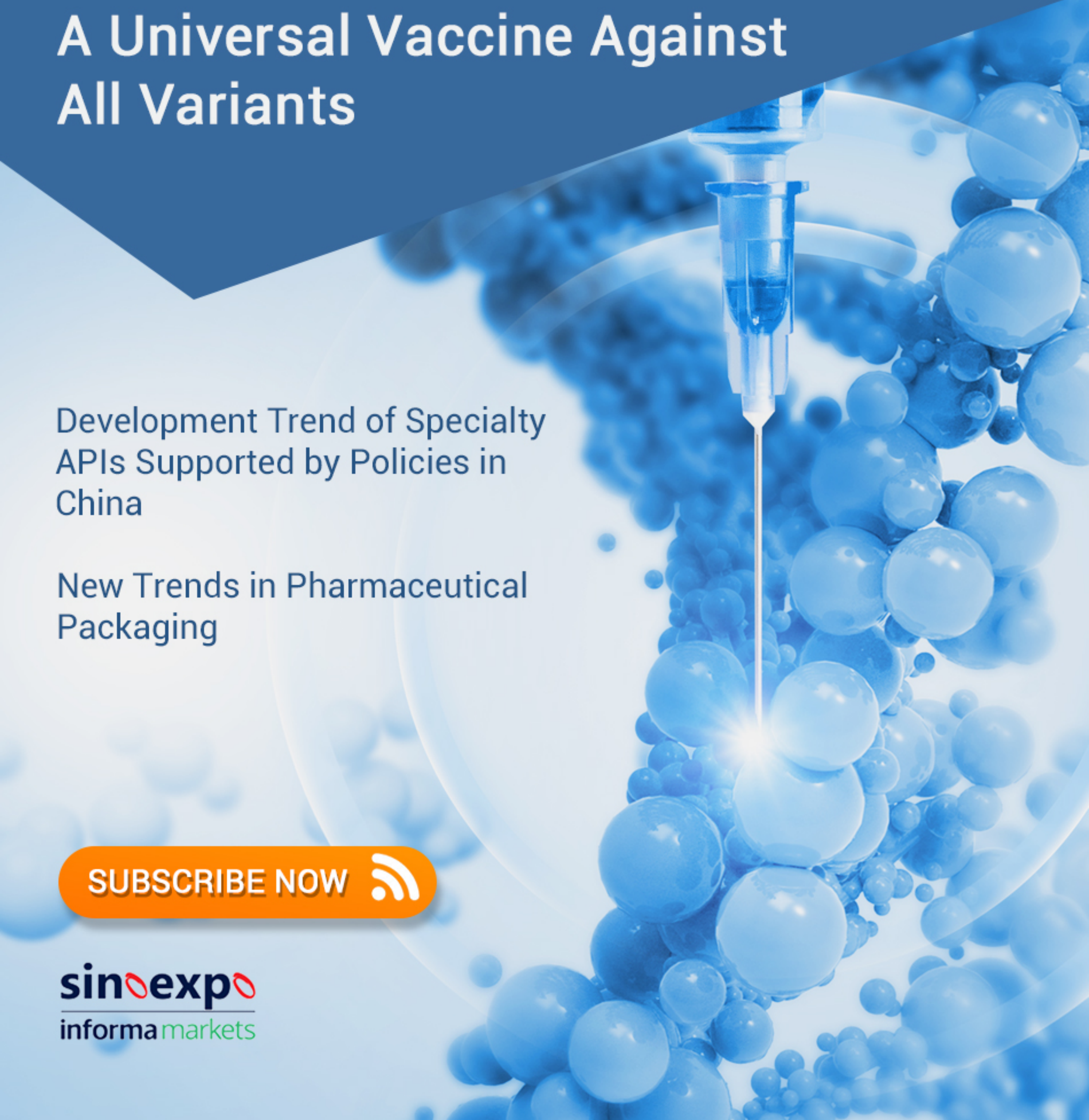
Pharma Sources Insight

APRIL 2022

A Universal Vaccine Against All Variants



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Webinars will be offered in Chinese to the Chinese audience and English to the international audience, with bilingual interpretation available.

Events Calendar 2022

30 March 2022	【Cell and Gene Therapy】 Chinese Language 13:20-14:00 New strategy for the Development of CAR-T Cell Therapy for Solid Tumors - Speaker: Zhao Yangbing | President & CSO, UTC Therapeutics Inc. 14:00-14:40 TCR-T Therapy for Solid Tumors, From Discovery to Clinical Research - Speaker: Wang Jianghua | Co-founder & CTO, CorreGene 14:40-15:20 AAV gene therapy current situation and development - Speaker: Yang Lin | Founder & Executive Director, AAVolution-Gene therapy 15:20-16:00 Experience in Preclinical Development of Cell Therapy - Speaker: Wang Quanjun | Professor, Beijing Institute of Pharmacology and Toxicology 16:00-16:30 TBC
31 March 2022	【The Future of Biomanufacturing: Capacity, Capability and Careers】 English Language - Speaker: Killian O'Driscoll, Director of Projects, National Institute for Bioprocessing Research and Training (NIBRT) - Speaker: Eric Langer, President and Managing Partner, Bioplan Associates, Inc
11-22 April 2022	【Innovative Formulation and Excipients R&D】 Chinese Language • Pediatric drug dosage form R&D strategies • Capsule Dosage Form Solutions in Drug Development - Speaker: Yang XiaoYi, Business Development of Capsugel • Sustained release dosage forms - trends of osmotic pumps • Long-acting Microsphere Dosage Form R&D and Commercial Barriers - Speaker: Shanghai Jemincare • Design and development of nano-injectable formulations • Novel excipients application in sustained-release injections R&D
13-15 April 2022	【Innovation and Development of Small Molecule Drugs】 Chinese Language · Discovery and development of therapeutics in respiratory and lung diseases (Topic TBC) - Speaker: General Manager of Ark Biosciences · Small molecules targeted agents R&D -- targeting energy metabolism in cancer · Innovation in crystal and particle engineering technology to promote CMC development · Key points of non-clinical CNS drug R&D -- from theory to practice · Trends of CDMO/CMO under the MAH system
20 April 2022 (TBC)	【Trends in peptides and oligonucleotides – choosing a partner CDMO】 English Language
27 April 2022	【Bio Insights: Cell and Gene Therapy】 English Language

Final topic and agenda are subject to change.

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Dear Readers,

In 2020, the first issue of Pharma Sources Insight launched with the early outbreak of the COVID-19 pandemic worldwide. Now, with the support of all the PharmaSources users, Pharma Sources Insight has ushered in the third year!

While the Russia-Ukraine conflict polarizing effect on the world, China is experiencing a "late spring cold" with 2000+ local confirmed cases increasing daily in the country. Although the fight against COVID-19 worldwide is tough, scientists are getting their way to discover the truth about the virus. In this issue, we will have a look at "**A Universal Vaccine Against All Variants of COVID and SARS**", and as China has been playing a key role in the supply of the COVID-19 products, it is time to review "**The Export Status of Chinese COVID-19 Vaccine in 2021**". And Dr. Preet Pal S.B. shares his opinion on "**The Impact of Russia-Ukraine Conflict on Pharma Business**".

On Feb.10th, 2022, the ODAC meeting held by FDA brought about widespread attention, which decided that Eli Lilly and Company and Innovent Biologics must conduct a trial for the Sintilimab to be applicable in the U.S. population. It means Innovent's PD-1 suffered a setback in the marketing of the overseas market. Two weeks later, Legend Biotech announced that CARVYKTI™ (ciltacabtagene autoleucel), a BCMA-directed CAR-T therapy, received FDA Approval to treat adult patients with relapsed or refractory multiple myeloma. Looking back to 2021, "**With Sky-high Price, CAR-T Therapy Sold at Least USD 1,709 Billion in 2021**". Besides, we will also discuss **trends and development in the HIV** and **bispecific antibody therapeutics market**.

According to our research, most PSI readers have indicated their interest in the API industry and the Chinese pharmaceutical market. In response to the readers, we will turn our perspective on "**The Development Trend of Specialty APIs Supported by Policies in China**", and "**A New Record of the Innovative TCM Approval with Chinese Reform of Review and Approval Systems**".

In "Industry Insight", as an expert of pharmaceutical engineering and technology, our newly joined writer, Mr. Muhammad Asim Niazi, will introduce "**New Trends in Pharmaceutical Packaging**" for the benefit of the users in the relevant areas.

It is no doubt that more is to come for the pharmaceutical market in 2022, including the rising cost of APIs and some crucial materials, the global supply chain tensions, and M&A across the pharma enterprises internationally. And China endeavors to increase the differentiation of innovative drugs and lowering the drug prices to improve patient accessibility.

Based on the Chinese market, Pharma Sources Insight seeks to bring more and more professional pharmaceutical news in the cutting-edge area, welcoming more and more new readers to join as members of PharmaSources.com. Thank you for being with us!

