The 8th Nikkei Communicable Diseases Conference

Tokyo Communicable Diseases Statement 2021

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0. Introduction

Beginning in 2014, the Nikkei FT Communicable Diseases Conference aims to bring together key players from various sectors and countries to deal with the never-ending struggle between humanity and communicable diseases, and to propose public-private partnership (P3) projects to solve related problems. In Japan, the peak of the 5th wave of the novel coronavirus infection (COVID-19) was in August 2021, and fortunately the epidemic was rapidly slowing down at the time of the conference. However, since there were still travel restrictions in place, remote technology was used to hold the 8th Nikkei FT Communicable Diseases Conference on October 27 and 28, 2021, in Chiyoda Ward, Tokyo, bringing together key persons in industry, academia, government, and private sectors from around the world.

〈Countermeasures Against COVID-19〉

It has now been nearly 2 years since the COVID-19 pandemic began to ravage the world in early 2020. The total number of infected people worldwide is approximately 240 million, and the total number of deaths is approximately 4.99 million (as of October 31, 2021). The cumulative number of infected people in Japan is approximately 1.7 million and the number of deaths is approximately 18,000. Throughout the world, the spread of the infection has caused a serious damage to the medical care system, which is a fundamental social infrastructure, and some countries and regions are still facing a crisis. Since the 7th Nikkei FT Communicable Diseases Conference held in November 2020, Japan has experienced the third wave, which peaked at the end of 2020, the 4th wave in May 2021, and the 5th wave in August 2021. The 5th wave was the largest peek ever due to the rapid spread of the Delta variant leading to a crisis in the medical care system.

The theme of the 8th Nikkei FT Communicable Diseases Conference was "Never to repeat the crisis" and discussions focused on COVID-19 measures and the country's experience during the 5th wave. The main issues discussed were: (1) testing systems, (2) vaccines, (3) medical care provision systems, (4) therapeutic drugs, (5) data utilization, (6) border control, (7) national decision-making, (8) the Tokyo Olympics/Paralympics, and (9) public involvement. The conference extracted what actually happened in Japan during the 5th wave, what issues remain, and pursued solutions through various discussions.

The results are summarized in this Tokyo Communicable Diseases Statement 2021 under "Countermeasures Against COVID-19 in Japan", which is recommended to read together with the "Yokohama Communicable Diseases Statement 2020" compiled last year (also titled the "7th Nikkei FT Communicable Diseases Conference Statement"). The statement outlines what industry,

academia, government, and citizens should do to prevent the crisis caused by the 5th wave. We hope that all stakeholders, including the government, local municipalities, private companies, medical institutions, academia, and citizens, will make use of these recommendations and actively promote preparations and countermeasures.

〈Public Private Partnership (P3)〉

In addition to COVID-19 measures, participants also discussed the progress and further development of P3 projects, which has been discussed and proposed by this conference since 2014. Through flat discussions involving a wide range of stakeholders from industry, academia, government, and private sectors, participants of the Communicable Diseases Conference once again confirmed the need and effectiveness of P3 projects to further tackle communicable diseases that threaten human health and economic activities. The Asia Africa Medical Innovation Consortium (AMIC), which consists of several consortiums, is managed by volunteers from the Nikkei FT Communicable Diseases Conference to develop and implement P3 projects throughout the year. In this 8th plenary session, it was reported that the P3 clinical trial platform proposed by AMIC's Asian Clinical Trials Platform consortium established facilities in Thailand and Indonesia with support from the Japanese government and has made progress despite the COVID-19 pandemic.

〈Completing the Tokyo Communicable Diseases Statement 2021〉

At the end of the plenary session, participants of the conference agreed on the adoption of "Tokyo Communicable Diseases Statement 2021". In addition to releasing this statement on the website and the media, results of the conference will be reported at relevant government meetings. This statement will be released not only in Japan but also to international organizations in a wide range of countries including those in Asia and Africa. Japan is expected to be committed even more to the global fight against communicable diseases by taking advantage of the international mutual understanding achieved through this conference.

Please refer to the previous statements listed below for details of the Nikkei FT Communicable Diseases Conference's discussions to date. The Nikkei-Asia Conference on Communicable Diseases has been renamed the Nikkei FT Communicable Diseases Conference since 2020, aiming to widen its contribution to the global society.

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*Information in the statements reflect the latest version at that time

1. Countermeasures Against COVID-19 in Japan

The COVID-19 pandemic has entered a new phase since the 7th Nikkei FT Communicable Diseases Conference was held in November 2020. With the efficacy and safety confirmed in clinical trials, vaccines have become commercially available at an unprecedented speed, and vaccination rollouts are underway around the world. The understanding of COVID-19 has improved, and treatment methods have been established. However, as the highly infectious Delta strain spread throughout the world making it difficult to implement a 'zero-corona' strategy, countries and regions have been forced instead to adopt a 'with-corona' strategy. In addition, in countries and regions where vaccinations started earlier, there was reoccurring of the spread of infection as the effectiveness of the vaccine decreased. In Japan, the number of infected cases reached a record high in the 5th wave in August 2021, severely affecting its medical care system. General medical treatment had to be restricted in urban areas and in Okinawa Prefecture.

This chapter, "Countermeasures Against COVID-19 in Japan", displays how the 8th Nikkei FT Communicable Diseases Conference reviews the 5th wave, identifies the issues, and proposes actions to be implemented in preparation towards the possible 6th wave. As it focuses on preparations against the 6th epidemic wave, the issues and actions cited are mainly short-term, but also include medium and long-term.

1-1 Tests

【Outline and Issues】

〈Inadequate Communication to the Public Regarding the Course of Direction and Purpose of Testing〉

In order to achieve both infection prevention and socioeconomic activities, it is essential that individuals and organizations are motivated to undergo testing. However, the government has not been able to provide a policy on the course of direction and purpose of testing. Hence, the public lacks the overall picture and understanding of COVID-19 tests.

In October 2020, the government's Novel Coronavirus Infectious Disease Control Subcommittee proposed the "Basic Rules and Strategies for Testing (Version 2)". As in the first version published earlier that year in July, testing subjects were classified into three categories: "(1)Symptomatic", "(2a)Asymptomatic with high risk of infection/high pre-test probability", and "(2b)Asymptomatic with low risk of infection/low pre-test probability".

The first version in July called for active testing on (1)Symptomatic individuals and (2a)Asymptomatic individuals with high risk of infection, and the government responded by expanding testing capacities. For (2b)Asymptomatic individuals with low risk of infection, it stated "testing may be carried out depending on individual circumstances and socioeconomic activities". This was revised in the second version in October, stating "it is important to understand the contents and precautions of the test when undergoing testing".

Testing on (1) and (2a) are "administrative tests" funded by public funds with no self-pay. Although (2b) are not subject to administrative testing, government and local municipalities are conducting tests on these individuals to prevent outbreaks in groups and facilities where clusters are likely to occur and to detect signs of the spread of infection at an early stage. Individuals are also getting tested at their own expense requesting it in regard with their social and economic activities.

Currently, there are 33,500 administrative testing facilities (33,000 medical institutions and 500 regional outpatient facilities), and 960 facilities conducting self-paid tests (879 medical institutions and 81 private testing facilities).

However, it cannot be said that the public has been thoroughly informed about the "basic

concept and strategy of testing". The Ministry of Health, Labour and Welfare has issued a notice to public health centers and medical institutions, but the information has not reached the public. There is a lack of public understanding on the purpose of testing in communicable disease control.

Japan's inadequate testing capacity was pointed out during the 2009 H1N1 pandemic in February 2020, but it did not lead to adequate preparedness. Hence, at the beginning of the spread of COVID-19 in February 2020, the country's PCR testing capacity was only 2,120 cases per day. During spring of 2020 when COVID first began to spread, the Ministry of Health, Labour and Welfare established a criteria for PCR testing as "fever higher than 37.5℃ or respiratory symptoms" to avoid overwhelming hospital capacity.

Since then, Japan's testing capacity was expanded to 142,000 cases per day as of February 1, 2021 for COVID-19 related PCR tests. The capacity almost doubled during the fifth wave, to a maximum of 270,000 PCR tests per day. As of October 2021, PCR testing capacity is 340,000 per day.

Testing for medical and public health purposes can be divided into three layers, differentiated by its tools and methods. First, the "Person" layer, in which over-the-counter test kits, such as antibody test kits and rapid antigen test kits help people seek medical advice, get diagnosed and treated by a doctor. Second is the "People (Group)" layer, in which health monitoring apps are introduced in workplaces to collect, record, and analyze data. If any abnormalities are detected, immediate testing and treatment will be conducted in order to prevent clusters. The third layer is the "Public (Society)" layer. Surveillance results are used to determine public health actions aiming to control clusters and the spread of infection.

The government and local municipalities are distributing antigen test kits to schools and other institutions, but these programs are not widely in operation. There is also no system that clarifies who has the authority to make decisions.

As a result of the government's efforts to expand testing capacity, administrative tests needed for surveillance and treatment for (1)Symptomatic individuals and (2a)Asymptomatic individuals with high risk of infection are now readily available.

As vaccination progresses, the percentage of mild cases is expected to increase. However, there is no structured testing system that is appropriate for the current situation, where the different layers of "Person" and "People (Group)" can be fully tested. What is needed is a grand design for testing covering society as a whole, including testing methods and testing costs for a "vaccination &

testing package".

The government has indicated that the general public should also be able get tested immediately when they are feeling ill, but there are no concrete plans for this.

〈Unable To Fully Visualize the Invisible Infection〉

With more people getting vaccinated, there is a concern that individuals with mild cases may spread the infection. A major issue in surveillance is how to "visualize" the invisible infection. It is essential to combine various types of surveillance, such as seroepidemiological surveys, sentinel surveillance, genome analysis, and sewage surveillance, in addition to notifiable disease surveillance using HER-SYS (Health Center Real-time Information-sharing System on COVID-19).

① Notifiable Disease Surveillance

For notifiable disease surveillance of COVID-19, along with the conventional framework of communicable disease surveillance that utilizes the National Epidemiological Surveillance System for Communicable Diseases (NESID) in which public health centers report the number of infected persons, HER-SYS, a separate system in which medical institutions directly input data, was put together and began operation at the end of May 2020. Although it took some time for the system to be fully operational due to issues such as the personal information protection ordinance, it gradually began to function as a surveillance system, and HER-SYS data was reported in the Ministry of Health, Labour and Welfare's Advisory Board documents beginning in January 2021.

However, HER-SYS is still not being utilized as initially expected. For example, follow-up data such as post-hospitalization information of the infected patients, has yet to be input in the system. It has also not been clarified how much of the collected data should be made public or shared.

Since notifiable disease surveillance relies on voluntary consultation of the infected individuals and diagnosis by medical practitioners, changes in the severity of disease, epidemiology, consultation behavior, etc., may not always be reflected in the surveillance data. Notifiable disease surveillance must be continued as a response to outbreaks, but it is also necessary to consider supplementary systems to "visualize" invisible infections, such as the following types of surveillances.

