biotechnology (青赛生物)	NDA	2024/10/18	Zagreb 4 doses & Essen 5 doses
	Qingfeng/C-FUSION Biotechnology (青峰药业/赛尔富森生物科技)	III	2022/01/18	Zagreb 4 doses & Essen 5 doses
Human Diploid Cell	Chengda Biotechnology (成大生物)	NDA	2024/08/31	Zagreb 4 doses & Essen 5 doses & 1-1-1-1
	ZFSW (智飞生物)	NDA	2024/10/16	Zagreb 4 doses & Essen 5 doses
	Chengdu institute of biological products (成都生物制品研究所)	III	2017/05/10	Zagreb 4 doses & Essen 5 doses
	Prokang Biotechnology (普康生物)	III	2024/07/18	Zagreb 4 doses & Essen 5 doses
	AIM (艾美疫苗)	III	2025/06/11	Zagreb 4 doses & Essen 5 doses & 1-1-1-1
		I	2025/05/19	Zagreb 4 doses & Essen 5 doses
	Ab&b Biotechnology (中慧生物)	I (completed)	2023/11/20	Zagreb 4 doses & Essen 5 doses

**Note: The dates for products in NDA stage are the dates handled by CDE*
By end of July 21st, 2025

Source: CDE, Frost & Sullivan

Marketed Human Rabies Vaccines in Global Market

Cell Line	Brand Name (Generic Name)	Company	NMPA approval date	Immunization Schedule*
Human Diploid Cell	Imovax	Sanofi	NA	Essen 5 doses
Primary chicken embryo cell	RabAvert/Rabipur	Bavarian Nordic	1997	Essen 5 doses

**Note: Post exposure vaccination program, in addition, all approved products can be used for the pre exposure prophylaxis 3-dose immunization program*
By end of July 21st, 2025

Source : FDA, Frost & Sullivan

Competitive Landscape of Rabies Vaccines in Global Market

Cell Line/Technical Route	Company	Clinical Stage	FPD	Immunization Schedule	Locations
Vero cell	Sanofi	III (completed)	2017/05/10	2-2-2-2	Thailand
	Yisheng Biopharma	III	2022/12/29	2-2-1 & Essen 5 doses	Pakistan, Philippines
		II (completed)	2016/11/06	1-1-1-1 & 2-2-1	Singapore
	Sinovac（科兴）	III	2025/07/09	Essen 5 doses	Pakistan
		III	2025/07/08	PrEP 1-1-1	Pakistan
mRNA	CureVac	I (completed)	2018/10/19	1-1-1 & 1/2-1/2	Belgium, Germany
saRNA	GSK	I (completed)	2019/08/20	1-1	U.S.

By end of July 21st, 2025

Source: ClinicalTrials.gov, Frost & Sullivan

Growth Drivers and Future Trends of the Chinese rabies vaccine market

Increase in pet ownership	• The number of pet owners in China is rising, with a significant increase in pet dogs. According to Chinese CDC, In 2024, the number of urban dogs and cats in China will be 124.11 million, of which 52.58 million are pet dogs. However, according to WHO's World Health Statistics reports, over 95.0% of human rabies cases worldwide are caused by dog-related injuries. Unlike developed nations, China has not yet effectively implemented widespread animal vaccination programs, leading to higher demand for human rabies vaccines.
Increased affordability and vaccination awareness	• Higher per capita disposable income enables more people to afford self-funded vaccines like human rabies vaccines. • In 2015, WHO proposed a global strategic plan to eliminate human rabies caused by dogs worldwide by 2030 at the Global Rabies Conference held in Geneva, Switzerland. In recent years, China has also released a series of guidelines, such as the "Expert Consensus on Rabies Exposure Prevention and Treatment (《狂犬病暴露预防处置专家共识》)" in 2019, "Guidelines for Rabies Exposure Prevention and Treatment (2023 Edition) (《狂犬病暴露预防处置工作规范（2023年版）》)", which recommended that individuals who are continuously and frequently exposed to rabies virus hazardous environments should receive pre exposure prophylactic rabies vaccination, and for post exposure prophylactic treatment, rabies vaccination should be administered as early as possible. Various provinces and cities in China have also set up 24-hour dog injury clinics and made public the list to help improve the vaccination rate after exposure.
Growth in Human Diploid Cell Rabies Vaccine Market Share	• The human rabies vaccine developed from human diploid cell is the WHO's gold standard for rabies vaccines, offering higher safety and stronger immune responses. While the current price of such vaccines, which is much higher than other human rabies vaccines, impacts vaccination rates, technological advancements may reduce production costs, improving affordability. With economic growth, the market share of human diploid cell rabies vaccines is anticipated to rise..

Source: Frost & Sullivan

Growth Drivers and Future Trends of the Chinese rabies vaccine market

Upgrading of serum-free culture and other processes promotes further development of rabies vaccines

- In the early stages of the development of rabies vaccines, natural animal fluid supplements such as animal serum (such as newborn bovine serum, premium fetal bovine serum, etc.) were added to cultured cells to maintain cell growth. However, the composition of serum culture media is complex, and viruses and mycoplasma present in animal serum, as well as prions related to bovine spongiform encephalopathy, pose a high risk of contamination. In addition, China‘s bovine serum is highly dependent on imports, which limits its supply. Serum free culture can solve the above pain points, with the advantages of stable components, low pollution, and high safety. The National Development and Reform Commission’s “Guiding Catalogue for Industrial Structure Adjustment (2019 Edition) （《产业结构调整指导目录（2019年本）》）" encourages the development and application of "serum-free and protein free culture medium cultivation, fermentation, and purification technologies for major disease prevention and control vaccines". However, serum-free culture technology has high barriers, and with the continuous upgrading of rabies vaccine cell matrix culture technology, serum-free culture technology is gradually being applied and will become a future trend. There are already relevant practices of low serum and serum-free cultivation of diploid cells in humans, which will promote the development of the rabies vaccine market

Growth in Human Diploid Cell Rabies Vaccine Market Share

- The human rabies vaccine developed from human diploid cell is the WHO’s gold standard for rabies vaccines, offering higher safety and stronger immune responses. While the current price of such vaccines, which is much higher than other human rabies vaccines, impacts vaccination rates, technological advancements may reduce production costs, improving affordability. With economic growth, the market share of human diploid cell rabies vaccines is anticipated to rise..

Source: Frost & Sullivan

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Overview of Shingles

- Shingles, also known as HZ, is a disease caused by reactivation of the varicella-zoster virus (VZV) from dorsal sensory or cranial nerve ganglia. This reactivation occurs when immunity to VZV declines because of aging or immunosuppression. Herpes zoster can occur at any age but most commonly affects the elderly population. Symptoms of shingles usually include a general feeling of malaise, pyrexia, chills, myalgia, headache, pruritus, numbness and rash. VZV can be spread from a person with active shingles to another person who has never had varicella or received vaccines. Following the resolution of varicella, the virus can remain dormant in the dorsal sensory and cranial ganglion for decades.