Sincerely,
Editor in Chief
Pharma Sources Insight

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A Universal Vaccine Against All Variants of COVID and SARS

By Lin Zhang

Keywords: Coronaviruses Vaccine, Spike-Ferritin-Nanoparticle, variants

The Covid-19 pandemic changed a massive influence on human life around the world and led to many negative consequences in terms of global health, tourism, economics, and many other things. Today, the pandemic continues across the world, although two mRNA-based vaccines and an adenovirus vector-based vaccine have been approved for emergency use in the United States and reduce mortality rates for COVID-19. (1-2)

However, there are currently significant and growing concerns about more contagious new COVID-19 variant, Omicron that will spread more easily than the original SARS-CoV-2 virus, more likely to reinfect individuals who have survived COVID, and even more resistant to vaccines according to the Centers for Disease Control and Prevention (CDC). (3) This is likely to contribute to a new wave with as many as a predicted 60% of people infected by March and 140 million new infections beyond that in the United States. (1, 4) Therefore, it is strongly suggested that only the effective and safer vaccine can control this vicious pandemic.

The universal SpFN vaccine

Currently, many platforms have been designed for developing the most efficacious and safe vaccines designed by different technologies including protein subunit, RNA, DNA, viral vector, inactivated, and live attenuated approaches.(5)

The good news is that recently U.S. Army, scientists at Walter Reed Army Institute of Research have developed a universal vaccine called Spike-Ferritin-Nanoparticle (SpFN) that effective against all variants of COVID and SARS including Omicron known to man and potential variants of the viruses.(6) Upon vaccination, the host will generate a strong immune response and broad protection against multiple COVID and SARS variants.

The mechanism of the SpFN vaccine

Unlike most currently available vaccines, which use mRNA to trigger the immune system. This novel vaccine is designed on a new platform called "self-assembling protein nanoparticle,"(7)

which operates based on a spike-ferritin nanoparticle or SpFN immunogen paired with two distinct adjuvants, Alhydrogel® or Army Liposome Formulation containing QS-21 (ALFQ, a vaccine adjuvant) for unique vaccine evoked immune signatures,(8) and offer the advantage of multivalent antigen presentation, which is a pivotal innovation as a vaccine adjuvant that provides excellent safety and potency and could lead to dual-use military and civilian benefits.

According to US Pentagon, Defense One, ferritin is a naturally occurring, ubiquitous, iron-carrying protein that self-oligomerizes into a 24-unit spherical particle. (9) Each of the molecule's 24 different faces could carry a different spike protein drawn from unique COVID variants, creating a strong and broad immune response through SARS-CoV-2 spike-specific T cells that might be effective across different strains. (8,10)

Furthermore, SpFN protected against a potent viral challenge, as replicating virus concentrations detected in the upper and lower airways of unvaccinated controls reached a mean of 106-107 copies/ml. SpFN also protected lower airway viral burden and disease as early as within one day of virus inoculation. (11)

Today's status of the vaccine

The vaccine is not yet fully developed. Early results in primates suggest the vaccine could work against COVID-19 variants and other coronaviruses as well. (6)

Currently, the vaccine is in its phase I clinical studies (NCT04784767)(12), which started in April 2021 is a first-in-human study of the safety, tolerability, and immunogenicity of different doses of SpFN vaccine against COVID-19 in healthy adults. This study enrolled a total of 72 healthy adult participants (age range 18-55) to evaluate the safety, reactogenicity, and immune response of the SpFN COVID-19 vaccine on human subjects who had neither been vaccinated nor previously infected with COVID. Next, the vaccine will need to be tested on human subjects who have been vaccinated or previously tested positive for the virus.

The official report of the results is yet to come and the preliminary results provide good reasons to be hopeful, it is sure to take some time to get approval and produced. It is believed that a new and better way of managing the COVID-19 pandemic is possible and that new and existing strains could be targeted through a single vaccine.

Advantages of the SpFN vaccine

The advantages of this universal vaccine are clear. One of the central concerns with variants like Delta and Omicron are their own danger, as well as the possibility of emerging new strains that could appear faster than individuals can get vaccinated for the previous strain. This new vaccine would negate this concern, as it could protect individuals from many strains, including emerging ones. Rather than needing several vaccines and boosters, the person would only require a single one to stay safe even if new, more contagious, or dangerous variants emerge. This makes it a strong line of defense against existing and emerging variants.

The second advantage is that the vaccine can create a strong immune response when applied that is likely to lead to stronger and longer protection according to preliminary results. This is good news in the situation when existing vaccines are proving less effective against new variants like Omicron.

It appears that the vaccine may be effective not only against the current strain of coronavirus but also against the SARS strain that emerged in 2002 and others. (8) This means that a single vaccine could do a lot to protect individuals from various strains, emerging viruses, and variants of the same one, by targeting a particular characteristic that is common among most coronaviruses.

What's the outlook?

This is very good news indeed and the future looks bright. This vaccine technology is still early in the development process, but the preliminary results suggest that it should have good outcomes with safe, effective and durable protection,(6) and might become a new first line of defense against multiple coronavirus strains, species and the next pandemic. Therefore, our immune response to the viruses could become a lot stronger and more enduring protecting people from damaging public health as much as has happened so far.

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About the Author:

Lin Zhang

Lin Zhang, Ph.D., senior director of a health care industry company in the United States. With the experience in clinical medicine, biotechnology, health industry and other fields, he is responsible for the research and development of plant medicine, functional food and health products. He was a clinician and worked for the National Cancer Institute, FDA and the National Cancer Center of Japan for many years.

A Look at the Export Status of Chinese COVID-19 Vaccine in 2021

By Xiaoyaowan

Keywords: human vaccine, vaccine export, Chinese vaccines

According to reports, the cumulative value of China's human vaccine exports reached RMB 101.04 billion in 2021. According to the press conference of the Ministry of Foreign Affairs and CCTV News, as of December 26, China has supplied more than 2 billion doses of COVID-19 vaccines or stock solutions to the world.

Five Chinese COVID-19 Vaccines Exported by China to Overseas Markets in 2021

On May 7, 2021, Sinopharm Beijing Institute has received emergency use authorization from the World Health Organization (WHO) for its inactivated viral vaccine to be promoted and used globally. The inactivated COVID-19 vaccine developed by Beijing Institute is the first in China and the sixth in the world to be added to the WHO's emergency use list.

In mid-October 2020, Sinovac applied to be included in the list of emergency use to WHO and handed in relevant materials according to WHO's requirements for continuous evaluation of vaccine safety, efficacy, and product quality. In early June 2021, with the WHO's approval, the inactivated COVID-19 vaccine was officially included in the emergency use list, followed by Sinopharm Beijing Institute, and Sinovac joined the COVAX program of WHO together with Sinopharm Beijing Institute. It supplied China's COVID-19 vaccine and brought the Chinese solution to the epidemic response for most developing countries where vaccines are in short supply.

On June 22 of the same year, the Chinese Ministry of Commerce and other three departments announced the inclusion of four vaccines that had been conditionally approved for marketing in China in the list of COVID-19 vaccine products available for export. It expressed support for the Chinese vaccine manufacturers to export in a self-operated manner. The list would be adjusted dynamically in due course according to the approval and marketing by the National Medical Products Administration.

Five Chinese COVID-19 Vaccines Exported in 2021

Manufacturer	Vaccine Type	Annual Capacity	Overseas Access
China National Biotec Group(CNBG)	Inactivated viral vaccine	More than 5 billion doses	Approved for emergency use in WHO EUL, 112+ countries, regions and organizations
Sinovac Biotech	Inactivated viral vaccine	More than 2 billion doses	Approved for emergency use or conditional marketing in WHO EUL, 50+ countries, regions and organizations
CanSino Biologics	Adenovirus vector vaccine	500 million doses	Approved for emergency use or conditional marketing in Mexico, Pakistan and other countries
Zhifei Biological	Recombinant subunit vaccine	300-600 million doses	Approved for use in Uzbekistan, Indonesia and other countries
Kangtai Biological	Adenovirus vector vaccine	200 million doses	Approved for emergency use in India

Source: The company's official websites, Guotai Junan Securities

In October, the COVID-19 vaccines of five Chinese vaccine manufacturers, Sinopharm Zhongsheng, Sinovac Biotech, CanSino Biologics, Zhifei Biological, and Kangtai Biological, were exported to the overseas markets, including three types of COVID-19 vaccine, with a total annual production capacity of over 8 billion doses.

The Top Five Countries in Chinese COVID-19 Vaccine Export

Globally, countries or regions with vaccine production or R&D capabilities in 2021 are mainly in Europe, the United States, Japan, India, and China, with high comprehensive and technical strength, and countries with relatively large populations such as Indonesia, Bangladesh, and Brazil.

China's vaccine export orders are increasing, and its products have covered more than 112 countries, regions, and international organizations worldwide. From the perspective of the export region, the main export destinations of the Chinese COVID-19 vaccines are Southeast Asia and the Middle East.

The value of exports for the whole year of 2021 exceeded RMB 100 billion, with the highest export value of RMB 16 billion in July and the lowest export value of about RMB 2.12 billion in January. Statistics from the General Administration of Customs show that the Top 5 exporters of COVID-19 vaccines in 2021 are Indonesia, Pakistan, the United Arab Emirates, Brazil, and Turkey. Overall, China is the major supplier of COVID-19 vaccines to developing countries.

China has Become a Major Supplier of COVID-19 Vaccines to Developing Countries

Since the outbreak of COVID-19 pandemic, General Secretary Xi has actively promoted the progress of international cooperation on vaccines on many international occasions.