② Seroepidemiological Surveillance

A serum antibody test is a test that examines the presence or absence of antibodies induced by pathogen infection. Although this test may not serve the purpose of detecting infected individuals in the early stages of infection, it can detect those who have been infected in the past and is suitable for epidemiological studies to investigate the cumulative occurrence of communicable diseases

within a group.

Because a certain number of COVID-19 cases are mild or asymptomatic, it is extremely difficult to identify every single case using PCR, which is an acute diagnostic method. A population-based seroepidemiological survey will enable a more accurate understanding of the scale of the epidemic from the past to the present.

Now that a large number of the population has been vaccinated, antibodies can be found in both naturally infected and vaccinated individuals. Differentiating these in the surveys is also important.

The "National Epidemiological Surveillance of Vaccine-Preventable Diseases" began in 1967 and includes seroepidemiological surveys. COVID-19 will be added from FY2021. Plans for surveillance are currently underway.

③ Sentinel Surveillance

Sentinel surveillance is testing conducted in a given region, to individuals with certain symptoms visiting a medical institution, regardless of whether they have a clear history of contact with someone infected with a specific disease (e.g., COVID-19 or influenza). This is contrary to notifiable disease surveillance which reports only those patients who are confirmed as infected following tests performed on the basis of strong suspicion of a specific disease. By surveying all cases with certain symptoms in a community, the percentage of patients who test positive for a specific disease can indicate how likely patients with certain symptoms are positive for a specific disease.

Mie Prefecture has been surveying the proportion of the SARS-CoV-2 causing acute upper respiratory tract infection on patients with influenza-like illness (ILI) and upper respiratory tract infection (ARI) since 2020. Patients presenting symptoms of acute upper respiratory infection were tested for COVID-19 and influenza. This survey found that the transition in "COVID positivity rate", which is the ratio of the number of COVID-positive results to the number of COVID tests conducted, preceded the increase in the number of new COVID cases based on the notifiable disease surveillance. It is also possible to estimate the total number of symptomatic infected individuals from the sentinel surveillance sites and the total number of patients examined.

Sentinel surveillance is thought to be effective as a preliminary indicator of the risk of COVID-19 spreading in a certain area, and as a means of gaining an overall picture of the spread of infection.

④ Genome Analysis

Genome information of pathogens can be used to identify invisible links between infected individuals and to take measures against clusters of communicable diseases. Genome analysis is utilized in measures against COVID-19 clusters. By tracing the footprints of random mutations in the genome we can trace the link of infection into the past. This aids active epidemiological investigations.

Since individuals who are asymptomatic or only have mild symptoms may not visit a medical institution, interviews in active epidemiological surveys are not always enough to follow the infection link. In addition to identifying cluster populations by epidemiological surveys, identifying cluster populations based on genomic information can supplement active epidemiological surveys and provide an overall picture of the transmission of infection.

The occurrence of new mutant strains can also be detected with genome analysis. During the 4th wave, Alpha strains originating from the UK were dominant, but a broad and comprehensive testing regime took place in cooperation with local governments and public health centers to collect negative samples. Genomic analysis on these negative specimens revealed the Delta variant in April 2021.

⑤ Sewage Surveillance

Detecting COVID genes in the sewage can lead to early detection of the spread of infection in the region. Sewage water contains viruses discharged from a large number of infected individuals, including those who are asymptomatic. This type of surveillance can be used to monitor the actual prevalence of the disease, including asymptomatic cases. It can also be useful for early estimation of new cases, since the release of viruses into the sewage system precedes symptoms and diagnosis.

Hokkaido University and Shionogi & Co., Ltd. have developed a method to determine the infection status of local municipalities and facilities based on the amount of COVID viruses contained in sewage water. For example, when the Hokkaido University-Shionogi method was used to conduct sewage surveillance at several locations in the athletes' village during the Tokyo Olympics and Paralympics, a correlation was found between the infection status and the number of viruses detected in the sewage. Furthermore, a large number of COVID RNA were detected even at sites where no positive cases had been confirmed. This high detection sensitivity of sewage surveillance suggested that it could perceive the presence of infected individuals more sensitively than regular testing being conducted in the athletes' village. The possibility of detecting the outbreak of infection at an early stage was also suggested.

⑥ Screening and Monitoring Tests

In Okinawa Prefecture, PCR tests were conducted in a large scale for local residents. The purpose of these PCR tests was to screen and monitor the situation.

The purpose of screening tests is to identify potentially infected individuals by widely conducting PCR tests on populations where it is clear that an epidemic is occurring. For example, in Okinawa Prefecture, PCR tests were conducted on staff and residents of the whole floor or entire facility of senior citizens homes where mass infection was suspected. If even one person was found to be positive, the entire facility was tested. In order to contain the infection, tests were conducted every other week until no more positive cases were found. Early intervention, extensive testing, and guidance on infection control measures must be combined to be effective.

Monitoring tests are conducted on populations in which an epidemic is occurring or likely to occur, examining the need for public health interventions and aiming to ascertain the status of the epidemic. Although it is not necessary to test all individuals, it is important to make testing more accessible. In Okinawa Prefecture, monitoring tests were conducted for essential workers and also multiple times in busy districts. In these districts, restaurants were asked to close based on the positivity rate of the monitoring tests, which contributed to stopping the spread of infection.

If tests are available only to those who wish to get tested (i.e., those with high awareness), isolating those who are positive among them will not be enough to suppress the epidemic. Assuming that there are many positive individuals among those who have not been tested, it is necessary to conduct screening tests or request the entire group (or region) to halt social activities.

It is also important to provide incentives for testing, such as providing guidance on infection control measures at the time of testing or offering tests at a lower price.

〈Nationwide System for Early Detection of Mild Cases Yet to be Developed〉

As the government expands testing capacity, the importance of early detection of minor cases is increasing, both in terms of treatment and in preventing the spread of the disease. Nagasaki Prefecture's health observation app "N-CHAT" is designed so that individuals feel comfortable about entering their data, and has been useful in the early detection of even slightly symptomatic cases. However, these efforts are limited to a few areas, and is hoped to be expanded nationwide.

When symptoms are mild, medical consultation is often delayed. This has led to delay in diagnosis and treatment and the occurrence of clusters. In order to start early treatment and prevent

the spread of infection, it is important that mild case patients are tested at an early stage. Medical examination should be encouraged whenever people are feeling ill. It is also imperative to formulate a system that easily provides testing whenever illness is noticed, to individuals and groups such as companies, workplaces, and schools.

For example, in the health observation app "N-CHAT" provided by Nagasaki Prefecture and others, employees input their body temperature and symptoms. It only takes about one minute. The app is useful in the early detection of symptomatic patients and administrators can recommend a qualitative antigen test to those with symptoms. The system does not require users to install the application. Users access the app via web browser and log in with an ID whenever entering their health data. This lowers the hurdle to those who do not wish to enter personal information. Administrators can check the aggregated data in graphs. If the number of symptomatic patients exceeds a certain number, the administrator will sound an alert. The system is designed to provide incentive for individual users, allowing them to not only keep track of their own health, but also feel the benefits of preventing mass infection in the company or group to which they belong.

〈Various Testing Technologies Developed by Private Companies Not Being Fully Utilized〉

Private companies have been developing a variety of testing technologies. However, these technologies have not been fully utilized since quality control procedures for testing have not been established. It is important for public and private sectors to work together in creating a set of rules. International harmonization in quality control is also required.

The accuracy of a PCR test or antigen test varies greatly depending on the test kit. It is essential to control the accuracy using standardized products developed by third-party organizations or the public sector. However, in the current situation where such external accuracy control system has not been established, intra- and inter-laboratory evaluation and verification using actual specimens by private testing labs are important. It is crucial that the whole testing process, including collection and storage of specimen, is conducted appropriately. Public and private sectors should work together to ensure and optimize the accuracy of the whole testing procedure from preparation to post-processing.

Although industry, government, and academia have come up with innovative testing and surveillance methods, horizontal development has not progressed. There is a need to involve various stakeholders (interested parties) and promote further innovation.

【Actions to Take】

① The government should indicate the course of direction and purpose of testing in order to gain

social understanding of COVID testing.

② Instead of relying only on notifiable disease surveillance based on HER-SYS, combining various other surveillance methods such as seroepidemiological surveys, sentinel surveillance, genome analysis, and sewage surveillance should be considered. In doing so, it will be necessary to identify operational obstacles and work to resolve them.

③ Expand initiatives such as the use of health observation apps that can aid with early detection of individuals with mild symptoms.

④ It is important for public and private sectors to work together to establish rules for quality control in testing. International harmonization is also required.

⑤ Promote innovation in testing and surveillance by involving various stakeholders.

1-2 Vaccines

【Outline】

Several COVID-19 vaccines have been commercialized, but Japan is falling behind in developing domestic vaccine. While the vaccination rate in Japan has reached 70%, current issues include how to increase the rate further, and whether vaccination should be administered to children who are at increased risk of infection as the dynamics of infection in Japan change. It will be difficult to fully resume global traffic and trade unless the vaccination rate increases worldwide, including low- and lower middle-income countries.

Universities, research institutes, pharmaceutical and biotechnology companies around the world have been conducting research and development of COVID vaccines at an unprecedented speed, making several vaccines commercially available since the end of 2020. The number of vaccines with confirmed efficacy and safety approved or granted emergency use authorization (EUA) varies depending on country or region. As of October 2021, 7 vaccines (*Details in Appendix) have been approved by WHO for emergency use by COVAX, the COVID-19 Vaccine Global Access Facility and 48.4% of the world's population (7.9 billion people) have received at least one dose of the vaccine.

In Japan, three vaccines have been approved so far, and as a result of promoting residential and workplace vaccination, 70% of the population have completed two doses of vaccination, and 76.7% have completed one dose of vaccination as of October 27, 2021. The government hopes to

complete vaccination to anyone willing to get vaccinated by November 2021. Although Japan lagged behind at the start, vaccination progressed rapidly after former Prime Minister Yoshihide Suga announced a policy to promote vaccination. As of October 22, 2021, Japan has the third highest vaccination rate in the world, after Canada and Italy.

In low-income countries, however, only 3% of the population has received at least one dose of vaccination. In countries such as Israel, where vaccination rollout began ahead of other countries, more than six months has passed since the start of vaccination, and the infection rate is rising once again. This is thought to be a result of the highly infectious Delta strain, and a decline in the effectiveness of the vaccine. Hence, there are moves to promote additional vaccinations. In Japan, several universities, research institutions, pharmaceutical and biotechnology companies have embarked on the R&D of COVID vaccines, but none have been put to practical use as of yet, thus none were available in time for Japan's vaccination rollout.

There are four major issues regarding vaccines: (1) the delay in practical application of vaccines developed in Japan, (2) the operation system of vaccination, (3) how to improve vaccination rate to those with vaccine hesitancy, and (4) how to apply vaccines for international contribution and national security.