Symptoms

- Shingles is a painful rash that develops on **one side of the face or body**. The rash consists of blisters that typically scab over in **7 to 10 days** and fully clears up **within 2 to 4 weeks.**
- Before the rash appears, people often have **pain, itching, or tingling** in the area where it will develop. This may happen several days before the rash appears.
- Most commonly, the rash occurs in **a single stripe around either the left or the right side of the body**. In other cases, the rash occurs **on one side of the face**.
- Shingles on the face can affect the **eye** and cause vision loss. In rare cases (usually in people with weakened immune systems), the rash may be **more widespread** on the body and look similar to a chickenpox rash.
- Other symptoms of shingles can include
  - Fever
  - Headache
  - Chills
  - Upset stomach

Complications

- The most common complication of shingles is long-term nerve pain called **postherpetic neuralgia (PHN).** PHN occurs in the areas where the shingles rash was, even after the rash clears up. It can **last for months or years** after the rash goes away. The pain from PHN can be so severe and debilitating that it interferes with daily life.
- Shingles may lead to serious complications involving the **eye, including blindness**.
- Very rarely, it can also lead to
  - pneumonia,
  - hearing problems,
  - brain inflammation (encephalitis), or
  - death.

Risk Factors

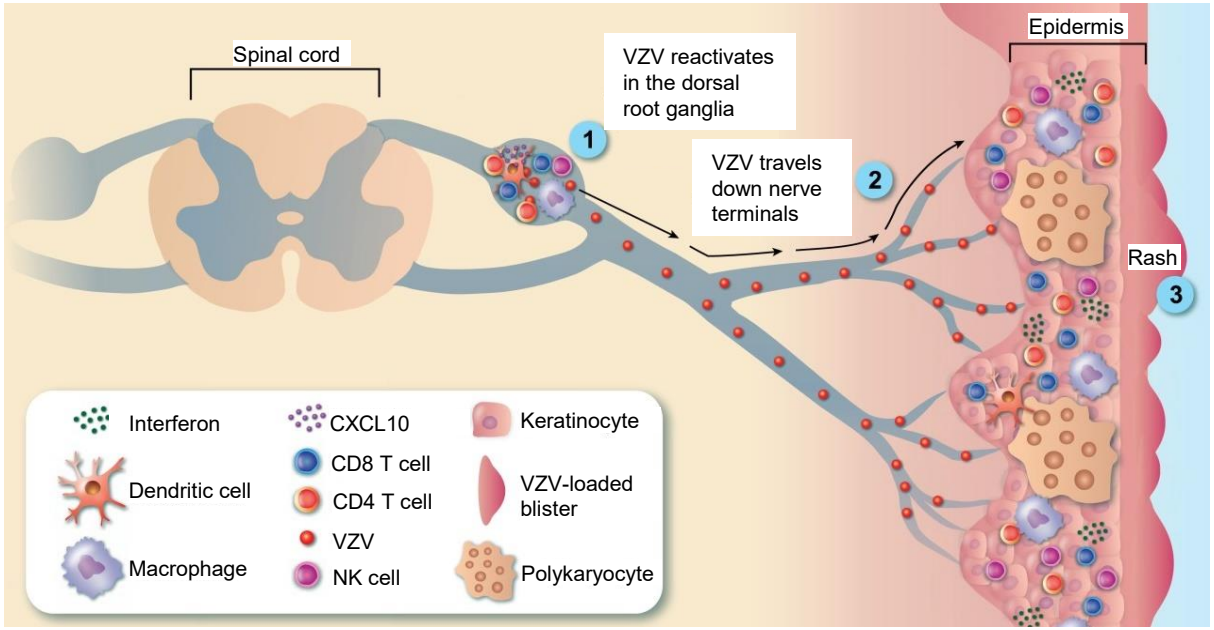
- The risk of getting shingles and having serious complications **increases with age**.
- People who have medical conditions or take medications that keep their immune systems from working properly have a higher risk of getting shingles.

Source: Literature review, Frost & Sullivan analysis

Overview of Varicella-Zoster Virus

VZV Reactivation Leads to HZ.

- Shingles is caused by **varicella zoster virus (VZV)**, the same virus that causes **chickenpox (varicella)**.
- **Primary infection** with VZV causes varicella.
- After a person recovers from chickenpox, the virus **stays dormant (inactive)** in the dorsal root ganglia.
- The virus can **reactivate later** in a person's life and cause a painful, maculopapular rash called **herpes zoster**.



Transmission

- **Active herpes zoster lesions** are infectious, through **direct contact** with vesicular fluid, until they dry and crust over.
- People with active herpes zoster lesions can **spread VZV infection and cause varicella** in people who have never had varicella or received varicella vaccine.
- Once varicella resolves, these people would **be at risk of herpes zoster**.
- People with active herpes zoster lesions should **cover their lesions and avoid contact with susceptible people** in their household and in occupational settings until their lesions are dry and crusted.

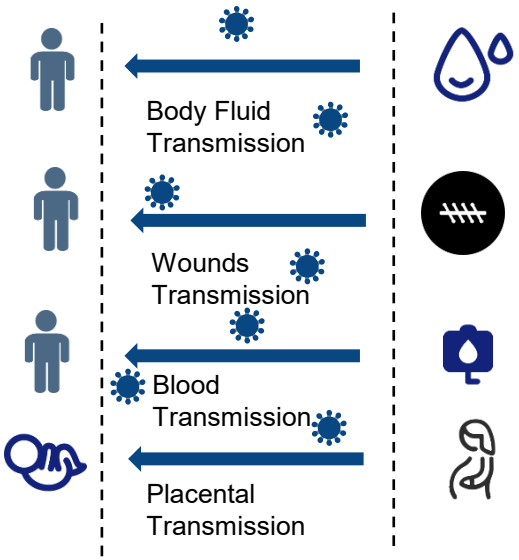
Source: Literature review, Frost & Sullivan analysis

Overview of Zoster (Herpes Zoster) Vaccine

- Humans are the only host of varicella-zoster virus. The virus enters the blood through the respiratory mucosa to form viremia. Varicella or recessive infection occurs. Later, the virus can be latent in the spinal dorsal root ganglia or cranial nerve sensory ganglia for a long time. Shingles affects nearly 3 million Chinese adults each year and most of them occur in adults over 50. According to the epidemiological survey in Guangdong Province, the prevalence rate of women is significantly higher than that of men.

Transmission

- Saliva spread
- Shingles is transmitted through the liquid of leaking herpes.
- Shingles can be spread through wounds
- Blood-borne infection
- Placental infection



Shingrix

- SHINGRIX is a zoster vaccine developed by GlaxoSmithKline. This is the only approved zoster vaccine in China.
- The vaccine is a kind of recombinant zoster vaccine which is capable of providing 90% protection among people over 50 years old according to clinical data.