On August 5, General Secretary Xi said at the first meeting of the COVID-19 vaccine Cooperation International Forum that China will strive to provide 2 billion doses of vaccines to the world in 2021. On November 12, when General Secretary Xi attended the APEC meeting, he reiterated the export commitment of 2 billion doses for the whole year. On August 5, at the first meeting of the International Forum, General Secretary Xi Jinping said that China will provide another 1 billion doses of vaccines to African countries, 600 million of which will be free of charge, and will also provide 150 million doses of vaccines to ASEAN countries free of charge.

As a major supplier of global public goods, China has actively contributed to achieving the availability and affordability of COVID-19 vaccines in developing countries.

About the Author:

Xiaoyaowan

Xiaoyaowan, a pharmaceutical industry practitioner, a word carrier in the We-media era focusing on changes of the pharma industry.

Worth Reading:

Fighting Against COVID-19: Summary of Key Products

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Global Market Review APRIL 2022

The Impact of Russian-Ukrainian conflict on Pharma Business

By Dr. Preet Pal S.B.

Keywords: Russia-Ukraine conflict, pharma industry, business opportunities

Russian-Ukraine is one of the biggest military conflicts since the end of the cold war. It had a polarizing effect on the world. However, this conflict has abruptly changed the business environment in the region. It would have a significant impact on how the pharma business is done in the ex-Soviet region.

Here, it is vital to understand that although impact of this conflict on the region involved would be largely negative, it may also offer specific opportunities.

In the short term, its impact is relatively easy to guess. It means a significant decline in the GDP of Ukraine, Russia, Belarus, and some other ex-soviet countries (and thus a decline in the pharma market). Moreover, it is likely to lead to prolonged stagnation in the business in the region.

Impact of economic and other sanctions on Russia on pharma business

The severe economic sanctions would significantly impact Russia, Belarus, and perhaps certain regions of Ukraine (separated territories). Some are already describing these sanctions carried out by the US and EU as one of the harshest ever.

However, it would have a broader negative impact on the regions. Countries that are significantly aligned with Russia, like Central Asian nations, may also experience economic hardships.

Although these sanctions do not include the pharmaceutical industry of healthcare products, at least at the time of writing of this article, but the industry would be affected due to other economic sanctions.

Although Russia produces 70% of drugs locally by volume, value-wise, it is just the opposite. It means Russia imports 70% of drugs in terms of value.

In 2021, EU and US pharma companies (Russia and neighboring

states) dominated the market in value terms. Some of the leading companies were Johnson & Johnson, Bayer Healthcare, Sanofi-Aventis, Roche, Novartis, Pfizer, Merck, GlaxoSmithKline, Sevier, Takeda, and so on.

As one can see, the EU and US dominated the pharma sector, and most of the top 10 companies in Russia are from the nations that have implemented the most stringent economic sanctions.

As already mentioned, these sanctions do not cover the pharma sector. Thus, these companies are expected to continue operating in the country. However, they would inevitably be affected by sanctions like those on the banking sector, transfer of technology, and others. This may have a considerable negative impact on their business.

It is worth understanding that most Russian banks have been sanctioned by the west, removed from Swift, and their assets were frozen. Thus, Russian banks are not likely to deal with many banks in the west. Of course, there are exceptions. Nevertheless, it is clear that EU and US-based pharma multinationals that traditionally dominated the market would see their turnovers and profits shrinking.

Moreover, they would also be influenced by changing public attitudes towards some of these companies in the region.

This impact would be significantly felt in Russia and Belarus. However, these companies may experience a decline in their business in Ukraine and Central Asia.

On the other hand, it may mean low competition for small to midcap companies. This may also pose a business opportunity for some.

Changes in patent laws and future regulatory changes, and their impact on pharma business

The Pharma industry is one of the most regulated industries. One of the ways in which big pharma multinationals from the EU and the US would be hit hard is due to changes in the Russian intellectual property laws.

Russia has already created a list of so-called non-friendly nations in response to Western sanctions, covering mainly the US and EU. As per this law, Russia may not respect any patent filings for companies from these nations. This means that suddenly, numerous drugs may become off-patent in Russia.

It may significantly open opportunities for some API sellers, traders, small pharmaceutical companies. Moreover, it means that Russian pharma companies may start manufacturing generic versions of patent-protected drugs in the coming months.

Some countries that have not ratified these treaties regarding patent protection like Bangladesh or Pakistan may start exploring the Russian pharma market. Of course, any such business comes with risk, as any business with Russia risks being sanctioned. However, for some smaller manufacturers, or those without any significant international footprint, that may not essentially be a barrier.

Additionally, it still remains to be seen if this conflict also results in regulatory changes in the country. However, considering the severity of the conflict, it is quite likely that Russia will implement significant regulatory changes in the pharma sector in the coming months.

Additionally, it is worth understanding that Russia has an economic union with Belarus, Kazakhstan, Kyrgyzstan, and Armenia (Eurasian Economic Union). Therefore, it means any changes in the patent laws and regulatory norms in Russia would directly impact these markets.

Impact of conflict on the local pharma industry of the region

For the local manufacturer of Russia and Eurasian Economic Union (EEU) at large, these sanctions may not have much negative impact. It is because they do not source much from Europe. Instead, it may mean an opportunity to expand their

business for them.

The local pharma producers in Russia are also quite likely to receive some additional support. Thus, the market share of local pharma manufacturers in Russia is expected to rise. Moreover, they would benefit from the lifting of specific patent protection for multinationals.

Additionally, it is worth understanding that many of the local manufacturing units have investments from multinational pharma companies. However, disinvestment by pharma giants from these units might not have any significant impact on the working of these units.

Ukraine also has significant local manufacturing of pharmaceuticals. In the short run, most companies may experience a substantial decline in business due to the economic impact of the conflict and outflow of the population. However, the long-term impacts of the war on the local pharma industry of Ukraine are more challenging to predict.

What business opportunities could this conflict create?

Any conflict or war results in significant human tragedy. Nevertheless, resulting changes in the legal framework in the region, changes in the regulatory environment, economic changes may also pose certain business opportunities for specific players of the industry.

Generally, it may provide business opportunities for the smaller companies in the midterm. And these opportunities will come due to many reasons like the exit of multinationals from the regions, reduced competition in the market, changes in patent laws, and other regulatory changes.

Generally, in the coming years, the market is expected to become more favorable for small-cap and mid-cap companies with a limited presence in the international market. It is because such pharma companies adapt faster to changing market conditions, they are more ready to find new ways of doing business. However, more importantly, such companies are less likely to be affected by economic sanctions against Russia.

Similarly, the market for pharma APIs, intermediates, excipients may fall in the coming year. However, it may show robust growth in the near future due to increased local production of generics.

To conclude, the Russian-Ukrainian conflict would have a significant negative impact on the business environment in the region. GDP of most nations, especially those of Russia and Ukraine, would shrink considerably. This conflict would also have an adverse economic impact on other EEU countries. All this means a significant recession in the industry in the near future. Nonetheless, significant regulatory changes in the region may also provide opportunities for certain businesses.

About the Author:

Dr. Preet Pal S.B.

Dr. Preet Pal S.B. is a physician (M.D. Medicine, Kazakh National Medical University) specializing in diabetes (Fellowship in diabetes), a lifetime member of the Indian Medical Association. Dr. Preet has vast business development experience in the ex-soviet republics/ CIS region (Ukraine, Kazakhstan, Uzbekistan, Russia, Kyrgyzstan, Azerbaijan, and so on). Dr. Preet is a multilinguistic. He has held senior management posts in various healthcare/pharmaceutical companies like SEARLE – central Asia (now a subdivision of Pfizer), Shreya life sciences, AGIO pharma, Indian Immunological Limited (Human and veterinary biologicals).

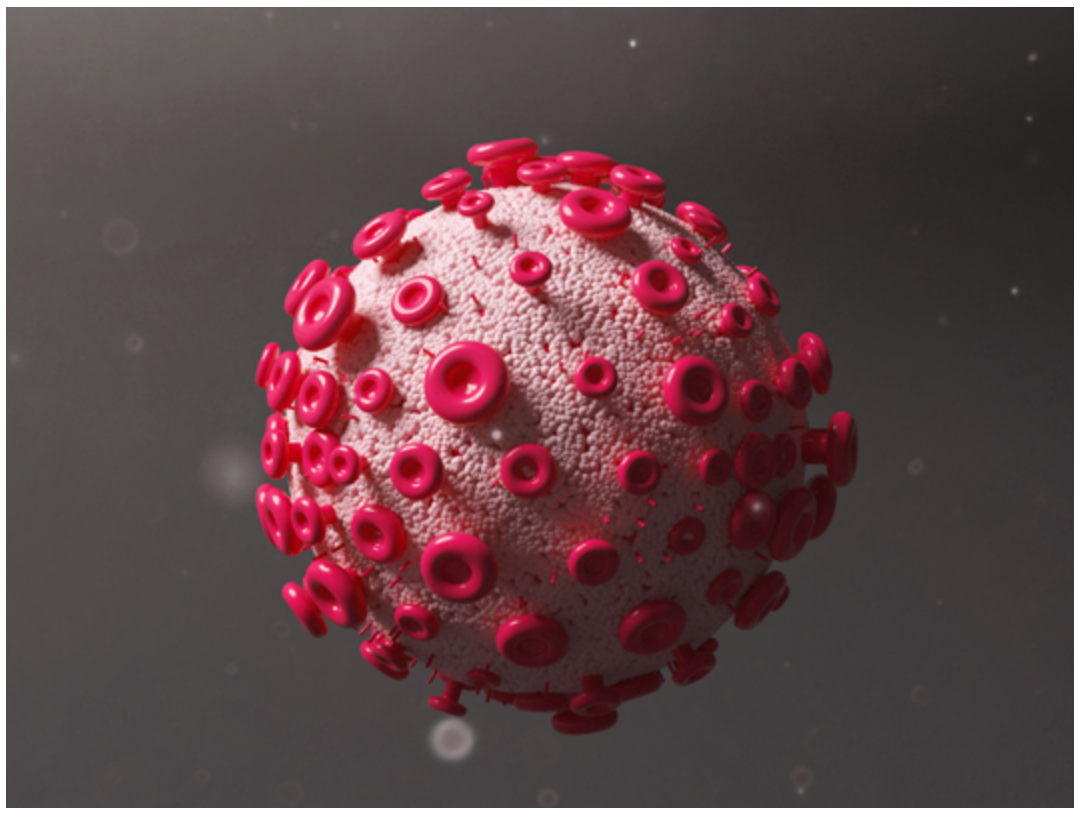
Dr. Preet is also a prolific writer and loves sharing my experiences. He firmly believe that an approach towards emerging markets differs considerably from developed markets. The bigger part of the global population resides in emerging markets. Yet, regretfully, most market reports remain focused on the developed markets. Even if they focus on emerging markets, they often use insights gained from developed markets.