1-2-1 The Delay in Developing Domestic Vaccines

【Issues】

Why is Japan lagging behind in the development and application of domestic vaccines? The reasons are;

(1) In the beginning of the outbreak, the scale of infection was not foreseeable. Unable to predict its marketability, companies were not able to make a quick decision on whether Japanese companies should embark on vaccine development.

(2) Since government or corporations had not been working on the development of new types of drugs, such as the mRNA vaccine, there was no established platforms for development and manufacturing.

(3) There were no large-scale budgetary measures to support the development and procurement of vaccines in response to a pandemic, like the Biomedical Advanced Research and Development Authority (BARDA) of the U.S. Department of Health and Human Services (HHS).

(4) There was no established base for research and development, such as networks for smooth virus acquisition and for conducting clinical trials in endemic areas.

(5) It was difficult to develop a vaccine manufacturing process quickly under a pandemic, and to secure manufacturing facilities and materials for large-scale production.

(6) In order to develop and obtain approval in Japan, it became necessary to comply with the so-called Cartagena Act (*). Smooth R&D is difficult due to legal and regulatory aspects as well, such as the requirement to pass a national lot release test.
(7) Lack of a flexible approval and licensing framework that simplifies the approval-review process and allows for rapid commercialization of domestic vaccines.
(8) There was no established centralized control tower function to support R&D and invest in R&D that could efficiently promote the research, development and manufacture of domestic vaccines in the event of an emergency.

Therefore, in June 2021, the Japanese government made a cabinet decision to approve the "Strategy for Strengthening Vaccine Development and Production" in order to strengthen the R&D and production system of domestic vaccines on a national level in preparation for future epidemics. The strategy calls for: (1) Formation of world-class R&D centers, (2) strengthening the funding function for strategic research, (3) development and expansion of clinical trial environments, (4) establishing the standards and speeding up the regulatory approval process, (5) setting up vaccine manufacturing bases, (6) fostering drug discovery venture companies, (7) fostering and promoting vaccine development and manufacturing, (8) promotion of international cooperation, and (9) strengthening the monitoring system as a precondition for vaccine development. These nine measures were proposed so Japan can devise a system for research, development, production, and supply of vaccines in preparation for emergencies. In addition, the government decided to establish a Strategic Center of Biomedical Advanced Research and Development for Preparedness and Response (SCARDA) within the Japan Agency for Medical Research and Development (AMED) to lead the domestic development of vaccines in order to achieve (2) strengthening the funding function for strategic research.

【Actions to Take】

① Steadily implement a "strategy for strengthening vaccine development and production" and immediately establish SCARDA within AMED to swiftly execute the budget and support R&D of domestic vaccines.
② For existing communicable diseases, mock-up and prototype vaccines should be developed regularly, so that domestic vaccines can be put to practical use in a short period of time in the event of an emergency.
③ Since it will be difficult to conduct clinical trials in Japan when the epidemic settles down and there are fewer infected people, Japan must further build networks to conduct clinical trials in endemic areas.
④ In the mid- to long-term, Japan should promote innovation in academia and industry by establishing a platform for research, development and manufacturing of new types of drugs

such as mRNA vaccines.

⑤ In the long term, Japan should reconsider existing laws and regulations, including pharmaceutical regulations, so the Cartagena Act can be dealt with promptly, and the national lot release tests can be cleared without delay.

⑥ The early approval system for pharmaceuticals based on the Pharmaceuticals and Medical Devices Law is not clear whether it can be applied to vaccines. The country needs to consider a framework that would enable the rapid commercialization of domestic vaccines.

⑦ Since the spread of communicable diseases is unpredictable, the marketability of vaccines is also unpredictable. The government should therefore consider purchasing or stockpiling domestic vaccines as well.

1-2-2 Vaccination System and Its Operation

【Issues】

Japan's vaccine rollout was conducted aiming to reduce the number of deaths and serious cases, while securing the country's medical care provision system. Thus, the priority order for vaccination was determined as follows; healthcare workers, the elderly, patients with underlying diseases, caretakers working in facilities for the elderly, and finally, others. Vaccines were distributed equally among prefectures, and residential vaccination was entrusted to local governments. At the same time, vaccinations were also conducted at workplaces.

The spread of the Delta strain and also the fact that vaccination has progressed, especially among adults is going to change the dynamics of the epidemic in Japan. Although children are less likely to become a severely ill, the risk of infection among children is relatively increasing. It must also be mentioned that neutralizing antibodies are known to decline after six months of receiving the mRNA vaccine. Additional vaccinations should be considered for the elderly and those with a high risk of turning severely ill.

Furthermore, long-term safety of new types of vaccines, such as mRNA vaccines has yet to be established. A system to evaluate their safety is crucial.

【Actions to Take】

① Currently in Japan, there is no approved vaccine for children under the age of 12. Children may be more prone to adverse reactions to vaccination. However, as the risk of infection is increasing among children, it is necessary to consider whether to promote the vaccination of children in Japan, taking into account the risks and benefits. In considering the risks and benefits, efforts should be made to gather information, such as by participating in the WHO's Strategic Advisory

Group of Experts (SAGE) and keeping up to date with the latest global trends.

② In view of the fact that there are individuals who do not wish to receive vaccinations due to fear of side effects, and that there is a need for vaccines with a high level of safety for the upcoming additional vaccinations, the development and commercialization of domestic vaccines with an emphasis on safety should be promoted swiftly.

③ In order to evaluate the long-term safety of vaccines, a system should be established to track and analyze vaccine recipients over time. In this system, various data should be linked such as suspected adverse reaction reports from medical institutions and vaccine manufacturers, the Vaccination Record System (VRS), and medical records of vaccine recipients who present symptoms suspected to be related to vaccination.

④ Clarify the range of compensation in the event of health damage due to adverse reactions after vaccination, including both short-term and long-term damage. This range of compensation and its details should be made widely known. Risk communication and media response in the event of serious health damage should also be considered.

1-2-3 Vaccination Rate and Vaccine Hesitancy

【Issues】

As of October 27, 2021, 70% of Japan's population has completed two doses of vaccination, while the remaining 30% has not. Since aiming for zero COVID cases is not realistic, we need to further increase the vaccination rate in order to curb the spread of infection, reduce the number of severe cases, and prevent the strain on our medical system.

According to an online survey conducted on 1,000 men and women in their 20s to 60s at the end of August by the Nikkei FT Communicable Diseases Conference, those who have not been vaccinated can be categorized into three types: They are either "thinking of getting vaccinated (but have not yet done so)", "have not decided yet", or "do not want to get vaccinated". Among these, those who "do not want to get vaccinated" are very determined to avoid vaccination, suggesting that it is difficult to reach out to them.

【Actions to Take】

① Now that the national vaccination rate has exceeded 70%, publicity should focus on the unvaccinated rate, i.e. the percentage of unvaccinated people. It should be actively informed that being unvaccinated is one of the risk factors for serious illnesses along with obesity and diabetes, and promote efforts to increase the vaccination rate.

② For those who are "thinking of getting vaccinated (but have not yet done so)" and those who "have not decided yet", vaccination should be encouraged with an approach that is in tune with

their values.

③ A large amount of information about vaccines, including fake news and false information to stir up anxiety, is being spread through the Internet and other media, so much so that we are in a state of a so-called infodemic. When providing information, it should not be in a condescending manner. It is important to be empathetic and respect their values.

1-2-4 Vaccines for International Contribution and National Security

【Issues】

Unless the infection is under control globally, it will be difficult to fully resume traffic and international trade. It is therefore essential to increase vaccination coverage worldwide, including low- and lower-middle-income countries.

COVAX, an international procurement framework in which high- and middle-income countries provide funds and vaccines free of charge, mainly to low-income countries, was launched at the initiative of international organizations such as WHO and the Gavi Vaccine Alliance. By October, over 300 million doses of vaccines had been supplied to 143 countries and territories.

However, India, which had been responsible for most of the production of vaccines for COVAX, restricted exports in order to prioritize domestic supply, and delays in production by AstraZeneca and Johnson & Johnson in the US have had a negative impact to the plan. The original target of supplying 2 billion doses worldwide by 2021 was thus revised downward to roughly 1.4 billion doses in the plan announced in September.

Japan has been making international efforts to ensure equitable access to vaccines in all countries and regions by contributing US$1 billion to COVAX, providing 60 million doses of vaccines free of charge (30 million doses so far), and aiding “last mile support” to help vaccine delivery to vaccination sites. The Japanese government is working to ensure equitable access to vaccines in all countries and regions. In addition to furthering these efforts, Japan should work to supply domestic vaccines and vaccines produced in Japan to low-income and low- and middle-income countries for international contribution.

The COVID pandemic highlighted the fact that Japan’s supply chain for medical supplies, including therapeutic drugs, vaccines, their raw materials, and other materials necessary for their manufacture, is heavily dependent on overseas sources. This has had the effect of making it difficult to develop and manufacture vaccines and therapeutic drugs originating in Japan. Therefore, it is important to prepare for emergency situations by building a supply chain that does not rely solely on overseas sources, and establish a system that enables the procurement, development, and manufacture of medical ingredients, intermediates, and other materials necessary for manufacturing in Japan.

【Actions to Take】

① In order to ensure a stable supply even in times of emergency, Japan should promote the domestic procurement of raw materials, intermediates and other materials necessary for the manufacturing of vaccines and therapeutic drugs, establish multiple supply chains, maintain and renew facilities and equipment necessary for their manufacture, and work on developing peripheral industries.

② Japan should also make international contributions through COVAX or other agencies, such as in supplying vaccines developed or manufactured in Japan to low-income and low- and middle-income countries, so that global traffic and trade can resume.

1-3 Medical Care Supplies

【Outline】

Japan's 5th wave recorded the largest number of infected cases, causing a shortage of hospital beds, with more patients quarantined at home or at accommodation facilities. Some hospitals were forced to restrict general medical care, putting Japan's medical care in a critical situation. The reason for this is Japan's unique medical care provision system, in which the number of healthcare workers is low by international standards and the number of hospital beds cannot be increased easily. During the 5th wave, there were cases where hospitals and medical personnel were forced to choose which lives to save.

As mentioned above, the 5th wave, which began in late June, plunged Japan's medical care, one of the social infrastructures, into a critical situation. Although vaccination rollouts had been underway throughout Japan, the rapid spread of the highly infectious Delta strain led to a sharp increase in the number of infected people in August, particularly in those who had not been vaccinated, mainly in the Tokyo metropolitan area and Okinawa. On August 20, 2021, the number of new infected cases nationwide was approximately 25,000, and the number of hospitalized patients temporarily exceeded 200,000. During this 5th wave, the number of individuals infected and quarantined at home or in accommodation facilities reached a record high. In Tokyo alone, the number of infected individuals quarantined at home temporarily exceeded 25,000 (excluding patients on waiting lists). 122 people died at home between January and September 2021 (according to data collected by the Ministry of Health, Labour and Welfare).