SHINGRIX
VACCIN CONTRE LE ZONA (NON VIVANT, RECOMBINANT, AVEC AS01$_B$ COMME ADJUVANT

Zostavax

- Zostavax is a zoster vaccine developed by Merck. The vaccine wasn't approved in China mainland.
- As a earlier developed vaccine, Zostavax applied attenuated vaccine technique which have several draw backs compared with recombinant zoster vaccine .

ZOSTAVAX®
Get your shingles

Draw Backs

- The price of Shingrix in China is 1560 CNY each dose and it usually takes 2 doses for each person, which reveals the lack of price advantage.
- The adverse reactions includes pain, redness, swelling, myalgia, fatigue, headache, chills, fever, and gastrointestinal symptoms.

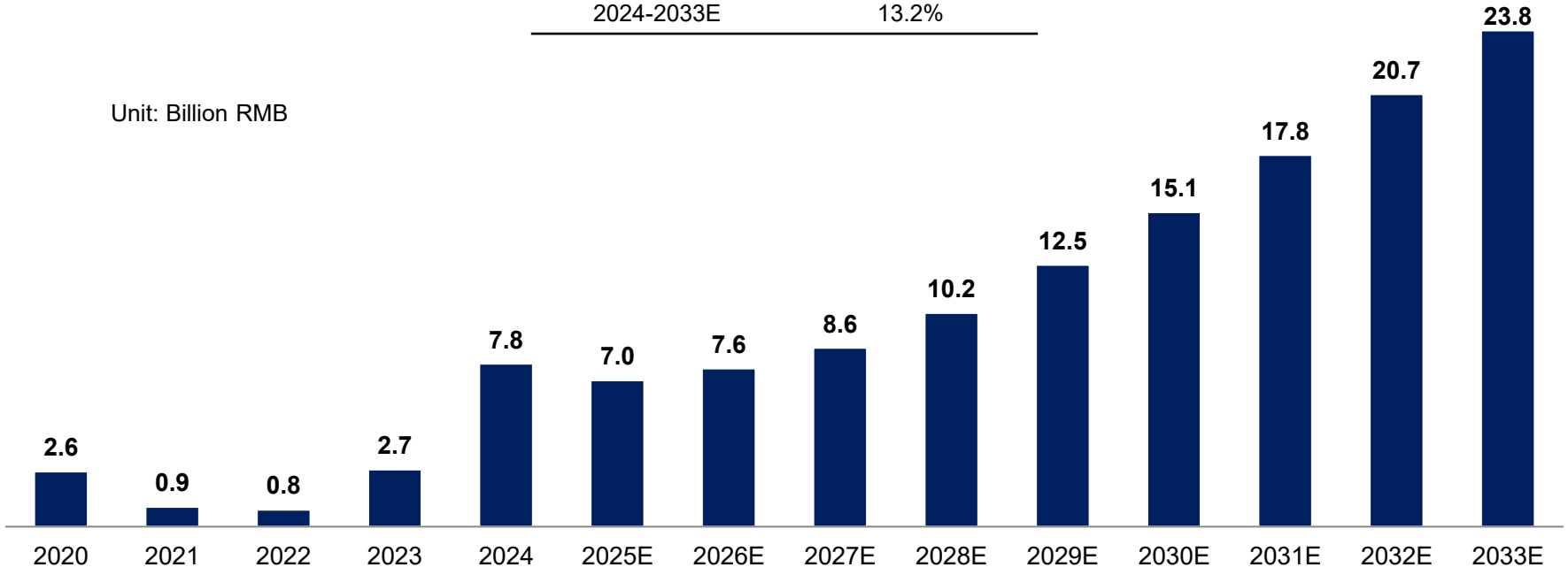
Source: Literature review, Frost & Sullivan analysis

China Zoster Vaccine Market Production Value, 2020-2033E

- The herpes zoster vaccine market in China reached RMB2.6 billion in terms of production value in 2020 after the first herpes zoster vaccine obtained approval from the NMPA in 2019. Driven by growing awareness of herpes zoster and the increasing number of available herpes zoster vaccine products, the herpes zoster vaccine market is estimated to increase from RMB7.8 billion in 2024 to RMB23.8 billion in 2033, at a CAGR of 13.2%.

China Zoster Vaccine Market Production Value, 2020-2033E

Period	CAGR
2020-2024	31.2%
2024-2033E	13.2%



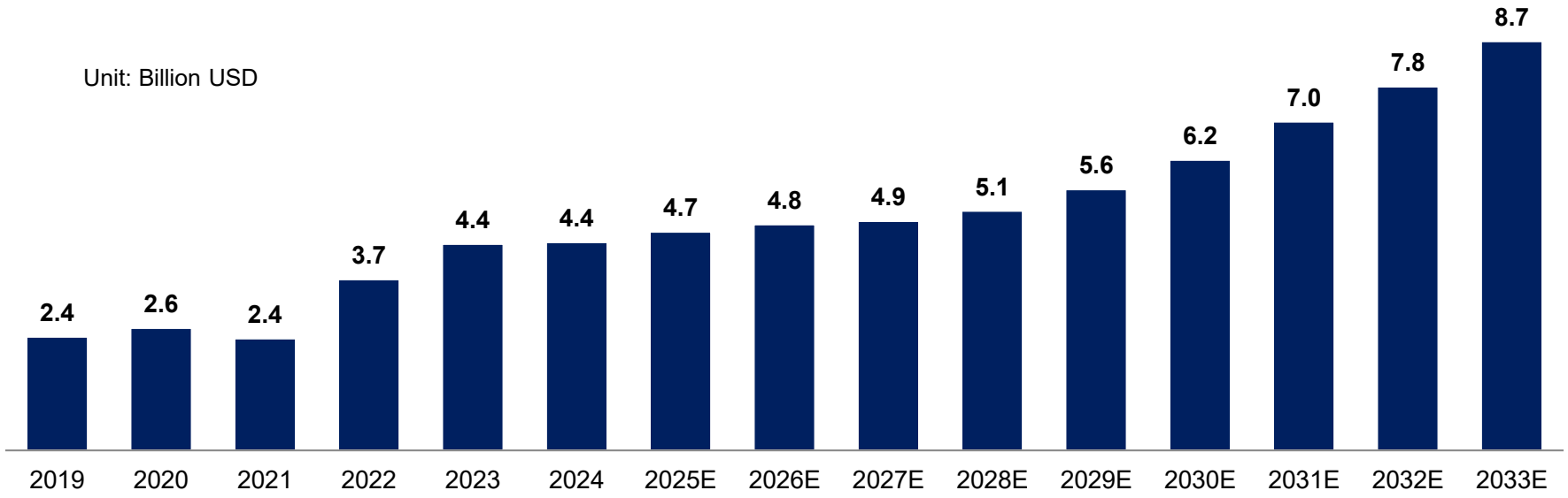
Source: Expert interview, NIFDC, Frost & Sullivan analysis

Global Zoster Vaccine Market Size and Forecasted, 2019-2033E

- The global herpes zoster vaccine market increased from US$2.4 billion in 2019 to US$4.4 billion in 2024, at a CAGR of 12.8%, and is estimated to reach US$8.7 billion in 2033, at a CAGR of 7.8% from 2024 to 2033.