Global Market Review APRIL 2022

Trends and Developments in HIV Research

By Neeta Ratanghayra

Keywords: HIV vaccines, HIV therapies, Imbokodo



Novel treatment strategies and advances in care have transformed the lives of people living with HIV (human immunodeficiency virus). Antiretroviral therapy (ART), once-daily single-tablet regimens (STRs), and PrEP (pre-exposure prophylaxis) are some major milestones that have changed the trajectory of the deadly disease.

The change has been disruptive, but HIV continues to remain a global public issue. Worldwide, around 38 million people are living with HIV and there is an unmet need for more effective drug candidates and strategies for treatment as well as prevention of new infections.

This article covers some recent developments in the management of HIV.

The Advent of Long-Acting Therapies

Long-acting therapies are set to make a huge difference in the lives of people living with HIV. These therapies don't need to be taken daily and can be dosed weekly or monthly - a feature that may improve patient convenience and improve treatment adherence by eliminating the daily reminder of treatment.

Long-acting therapies can be specifically useful in the pediatric populations with HIV, a group with huge unmet needs. By reducing the frequency of treatment administration in children, long-acting therapies can improve quality of life and adherence to regimens.

ViiV Healthcare's CABENUVA, approved by the FDA in January 2021, is the first long-acting injectable HIV treatment in the market. The therapy consisting of one cabotegravir injection and one rilpivirine injection needs to be administered just once a month. FDA also approved VOCABRIA (cabotegravir) 30 mg tablets which should be taken in combination with oral rilpivirine (EDURANT) for one month before starting treatment with CABENUVA to ensure the medications are well-tolerated before switching to the extended-release injectable formulation.

In December 2021, FDA approved ViiV's Apretude (cabotegravir extended-release injectable suspension) for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV. Apretude is given first as two initiation injections administered one month apart, and then every two months thereafter.

Apart from ViiV Healthcare, Gilead is expected to complete regulatory filings this year for their long-acting self-injectable HIV treatment lenacapavir. Lenacapavir must be injected once every six months. If approved, the HIV-1 capsid inhibitor will be the first approved treatment of its kind. Lenacapavir (in combination with other treatments) is being developed for heavily treated patients who have become resistant to multiple drugs, a particularly difficult-to-treat group of patients.

HIV Vaccines – A Promising Strategy to Fight HIV

An effective HIV vaccine can help combat HIV and is seen as a potential strategy to curb this deadly disease. Mosaic-based vaccines and messenger RNA (mRNA) vaccines are some novel technologies being evaluated.

Mosaic-based vaccines consist of mosaic immunogens, such as a mosaic glycoprotein 140 (gp140). These immunogens, which are delivered through viral vectors, have the capacity to

induce a broad immune response as they are made up of pieces of different HIV strains.

In September 2021, Janssen's mosaic-based HIV vaccine candidate failed to offer substantial protection against the disease in the Phase IIb Imbokodo clinical trial in women in sub-Saharan Africa. The company decided to discontinue the Imbokodo study.

The Imbokodo study is discontinued, but Janssen is continuing the Phase 3 Mosaico study. The Mosaico study is testing the safety and efficacy of a different composition of the HIV vaccine regimen among men who have sex with men (MSM) and transgender individuals. The trial is being conducted in the Americas and Europe where different strains of HIV are circulating.

The success with mRNA vaccines for COVID-19 has generated hopes that mRNA techniques can also be used in HIV. Many research groups including the International AIDS Vaccine Initiative (IAVI) are working towards this mission. Moderna, the company which developed the COVID-19 mRNA vaccine is set to test its vaccine candidate mRNA-1644 for HIV. mRNA-1644 is based on the same mRNA platform as the COVID-19 vaccine.

Apart from mRNA vaccines, researchers are also considering replicating viral vector-based (Vesticular Stomatitis Virus) vaccine comprising a recombinant VSV vector that incorporates an HIV envelope gene.

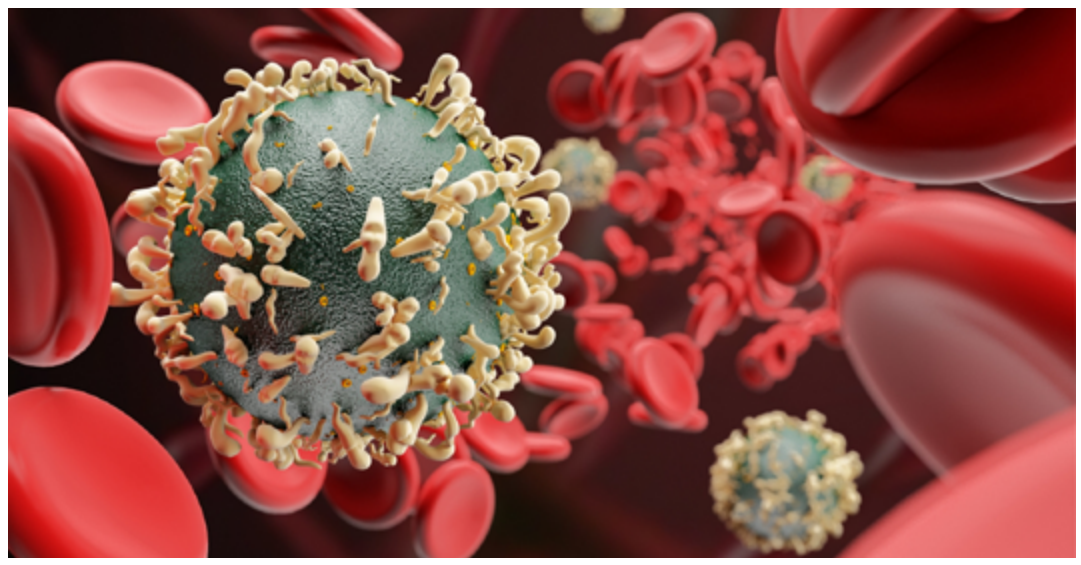
A vaccine can do wonders, but the development of an HIV vaccine is easier said than done. HIV is a highly variable virus and can easily target immune cells and integrate into the host genome causing infection as well as latent infection. Another factor is the lack of evidence for what exactly constitutes an appropriate immune response to HIV.

A Cure for HIV - How Close are We?

A cure for HIV may be the final phase of HIV control but developing a cure is challenging. HIV has the ability to hide itself and lay dormant in pockets of host T cells. These pockets, known as “latent viral reservoirs", can be found in peripheral blood, lymph nodes, gut-associated lymphoid tissue, T lymphocytes, and the central nervous system.

Latent viral reservoirs are unrecognized as harboring HIV by the immune system and can remerge if ART is stopped after achieving successful HIV suppression. Additionally, these viral reservoirs can persist despite years of treatment with anti-HIV drugs.

Elimination of the viral reservoirs is key to HIV cure, but evidence suggests that more than 70 years of continuous, fully suppressive HIV treatment is required to completely eliminate the HIV reservoir. Another option is the induction of HIV from its latent state, which would decrease reservoir load and reduce the time to eradication. Several concepts have been explored to combat latency and a few are described below:



- Shock-and-kill approaches – This involves the administration of latency reversal agents, which reactivate latent HIV hiding in immune cells. The next step is the elimination of the reactivated cells using the body's immune system (host immune clearance and HIV-cytolysis) or anti-HIV drugs.
- Induction of deep latency – In this approach, the HIV reservoirs are deeply silenced to induce the proviral HIV so that HIV would not rebound, or the rebound is significantly delayed even when treatment is stopped.
- Precise excision of integrated proviruses via CRISPR-Cas9 or other precision nuclease technologies

ViiV Healthcare, Gilead Sciences, and Excision Biotherapeutics are some companies working towards developing a cure for HIV.

HIV therapies - Developments in China

HIV remains a major problem in China, with AIDS-related mortality rising sharply in recent years. The HIV market landscape in China is largely dominated by global companies, but due to the huge potential for HIV treatment in China, many local companies have joined the race.