The country worked on constructing a medical care provision system by securing hospital beds and quarantine facilities and distributing/deploying therapeutic drugs and medical equipment. With regard to hospital beds, each prefecture increased the number of COVID hospital beds under the initiative of the Ministry of Health, Labour and Welfare. As of August 18, 2021, there were approximately 38,000 COVID hospital beds, and approximately 5,500 hospital beds for severe COVID patients secured nationwide.

Until the 4th wave, most of the infected patients in Japan were hospitalized, including those with mild cases. In the 5th wave, however, the rapid increase in the number of infected individuals filled hospital beds, especially in the Tokyo metropolitan area, with many people on the waiting list to be hospitalized. As a result, the workload at public health centers exceeded its capacity, and it took longer for health observation services to begin. At the same time, the number of patients evolving into serious cases while quarantining at home or at accommodation facilities increased, and emergency medical care became dysfunctional. It turned into a vicious cycle where more and more patients in need of hospitalization could not find a place to be admitted. In some cases, even moderate II patients could not find a hospital, and cases involving pregnant women had difficulty finding emergency rooms. Although some doctors and nurses engaged in home medical care and began to take charge of health observation on behalf of public health centers and provided treatment on behalf of hospitals, they were short-staffed, and the system did not work well, especially in the Tokyo metropolitan area. Furthermore, due to a shortage of hospital beds and medical personnel, some hospitals were forced to restrict general medical care not related to COVID, and the ambulance response rate declined. Some facilities also experienced shortages of medical supplies such as oxygen concentrators.

On the other hand, there were quite a few prefectures and municipalities that survived the 5th wave through their own efforts, even with the sharp increase in the number of infected cases. For example, Sumida Ward in Tokyo shortened the period of hospitalization by securing back-up beds to which patients recovering from the acute stage could be transferred. In addition to augmenting the system of public health centers, the city ward promoted health observation of patients quarantined at home in cooperation with local medical associations and pharmacies, and utilized local medical resources by allocating roles between hospitals, clinics, pharmacies, and other organizations. In Okinawa Prefecture, the number of new infections per population in early August recorded the highest in Japan, similar to the infection situation in Europe and the US. The prefectural government took initiative, to share and grasp real-time data on the operational status of hospital beds, while emergency doctors of the stationed Disaster Medical Assistance Team (DMAT) assessed treatment policies, the need for hospitalization, and matched the severity of patients' illnesses with the status of available hospital beds, nurses and other factors of receiving

hospitals. By clarifying the roles of public health centers, medical institutions, and nursing care facilities, and encouraging the transfer of patients out of the acute stage to other facilities, the system maximized the use of local medical resources.

The COVID-19 pandemic has had a serious impact on healthcare not only in Japan, but also in other countries. In the UK and US, 30% of all deaths due to COVID-19 occurred outside of hospitals, such as at home or in elderly care facilities. In addition, in the UK, the number of excess deaths, which indicates how much the actual number of deaths exceeded the number of deaths per population estimated from historical data, increased in 2020, which may be caused by the restrictions in general medical care.

1-3-1 Japan's Unique Medical Care Provision System

【Issues】

The reason behind the critical shortage of hospital beds during the 5th wave is Japan's unique medical care provision system. Compared to Europe and the US, Japan has more hospitals and hospital beds per capita, but the number of doctors per capita is the same, which means the number of doctors per hospital bed is low. In Japan, where the aging rate is highest in the world, the majority of hospital beds are used for convalescent and chronic care for the elderly, leaving only a limited number of beds available to treat acute patients. Another aspect is that hospitals in the community are not differentiated according to their function. Furthermore, the number of doctors, nurses, and other medical personnel who can provide acute care, including communicable diseases and emergency care, is limited. Those medical personnel are also scattered throughout the region.

Moderate or severe cases of COVID-19 cannot be treated simply by having available hospital beds. Doctors and nurses with the expertise to carry out treatment are needed. In addition, treatment of moderate and severe cases of COVID-19 requires more than 1.5 times more manpower than, for example, medical care for chronic elderly patients. Therefore, even if there are a large number of hospital beds, if there are not enough doctors and nurses, the beds cannot be fully utilized and hospital beds cannot be operated at 100%. In addition, because COVID patients must be placed separately from other patients, entire wards must be converted to COVID wards. This means that originally hospitalized patients need to be discharged or transferred, however, such coordination is a hassle for medical personnel, and takes time to implement.

In Japan, based on the revised Infectious Diseases Law, local governments are now allowed to disclose the names of medical institutions that fail to respond to requests for cooperation in securing hospital beds without justifiable reasons. During the 5th wave, some local governments

took advantage of this law to request cooperation in securing hospital beds, but the effect was limited and did not lead to a significant increase in hospital beds.

【Actions to Take】

① In the 6th wave, it is essential to take on patients not in a hospital-based manner, but in a community-based manner and maximize the use of local medical resources. Specifically, by establishing a system in which patients can be admitted from an early stage according to the function of the hospital: serious cases should be admitted to large hospitals, while patients with relatively mild symptoms should be admitted to small and medium-sized hospitals. Beginning treatment from an early stage should reduce the number of patients evolving into serious cases.

② In preparation for the 6th wave, prefectures and local municipalities must act as headquarters so that patients are admitted according to the severity of their illness and function of the hospital. For this purpose, data on the availability of hospital beds and medical personnel should be shared.

③ In preparation for the 6th wave, not only hospitals, but clinics and nursing homes must also be able to cooperate. Patients who are out of the acute stage should be transferred to back-up medical facilities, while patients with mild cases or those who have recovered should be treated at home. These efforts will also lead to an ideal form of regional medical care.

④ In the medium- to long-term, all doctors and nurses, not just those with specialties in communicable diseases or emergency medicine, should receive training in the handling of PPE (personal protective equipment), the operation of respirators and other equipment so they are prepared for emergencies.

⑤ In the medium- to long-term, create a system that can provide intensive care for severe cases even in rural areas where medical resources are limited, by utilizing a tele-ICU/eICU system in which doctors and nurses with expertise in advanced treatment can provide remote support.

⑥ For areas where the number of infected cases is rapidly rising and medical resources are in short supply, establish a system, like EMT (Emergency Medical Team) and DMAT (Disaster Medical Assistance Team) to temporarily dispatch doctors and nurses with expertise.

1-3-2 Discussing the Choice of Life in Contingencies

【Issues】

In the 6th wave and beyond, or in epidemics arising in the future, the possibility cannot be denied that the number of severe cases will increase rapidly, and medical personnel will be forced to make choices on which lives to save. Which patient should be admitted to the hospital? Which severe case patient should use ECMO or receive other extensive treatment? It is also possible that some critically ill patients may not be able to communicate whether they wish to be initiated

cardiopulmonary resuscitation measures in the event of cardiopulmonary arrest, i.e., their intention of DNAR (Do Not Attempt Resuscitation). The situation may also cause emergency and general medical care to be significantly restricted.

【Actions to Take】

① With regard to DNAR wishes in critical situations, there is a need to promote awareness to the general public that one may express their wishes. Patients should be advised to confirm their wishes with their families.

② Policy making regarding triage and non-initiation of cardiopulmonary resuscitation in the event of emergencies should not be left to hospitals and those working in the medical field. Immediate discussions should take place in various fields such as academic societies, including experts in bioethics, to sort out the issues and guiding principles. After that, we urge the government to take the lead in presenting a perspective.

1-4 Therapeutic Drugs

(Neutralizing Antibody Drugs and Oral Therapeutic Drugs)

【Outline and Issues】

Neutralizing antibody drugs have been approved for mild and moderate COVID-19 cases with a high risk of severity. Development of orally administered small molecule drugs, which are expected to have a significant impact on medical care, is also underway. However, tests for identifying infected individuals and predicting the risk factor for severity have not been fully utilized. Consequently, neutralizing antibody drugs and other therapeutic drugs are not being used efficiently.

With the efficacy and safety being confirmed in clinical trials, etc., several therapeutic drugs(*) are now used to treat COVID-19 patients. In particular, neutralizing antibody drugs for patients with mild or moderate cases have been put to practical use beginning in autumn, 2020. Initially, the Ministry of Health, Labour and Welfare allowed the administration of the neutralizing antibody drug (Lonapreve) only to hospitalized patients with mild or moderate cases who were at risk of turning into a severe case, as drug supply was limited. In August 2021, the administration was also approved for patients being treated in accommodation facilities, and also to outpatients by the end of August. During the 5th wave when the number of infected patients increased rapidly

mainly in the Tokyo metropolitan area due to the spread of the Delta strain, the drug was also actively administered for patients resting at home and at oxygen stations.

The development of orally administered small molecule drugs(*), which are expected to have a major impact in medical care, is also in progress. In the US and Europe, interim analyses of clinical trials have confirmed the safety and efficacy of small-molecule drugs, and applications for approval are now under review for emergency use authorization (*EUA). In the UK, the first orally administered small molecule drug was approved in November 2021. If orally administered small-molecule drugs can reduce the number of patients who become severely ill by administering them before the onset of exposure or early in the course of the disease, this will help to reduce the burden on the medical system.

Neutralizing antibody drugs approved for patients with mild or moderate cases who are at risk of severity are currently more expensive compared to small molecule drugs. In Japan, due to the critical situation of medical care in the 5th wave, neutralizing antibody drugs were widely used even for patients being treated at home or at accommodation facilities. In some cases, they were administered to mild case patients who did not have a high risk of severity.

In order to effectively utilize neutralizing antibody drugs and orally administered small molecule drugs that will be put to practical use in the future, it is essential to quickly identify infected individuals and begin treatment at an early stage. However, sufficient testing to identify infected individuals may be difficult, due to the lack of easy access to testing and the lack of a well-functioning system to identify close contacts.

Furthermore, in order to effectively utilize neutralizing antibody drugs, it is necessary to identify those patients at risk of turning severely ill and administer the drugs at an early stage. In Japan, two types of blood markers (interferon- λ 3: IFN- λ 3 and TARC - thymus and activation-regulated chemokine) that can predict the risk of severe illness have been developed, and they can be covered with national health insurance. However, they are not being fully utilized due to the fact that it takes time for the results to come back.

【Actions to Take】

① To efficiently utilize small molecule drugs and neutralizing antibody drugs, a system for rapid identification of infected patients and early treatment should be established.

② Establish a system to easily conduct tests and quickly obtain results for blood markers that can predict the risk of severe illness.

1-5 Utilizing ICT and Bigdata

【Outline and Issues】

〈Difficulties in Collecting Data〉

Data-driven decision-making (data utilization) is essential for implementing communicable disease control measures based on scientific evidence. HER-SYS lacks a perspective on what kind of data is necessary for infection control and how data can be input easily, making the system difficult to gather information. It is necessary for communicable disease specialists and IT specialists to cooperate further and design a system that is easier to use.