Global Zoster Vaccine Market Size and Forecasted, 2019-2032E

Period	CAGR
2019-2024	12.8%
2024-2033E	7.8%



Source: Expert interview, Annual Report, Frost & Sullivan analysis

Marketed Zoster Vaccines in global market

Brand Name (Generic Name)	Technical Route	Company	FDA approval date*	Age Coverage
Zostavax	live attenuated	Merck	2006/05	50 years of age and older
SHINGRIX	recombinant	GSK	2017/10	50 years and older/18 years and older who are or will be at increased risk

Note: The approval date is the time when the vaccine was first approved, without considering the expansion of the age group of the vaccinated population
By end of July 21st, 2025

Source : FDA, Frost & Sullivan

Marketed Zoster Vaccines in China

Brand Name (Generic Name)	Technical Route	Company	NMPA approval date*	Age Coverage
SHINGRIX	recombinant	GSK	2019/05	50 years of age and older
感维	live attenuated	BCHT（百克生物）	2023/01	40 years of age and older

Note: The approval date is the time when the vaccine was first approved, without considering the expansion of the age group of the vaccinated population
By end of July 21st, 2025

Source： NMPA, Frost & Sullivan

Competitive Landscape of Zoster Vaccines in China

Technical Route	Company	Clinical Stage	FPD*	Age Coverage
recombinant	Recbio （瑞科生物）	III	2024/10/9	40 years of age and older
recombinant	Lvzhu biotech （绿竹生物）	NDA	2025/2/9	*The age for submitting NDA for this product has not been disclosed
		III	2023/9/25	40 years of age and older
		II	2024/11/4	50 years of age and older
		II (completed)	2022/4/19	50-70 years of age
recombinant	MaxVax （迈科康生物）	III	2024/6/3	40 years of age and older
		II	2023/5/8	30 years of age and older
		I	2022/10/21	18 years of age and older
recombinant	Varnotech （华诺泰生物）	II	2024/10/29	40 years of age and older
recombinant	Ab&b Biotechnology （中慧生物）	I/II	2025/2/19	40 years of age and older
recombinant	SinoCellTech （神州细胞工程）	I/II	2025/1/24	40 years of age and older
recombinant	Lvye pharma （绿叶制药）	I	2025/3/5	40 years of age and older
recombinant	CGE Healthcare （远大赛威信）	I	2024/12/10	40 years of age and older
recombinant	Shanghai institute of biological products （上海生物制品研究所）	I	2025/4/25	40 years of age and older
recombinant	GeneVax （吉诺卫）	II	2025/6/10	40 years of age and older
live attenuated	Changsheng biotechnology （长生生物）	III	2017/10/7	40 years of age and older
live attenuated	Shanghai institute of biological products （上海生物制品研究所）	I/II (completed)	2018/12/19	40 years of age and older

**Note: The dates for products in NDA stage are the dates handled by CDE*
By end of July 21st, 2025

Source: CDE, Frost & Sullivan

Competitive Landscape of Zoster Vaccines in China

Technical Route	Company	Clinical Stage	FPD*	Age Coverage
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recombinant	Shanghai institute of biological products （上海生物制品研究所）	I	2025/4/25	40 years of age and older
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**Note: The dates for products in NDA stage are the dates handled by CDE*
By end of July 21st , 2025

Source: CDE, Frost & Sullivan

Competitive Landscape of Zoster Vaccines in China

Technical Route	Company	Clinical Stage	FPD*	Age Coverage
mRNA	CSPC （石药集团）	I	2025/4/29	40 years of age and older
mRNA	ABOGEN （艾博生物）	I	2025/5/14	40 years of age and older
mRNA	RHEGEN （瑞吉生物）	I	2025/5/16	40 years of age and older

**Note: The dates for products in NDA stage are the dates handled by CDE*
By end of July 21st, 2025

Source: CDE, Frost & Sullivan

Growth Drivers of zoster vaccine Market

Aging Society	• The lifetime risk of Herpes Zoster (HZ) in the general population ranges from 20–30% but the risk increases dramatically after 50 years of age with a lifetime risk of HZ reaching 50% at age 85 years. With the aging of the global society, the number of people over 50 years old is increasing, indicating a growing amount of people that are prone to shingles. People with herpes zoster are likely to develop postherpetic neuralgia (PHN), which is the most common and a severe complication of herpes zoster. PHN can last for weeks, months or even for years, which can dramatically affecting the life quality of the patient. Furthermore, a person's risk of having PHN after herpes zoster increases with age, indicating a considerable disease burden for the old. Therefore, effective vaccine of HZ are of great market potential.
High Reactivation Rate	• According to studies, Herpes Zoster (HZ) persists for life in the host after a primary infection (varicella or chickenpox). It is estimated that up to one third of infected individuals will clinically reactivate VZV in their lifetimes, usually in their elderly years when immunity is naturally senescing, or when immunity is suppressed by disease or iatrogenic cause. Each year, more than 1.5 million people in China are afflicted by HZ and its most common complication the persistence of neuropathic pain (post-herpetic neuralgia, [PHN]), with a total cost of over 1 billion RMB across China. Such huge amount of potential reactivation patient suggest a huge market of HZ vaccine.
Technical Upgrade	• Zostavax, the first zoster vaccine, was a live attenuated vaccine approved by the FDA in 2006. Although Zostavax's efficacy declines significantly within six to eight years after vaccination, the market has evolved with the introduction of Shingrix in 2017. Shingrix, a recombinant protein vaccine, offers significantly better protection as proven in clinical trials. This technical advancement resulted in Shingrix's revenues reaching US$4.3 billion in 2023, when FDA discontinued lot release of Zostavax in the same year, underscoring an expanded market share for new vaccines.

Source: Frost & Sullivan analysis

Future Trends of zoster vaccine Market

Safe and Effective	• Advances in biotechnology and production process are leading to development of zoster vaccines with improved durability and stronger immunogenic responses. These developments are suitable not only for healthy individuals but also for the elderly and immunocompromised population. Innovations such as the mRNA zoster vaccine, which are currently being tested in rhesus monkeys, show promising extended immune responses with acceptable side effects.
High Penetration	• Improved processes and technology could reduce the cost of producing zoster vaccines, thus lowering their price and driving more people to get vaccinated. In addition, the increased safety and protective efficacy of the herpes zoster vaccine can expand the applicable population of the vaccine. These two factors would increase the penetration of the zoster vaccine market.