In 2018, the first Chinese proprietary HIV therapy injectable Ai Ke Ning (albuvirtide) was approved. Albuvirtide is a long-acting fusion inhibitor developed by Frontier Biotechnologies. The drug is to be administered by a once-weekly injection.

National Medical Products Administration (NMPA) has

approved the Abbreviated New Drug Application (ANDA) for the generic version of Truvada (emtricitabine/tenofovir). The generic made by Chai Tai-Tianqing Pharmaceutical will be the first Chinese-made HIV combination tablet in the country.

In June 2021, China's Jiangsu Aidea Pharmaceuticals received marketing approval from Chinese health authorities for Ainuovirine (ACC007), a new -nucleoside reverse transcriptase inhibitor (NNRTI). As the first oral HIV treatment in China, Ainuovirine is expected to take a huge market share.

In July 2021, NMPA gave conditional approval to Henan Sincere Biotech Co. Ltd.'s dual-targeting, oral HIV drug, azvudine, to treat HIV-1-infected adult patients with high viral loads.

Ascletis is developing ASC09F, a combination tablet containing ritonavir and ASC09, a protease inhibitor. In 2020, Ascletis received investigational new drug (IND) approval for ASC09F. A phase I pharmacokinetic trial has been completed in China for the drug.

The Need for Continuous Research

By transforming care, innovations can change the trajectory of the HIV epidemic and improve patient outcomes. Identifying knowledge gaps and priority areas as well as including knowledge from fields such as COVID-19 can facilitate progress in HIV research.

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Neeta Ratanghayra is a freelance medical writer, who creates quality medical content for Pharma and healthcare industries. A Master's degree in Pharmacy and a strong passion for writing made her venture into the world of medical writing. She believes that effective content forms the media through which innovations and developments in pharma/healthcare can be communicated to the world.

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With Sky-high Price, CAR-T Therapy Sold at Least USD1.709 Billion in 2021

By Yi

Keywords: CAR-T therapy, CAR-T therapy Price, CAR-T therapy Approval

Currently, six CART-cell immunotherapies have been approved in China and abroad, as shown in the table below. Except for Abecma, the other five therapies are all targeted at CD19.

Globally Approved CAR-T Therapy

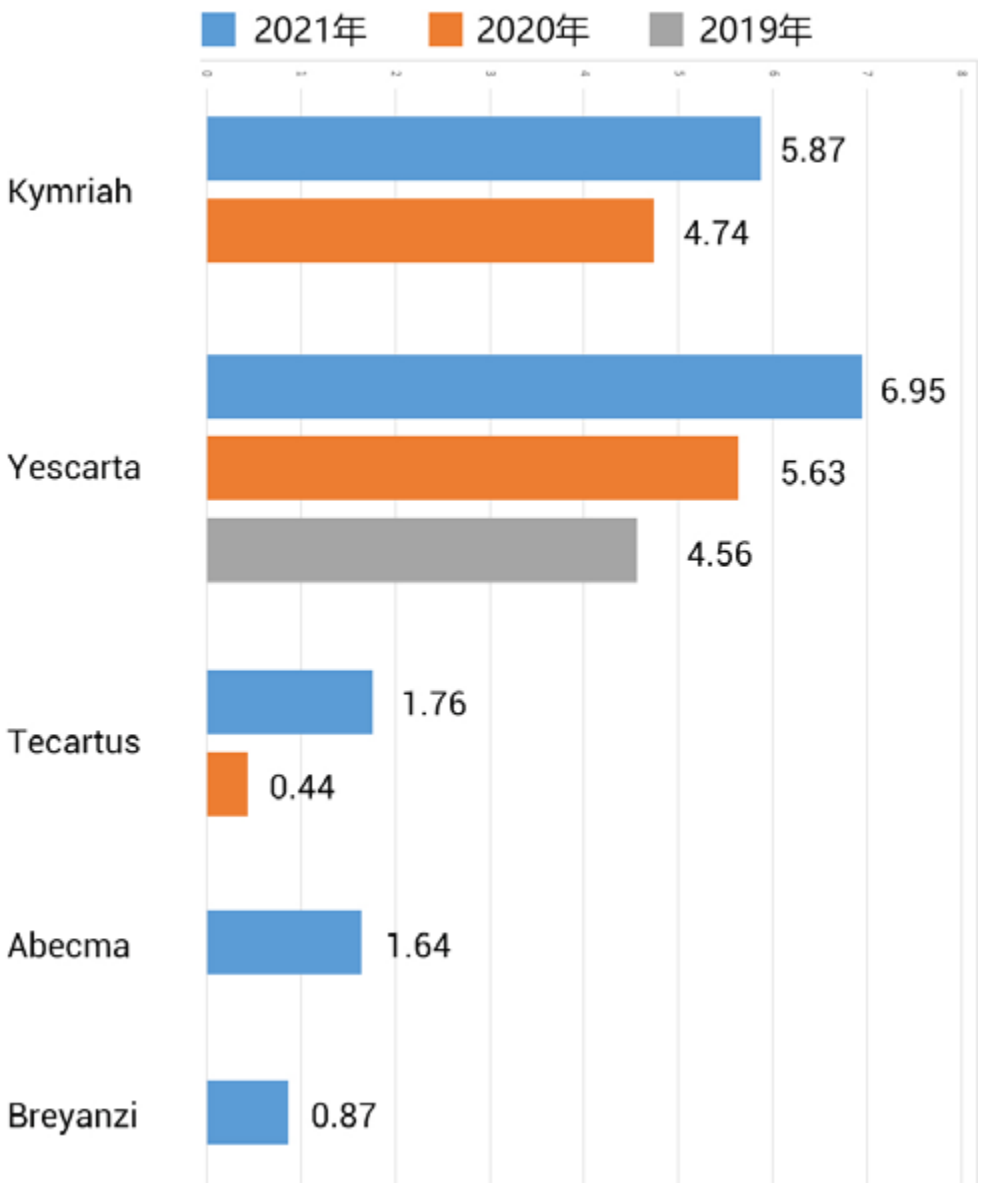
Trade name	Generic name	Effect target	Company
Kymriah	Tisagenlecleucel	CD19	Novartis
Yescarta	Yescarta	CD19	Gilead
Tecartus	Brexucabtagene Autoleucel	CD19	Gilead
Breyanzi	Lisocabtagene Maraleucel	CD19	BMS
Abecma	Idecabtagene Vicleucel	BCMA	BMS/Bluebird Bio
Beinuoda	Relmacabtagene Autoleucel	CD19	JW Therapeutics

Source: Public information

With the announcement of the companies' financial report, the sales volume of the above five CAR-T therapies in 2021 also came out along. Relmacabtagene Autoleucel is CART-cell immunotherapy developed by JW Therapeutics based on Juno's JCAR017 (i.e. Breyanzi), approved by NMPA in China in September 2021 to treat relapsed or refractory large B-cell lymphoma in adult patients after second-line or above systemic therapy.

In terms of timeline, the CAR-T therapy market size is expanding from 2019 to 2021. The market sizes in these three years were US $734 million, US $1081 million and US $1.709 billion respectively. And according to Frost & Sullivan's report: From 2019 to 2024, the compound annual growth rate of CAR-T therapy market size is 55.0%, and the market size will expand to USD 6.6 billion in 2024; The compound annual growth rate from 2024 to 2030 is expected to be 22.1%, and will further expand to USD 21.8 billion in 2030. It shows that the current CAR-T market is far from saturated and needs to be explored by companies.

Sales of Marketed CAR-T Therapies (USD100 million)



Back in 2021, many CAR-T therapies have made new progress in supervision:

Breyanzi

Approved by the FDA in February 2021 for the treatment of adult patients with relapsed or refractory large B-cell lymphoma (R/R LBCL) who have received two or more systemic therapies.

Approved in Japan in March 2021 for the treatment of relapsed or refractory large B-cell lymphoma (R/R LBCL) and relapsed or refractory follicular lymphoma (R/R FL).

Abecma

FDA approved Abecma in March 2021 to treat adult patients with relapsed/refractory multiple myeloma (R/R MM) that have received four or more therapies (including immunomodulators, protease inhibitors, and anti-CD38 antibodies).

Abecma received EC conditional approval in August 2021 to treat adult patients with R/R MM that have received at least three prior therapies (including immunomodulators, a protease inhibitor, and an anti-CD38 antibody) with disease progressed during treatment with the prior therapies.

Tecartus

Approved by the FDA in October 2021 for the treatment of adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

Yescarta

Approved in Japan in January 2021 for the treatment of certain adult patients with relapsed/refractory large B-cell lymphoma (LBCL) .

The FDA approved Yescarta in March 2021 to treat adult patients with relapsed or refractory (R/R) follicular lymphoma

(FL) who have previously received two or more systemic therapies.

sBLA was submitted to the FDA in October 2021 for second-line treatment of adult patients with relapsed or refractory large B-cell lymphoma (LBCL).

Kymriah

In October 2021, FDA and EMA received and accepted the marketing application of a new indication to treat adult patients with relapsed or refractory follicular lymphoma (r/r FL) who have received at least 2 prior therapies.

In addition, Carvykti (cilta-cel), a BCMA-targeted CAR-T therapy jointly developed by Janssen and Legend Biotech, submitted BLA to the FDA in 2021 for Carvykti to treat adult patients with relapsed/refractory multiple myeloma (MM). It is believed that with the approval of the new indications and the new products,

the CAR-T therapy market will further expand in the future.