Currently, all local governments are entering data regarding infection cases into HER-SYS, allowing the Ministry of Health, Labour and Welfare to consolidate data. Nevertheless, not all the information necessary for decision-making on communicable disease control is available via HER-SYS.

One of the reasons for this is that the number of items to be entered in HER-SYS was drastically reduced in order to lower the burden on medical institutions and public health centers. Therefore, despite the accumulation of detailed information at medical institutions and public health centers, there is no mechanism to systematically collect all the data.

Adding to that, there are many medical institutions that do not enter information on COVID cases into HER-SYS, and the reality still remains that hospital administrative staff are sending information by fax, and public health centers are entering the information in the system.

The fundamental problem is that the system was not designed to provide the best UX (user experience) and UI (user interface) for the people working on the front lines of communicable disease control. This should have been done by infection control experts and IT experts who understand how to make it easier for medical personnel to enter data and what kind of data is necessary for communicable disease control.

Furthermore, although HER-SYS is structured to collect prognostic information such as hospitalization, discharge, and death of infected patients, this information is not systematically consolidated.

〈Too Many Systems Causing Inadequate Data Coordination〉

There are now too many communicable disease control data systems which is increasing the input burden on the frontline. It is difficult to perform detailed analysis because the data is not linked. It is necessary to change the vertical administrative structure, clarify the responsibilities of ministries, government and local municipalities, and coordinate the data.

In addition to HER-SYS, the government has developed COCOA, a contact confirmation app, and G-MIS, a novel coronavirus infection information support system for medical institutions. Also, the Ministry of Health, Labour and Welfare has developed V-SYS, a system for facilitating vaccine delivery, and the Cabinet Secretariat has developed VRS, a system for recording vaccine inoculations.

However, since VRS is recorded in connection with My Number (Japan's social security and tax number system) and the others are not, it is difficult to analyze the data in a coordinated manner. The data is not organically linked, making it time-consuming to input data. It can be said that there was a lack of perspective in designing the entire IT system used for communicable disease control.

Discussions are required on the realization of a Personal Health Record (PHR) system, a platform for individuals to input personal health information, including vaccination records.

〈Lack of User Perspective in System and App Development〉

The lack of a user perspective has led to the proliferation of various apps that are not necessarily easy for users to use. There is also a lack of UX/UI design that leads to behavioral changes with daily use.

The contact confirmation app "COCOA" was initially planned to display a graph of close contact behavior. This did not happen, and the app did not lead to personal behavioral changes.

In an effort to balance socioeconomic activities with communicable disease control, the government has announced a policy of using a "vaccine/test package" and a QR code tracking system. The "vaccine/test package" is a system that allows people to loosen restrictions on their activities by either receiving two doses of a vaccine or providing a negative test result. Experiments are being conducted in many municipalities beginning in October 2021. It is still under consideration how COCOA, the proof of vaccination app, proof of a negative test result, and QR code tracking system, will be utilized depending on the size, shape and frequency of use of various venues and shops.

Experiments have also begun to link the list of visitors with HER-SYS. This way, when an infected individual is found, it will be possible to test those who had close contact, i.e., the people who were in the same place at the same time.

More and more private companies have announced that they will begin offering vaccination apps, which calls for a set of rules to be put in place. However, there are fears that this could lead to discrimination against those who cannot be vaccinated. There is also a need to consider devising a way to display "verified" on the smartphone screen regardless of whether the person has been vaccinated or tested negative for the disease.

Many local municipalities have already established their own COVID-19 tracking systems using two-dimensional codes (QR codes). It is not user-friendly for users to have a number of apps for communicable disease control in their smartphones. Apps should be designed with UX/UI in mind so that users can benefit from using them in their daily lives.

〈The Need for Public Consensus on Privacy Protection〉

In utilizing various data, it is essential to relieve public anxiety. Many worry that their privacy may be violated. It is necessary to clarify, for what purpose and how the information will be used, and to make this widely known.

The fact that each municipality makes personal information of infected individuals public, such as their area of residence, occupation, prognosis, is a problem. Although the format of information varies, this is detailed personal information. This information has been utilized for cluster countermeasures, as it is difficult to obtain sufficient data on infected individuals through the system. However, it cannot be said that their privacy is protected.

Retrospective epidemiological surveys and contact tracing will be dramatically improved by utilizing tracking systems using QR codes. As vaccination progresses and the number of mild cases increases, it becomes difficult to grasp the actual state of infection. A QR code-based system can collect various contact history data, for example, when entering restaurants and other facilities. Information that could not be seen with previous cluster countermeasures can be made visible. It will be possible to grasp quantitatively what kind of circumstances, restaurants or event venues bear how much of a risk of spreading the infection.

In utilizing various data, it is essential to relieve public anxiety. Many worry that their privacy may be violated. In terms of this consideration for privacy, COCOA is a difficult system for

health authorities to use. It is necessary to clarify, for what purpose and how the information will be used, and to make this widely known.

It is also necessary for industry, government, academia, and citizens to cooperate, and use their combined wisdom to work on communicable disease control as it is their own problem. It should not be conducted in an authoritative way.

【Actions to Take】

① Enhance the usability of systems and applications with a user's perspective.
② Deepen collaboration between communicable disease specialists and IT specialists.
③ Put an end to vertical administrative structures. Clarify the responsibilities of each ministry, government and local municipalities and strengthen data coordination.
④ Promote the Personal Health Record system.
⑤ Explain carefully to the public how their personal information will be used.
⑥ Each municipality should establish privacy guidelines on the release of information about infected individuals.
⑦ Industry, government, academia, and citizens should cooperate, and use their combined wisdom to work on communicable disease control as it is their own issue.

1-6 Border Control

1-6-1 Recent Status and Future Changes

【Outline and Issues】

〈**Easing Measures to Resume International Travel** and Business〉

Japan's border control measures have been strict by global standards, such as setting a 14-day quarantine period for entry and re-entry to Japan, except for those with special exceptional circumstances. Among major countries, only China and Australia are enforcing stricter measures than Japan, mandating a 14-day quarantine. Now that vaccination has progressed worldwide and the number of infected cases is declining in Japan, the question is how to ease border control measures so that international travel and business can resume.

In October, Japan reduced the 14-day quarantine period for vaccinated individuals entering the country to 10 days, except for those entering from South America and some other

regions. Meanwhile, the UK has taken further steps, eliminating the need for self-isolation for travelers with proof of vaccination, starting in October. It is impossible to reduce the number of infected cases to zero. So, how can we coexist with COVID-19 while also revitalizing the economy? Future border control measures must aim to achieve this.

〈Mutant Strains Raising Concerns〉

Genome analysis experts say that COVID-19 will continue to mutate. Compared to noroviruses and influenza viruses which have accumulated a wide variety of mutations over a long time, COVID-19 is only two years into its epidemic and there has only been about 40 mutations overall. The likelihood of future mutated strains and the course of this epidemic is still uncertain. There could be new strains that slip past the current PCR tests. It should be understood that the world will continue to be threatened by new mutant strains of SARS-CoV-2.

In order to stop the spread of new mutant strains, border control measures should not be eased casually. In fact, the number of infected cases in the UK, which has taken the lead in mitigation measures, is once again at a high level.

〈Proof of Vaccination and Testing Specifications〉

Requests for international compatibility of vaccination certificates are being heard from outside Japan. A prerequisite for such compatibility is the standardization and compatibility of testing standards in each country. The principle of border control is “reciprocity”, in which the same conditions are imposed on the entry and exit of both sides. The Ministry of Health, Labour and Welfare, the Ministry of Foreign Affairs, and the Immigration Services Agency of Japan must coordinate and respond quickly to changes in the situation.

【Actions to Take】

① In order to keep the level of infection at a certain level where death or serious cases can be prevented, at the same time as enabling international business and travel in line with global trends, new border control measures in response to the situation must be put in place.
② Border control measures should be flexible in response to changes such as the emergence of new mutant strains and epidemics.
③ In order to detect new mutant strains at an early stage and link them to communicable disease control measures, testing with genome analysis should be expanded.
④ Immigration documents regarding communicable diseases testing results and proof of vaccination should be made compatible internationally.

1-6-2 Border Control Measures for the Olympic and Paralympic Games

【Outline and Issues】

〈Entry Granted for Special Exceptional Circumstances〉

In the second year of the COVID-19 epidemic, Japan's border control measures were put to the test in the country's response regarding the Tokyo Olympic and Paralympic Games. During that time, Japan required people entering or re-entering Japan to voluntarily quarantine at home or in other accommodations for 14 days, even if they tested negative for COVID-19.

However, various special measures were granted to those involved in the Olympic and Paralympic Games. These special measures were even applied to foreign media personnel, allowing them to shorten their quarantine period to 3 days if they agree to be under strict surveillance using GPS from the fourth day onward. This special treatment to Olympic staff was criticized, as Japan was experiencing a rapid spread of infection by the Delta strain at that time.

The Tokyo Olympics and Paralympics did not accept spectators from abroad, which meant that quarantine measures were limited to athletes and related professionals, allowing for careful and thorough supervision. Even so, some problems arose such as when the Ugandan delegation entered Japan in June. Out of the nine members, one tested positive for COVID at the airport and another at their accommodation. Both were quarantined temporarily. They had tested positive even though they had been vaccinated twice and had a negative certificate.

Questions were raised about the fact that the rest of the delegation who had close contact with the individual who tested positive was granted "special treatment" and was allowed to enter the country and move to Izumisano City, Osaka Prefecture, where the training camp was located. It was also pointed out that there were inadequacies in the quarantine law to ensure the effectiveness of the quarantine officer's order.

〈Issues with Publicizing Infection Cases〉

There was also a case in which a problem arose over the disclosure of infection information. The Lambda strain, a mutated form of SARS-Cov-2, was confirmed for the first time in Japan in an Olympic staff who had entered the country from Peru. The case was reported on Aug. 16, after the Olympics were closed. According to the Ministry of Health, Labour and Welfare and other officials, the woman had arrived at Haneda Airport from Peru in South America on July 20. She tested positive for COVID-19, and the National Institute of Infectious Diseases later analyzed the virus and found it to be of the Lambda strain. The announcement was postponed because it did not fall under the category of "VOC" (Variant of Concern). This raised concerns in Japan's border control measures in terms of rapid announcement of infections and its criteria.

On the other hand, the COVID epidemic has helped in establishing Japan's quarantine model, in which quarantine is concentrated at the five major international airports of Narita, Haneda,

Kansai, Chubu Centrair and Fukuoka. Japan should learn from this experience and discuss border control measures in the event that a more powerful communicable disease strikes in the future.

【Actions to Take】

① When special measures are conducted for border control measures, the reasons for such measures should be fully explained to the public, and the operation and management of such measures must be thoroughly implemented.

② Clarify the criteria for announcing cases of infection, referring to the WHO's list of mutant strains and other sources.