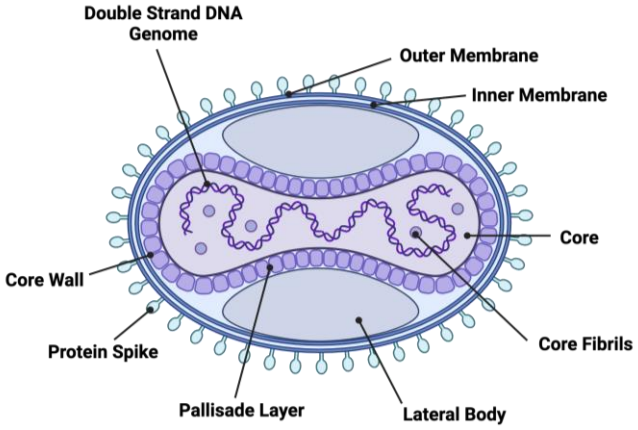
Source: Frost & Sullivan analysis

Table of Contents

Overview of Orthopoxvirus

- The genus *Orthopoxvirus* within the *Poxviridae* family includes several species, such as the variola virus (VARV), which causes smallpox and exclusively infects humans; zoonotic species like monkeypox virus (MPXV), cowpox virus (CPXV), vaccinia virus (VACV), and camelpox virus (CMLV); along with other related viruses. These orthopoxviruses share immunological cross-reactivity and cross-protection, meaning infection with one virus in this genus provides immunity against others within the same genus.

Orthopoxvirus virus structure



- Structure and Size: Orthopoxviruses (OPV) are enveloped, brick-shaped viruses measuring approximately 350 × 270 nm.
- Genome: They possess a double-stranded DNA genome of about 200 kb, with covalently linked ends.
- Antigenic Relationship: OPV species share close antigenic relationships.
- Genomic Homology: OPV exhibit significant genome-level homology across species.

Host and host specificity

Virus	Infections in	Spectrum of hosts	Natural host
Variola (VARV)	human	broad	unknown
Vaccinia (VACV)	human, buffalo, cattle, elephant, pig, rabbit, etc.	broad	rodent
Monkeypox (MPXV)	human, ape, monkey, rodent, prairie dog, etc.	broad	rodent, sciuridae
Cowpox (CPXV)	human, cat, cattle, elephant, rodent, rhinoceros, etc.	broad	rodent
Camelpox (CMLV)	camel	narrow	unknown

Transmission Routes

VARV
- Transmitted via **droplets or aerosols**.
- Initial infection occurs in the nasopharynx or respiratory tract mucosa.

MPXV
- **Zoonotic transmission** through African gophers and rodents (animal reservoirs).
- Transmission occurs via **direct contact with infected animals or their secretions**.

CPXV
- Transmitted via **skin lesions or direct contact** with infected cats, rats, or tissues.
- Human-to-human transmission is not typically reported

Other Poxvirus Species
- Typically transmitted via **direct contact** with infected animals, tissues, or secretions.

Source: Literature research, Frost & Sullivan

Overview of Orthopoxvirus

Clinical Presentation

Clinical characteristics	Smallpox	COWPOX, VACCINIA, OR SIMILAR ORTHOPOXVIRUSES
Incubation period(Days)	7-19	2-4
Fever, Malaise, Headache	Yes	Yes
Lymphadenopathy	No	Yes
Lesion distribution	Spread in a centrifugal pattern; frequently appears on the palms and soles.	Commonly confined to the hands, face, and neck.
Lesion characteristics	• Deep-seated, well-circumscribed lesions with a central umbilication. • Rash evolves gradually through stages: macule → papule → vesicle → pustule → crust. • Entire progression spans 2–4 weeks.	

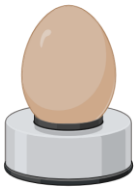
Risk, Endemicity, and Prevention

	Smallpox	COWPOX, VACCINIA, OR SIMILAR ORTHOPOXVIRUSES
Infectious agents	Variola virus	Cowpox virus, Vaccinia virus, Akhmeta virus
Endemicity	• Eradicated worldwide; • Possibility of reemergence through deliberate release (e.g., bioterrorism)	• Cowpox virus: Europe and the Caucuses • Vaccinia virus: the Americas (Argentina, Brazil, Colombia); Asia (Bangladesh, India) • Akhmeta virus: Georgia
Great Risk population	None	Travelers with direct contact with animals, particularly bovids.
Prevention method	• Vaccination	• Avoid diseased agricultural bovids. • Use appropriate personal protective equipment (PPE).

Source: Literature research, Frost & Sullivan

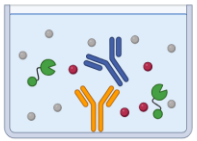
Overview of Orthopoxvirus

Diagnostic Methods

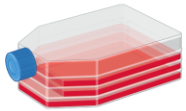


1.Chorioallantoic Membrane (CAM) Inoculation: Classical method using embryonated hen's eggs; distinguishes OPV based on morphology and histology, used in specialized labs.

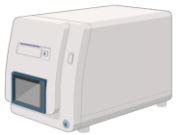
2.Electron Microscopy: Differentiates OPV from other pathogens like PPV and bacteria (e.g., Bacillus anthracis); cannot differentiate between OPV species.



3.Serology: ELISA and immunofluorescence to detect OPV-specific IgM; neutralization tests for immune status evaluation.



4.Cell Culture: OPV cultured in human or monkey cells; species differentiation performed by PCR and sequencing.



5.Nucleic Acid Test (NAT): PCR and real-time PCR methods identify and differentiate OPV species; real-time PCR provides genome quantification and melting curve analysis.

Therapy and Prophylaxis

Prophylactic Vaccination:

- VACV vaccines are available but have significant adverse reactions.
- **Post-9/11**, certain populations (e.g., military, healthcare workers) in the USA were vaccinated with VACV.
- New third-generation vaccines like **MVA and LC16m8** (licensed in Japan) are being developed with fewer side effects.
- **MVA-based vaccine (IMVAMUN**E) has shown progress in clinical trials, providing effective protection even after OPV exposure.

Chemotherapy:

•Cidofovir:

- A nucleoside phosphate inhibitor of viral DNA polymerase.
- Effective against OPV but limited by kidney toxicity and the need for intravenous administration.
- Derivative CMX001 is orally bioavailable and less toxic.

•ST246:

- Inhibits OPV exit from infected cells by targeting the F13L envelope protein.
- Effective post-symptom onset in animal models.
- Combined vaccination and ST246 administration induce protective immune responses.
- Successfully used to treat severe eczema vaccinatum in a child.

•Combination Therapy:

- CMX001 and ST246 showed synergistic effects in experimental treatments.