However, the price issue must be resolved for CAR-T therapy to reach more patients. At present, the price of CAR-T is sky-high, and the cheapest one is over 1 million yuan.

Drug name	Price
Kymriah	USD 475,000/needle
Yescarta	USD 373,000/needle; RMB 1,200,000/needle (China)
Tecartus	USD 373,000/needle
Abecma	USD 437,968/needle
Breyanzi	USD 410,300/needle
Beinuoda	RMB 1,290,000/needle

Source: Public information

About the Author:

Yi

Yi, a pharmacist pays attention to the research and development trends of new drugs at home and abroad, expects to improve himself in the continuous input and output, and grow together with medical we-media.

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The Sales of BTK Inhibitor Reached at Least USD11 Billion Worldwide in 2021

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The Boosting Bispecific Antibody Therapeutics Market: Market Size Exceeded USD3.5 Billion by 2021

By Yi

Keywords: Bispecific Antibody, Transaction, Teclistamab, Vabysmo

So far this year, there has been good news on the bispecific antibody therapeutics market.

- *In mid-January, Johnson & Johnson submitted a BLA to the FDA for BCMA/CD3-targeted bispecific antibody teclistamab to treat patients with relapsed or refractory multiple myeloma (MM).*

- *On January 31, Roche's Vabysmo (faricimab-svoa), an Ang-2/VEGF-A-targeted bispecific antibody, was approved by the FDA to treat patients with neovascular age-related macular degeneration (nAMD) and diabetic macular edema (DME).*

- *On February 17, ZW25, a HER2-targeted bispecific antibody introduced by BeiGene from Zymeworks, was proposed by CDE to be included as a breakthrough therapy. The indication was monotherapy for HER2-positive locally advanced unresectable or metastatic biliary tract cancer (BTC) with failed systemic chemotherapy.*

The bispecific antibody is a popular area of pharmaceutical R&D, with five varieties approved globally (see the table below for details, of which Removab exit market in 2017 due to poor sales after marketing.) The marketed bispecific antibody drugs have a broad range of indications, covering oncology, rare diseases, ophthalmic diseases, etc.

Bispecific Antibody Approved Worldwide

Drug name	Effect target	Enterprise name	Indication
Removab (catumaxomab)	CD3、EpCAM	Feisenmei Bio and Sanlong Pharmaceutical	EMA 2009.04 Malignant ascites
Blincyto (blinatumomab)	CD3、CD19	Amgen	In December 2014, FDA approved the drug for refractory B-cell acute lymphoblastic leukemia treatment.
Hemlibra (emicizumab)	FX、FIX	Roche	In November 2017, FDA approved the drug for hemophilia A treatment.
Rybrevant (amivantamab-vmjw)	EGFR、c-MET	Johnson & Johnson	In May 2021, FDA approved the drug for disease progression after failure of platinum-containing chemotherapy, and EGFRex20ins+ in adults with mNSCLC treatments.
Vabysmo (faricimab-svoa)	Ang-2、VEGF-A	Roche	In January 2022, FDA approved the drug for neovascular age-related macular degeneration and diabetes mellitus treatments. Macular edema

Source: Public data

In terms of the sales volume we know, the global bispecific antibody market has been growing in recent years, with Roche's Hemlibra being a blockbuster product with a sales volume of over USD 3 billion.

Known Sales of Bispecific Antibody

Drug name	Enterprise name	2021	2020	2019
Blincyto	Amgen	USD 472 million	USD 379 million	USD 312 million
Hemlibra	Roche	CHF 3,022 million	CHF 2,190 million	CHF 1,380 million

Besides, there are many other bispecific antibodies in the late

stage of clinical development, with at least 8 in Phase III and 25 in Phase II. According to public information, Chinese bispecific antibodies under research are mainly for tumors treatment. Nevertheless, these bispecific antibodies have very diverse targets, with PD-L1/4-1BB, EGFR/MET, CD3/CD20, and others being popular targets.

Some of the Bispecific Antibody in the Pipeline in China

Drug name	Target	Enterprise name	R&D phase
Candonilimab	Effect target	Zhongshan Akeso, Inc.	In the progress of marketing application
KN026	HER2	Alphamab Co. Ltd	Phase III clinical trial
Ivonescimab	PD-1,VEGFA	Zhongshan Akeso, Inc.	Phase III clinical trial
Zanidatamab	HER2	BeiGene	Phase III clinical trial
Mosunetuzumab	CD20,CD3	Roche Group	Phase III clinical trial
Amivantamab	EGFR,MET	Johnson & Johnson	Phase III clinical trial
Glofitamab	CD20,CD3	Roche Group	Phase III clinical trial
IBI318	PD-1,PD-L1	Suzhou Innovent Biologics, Inc.	Phase III clinical trial
KN046	CTLA4,PD-L1	Alphamab Co. Ltd	Phase III clinical trial
CM350	CD3,GPC3	Keymed Biomedical Technology (Chengdu) Co., Ltd.	Phase II clinical trial
ZG005	PD-1,TIGIT	Suzhou Zelgen Pharmaceutical Co., Ltd	Phase II clinical trial
PSB205	PD-1,CTLA4	Qilu Pharmaceutical	Phase II clinical trial
ES104	VEGF,DLL4	Elpiscience	Phase II clinical trial
Elranatamab	BCMA,CD3	Pfizer	Phase II clinical trial
LBL-024	PD-L1,4-1BB	Nanjing Leads Biolabs Co., Ltd.	Phase II clinical trial
EMB-06	CD3,BCMA	EpimAb Biotherapeutics	Phase II clinical trial
Talquetamab	CD3,GPRC5D	Janssen Pharmaceuticals	Phase II clinical trial
CM355	CD3,CD20	Beijing Innocare Pharmaceutical Technology Co., Ltd.	Phase II clinical trial
PM1003	PD-L1,4-1BB	Biotheus (Zhuhai) Co., Ltd.	Phase II clinical trial
LBL-015	PD-1,TGFB	Nanjing Leads Biolabs Co., Ltd.	Phase II clinical trial
Izokibep	IL17A,Albumin	Inmagene	Phase II clinical trial
6MW3211	CD47,PD-L1	Mabwell (Shanghai) Bioscience Co., Ltd.	Phase II clinical trial
SI-B001	EGFR,HER3	Sichuan Biokin Pharmaceutical Co., Ltd	Phase II clinical trial
EMB-02	PD-1,LAG3	EpimAb Biotherapeutics	Phase II clinical trial
M701	EPCAM,CD3	Wuhan YZY Biopharma	Phase II clinical trial
HX-009	PD-1,CD47	Hangzhou Hansi Biological Pharmaceutical Co., Ltd.	Phase II clinical trial
MCLA-129	EGFR,MET	Betta Pharmaceuticals Co., Ltd.	Phase II clinical trial
IBI302	complement	Suzhou Innovent Biologics, Inc.	Phase II clinical trial
ES101	PD-L1,4-1BB	Elpiscience (Suzhou) Biomedical Technology Co., Ltd.	Phase II clinical trial
PM 8002	PD-L1,VEGF	Biotheus (Zhuhai) Co., Ltd.	Phase II clinical trial
Odronextamab	CD3,CD20	Zai Lab Medicine (Shanghai) Co., Ltd.	Phase II clinical trial
PM8001	PD-L1,TGFB	Biotheus (Zhuhai) Co., Ltd.	Phase II clinical trial
ZL-1301	LAG3,PD-1	Zai Lab Medicine (Shanghai) Co., Ltd.	Phase II clinical trial
EMB-01	EGFR,MET	EpimAb Biotherapeutics	Phase II clinical trial

Source: insight database

The same to the global bispecific antibody field, in which the competition is unquestionably more fierce. As the current progress, there will be explosive growth in the bispecific antibody market in the years to come. Some institutions predicted that its global market size will reach USD 80 billion in 2030, while the size of the Chinese market will hit USD 10.8 billion.

Furthermore, to capture the bispecific antibody market, Sanofi entered into an exclusive global collaboration and licensing agreement of over USD 1 billion with South Korea's ABL Bio in January 2022. They will jointly develop and commercialize ABL301, an α-synuclein, and IGF1R-targeted bispecific antibody. The drug employs Grabody-B platform technology to enhance the blood-brain barrier (BBB) penetration of antibodies to treat Parkinson's disease and other potential indications.

About the Author:

Yi

Yi, a pharmacist pays attention to the research and development trends of new drugs at home and abroad, expects to improve himself in the continuous input and output, and grow together with medical we-media.

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8	Tofflon Science and Technology Group Co. Ltd.
9	Hebei Changshan Biochemical Pharmaceutical Co., Ltd.
10	VEGA PHARMA LIMITED (HANGZHOU VEGA CO., LTD)

Perspective on the Development Trend of Specialty APIs Supported by Policies in China

By Xiaoyaowan

Keywords: Specialty API, API policy, API trends

On November 9, 2021, the National Development and Reform Commission and the Ministry of Industry and Information Technology issued the Notice on the Implementation Plan of Promoting the High-quality Development of API Industry. China intends to develop value-added and high-growth varieties, green and low-carbon technologies, and equipment supporting leading enterprises to gain international competitiveness and create industrial hubs and production bases with global influence by 2025. This plan is the first policy document for the overall development of the API industry published by two significant ministries in recent years, which has crucial guiding significance.

