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Japan's API Challenges

(Sources: Staff articles by Pharma Japan)

The import of APIs to Japan has been recently impacted by adverse global factors. Air cargo costs for Japan-bound flights from Europe are soaring due to airspace closures over Russia, with API import prices for certain medicines starting to surge from the war in Ukraine.

While rising prices may not put immediate pressure on manufacturing costs, if the current situation continues for a considerable length of time, it will drive up the manufacturing cost rate with cheaper APIs likely to see larger increases, according to Ichiro Fujikawa, chairman of the Japan Pharmaceutical Traders' Association, a group of API/intermediate importers.

While Japan imports no APIs from Ukraine or Russia, the closure of airspace is having a direct impact on airfreight. In the wake of Russia's invasion of Ukraine, the number of cargo flights taking southern routes from Europe to Japan that were carrying goods, including pharmaceutical products, increased, causing congestion in logistics.

This has prompted competition for space in limited cargo capacity. As of the week ending March 8th, the market had already seen a spike in airlines' freight fees. And while there are virtually no medicines imported from Ukraine or Russia, imports from Italy, Eastern Europe and other European countries of origin would see cost increases for airfreight due to ballooning transportation costs.

According to Mr. Fujikawa, freight charges are included in API import prices, with API manufacturers typically setting prices for their products that incorporate transport expenses. Freight fees fluctuate daily, and API manufacturers set prices with certain buffers to absorb these fluctuations. Once air freight costs move above these buffers, additional costs would need to be passed on to the API import prices. The cheaper the API, the larger the impact, according to Mr. Fujikawa. However, the amount of increase remains unclear.

"Prices are just starting to go up. It's inevitable that we'll see a further rise in prices going forward (given the war and ensuing impact on logistics.)" Mr. Fujikawa pointed out. "Air transport over Europe was affected when there was a big volcano eruption in the past, but it's a war this time, not a natural disaster," he said, not that it is difficult to foresee a long-term impact on API prices.

The Japanese government is considering ways to create a drug pricing system that would ensure the repatriation of active pharmaceutical ingredient (API) manufacturing back to Japan to overcome potential challenges due to these global factors and potentially others on the horizon.

When asked about the importance of domestic API production during an Upper House budget committee meeting, Japan's Prime Minister, Fumio Kishida, explained that Japan is currently

(continued on page 2)

In Brief...

- **Sanofi** and **Seagen Inc.** announced an exclusive collaboration agreement to design, develop, and commercialize antibody drug conjugates (ADCs) for up to three cancer targets. The collaboration will utilize Sanofi's proprietary monoclonal antibody (mAb) technology and Seagen's proprietary ADC technology. ADCs are antibodies engineered to deliver potent anti-cancer drugs to tumor cells expressing a specific protein and Sanofi currently has one ADC in development.
- **Walgreens Boots Alliance** (WBA) announced second quarter financial results. Q2 sales from continuing operations increased 3.0% year-over-year to US$33.8 billion, up 3.8% on a constant currency basis. Second quarter operating income from continuing operations increased to US$1.2 billion, compared with operating income of US$832 million year-over-year; adjusted operating income from continuing operations increased to US$1.7 billion, up 35.9%. Separately, WBA CEO *Rosalind Brewer* has been named USA TODAY's Women of the Year, a recognition of women across the country who have made a significant impact. Brewer is one of corporate America's most prominent women and Black female executives and is the only Black woman serving as chief executive of an S&P 500 company.
- **Sigma Healthcare** (Australia) reported FY2022 financial results, with a revenue increase of 1.3% year-over-year to US$3.45 billion. Hospital sales rose 5.6% over 2021 and retail brands sales were up 6.4% for the year. *Vikesh Ramsunder* has taken the reins as CEO and Managing Director of Sigma Healthcare. Most recently, he held the position of CEO of Clicks

(continued on page 2)

A Potential New COVID-19 Vaccine Could Be Accessible for More of the World

(Source: A staff article by World Pharma News)

A new vaccine developed at MIT and Beth Israel Deaconess Medical Center may aid in efforts to vaccinate those in poorer countries, offering an inexpensive, easy-to-store, and effective alternative to RNA vaccines.

In a new paper, researchers report that the vaccine, which comprises fragments of the SARS-CoV-2 spike protein arrayed on a virus-like particle, elicited a strong immune response and protected animals against viral challenge. The vaccine was designed so that it can be produced by yeast, using fermentation facilities that already exist around the world. The Serum Institute of India, the world's largest manufacturer of vaccines, is now producing large quantities of the vaccine and plans to run a clinical trial in Africa.

"There's still a very large population that does not have access to COVID vaccines. Protein-based subunit vaccines

(continued on page 2)

APIs (cont.)...

dependent on imports from China and India for many APIs due to profitability and other reasons. He also highlighted government initiatives that have been taken thus far to alleviate the situation, including support for repatriating API manufacturing for antibiotics to Japan and requests for pharmaceutical companies to diversify API sources.