1-7 Nation's Decision Making

【Outline and Issues】

In national decision making during the COVID-19 pandemic, the opinion of experts was always heard, however, the reasons for why the final decision was adopted or not, and the process of decision-making was not always clearly revealed. The relationship between the national government and local governments was also not clear, and some decisions were delayed in that respect. As the policy decision-making process was unclear and risk communication with the public was not effectively conveyed, national decisions and messages did not foster a sense of unity.

The opinions of experts have not always been reflected in the government's tourism support measures "Go To Travel" or in the measures to boost demand for food service "Go To Eat." In some respects, communicable disease control had taken a back seat to economic priorities.

In regard to the Tokyo Olympics and Paralympics, it is difficult to say that the government had fulfilled its responsibility to fully explain why the Games had to be held amid a pandemic. It is expected that opinions of the government and the experts would differ, but the issue of accountability to the public has emerged, as to the process of how the decision was made to adopt, partially adopt, or reject the experts' opinions.

It is important to develop highly specialized human resources to serve as core personnel in preparation for pandemics. As the state of emergency was declared repeatedly, administrative issues emerged, such as how to increase the number of tests and hospital beds, and how to maintain the functions of public health centers. The concept of an "active roster" is a good way to identify

essential core personnel, including politicians, experts, and bureaucrats, in case of emergencies. It is necessary to clarify the chain of command and create a system that can promptly respond to controlling communicable diseases.

Issues also remain with the media. Since the outbreak of COVID-19 in 2020, the media has reported on the severity of the pandemic, basically by announcing the number of newly infected people. However, it is questionable whether the media has made efforts to conduct steady investigative reporting, such as uncovering the actual circumstances of securing hospital beds. Overall, news coverage tended to be partial, biased toward negative aspects, and chose catchy topics without much follow up.

Issues have also emerged regarding the relationship between the national government and local governments. Local governments are more likely to have specific information on the infection situation and to make accurate decisions. Wakayama Prefecture was recognized for its "Wakayama Model" in which it successfully contained clusters within a public hospital. As Japanese healthcare has always been localized, it is difficult for the national government to take a leadership role. However, communicable diseases are a nationwide problem, and without common data and standards for all 47 prefectures, comparisons cannot be made. The role of the national government and prefectural governors should be made clear, so that national and local governments understand clearly their responsibilities and tasks in times of emergencies.

【Actions to Take】

① Summarize and review the national policy decision-making of the COVID-19 pandemic as soon as possible, and use the lessons learned to prepare for the next contingency.
② In the event of an emergency, leaders of the national government, local governments and other organizations need to have a common goal to solve the problem, convey the message as one voice, and engage in dialogue through risk communication to reduce the division among citizens.
③ Strengthen national contingency preparedness to deal with new pandemics. For example, create an active roster, in which core personnel can be called upon immediately and take actions.

1-8 Tokyo Olympic and Paralympic Games

【Outline and Issues】

〈Accountability of the Government as Hosting Country〉

The Tokyo 2020 Olympic and Paralympic Games were postponed for one year due to the COVID-19 pandemic. They were held from July to September in 2021. This one-year postponement did indeed have an effect in terms of communicable disease control. The understanding of the virus was better, making it easier to take measures. Vaccination had also begun. However, the games were held in the midst of the Delta variant spread, with the number of infected cases significantly higher than the year before. With the exception of the 1920 Antwerp Games in Belgium held 100 years ago in the immediate aftermath of World War I and before the Spanish flu pandemic was under control, this was the first time that both the Olympics and Paralympics was held amid a pandemic.

As a state of emergency was declared in Tokyo and the medical care system was under a lot of stress, public opinion in several surveys showed that the majority of people were in favor of canceling or postponing the event. Despite the fact that experts were calling for cancellation or postponement due to the overwhelmed healthcare system, the government insisted on holding the event. It is difficult to say that the Japanese government, as the host country, had adequately explained to its citizens and the world why the event had to be held under a pandemic. Risk communication and consensus building remain an issue.

The International Olympic Committee (IOC) officials did not give enough consideration to the actual situation or the public sentiment in Japan. Unconvincing statements were made including how Japanese people have the mental strength to overcome this difficulty. This too can be blamed on the lack of explanation by the government, the Tokyo Organizing Committee for the Olympic and Paralympic Games, and the Japanese Olympic Committee (JOC). There was not enough risk communication to the general public. Unfortunately, consensus building involving the public regarding the event were not necessarily successful.

〈Effectiveness of the Bubble System〉

A “bubble system” was adopted for the Tokyo Olympic and Paralympic Games in which the host city was enclosed in a bubble to cut off contact between the people involved in the Games and the outside world. Although there were cases of infection and some individual issues, it can be said that the bubble system itself functioned effectively as a measure to prevent the spread. The IOC spokesperson called this a “parallel world” and emphasized the fact that the athletes’ village was

under one of the strictest "lockdowns" in the world. Instead of avoiding the 3C's, it was a way for the public and the Olympic athletes and staff to operate in "separate worlds where they do not mix." PCR testing on the athletes and staff was also conducted on a daily basis at a high level of thoroughness.

The organizing committee distributed a "playbook" which outlines the rules necessary to prevent infection and asked for written pledges to tighten up and ensure compliance. Rather than issuing the playbook abruptly, the organizing committee built a consensus beforehand and communicated closely with the involved parties to create a momentum for compliance with the rules. There were cases where foreign athletes violated the rules by leaving the village for sightseeing purposes, but this was prevented from happening again with penalties such as revoking their Olympics accreditation.

According to the Olympic Organizing Committee, the total number of Olympic-related COVID-19 cases since July 1, when the playbook was applied, was 863. This included 41 athletes, 201 event officials, 50 media personnel, 29 organizing committee staff, 502 tournament contractors, and 40 volunteers. As shown by the high number of infected contractors, moving in and out of the bubble created a hole in the bubble and the risk of infection tended to increase. Even when they stayed within the bubble, there were cases of concern about contact with other hotel guests. However, there were no clusters within the bubble, and no secondary or tertiary spread of infection.

〈The Ban of Spectators and its Effect〉

The decision to hold the Games without spectators was made late in response to the spread of infection and intensifying public pressure. But in the end, the decision to hold the Games without spectators had a certain effect in preventing the spread of infection. Among the host cities, Tokyo and 4 prefectures banned spectators, the 3 prefectures allowed only local spectators. No foreign spectators were allowed. The Cabinet Secretariat's "Coordination Meeting for COVID-19 Countermeasures at the Olympic and Paralympic Games Tokyo 2020" examined the bubble system and discussed how to maintain the "core of the Olympics" while holding the Games amidst a pandemic. The "core" was defined as "a group of world-class athletes competing to become number one", which allowed for no spectators to become an option.

The timing of the Olympics coincided with the 5th wave of the highly infectious Delta strain. For this reason, many criticized the Olympic Games for possibly triggering the 5th wave. However, in reality, while the Games were held without spectators, the flow of people decreased, and the effective reproduction number of COVID-19 also dropped. This may have been due to traffic restrictions and widespread calls asking people to stay at home. Looking at the number of

infected cases, the peak of the 5th wave came in August, while the peak of the number of athletes and tournament officials entering Japan was in mid-July. Assuming that the bubble system was functioning to a certain extent, there is a one-month gap. Thus, the Olympics cannot simply be linked to the 5th wave.

〈"Passing Mark" Thanks to On-Site Efforts〉

Even though the overall tactics and specification of roles had not been clearly established by the organizing committee, on-site leaders dealt with various specific issues and managed to carry out their duties. For example, those in charge of transporting PCR test specimens were often unsure of where to submit them, among the 60 collection points. Many of the staff were temp workers and had no choice but to handle the specimens with their bare hands when carrying out their duties. Their working environment did not protect them, nor were there any laws to protect them. In many respects, the effort of on-site leaders working to solve daily problems earned the organizing committee a "passing mark" in the management and smooth execution of the event.

If you look at only one side of the parallel world, inside the bubble of the Olympic and Paralympic Games, the Games may have been a success even under the state of emergency. However, when we look outside the bubble at Japanese society, it is clear that the status of the epidemic had become more serious, into a state where some citizens could not receive adequate medical care. As an international event that puts national pride on the line, it can only be a true success if it is held with the consensus of the people, ensuring the safety of the practitioners, and with the cooperation of the majority of the people.

【Actions to Take】

① Summarize and review the Tokyo 2020 Olympics and Paralympics, including proof of vaccination, effectiveness of testing, and decisions made by the management, to use as a reference in dealing with future contingencies.

② For large-scale events hosted by international organizations such as the IOC, the government should explain the current status of the host country's medical system and public sentiment to the organizers and encourage them to adjust the method and timing of the event to better suit the hosting country.

③ Rather than relying on on-site efforts, create a system that functions as an organization by checking the chain of command, clarifying the command post, and promoting the development of laws to ensure the safety of those in charge of practical operations.

④ In order to make use of the experience gained from the Tokyo Olympics and Paralympics in future international events such the next Olympics and Paralympics in Beijing and Paris, share the accumulated knowledge and data with the rest of the world.

1-9 Public Involvement

【Outline and Issues】

The cooperation of the general public is essential for communicable disease control.

In the ongoing COVID disaster, the expression *jishuku-zukare*, that can be translated as "fatigue from self-imposed restraint", is being used. It describes the situation where the public's cooperation with requests from the government and local municipalities became less and less forthcoming. At the root of the problem is a sense of being "forced" to do things that are not based on their will.

In another case, HER-SYS and COCOA lacked the user's point of view in development, thus turned out to be an inconvenient system, troublesome for the users to input data.

In order to solve these types of problems, such as the public feeling forced to do things and the lack of user friendliness, it is important to have a "social marketing" perspective that utilizes marketing concepts to solve social issues.

Instead of launching messages or policies straight away, the key is to identify groups not only by external criteria such as age and occupation, but by groups that have similar beliefs, attitudes, and behavioral patterns. Messages that are attuned to the values and awareness of each group should be sent out. Rather than taking an "authoritative approach", leaders should listen to the concerns and opinions of the public, create policies together with them, and implement them together. By doing so, the public will have a sense of involvement and will be able to commit themselves proactively.

Listening to the public about the circumstances and feelings behind the dissatisfaction and resistance, as well as the reasons why they are unable to act, and then working together to find ways to resolve the issues can often lead to innovation. By sharing with the whole society, examples of the things that are not working well, it may increase the possibility of breaking through barriers. We can also expect countermeasures against communicable diseases to evolve by tapping into the latent ideas of the citizens and utilizing them in society.

As the situation of the epidemic changes, it becomes necessary for the people to cooperate with new policies. When introducing new policies and systems, it is important to recognize that

having to change their actions is something that feels like a burden (an extra cost) to the people. Thus, it is also important to reduce their anxiety and offer benefits that exceed that burden.

The Nikkei FT Communicable Diseases Conference, under the supervision of Associate Professor Yoko URYUHARA of Doshisha University, conducted a public opinion survey on COVID-19 among 1,000 men and women in their 20s to 60s via the Internet at the end of August 2021.