Passive Immunisation:

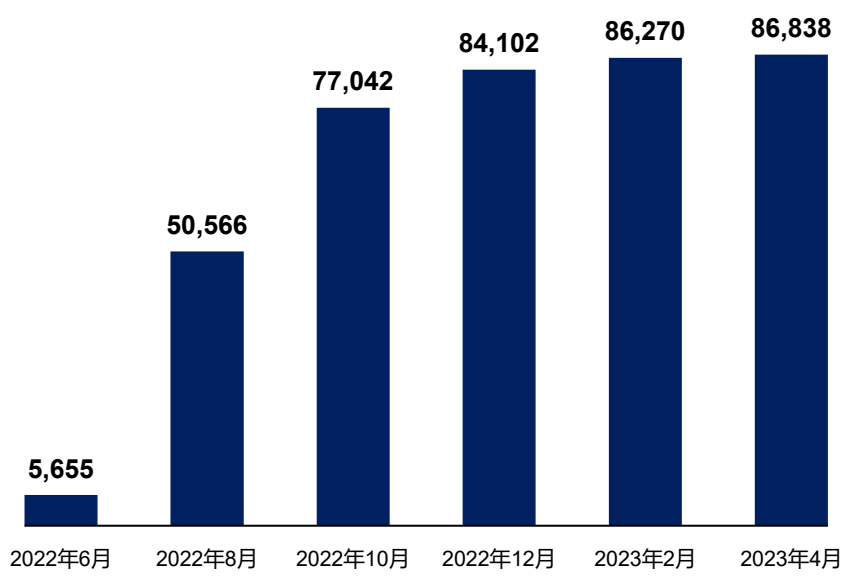
•Immunoglobulin preparations (VIG) recommended for complications associated with vaccination, limited global availability of VIG.

Source: Literature research, Frost & Sullivan

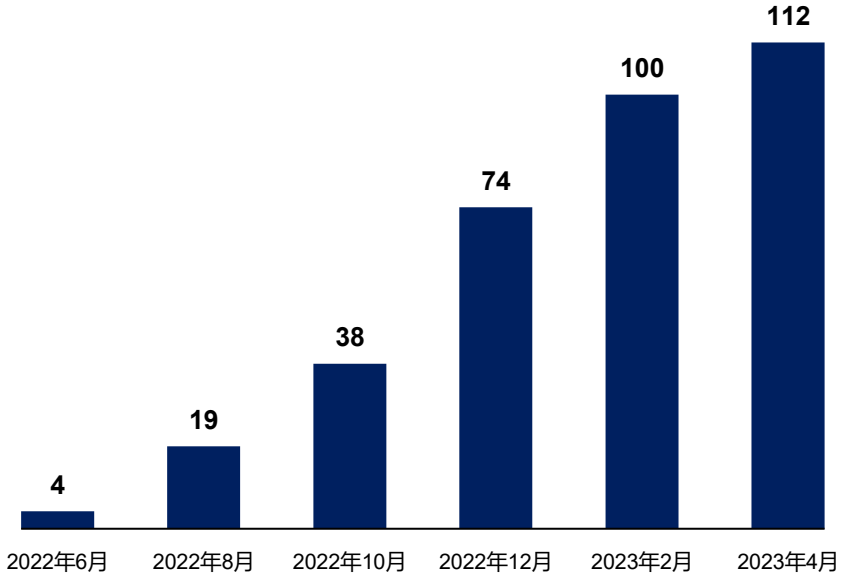
Accumulated Number of Confirmed Cases and Deaths of Monkeypox

- According to WHO data disclosure, as of April 4, 2023, there have been a total of 86,838 confirmed cases worldwide, including 112 confirmed deaths.
- According to WHO data disclosure, as of March 28, 2023, there have been a total of 24 confirmed cases of monkeypox in China, with no deaths reported.

Accumulated Number of Confirmed Cases of Monkeypox worldwide



Accumulated Confirmed Deaths from Monkeypox worldwide



Note: Data for April 2023 as of April 4, 2023

Source: WHO, Frost & Sullivan

Recommended Monkeypox vaccine by WHO and Chinese CDC for Disease Control and Prevention

WHO

- It is recommended that case contacts receive the post exposure prophylaxis vaccine (PEPV) within 4 days after their first contact (up to 14 days if asymptomatic);
- The vaccination plan should include continuous tracking and monitoring of contacts, strong information dissemination, a sound adverse drug reaction monitoring system, ideally accompanied by data collection tools and standardized protocols for conducting vaccine efficacy research, further ensuring vaccine safety, and providing effective data support for subsequent experiments.
- Whether to use monkeypox vaccine should be based on a comprehensive assessment of individual risks and benefits;
- At present, large-scale vaccination against monkeypox is not recommended. The level of exposure risk may vary by population, and in situations where vaccine supply is limited, countries can use exposure risk levels to determine priority;

WHO recommends high-risk populations to receive primary preventive vaccines

- Men who are homosexual, bisexual, or have sexual relations with multiple sexual partners
- Individuals with multiple temporary sexual partners
- Sex worker
- Laboratory personnel responsible for handling smallpox virus
- Clinical laboratories and medical staff conducting monkeypox diagnostic tests
- Members of the epidemic response team

Chinese CDC

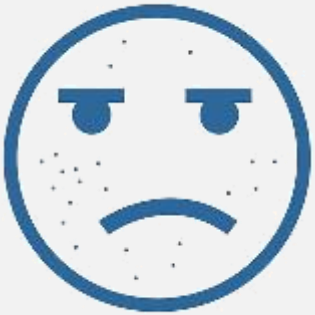
- Due to the relatively limited prevalence of monkeypox in previous areas, and the fact that monkeypox infection is a self limiting disease with usually mild clinical symptoms, comprehensive prevention and control measures mainly focused on managing the source of infection are generally adopted for monkeypox prevention. China currently does not provide widespread vaccination for the population, but specific populations can be prevented through vaccination.
- Due to the cross immunity, vaccination with smallpox vaccine can prevent monkeypox, and vaccination with smallpox vaccine before exposure can effectively protect the population from infection; Within 2 weeks after exposure, especially within the first 4 days of vaccination, about 85% of individuals can develop immunity and alleviate the severity of symptoms.

Source: WHO, Chinese CDC, Frost & Sullivan

Overview of Chickenpox

- Chickenpox is an acute systemic infectious disease caused by the varicella-zoster virus (VZV). In immunocompetent children, chickenpox is typically a benign, self-limiting illness; however, it tends to be more severe when it occurs in adults.

Symptoms



- Typically, after exposure to VZV for 14-16 days (range: 10-21 days), patients may develop the chickenpox rash. One to two days before the rash appears, patients may experience fever, fatigue, malaise, loss of appetite, and headache, with occasional mild abdominal pain. These symptoms usually resolve on their own 2-4 days after the rash appears.

Complication

- Although chickenpox is usually self-limiting, it can be accompanied by serious complications, typically caused by VZV itself or secondary bacterial infections. Non-skin complications affecting the central nervous system include conditions with a generally good prognosis, such as cerebellar ataxia, as well as more severe conditions with a poorer prognosis, such as encephalitis.
- In rare cases, these complications may lead to death, particularly in immunocompromised individuals. The most common complication in children is secondary bacterial infection, whereas in adults, the most frequent complication is pneumonia (usually viral pneumonia).

High-risk population

- Infant
- Children
- Adult
- Pregnant women
- Immunocompromised Individuals

Transmission routes

Chickenpox is highly contagious, with the highest infectivity occurring during the prodromal phase and the early stages of skin lesion appearance. It is transmitted in the following ways:

- Through inhalation of infected airborne droplets or aerosolized particles, which infect the mucous membranes (usually the nasopharynx).
- Direct contact with the virus, such as through broken skin.