Specialty APIs

API refers to any substance or a mixture of substances becoming an active ingredient of medicine when used in pharmaceutical manufacturing. There are three kinds of APIs: bulk, specialty, and patent API in terms of differences in the patent period of downstream preparations. The specialty APIs are mainly chronic disease drugs, antiviral agents, anti-tumor drugs, contrast agents, etc. The downstream of specialty APIs are "new" generic, whose patents have just expired or are about to expire. Compared to bulk API, the technical barriers of specialty APIs are relatively high, with a looser market competition pattern and a relatively high gross profit ratio.

Most pharmaceutical enterprises of specialty API take total synthesis, fermentation, and chiral compounds as their major technology platforms. A few specialty APIs, such as nucleosides, polypeptides, and PEG, belong to emerging technology platforms. Compared with traditional small molecule drug synthesis, specialty APIs based on new technology platforms are relatively scarce, and the technical threshold for R&D is high. Therefore, manufacturers with the production capacity of related categories have a unique competitive edge.

Market Positioning of Specialty APIs in China

China is a large manufacturer of chemical raw materials, the

overall industrial chain layout in China is good for developing the pharmaceutical intermediate and the API industry. At the beginning of industrial development, due to a series of backwardness in technology, capital, and equipment, the development of the entire API industry is extensive, and the proportion of specialty API, with high technical barriers and high gross profit ratio, is relatively low. In the early period, the advantages of the Chinese API industry chain are: more concentrated in intermediates and some bulk API, and the specialty APIs with high added value are mastered mainly by European, American, and Indian enterprises.

At present, China is the world's largest API manufacturer and exporter. But in the standardized market with higher cost performance, specialty API is confronted with competition from mature suppliers in India and China. API products in the Indian market are mainly penicillin, clopidogrel, atorvastatin, and other varieties. These are all specialty API varieties used to treat diabetes, swelling, cardiovascular and other fields. India's specialty APIs account for a leading position in the standardized market, second only to the United States.

With the progress of the pandemic, China's API industry has ushered in an opportunity for development, and the growth of the specialty API industry has accelerated. From the perspective of industry attributes, the specialty API is a technology-driven industry. The industry enterprises are usually marked by a high proportion of R&D personnel, R&D expense rate, and a relatively stable net profit ratio. The industry has a high threshold and barriers in safety, environmental protection, quality, and cost control. Also, corporate champions have established multi-dimensional competitive advantages in production technology, capacity certification, and customer stickiness.

Development Trend in China

Early specialty API manufacturers in China represented by Huahai Pharmaceutical Co., Ltd and Zhejiang Hisun Pharmaceutical Co., Ltd, focus on statins, sartans, and other specialty APIs. In recent years, new and cutting-edge APIs such as tinib and saban have emerged and been popular on the market. Some API manufacturers such as Menovo, Apeloa, Ausun, and Aurisco have gradually developed and expanded.

Driven by the continuous improvement of the production process of specialty API, and the price advantage in China, the substitution effect of Chines specialty APIs on overseas imported ones will gradually increase in the future. The specialty API industry in China has been in rapid development.

In the short and medium-term, influenced by the upstream costs and the downstream inventory digestion, specialty APIs in China are to start a new round of price increase cycles. At present, the price of valsartan in China has reached the bottom, the prices of telmisartan, irbesartan, calcium pantothenate, and caffeine are about to rise.

In addition, in early November of 2021, NMPA issued a notice on the enabling of the API production and supply information collection module, requiring enterprises to collect the production, supply, and inventory information of APIs, which approved through associated approval and review quarterly, and provide supervision and inquiry functions. The provincial drug regulatory departments can inquire about the API manufacturing and supply information according to their authority.

The transparency of API production information will further standardize the industry, accelerate the normalization of the small and medium-sized enterprises, and benefit the leading enterprises that have scale advantages. At the same time, the standardization of API information makes it easier to implement centralized procurement of drugs, and the integration of API and preparations is the development direction. For API pharmaceutical enterprises, the consistency evaluation and volume-based procurement policy have greatly reduced the sales threshold, and API enterprises with cost advantages can significantly increase their income in the field of preparations. Therefore, it is a good choice for enterprises to enter the downstream preparation vertically and quickly increase their income.

At the same time, in the short term, the US dollar interest rate hike is expected to lead to the depreciation trend of CNY, which

will bring obvious exchange rate benefits of export-oriented API enterprises and is conducive to the increase of apparent income. Among many A-share API enterprises, the major clients come from foreign countries, playing a dominant role in China's API export. Among them, the overseas business of Huahai Pharmaceutical, Synergy Pharma, Hepalink, Menovo, and other enterprises accounts for a relatively large proportion of the income structure, and the depreciation of CNY is beneficial to the improvement of their performance.

In the medium and long term, with the orders from the key customers keeping generating revenue, specialty API enterprises will achieve the transformation to a CDMO business model. According to follow-up reports from industry insiders during industrial upgrading, leading enterprises in China have accelerated the industrial transfer to high-value-added and high-growth varieties by innovation and upgrading of production technology. The transformation business of leading API pharmaceutical enterprises has entered the cash period. In the first three quarters of 2021, the CDMO/CMO business income of Jiuzhou Pharmaceutical, Apeloa, and Tianyu Pharmaceutical achieved rapid growth of 35%+ year-on-year.

In the past three years, Chinese specialty API enterprises, especially leading enterprises have experienced a large-scale production expansion. Chinese API enterprises have been preparing for the explosive growth of the generic drug market. Specialty APIs with growth potential and parallel CDMO expansion are still the growth logic deserving attention in the future.

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Xiaoyaowan, a pharmaceutical industry practitioner, a word carrier in the We-media era focusing on changes of the pharma industry.

A New Record of the Innovative TCM Approval with the Reform of China's Review and Approval Systems

By Zhulikou431

Keywords: TCM reform, TCM approval, Traditional Chinese Medicine, Chinese patent medicine

The Chinese civilization has been in existence for over five thousand years, and traditional Chinese medicine is one of the most magnificent treasures, which embodies the vast wisdom of the Chinese people and the Chinese nation. During the long times of Chinese history, traditional Chinese medicine has played and has always played an irreplaceable historical role. From the Yellow Emperor's Inner Canon to the Compendium of Materia Medica, from Cow-bezoar Bolus for Resurrection to artemisinin, the traditional Chinese medicine has made indelible and outstanding contributions. Especially since the outbreak of the COVID-19, the participation breadth and depth of traditional Chinese medicine in the fight against the pandemic have been unprecedented, and the results achieved are remarkable, which also fully confirms the peculiar curative effect of Chinese medicine.

Summary of Approved Varieties of Traditional Chinese Medicine in 2021

Recently, the National Medical Products Administration approved the application of the registration of three traditional Chinese medicine innovative drugs, namely Xuanqi Jiangu Tablets, Qizhi Yishen Capsules, and Kunxinning Granules. In addition, another innovative drug of traditional Chinese medicine, Yinqiao Qingre Tablets, was also approved for marketing in November.

According to the announcement of the Chinese National Medical Products Administration, up to now in 2021, NMPA has approved six new drugs of traditional Chinese medicine based on the emergency approval of Qingfei Paidu Granules, Huashi Baidu Granules, and Xuanfei Baidu Granules. The year 2021 is proved to be the year of the most number of TCM new drugs approved in the past five years. (See Table 1 for details)

Table 1 Innovative Drugs of the Traditional Chinese Medicine Approved by NMPA in 2021

	Drug name	Time of approval	Indications	MAH
1	Qingfei Paidu Granules	Mar-21	COVID-19	Institute Of Basic Research In Clinical Medicine, China Academy Of Chinese Medical Sciences

2	Huashi Baidu Granules	Mar-21	COVID-19	Guangdong Efang Pharmaceutical Co., Ltd.
3	Xuanfei Baidu Granules	Mar-21	COVID-19	Buchang Pharmaceuticals
4	Yishen Yangxin Anshen Tablets	Sep-21	Insomnia	Shijiazhuang Yiling Pharmaceutical Co., Ltd.
5	Yiqi Tongqiao Pills	Sep-21	Seasonal allergic rhinitis	Tianjin Dongfang Huakang Pharmaceutical Technology Development Co., Ltd
6	Yinqiao Qingre Tablets	Nov-21	Wind-heat common cold	Jiangsu Kanion Pharmaceutical Co., Ltd.
7	Xuanqi Jiangu Tablets	Nov-21	Mild and moderate knee osteoarthritis	Hunan Fangsheng Pharmaceutical Co., Ltd
8	Qizhi Yishen Capsules	Nov-21	Early diabetic nephropathy	Shandong Fenghuang Pharmaceutical Co., Ltd.
9	Kunxinning Granules	Nov-21	Female climacteric syndrome	Tasly Pharmaceutical Group Co., Ltd.
10	Huzhen Qingfeng Capsules	Dec-21	Mild and moderate acute gouty arthritis	Yili Pharmaceutical Co., Ltd
11	Jieyu Chufan Capsules	Dec-21	Mild and moderate depression	Shijiazhuang Yiling Pharmaceutical Co., Ltd.