The results are mainly as follows:

1) When asked about the source of information they trusted and used as a basis for making decisions about COVID-19 measures, such as whether to get vaccinated, the highest percentage of respondents trusted "information from public agencies" (59%), followed by "TV" (57%) and "information from family" (55.4%).
On the contrary, the most common source of information respondents did not trust was "information from influencers" (44.9%), followed by social networking sites (SNS) and video sharing websites.

2) When asked about providing proof of vaccination, negative test result, or cell phone numbers using two-dimensional codes (QR codes) in order to reduce the risk of infection several times a month for leisure activities such as eating out or watching sports events, more than 70% of respondents said they would be willing to cooperate. About 70% of the respondents were willing to cooperate when going on vacation a few times a year, and 60-70% were willing to cooperate for frequent errands such as daily shopping. Overall, many are willing to cooperate.

3) A detailed analysis of the open-ended responses regarding the willingness to cooperate showed that the 38 respondents who "Do not want to cooperate at all" in any of the categories of providing proof of vaccination, negative test result, or cellphone number via QR code, expressed much anger and sadness, in which many of the criticisms were not related to the measures themselves. On the other hand, the majority of the 111 respondents who answered "Undecided" to all 3 methods gave "No particular reason". For those who did not show willingness to cooperate, their reasons varied greatly, so it would be advisable to prioritize and provide different measures and information according to each group rather than take a uniform approach.

4) When asked to choose what would make people more willing to cooperate in showing proof of vaccination or negative test results, the top response for those in their 40s and 60s was "When experts show scientific evidence of effectiveness and benefits", while for those in their 20s and 30s it was "When there are financial benefits", and for those in their 50s it was "When I see or hear news

that my generation is prone to become severely ill". In order to encourage people to cooperate, it was suggested that it is necessary to design a detailed system that can send messages in a way appropriate for each generation.

5) When asked about the idea of mandatory health monitoring at workplaces and schools using apps etc. to "swiftly conduct tests when a few people are feeling ill in order to prevent the spread of infection", 77% of the respondents were willing to cooperate in adopting such a system. While the percentage of people who want to cooperate in installing apps and reporting their health condition on a regular basis dropped to about 60%, 76% of the people want to cooperate with testing when someone in their group becomes ill. Detailed analysis is required to determine exactly what makes people hesitant to change their behaviors.

【Actions to Take】

Send out messages that are based not only on external criteria such as age and occupation, but also on the values and awareness held by groups with similar beliefs, attitudes, and behavioral patterns. Instead of taking an "authoritative approach", implement policies together with the public based on a thorough understanding of their concerns and ideas. "Social marketing" methods may also be a good idea. When introducing new policies and systems, attention should be paid to reducing the anxiety of the public, while at the same time, ensuring that they can feel the benefits exceed their anxiety.

2. P3 projects from the Conference and their Future Issues

2-1 Malaria P3 Project Report

With 200 million cases of malaria reported globally, the AMIC Malaria consortium has been developing P3 projects in Asian and African regions since its launch in 2016, in the following three areas; testing and diagnosis, drug discovery, and vector control for prevention. Since last year's conference in November, the project's activities have deepened with progress in vaccine development and the detection of resistant protozoa. However, malaria control continues to lag behind globally in the wake of the COVID-19 pandemic, and the conference reaffirmed the need for continued efforts to combat malaria.

For malaria in Asia, the progress of the industry-government-academia project that centers around the National Center for Global Health and Medicine (NCGM) focusing on the development of new diagnostic and therapeutic methods was reported. They will continue clinical performance testing and activities to obtain WHO prequalification (PQ) for high-sensitivity testing methods (Eiken Chemical: ultra-sensitive test method using LAMP technology for Malaria gene detection, Sysmex: XN-31 automated hematology analyzer that can test for plasmodium at high-speed using flow cytometry). Approved by the PMDA in Japan last year, the insurance coverage of XN-31 has started since September 2021. The LAMP method, along with the flow cytometry method, has been added to the notification criteria under Japan's Infectious Diseases Control Law. Malaria-LAMP has undergone a performance evaluation study at Mahidol University Hospital of Tropical Diseases in Thailand, and its feasibility of detecting asymptomatic malaria in endemic areas is being examined. With regard to a new treatment (Neo-Pharma Japan: 5-ALA supplement to eradicate protozoan parasites and prevent reinfection after treatment), clinical trials are being prepared in Thailand through the Asian Clinical Trial Platform launched by the Communicable Diseases Conference, and the results of a double-blinded cohort study in Laos is being compiled. In addition, 5-ALA was found to completely inhibit the replication of SARS-Cov-2 in vitro, and specific clinical studies on its effects on treatment and sequelae are underway.

For the fight against severe childhood malaria in Africa, the feasibility of malaria eradication in tropical Africa is continuing to be examined, with the SATREPS project of Osaka City University at its core. Through the establishment of local offices and other means, they will strengthen activities in the areas of diagnosis, treatment (XN-31 and 5-ALA supplements mentioned above) and vector control (Sumitomo Chemical: Olyset Plus, a long-lasting insecticidal net that can control insecticide-resistant mosquitoes, and SumiShield, an indoor residual spray), along with local educational activities. Fieldwork with local universities is also planned to become more active. The African Business Consortium, linked to the African Business Council of the Japanese government and launched in the event of TICAD7 in 2019, has started new industry-government-academia collaborations during this COVID-19 pandemic. Under a joint project (Sysmex, Ajinomoto and NEC) in Ghana, a cross-industrial collaboration model to solve local social issues is being explored. In collaboration with the local Ministry of Health and hospitals, projects are moving forward such as human resource training using ICT and addressing malnutrition, a risk factor for malaria, by improving the health of the mothers and their children. There are plans to strengthen activities ahead of TICAD 8, scheduled to be held in Tunisia, Africa in 2022.

2-2 Antimicrobial Resistance (AMR) P3 Project Report

Communicable diseases caused by drug-resistant (AMR) bacteria are predicted to cause about 10 million annual deaths worldwide by 2050 if no action is taken. In Japan, it has been estimated that about 8,000 people die annually from two types of drug-resistant bacteria. On the other hand, the development of new antimicrobials to treat drug-resistant bacteria infections has been drastically reduced, due to its difficulty, high costs, and low profitability. Even if commercialized, the use of antimicrobial drugs is usually held back in order to prevent the emergence of drug-resistant strains, and therefore it is difficult to secure retail sales and expect enough profit that matches investment. Many countries are adopting "push incentives" which support the funding of R&D, however, except for a few experimental cases, there aren't any fully established "pull incentives" that offer support after drug approval. Aiming to secure profit after approval and to build a pull incentive system to sustainably support R&D of AMR drugs, AMIC decided to launch its 5th consortium, the "AMR consortium" at the 6th Nikkei Asia Africa Conference on Communicable Diseases.

Even as we face the COVID-19 pandemic worldwide, steady progress has been made in 2021 on AMR measures both domestically and internationally. At the G7 summit held in the UK in June, it was agreed not only at the Health Ministers Meeting but also at the Finance Ministers Meeting that AMR is a "silent pandemic" that needs to be addressed quickly and surely. In Japan, it was clearly stated in the Basic Policy on Economic and Fiscal Management and Reform (*Honebuto no Hoshin*) approved by the Cabinet in June, that the government will play a leading role in AMR measures, and the "Pharma Industry Vision 2021" published by the Ministry of Health, Labour and Welfare in September points out the low profitability of drugs for communicable diseases, including antimicrobial agents. It was also stated that the introduction of pull-type incentives should be considered.

At the meeting, Sally Davies, the government's special envoy for AMR in the UK (host country of the G7 summit), gave a video presentation, saying that the COVID-19 pandemic is a wake-up call to take action before a health crisis caused by AMR occurs, and expressed hope for Japan's leadership in the fight against AMR. She also emphasized that investment initiatives are playing a growing role in the private sector.

It was reported at the conference that the AMR consortium released a proposal to the government in March regarding the introduction of a pull-type incentive system in the antimicrobial market (See reference link below), and also that the group has been continuously working on the proposal since then. The proposal focuses on the Market Entry Reward (MER), which guarantees an appropriate return on investment in addition to sales based on the amount of antimicrobial use, the Subscription Model (SM), which pays a fixed fee periodically regardless of the amount used, and

the Profit Guarantee Scheme, which guarantees the same level of annual profit as drugs other than antimicrobial agents. The total budget scale is estimated to be 20 to 80 billion yen (200–800 million USD) per product (which equates to 2 to 8 billion yen [20-80 million USD] annually if paid over a 10-year period). Pharmaceutical companies pointed out the importance of industry-government-academia collaboration, noting that the UK, for example, which is experimenting with pull-type incentives, has established an environment in which a large number of antimicrobial drugs are available. They also pointed out the importance of collaboration, in light of the fact that a list of resistant bacteria requiring priority measures in Japan was compiled by the "AMED Industry-Academia-Government Liaison Committee for Infectious Disease Drug Discovery" formed by the Agency for Medical Research and Development (AMED) under the jurisdiction of the Ministry of Health, Labour and Welfare, academia, and the Japan Pharmaceutical Manufacturers Association.

Japan will host the G7 summit in 2023. In addition to antimicrobial drug development, standard precautions such as disinfection are also important. AMR is a cross-border threat, and it is essential to include developing countries in these measures. Moreover, both COVID-19 and AMR are zoonotic diseases, and it was confirmed that there is a need to discuss them in a "One Health" perspective within health crisis management. In addition to deepening discussions to organize financial resources for pull-type incentives, the consortium reported that it will continue to work on education and raising public awareness.

Reference link: https://www.amralliancejapan.org/wp/wp-content/uploads/2021/03/RecommendationsOnPullIncentivesForAMRInJapanExecutiveSummary_JPN.pdf

2-3 Candidates for the Next Communicable Disease P3 Project

The P3 project has achieved a certain level of success in each of the AMIC consortiums, paving the way for seeds of Japan's technology to contribute to global communicable disease control. The possibility of the next P3 project was also discussed at the conference.

On neglected tropical diseases (NTDs), the establishment of a new consortium was suggested. NTDs are parasitic and bacterial infections that are widespread mainly in among the poor in tropical regions, and the Japanese government has been playing a leading role in the fight against these diseases alongside with the fight against global poverty. However, in terms of actual corporate activities, it cannot necessarily be said that projects related to this field has been making

significant contributions, including profit wise, and thus more support is necessary in order to strengthen Japan's further contributions in this field. To enhance Japan's presence in global health at TICAD8 and other forums, it is necessary to strengthen industry-government-academia collaboration that promotes concrete social implementation of related products and technologies.

In terms of communicating to the public via mainstream media and social networking platforms to incite behavioral changes such as receiving vaccination, the UK had published a guideline in July 2020. A preparatory meeting to initiate national discussions for the next conference in preparation for the next pandemic was also suggested.