资料来源：文献资料，弗若斯特沙利文分析

Treatment and Prevention of Chickenpox

- Mild cases of chickenpox require only routine treatment. However, for patients with disseminated chickenpox and those at high risk of severe disease, antiviral therapy and post-exposure prophylaxis (using antiviral medications or immune globulin) are the primary treatment options.
- The cost of the chickenpox vaccine is relatively low compared to the expenses of treating the disease, making it an economical choice that can effectively reduce individual financial and disease burdens. Vaccination is the most effective method for preventing chickenpox, making it especially necessary and urgent to use the chickenpox vaccine for prevention.

Chickenpox treatment

Routine Treatment

- Mild cases of chickenpox only require symptomatic treatment. It is important to relieve itching and avoid scratching to prevent secondary bacterial infections.
- For patients with severe itching, options include wet compresses, systemic antihistamines, or oatmeal baths to help soothe the skin.

Antiviral therapy

- Immunocompromised individuals and patients with severe complications generally require intravenous antiviral medications.
- In immunocompromised children, post-exposure prophylaxis with oral antiviral medications, such as acyclovir, can also safely and effectively prevent secondary chickenpox infections.

Immune globulin

- For high-risk individuals susceptible to severe chickenpox, post-exposure prophylaxis with VZV immune globulin is an option. However, VZV immune globulin is expensive and is not widely available in many parts of the world.

Chickenpox prevention

- Since chickenpox is highly contagious and primarily spreads through respiratory droplets and direct contact, it has a high infectivity rate, and people are generally susceptible. Chickenpox can occur year-round, with peak incidence in winter and spring, making prevention especially important.
- Currently, vaccination is the only effective method for preventing chickenpox and plays a critical role in controlling outbreaks and epidemics.

Source: WHO, Research paper, Frost & Sullivan

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Overview of Tetanus

- Tetanus is an acute specific infection caused by the entry of *Clostridium tetani* into the body through wounds.
- Tetanus is classified into neonatal tetanus and non-neonatal tetanus. China eliminated neonatal tetanus in 2012; however, non-neonatal tetanus remains a serious public health issue.

Pathogenesis

- When *Clostridium tetani* spores enter body tissues, they develop into vegetative forms in an anaerobic environment. These forms proliferate extensively and release tetanospasmin, triggering tetanus. Common causes include:

- A history of skin or mucosal injury or damage (such as animal bites, injection of drugs, childbirth, or abortion)
- A history of bacterial infection in the skin, mucosa, or soft tissues (such as chronic otitis media, chronic sinusitis, periodontal infection, perianal infection, etc.)
- A history of gastrointestinal tract injury (such as gastrointestinal surgery or perforation)

Transmission routes

Clostridium tetani is an obligate anaerobe that is widely distributed in nature, found in dust, soil, and human or animal feces. It primarily enters the body through skin or mucosal wounds, most commonly in:

- ✓ Patients with trauma or burn injuries
- ✓ Newborns delivered in unsanitary conditions
- ✓ Cases involving inadequately sterilized surgical instruments。

Clinical manifestation

The incubation period for non-neonatal tetanus is typically 3–21 days, though it can be as short as 1 day or, in rare cases, extend to over six months. The clinical manifestations of non-neonatal tetanus are classified into three types:

- ✓ Generalized Tetanus: Characterized by profuse sweating, arrhythmias, unstable hypertension or hypotension, and fever.
- ✓ Localized Tetanus: Involves tonic and spasmodic muscle contractions in a single limb or a specific area near the wound.
- ✓ Cephalic Tetanus: Presents with difficulty swallowing and cranial nerve paralysis, often accompanied by trismus (lockjaw).

Source: 非新生儿破伤风诊疗规范（2019 年版），Frost & Sullivan

Tetanus Prevention Measures and Existing Challenges

- Based on studies on various wound exposures and misconceptions in immunoprophylaxis, proper wound care and vaccination are crucial in preventing tetanus infection.
- Currently, there are certain issues within China's tetanus vaccination system; additionally, clinical standards for the use of tetanus preparations in preventive treatment are not fully standardized. As a result, there is a general lack of uniformity in preventive measures, leading to inconsistencies in tetanus prophylaxis practices.

Prevention Measures

Wound management

- Wounds are categorized based on exposure as follows: (1) clean wounds, (2) unclean wounds, and (3) contaminated wound
- Wound management measures: (1) For wounds with heavy bacterial contamination and debris, wound debridement is recommended. (2) Wound irrigation is time-sensitive and should be performed as soon as possible. (3) In some cases, patients should consider receiving oral penicillin antibiotics.

Immunoprophylaxis

- Tetanus prevention primarily relies on antibodies and can only be achieved through primary or secondary prevention.
- Primary Prevention (Active Immunization): Involves administering a vaccine containing tetanus toxoid (TT) to induce acquired immunity in the body.
- Secondary Prevention (Passive Immunization): Involves introducing immune effectors, such as Tetanus Antitoxin (TAT) or Tetanus Immunoglobulin (TIG), into the body to provide immediate immunity.

Existing Challenges

I
- There are issues within China's tetanus immunization system, as active immunization is administered by local preventive clinics, while passive immunization is handled by hospital emergency departments, creating a degree of disconnection between the two.

II
- The use of Tetanus Antitoxin (TAT) or Tetanus Immunoglobulin (TIG) results in substantial waste of limited medical resources and, in some cases, the inappropriate use of TAT poses greater medical risks than tetanus itself.

III
- Due to inadequate understanding of tetanus, many healthcare providers inform patients that immunoprophylaxis must be received within 24 hours post-injury to be effective, and some facilities even refuse immunoprophylaxis to patients if more than 24 hours have passed since the injury.

IV
- Furthermore, due to limited awareness of passive immunization, many physicians believe that patients will not develop tetanus after receiving TAT or TIG.