The government is reviewing the drug pricing system so as "to balance the promotion of innovation and the sustainability of universal coverage," said Mr. Kishida, adding that NHI prices are raised for low-priced medicines with high medical needs for which continuous supplies are deemed difficult. "We should manufacture and supply needed medicines in Japan. From this standpoint, we need to continue discussions on how NHI prices should be set," he said.

COVID Vaccine (cont.)...

are a low-cost, well-established technology that can provide a consistent supply and is accepted in many parts of the world," says J. Christopher Love, the Raymond A. and Helen E. St. Laurent Professor of Chemical Engineering at MIT and a member of the Koch Institute for Integrative Cancer Research and the Ragon Institute of MGH, MIT, and Harvard.

Love and Dan Barouch, director of the Center for Virology and Vaccine Research at Beth Israel Deaconess Medical Center (BIDMC) and a professor at Harvard Medical School, are the senior authors of the paper, which appears in Science Advances. Love's lab, working closely with Barouch's lab at BIDMC, began working on a COVID-19 vaccine in early 2020. Their goal was to produce a vaccine that would be not only effective but also easy to manufacture. To that end, they focused on protein subunit vaccines, a type of vaccine that consists of small pieces of viral proteins. Several existing vaccines, including one for hepatitis B, have been made using this approach.

"In places in the world where cost remains a challenge, subunit vaccines can address that. They could also address some of the hesitancy around vaccines based on newer technologies," Love says. Another advantage of protein subunit vaccines is that they can often be stored under refrigeration and do not require the ultracold storage temperatures that RNA vaccines do.

For their subunit vaccine, the researchers decided to use a small piece of the SARS-CoV-2 spike protein, the receptor-binding domain (RBD). Early in the pandemic, studies in animals suggested that this protein fragment alone would not produce a strong immune response, so to make it more immunogenic, the team decided to display many copies of the protein on a virus-like particle. They chose the hepatitis B surface antigen as their scaffold and showed that when coated with SARS-CoV-2 RBD fragments this particle generated a much stronger response than the RBD protein on its own.

The researchers also wanted to ensure that their vaccine could be manufactured easily and efficiently. The MIT team designed the RBD protein so that it could be produced by the yeast Pichia pastoris, which is relatively easy to grow in an industrial bioreactor. Pichia pastoris is already used to produce vaccines in bioreactors around the world. Once the researchers had their engineered yeast cells ready, they sent them to the Serum Institute, which ramped up production rapidly.

Once the researchers had their vaccine candidate ready, they tested it in a small trial in nonhuman primates. For those studies, they combined the vaccine with adjuvants that are already used in other vaccines. In those studies, the researchers showed that the vaccine generated antibody levels similar to those produced by some of the approved COVID-19 vaccines, including the Johnson and Johnson vaccine. They also found that when the animals were exposed to SARS-CoV-2, viral loads in vaccinated animals were much lower than those seen in unvaccinated animals. For that vaccine, the researchers used an RBD fragment that was based on the sequence of the original SARS-CoV-2 strain that emerged in late 2019. That vaccine has been tested in a phase 1 clinical trial in Australia. Since then, the researchers have incorporated two mutations (similar to ones identified in the natural Delta and Lambda variants) that the team previously found to improve production and immunogenicity compared to the ancestral sequence, for the planned phase 1/2 clinical trials. The approach of attaching an immunogen RBD to a virus-like particle offers a "plug and display"-like system that could be used to create similar vaccines, the researchers say.

If the clinical trials show that the vaccine provides a safe and effective alternative to existing RNA vaccines, the researchers hope that it could not only prove useful for vaccinating people in countries that currently have limited access to vaccines, but also enable the creation of boosters that would offer protection against a wider variety of SARS-CoV-2 strains or other coronaviruses.

In Brief (cont.)...

and was previously CEO of UPD (South Africa).

- Pharmacy organizations, including the **National Association of Chain Drug Stores, the American Pharmacists Association**, and the **American Society of Health-System Pharmacists**, praised the **U.S. House of Representatives** for the introduction of bipartisan legislation (HR 7213) that would help ensure the continuity of accessible pharmacy-based care with the introduction of *H.R. 7213, the Equitable Community Access to Pharmacist Services Act*, bipartisan legislation that would ensure patients continue to have access to essential pandemic and pandemic-related health services provided by pharmacists, including services to keep communities safe from COVID-19 and future public health threats. More than 100 national and state-based associations representing patients, pharmacists, community pharmacies and rural and underserved communities applauded the legislation.
- **Moderna** is adding another two vaccine programs to its roster: a combination respiratory candidate and a shot targeting all four endemic human coronaviruses that cause the common cold. The respiratory combo candidate, mRNA-1230, will go after the three most significant viruses that cause respiratory diseases in adults: SARS-CoV-2, influenza and respiratory syncytial virus (RSV) and is designed to be used as an annual booster. The second, mRNA-1287, is a four-pronged attack against viruses that are a significant cause of common respiratory disease worldwide. Separately, Moderna received emergency use authorization for its COVID-19 booster in children under the age of 6.

(Sources: Company Press Releases, Drug Store News, Fierce Biotech, Scrip Intelligence and World Pharma News)