The traditional Chinese medicine industry is an essential part of China's pharmaceutical industry, with strategic advantages and broad market prospects in China's national economy and social development. Currently, traditional Chinese medicinal materials, traditional Chinese medicine decoction pieces, and Chinese patent medicine are the three pillar industries of China's traditional Chinese medicine industry. Recently, Chinese medicine has got more and more public awareness, and the status of Chinese patent medicine in the national economic development has enhanced. Taking the nation's basic medical insurance drugs as an example, the newly announced 2021 national basic medical insurance drugs catalog contains 2,860 kinds of drugs, including 1,486 chemicals and 1,374 Chinese patent medicine. The proportions of pharmaceutical chemicals and traditional Chinese medicines are the same.

In addition, the traditional Chinese medicine industry has made great progress driven by such factors as the encouragement of national policy, market demand, and modernization of traditional Chinese medicine. However, we have to admit that there is a certain lack of momentum for the development of Chinese patent medicine in some areas in China, and the homogenization of products is clear. In addition, the products from Chinese patent medicine enterprises are in a low degree of innovation, low level of technology, and imbalanced product structure.

About the Author:

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Zhulikou431, as a senior engineer, PDA member, ISPE member, ECA member, PQRI member, senior aseptic GMP expert, has deep knowledge in aseptic process development and verification, drug development and registration, CTD document writing and review, regulatory audit, international certification, international registration , quality system construction and maintenance, as well as sterile inspection, environmental monitoring and other fields. In recent years, he has focused on the analysis of trends in the macro pharmaceutical field and the risk management of pharmaceutical enterprise mergers and acquisitions projects.

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Summary and Brief Analysis of New Drugs Approved by NMPA in 2021

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New Trends in Pharmaceutical Packaging

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Pharmaceutical packaging is the critical stage of the drug manufacturing process. Its primary purpose is to maintain the drug's properties until it reaches its intended user. It protects the drug from damaging external factors such as Human mishandling, counterfeiting, and tempering that could affect its properties. It maintains its efficacy throughout different stages of a drug supply chain, such as sampling, transportation, and storage. It also protects and possesses properties against various environmental factors such as Heat, Dust, and Moisture.

Regulatory bodies worldwide have special regulations for pharma packaging, and they keenly inspect the packaging practices of a pharmaceutical company during their routine inspections. They inspect to see whether the company has invested enough in quality packaging machinery, and the packaging processes are according to approved regulations. If the regulatory bodies find any major non-conformance in a pharma company's packaging practices, it can result in a warning, fines, or complete shutdown of operations.

As with other pharmaceutical sectors, the packaging also witnessed new trends and innovation. The use of advanced engineering techniques such as Automation, improved mechanical design, and software solutions are the main building blocks behind the innovation.

Drivers of New Trends in Pharma Packaging

New trends in the Pharmaceutical sector is not overnight, but it is the result of tireless efforts of different experts to achieve improvements. These improvements pave the way for new trends. Some factors that have contributed significantly to packaging include the following.

- *Research: Constant research in different areas of pharma packaging such as Packaging material, engineering design has helped in creating new designs.*
- *Learning from past experiences*
- *Desire for improvement*

Advantages of Innovation and New Trends

There are many advantages of new trends that have benefitted both the manufacturers and patients. Let's look at some benefits of recent trends in pharmaceutical packaging.

Cost effective: It has enabled the manufacturers to increase their production capacities with fewer resources and less time. This helps to compete with their competitors and increases their market share. Similarly, patients also benefit by having low-cost medicines and drugs.

Reduced Operating Cost: It also results in reduced operating costs which is the most crucial benefit. New energy-efficient machines consume fewer energy resources, such as Electricity and Compressed Air, compared to older packaging machines.

Ease in Operation: New packaging machines can be operated with little expertise. It enables the manufacturers to hire manpower without highly technical knowledge and skills. It also eliminates the need for specialized training during commissioning. Manpower with the basic machine and engineering knowledge can be easily trained to operate these machines.

Lower changeover times: Changeover times are critical in every manufacturing process, and they are one of the main reasons for machine downtime. Additionally, they require skillful personnel to carry out changeover successfully, without creating problems for the machine and the operators. New technologies in packaging machines enable the operator to perform machine changeover in less time and at the same time prevent post-changeover problems.

New Trends

Let's look at some latest trends in pharmaceutical packaging machine.

Blow fill seal (BFS)

Blow Fill Seal is the latest aseptic filling and offers many advantages over traditional ampoule filling. In this technology, the container is formed by placing the raw plastic in granules in a mold. In the mold, plastic undergoes a process known as Extrusion, in which it is forcefully pressed. This process causes the plastic to take the shape of the mold, which is essentially the shape of the container. After formation, the plastic container is filled with the product. Sterile air is injected into it before filling, and the plastic mold is closed and sealed.

The main advantage of the BFS technique is that filling is carried out without human intervention. This reduces the risks associated with human involvement, such as contamination. BFS is also common in the manufacturing of Biotech products such as Vaccines.

BFS prevents problems related to glass container such as glass particles, as the glass sealing process are eliminated.

In a BFS machine, only a small area of the machine is required to be under environmental control compared to traditional filling machines, where the entire machine needs to be under environmental control.

Plasma impulse chemical vapor deposition (PICVD) coating technology

This is a particular type of chemical vapor deposition, which uses low-pressure gas. This helps to lower the temperature of the reaction. The plasma is used to activate the deposition process, creating glass-friendly properties such as easy to clean and anti-scratch properties.

They are widely used in Biotechnology products due to low operating temperatures, as bioproducts require temperature in the lower range.

Despite the above-mentioned advantages, PICVD coating has two significant difficulties. The equipment is costly as

compared to other alternative equipment. The maintenance of PICVD coating equipment is also expensive and requires specialized training and skills. Similarly, its parts are expensive, making any maintenance or replacement expensive.

Secondly, PUCVD coating technology uses Silicon Oxide and Silicon Nitride, which are not human and environmentally friendly. These gasses are toxic and can create harmful working conditions. Additionally, they require specialized protective arrangements during their coating process.

Unit dose vials

Unit dose vials are specialized packaging designs in which the medicine can only be used once. They are typically filled in the required quantity, utilized only once, and consumed by a single patient. The drug should be discarded if leftover. It can cause harmful effects if used again.

Unit dose vials often consist of a plastic bulb, which can be twisted to open. The vial body is squeezable, which is squeezed to administer the drug.

Unit dose filling is performed by a machine that operates under a controlled environment commonly called Cleanrooms. Their speed can range up to 120 vials per minute, and the speed decreases as the fill volume increases. Their fill volume can range up to 0.3 to 10 ml.

After the filling process is completed, the vials are labelled with the necessary product information. This is in contrast to traditional glass-based vials and ampoules where the product information is printed on the glass container.

Two-in-one prefilled vial design

Two in one design is a design that is used to protect the drug container against tampers. It easily indicates to the user if the drug has been tampered with.

There are two chambers on the upper and lower sides in this design. The lower chamber is separated by a spacer so that constituents do not mix with each other. This formation is used to pack the pharma product with the water for injection.

Prefilled syringes

The prefilled syringe is the latest method of administering injectables to humans. It is a single-dose drug delivery method in which the needle is placed in the container. There was a trend of using glass body in the past, but nowadays, plastic body is used. The syringes and plastic bodies are disposable and cannot be used more than once.

They are safe and allow for easy handling. Transportation of Prefilled syringes is also easy, as there is no chance of breakage. This is in contrast to glass ampoules, which can break during transport. They are also lightweight, significantly reducing transportation costs and resources. They are also easy to use and can be administered easily as compared to glass-based containers. They have preferred delivery methods of different specialized drug types such as vaccines and erythroproteins.

There are two types of Prefilled syringes – Needle-free PFS and Needled PFS.

Needle-free PFS is commonly used for administering Vaccines and can be used for subcutaneous and intradermal injection. They are calibrated for a specific fill volume and can be used for a 0.5mL or 0.1mL dose. While this type can be used for consistent delivery, it is dependent on the provider's handling capabilities. So it is recommended to have proper training of the technical personnel.

The Needled PFS is generally used for biotech and pharmaceutical products. They consist of a needle cannula inserted through a nozzle and require siliconization. The Silicon

is applied at the syringe barrel and on the needle surface. Silicon on the needle helps in easy skin penetration during its usage on the patients.

The Silicon used must be of medical grade and should not contaminate or change the properties of the drug.

Child-resistant packaging

Child-resistant packaging is a packaging that is difficult for a child to open. However, adults, including those with disabilities, can easily open the packaging and consume the drug. Manufacturers implement child-resistant packages by an additional cap which is challenging to open. The cap comes with a locking mechanism, which can only be open with a specific opening technique. Examples of such techniques include Push & turn and Turn & lift.

Blister packaging also comes in the variant of child-resistant, where manufacturers deploy an additional layer over the original blister layer. This extra layer makes it difficult for the children to open the blister packs, although the adult can easily open the blister packs.

Conclusion

As with other industries and sectors, Pharmaceuticals also witnessed innovations and trends. At first, they seem to be expensive and resource-intensive, but they benefit the company in the long run. Innovation helps a manufacturer remain at the top of their competitors and results in increased revenue.

About the Author:

Muhammad Asim Niazi

Muhammad Asim Niazi has a vast experience of about 11 years in a Pharmaceutical company. During his tenure he worked in their different departments and had been part of many initiatives within the company. He now uses his experience and skill to write interested content for audiences at PharmaSources.com.

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