Source: 中国破伤风免疫预防专家共识, Frost & Sullivan

Classification of Tetanus Vaccines

Vaccine Type	Common Classification	Indications	Target Population	Representative Manufacturers
Tetanus Vaccine (Monovalent)	Adsorbed Tetanus Vaccine	• Used to prevent tetanus	Primarily for individuals at high risk of injury, pregnant women in need of booster doses, as well as newborns and postpartum women.	• Olymvax • Wuhan institute of biological products
Multivalent Vaccines	Adsorbed Diphtheria-Pertussis-Tetanus Combination Vaccine	• For booster immunization of diphtheria, pertussis, and tetanus in children who have completed the primary immunization series	Children under 12 years old	• Wuhan institute of biological products, etc.
	Acellular Pertussis Diphtheria-Tetanus Combination Vaccine	• For prevention of diphtheria, pertussis, and tetanus	Children aged 3 months to 6 years	• Wuhan institute of biological products • Beijing institute of biological products • GSK Pharmaceuticals • Chengdu institute of biological products • Sanofi • Changchun institute of biological products, etc.
	Acellular Pertussis Diphtheria-Tetanus-Influenza Type B Vaccine	• For prevention of diphtheria, tetanus, pertussis, Haemophilus influenzae type B infections, and related respiratory infections	Infants and toddlers 3 months and older	• Minhai Biotech, • Sanofi • GSK Pharmaceuticals, etc
	Acellular Pertussis Diphtheria-Tetanus-Haemophilus Influenzae Type B and Influenza Vaccine	• For prevention of diphtheria, tetanus, pertussis, Haemophilus influenzae type B infections, and influenza-related respiratory infections	Infants and toddlers 2 months and older	• Sanofi • GSK Pharmaceuticals, etc.
	Diphtheria-Tetanus-Pertussis-Polio-Haemophilus Influenzae Type B-Hepatitis B Vaccine	• For prevention of diphtheria, tetanus, pertussis, polio, Haemophilus influenzae type B infections, and hepatitis B	Infants and toddlers 6 weeks to 4 years	• Sanofi, Merck Sharp & Dohme Co., Inc.

Source: Research paper, Frost & Sullivan

Confirmation

1. According to WHO, there are around a billion cases of seasonal influenza annually, including approximately 3 to 5 million cases of severe illness that led to approximately 290,000 to 650,000 respiratory deaths annually.
2. Whole-virion inactivated influenza vaccine variant involves cultivating the influenza virus and subsequently inactivating it using heat or chemical methods.
3. IPD has a notably high mortality rates in children, particularly in low- and middle-income countries, where the mortality rate for sepsis associated with IPD can reach up to 20%, while that for meningitis can be as high as 50%.
4. Currently, PCV13 are used in infants and children and PPSV23 are used in people aged 50 years and above or people over 2 years old with increased infection risks.
5. The incidence of herpes zoster in China increased from 7.0 million in 2019 to 7.7 million in 2023. The global incidence of herpes zoster also increased from 31.0 million in 2019 to 40.8 million in 2023.
6. Initially concentrated in parts of Central and West Africa, the virus began to spread more widely, with outbreaks reported in several countries across Europe, North America and Asia. According to WHO, between January 1, 2022 and November 30, 2024 there had been a total of 117,663 confirmed cases of monkeypox worldwide, including 263 confirmed deaths.
7. Monkeypox cases also emerged sporadically in China, with a total of 951 confirmed cases between September 2023 to November 2024.
8. In terms of production revenue, the Class II vaccine market in China increased from RMB51.4 billion in 2019 to RMB92.5 billion in 2024, at a CAGR of 12.5%. Driven by increased awareness and ability to pay and introduction of new vaccines, particularly with the anticipated increase in the manufacturing of Class II vaccines in the coming years, the Class II vaccine market in China is expected to reach RMB324.4 billion in 2033, at a CAGR of 15.0% from 2024 to 2033.
9. China's quadrivalent influenza vaccine market has grown significantly. The total number of lot release increased from 9.7 million in 2019 to 46.6 million in 2024, at a CAGR of 36.8%.
10. Referencing a vaccination coverage rate of 49.3% in all people aged 6 months and older in the U.S. during the 2022-2023 season compared to an overall vaccination coverage rate of 3.8% in China for the same year, there is considerable room for improvement in China.

Confirmation

11. The global influenza vaccine market increased from US$5.3 billion in 2019 to US$6.6 billion in 2024, at a CAGR of 4.5%, and is estimated to further increase to US$12.7 billion in 2033, at a CAGR of 7.5% from 2024 to 2033. The global subunit influenza vaccine market has gradually increased from US$0.4 billion in 2019 to US$0.5 billion in 2024, and it is estimated to further increase to US$1.2 billion by 2033.
12. The PPSV23 market in China, in terms of production value, was RMB1.8 billion in 2019. Driven by the increase awareness of pneumonia awareness after the COVID outbreak in 2020, the PPSV23 market significantly increased to RMB3.4 billion in 2020, with the total number of lot release of PPSV23 vaccine also increased from 9.5 million in 2019 to 17.4 million in 2020. However, after the marketing of COVID-19 vaccines in 2021, the market size and lot release of PPSV23 have declined, remaining at approximately the same level as in 2019. The market of PPSV23 in China decreased to RMB1.2 billion in 2024 and the total number of lot release decreased to 6.2 million in 2024. However, with the increased availability more advanced products in China, the PPSV23 market in China is expected to grow in the next few years, reaching RMB5.0 billion in 2033, at a CAGR of 17.4% from 2024 to 2033.
13. The advantage and limitations of each vaccine or vaccine candidate largely depend on the technical design of the vaccines
14. As of June 19th, no RSV vaccine had been approved by the NMPA. As of the same date, there were 14 RSV vaccine candidates under clinical development in China.
15. As of June 19th, there were three RSV vaccines approved by the FDA, including two recombinant vaccines and one mRNA vaccine. As of the same date, there were 22 RSV vaccine candidates under clinical development outside China.
16. As of June 19th, there were eight marketed varicella vaccines in China, all of which are live attenuated vaccines. As of the same date, there were two varicella vaccine candidates under clinical development in China, both of which are live attenuated vaccines.
17. As of June 19th, there were six marketed single-component tetanus vaccines in China, all of which were adsorbed vaccines. As of the same date, there were four single-component tetanus vaccine candidates under clinical development in China, all of which were adsorbed vaccines.
18. As of the June 19th, no mpox vaccine had been approved by the NMPA and there was one mpox vaccine candidate under clinical development in China. As of the same date, there were two mpox vaccine approved by the FDA, which was a live attenuated vaccine, and three mpox vaccines (one live attenuated vaccine and two mRNA vaccines) under clinical development outside China.

Confirmation

19. The average bidding prices for influenza vaccines in China decreased from RMB126 per dose in 2022 to RMB125 per dose in 2023, and further decreased to RMB93 per dose in 2024. In particular, the average bidding price of split-virion vaccine dropped significantly, from RMB122 per dose in 2022 to RMB119 per does in 2023 and further to RMB85 per dose in 2024. However, influenza vaccination rate in China increased from 2.5% in the 2021-2022 influenza season to 3.8% in the 2022-2023 influenza season. For the 2023-2024 season, while no official overall influenza vaccination rate is available, it is estimated that the influenza vaccination rate in China remained relatively stable at 3.0% to 3.5%. In 2029, the influenza vaccination rate is estimated to reach approximately 9.0% to 9.5%, with an estimated average price of approximately RMB85 to RMB88 per dose. In 2033, the influenza vaccination rate in China is estimated to reach approximately 15.0% to 15.5%, with an estimated average price of approximately RMB80 to RMB85 per dose.
20. In China, varicella incidence shows a seasonal pattern, with peaks from May to June and from October to January of the following year. There were approximately 516.6 thousand reported cases of varicella in China in 2024.