3. Conclusion

It is still a long way before the global society defeats COVID-19. However, now that Japan and the rest of the world are now acquiring powerful weapons to curb the COVID-19 pandemic compared to the previous year: vaccines, neutralizing antibodies, and oral therapeutic drugs, it is becoming possible to control the infection and gradually resume socioeconomic activities. This statement is a proposal to further achieve this. Participants of the 8th Nikkei FT Communicable Diseases Conference have agreed to this statement.

4. Appendix

(Information as of October 24, 2021)

[Commercialized Vaccines]

mRNA

- Moderna(US) **mRNA-1273**（Approved in 76 countries）
- Pfizer (US) /BioNTech (Germany) **BNT162b2**（Approved in 103 countries）

Viral vector

- Janssen (US - Johnson & Johnson) **Ad26.COV2.S**（Approved in 75 countries）
- University of Oxford (UK)/AstraZeneca (UK) **AZD1222**（Approved in 124 countries）
- Serum Institute of India (India) **Covishield** (Formulated by University of Oxford and AstraZeneca)（Approved in 46 countries）

Inactivated

- Sinopharm (China) **BBIBP-CorV（Vero Cells）**（Approved in 68 countries）
- Sinovac (China) **CoronaVac**（Approved in 41 countries）

[Vaccines Under Development in Japan]

mRNA

- Daiichi Sakkyo **DS-5670**（Phase II clinical trial starting in November）
- VLP Therapeutics Japan **VLPCOV-01**（Phase I clinical trial）

Recombinant protein

- Shionogi **S-268019**（Phase II/III clinical trials）

Inactivated

- KMBiologics（Meiji Seika Pharma）**KD-414**（Phase II/III clinical trials）

Plasmid DNA

- Anges **AG-0301、AG-0302** (Phase III clinical trial)

Viral vector

- ID Pharma (I'rom Group) **IRO-203** (Under discussion for clinical trial)

[Vaccines Manufactured and Formulated in Japan]

Viral vector

- University of Oxford (UK)/AstraZeneca (UK) **AZD1222** (manufactured by JCR Pharma, formulated by KM Biologics and Daiichi Sankyo)

[The Cartagena Act]

The Cartagena Act is the commonly known name for the Act on the Conservation and Sustainable Use of Biological Diversity Through Regulations on the Use of Living Modified Organisms. In Japan, the law also applies when using living modified organisms in pharmaceuticals, and procedures such as ministerial approval are required for manufacturing.

[Emergency Use Authorization (EUA)]

Emergency Use Authorization (EUA) is a system under which the US Food and Drug Administration (FDA) allows the use of unapproved drugs or expands the indications of already approved drugs in emergency situations. It is applied when it is determined that the following criteria are met: (1) the disease is life-threatening; (2) the product has a certain level of efficacy in treating the disease; (3) the benefits of using the product outweigh the potential risk of using the product; and (4) there are no adequate alternatives available for diagnosing, preventing, or treating the disease. However, EUA is not an official approval and can be revoked flexibly if new data on safety and efficacy emerge.

[Therapeutic Drugs Approved in Japan]

- For moderate to severe cases
- Gilead Sciences' antiviral drug **Veklury** (remdesivir)
- Immunosuppressant steroid (dexamethasone)
- Eli Lilly Japan's immunosuppressant drug **Olumiant** (baricitinib)
- For mild to moderate cases with risk of severity
- Chugai Pharmaceutical's neutralizing antibody drug **Ronapreve** (casirivimab/imdevimab)
- GlaxoSmithKline's neutralizing antibody drug **Xevudy** (sotrovimab)

[Orally Administered Small-Molecule Drugs Under Development]

- Fujifilm Toyama Chemical's antiviral drug **Favipiravir** (Phase III clinical trial)
- Merck's antiviral drug **Molnupiravir** (Preparing request for approval)
- Pfizer's antiviral drug **PF-07321332** (Phase II/III clinical trials)
- Shionogi's antiviral drug **S-217622** (Phase II/III clinical trials)
- Swiss drugmaker Roche's antiviral drug **AT-527** (Phase 3 clinical trial)

[The 8th NIKKEI FT Communicable Diseases Conference]

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〈Reference〉

Contents of the 8th the Nikkei FT Communicable Diseases Conference
Special Agenda / Special Sessions / Breakout Sessions

Special Agenda (The Japan Pharmaceutical Manufacturers Association)
"Preparedness for Emerging and Re-emerging Infectious Diseases Including Antimicrobial Resistance (AMR) – Expectations for economic security and control tower function"

Throughout history, we have experienced numerous communicable disease pandemics, and it is expected to occur in the future every few years. Meanwhile, antimicrobial resistance (AMR) bacteria, which have emerged from the overuse of antimicrobial agents, is also a major threat to humanity. To prepare for emerging and re-emerging communicable diseases, the development of vaccines and therapeutic drugs is crucial for the nation's economic security. Japan needs to quickly establish a system that will allow the country to keep pace with other G7 countries in the development of vaccines and therapeutic drugs.

In June, the Japanese Cabinet approved the "Strategy for Strengthening Vaccine Development and Production". It announced a policy to newly establish the "Strategic Center of Biomedical Advanced Vaccine Research and Development for Preparedness and Response (SCARDA)" within the Japan Agency for Medical Research and Development (AMED) in order to swiftly conduct R&D of vaccines during emergencies. Research funds should be strategically provided to the center on a regular basis during normal times.

Japan must become a leader in combating emerging communicable diseases, and AMR is extremely important for both diplomatic and public health reasons. Industry, government, and academia need to work closely together in order to have the capacity to conduct research, develop, and produce not only vaccines but also therapeutic and diagnostic drugs in Japan. Moreover, it is important to develop human resources and a framework for speeding up and allowing more freedom on research. This can be done, for example, by bridging academia and bio-ventures to pharmaceutical companies. In order to do so, it is essential to have a government command center that not only plays the role of coordinating, but also has strong responsibility and authority.

Special Agenda (AiPharma)
"How International Consortium Accelerates Drug Development for COVID-19"

Ai Pharma, a biotechnology company with offices in the US (Boston), Dubai, UAE, and Japan (Tokyo), focuses on the development of antiviral drugs. Currently, they are conducting Phase III clinical trials of favipiravir under the license of Fujifilm. The company's CEO,

Alessandro GADOTTI, said in a video message at the beginning of the special agenda that the subject of discussion, "How international consortiums should operate" was "in line with the corporate philosophy".

Regarding international cooperation in drug development, the importance of international clinical trials emerged as a topic as the world faces the COVID-19 pandemic. With regard to vaccines in particular, Japan has not been able to conduct joint clinical trials because of a low case rate. The management of international clinical trials should be considered an important matter that will give Japan an opportunity to demonstrate its leadership to the world. There are high expectations towards Japan and the country's scientific capabilities.

In terms of achieving international cooperation, the Nagoya Protocol or the Cartagena Convention, international frameworks for the transboundary movement of endangered species and living modified organisms, are an issue. Because these biodiversity conventions also apply to viruses and bacteria, they sometimes become an obstacle in obtaining viruses and bacteria for the development of vaccines, diagnostics, and therapeutic drugs. We need to consider how to overcome this problem in the context of a new global treaty on pandemics and preparedness. It is also necessary to create a "bio-hub" system where pathogens that pose a danger to the health and safety of the world are collected at specific locations and provided to various research institutions.

In the midst of the COVID-19 pandemic, the business model for drug development has also changed. Major pharmaceutical companies Pfizer, Moderna, and AstraZeneca did not create vaccines from scratch, but rather took up the seeds that had been nurtured by start-up companies and academic institutions. If Japanese pharmaceutical companies do not adapt to such a business model, they will not be able to keep up with the speed of global drug development. Establishing a system to speed up the process of drug development and commercialization, such as the Emergency Use Authorization (EUA) in the US, will also be an important key for Japan in order to promote collaborative and cooperative development with the rest of the world. Global standardization of data is also necessary in order to efficiently conduct clinical trials simultaneously around the world.

Special Session① (ICheck)

"Effectiveness of Antigen Testing in the Prevention of COVID-19 Infectious Diseases"

People with COVID-19 can transmit it to others within 4 or 5 days after being infected. Many patients are asymptomatic or have only mild symptoms. Another characteristic of COVID-19 is that the condition can deteriorate rapidly. Epidemiological studies outside Japan suggest that frequent use of low-sensitivity tests, such as antigen tests, can identify infected individuals more quickly and help control the spread of infection, compared to less frequent use of high-sensitivity tests, such as PCR tests. At workplaces, nursing homes, and schools where there is a high risk of

infection clusters, frequent and repeated antigen testing can identify clusters at an early stage and prevent the wide spread of infection.

Clinical studies are showing that early testing, diagnosis, and drug administration allows antiviral drugs to be more effective. In a clinical trial of Fujifilm Toyama Chemical's anti-influenza drug Avigan (generic name: favipiravir), they took out and examined a group of people that participated in the trial within 72 hours after the onset of the illness. Patients who took the Avigan tablets recovered faster compared to those who took placebos.

Establishing a system of early testing, early diagnosis, and early treatment would not only benefit individual patients, but also benefit the community by preventing hospitalization and thereby securing hospital beds. It was agreed that early testing and diagnosis is crucial to maximize the effectiveness of oral antiviral drugs.

Special Session② (Daiichi Sankyo Co., Ltd.)

"Collaboration among Stakeholders to Implement the 'Strategy for Strengthening Vaccine Development and Production'"

The delay in commercialization of domestically produced vaccines against COVID-19 can be explained by the fact that Japan's vaccine industry has not been strategically nurtured and accelerated compared to Europe and the US in creating an environment that encourages sustained R&D of vaccines, reviewing pharmaceutical regulations, and developing a system that enables stable manufacturing, supply, and distribution. Furthermore, public support for R&D of vaccines to prepare for pandemics has been insufficient, and innovative production technologies and development skills have not been accumulated.

In order to prepare for contingencies such as a pandemic, it is important that all stakeholders in industry, academia, and government work together to revitalize the vaccine industry by improving the environment for vaccine research and development, production, and distribution. In addition, there is a need for a system that enables the early commercialization of domestically developed and manufactured vaccines by quickly creating domestic seeds or adopting overseas seeds in the event of a contingency. The rapid commercialization of domestically produced vaccines will not only bring safe and effective vaccines to the citizens of Japan as quickly as possible, but will also lead to international contributions by providing them to low-income and lower-middle-income countries.

In June 2021, the Japanese government made a cabinet decision to approve the "Strategy for Strengthening Vaccine Development and Production" in order to strengthen the R&D and production system of domestic vaccines on a national level in preparation for future epidemics. The strategy includes nine measures: (1) formation of R&D centers, (2) strengthening of funding functions, (3) development and expansion of clinical trial environments, (4) establishing the

standards and speeding up the regulatory approval process, (5) setting up manufacturing bases, (6) fostering drug discovery venture companies, (7) fostering and promoting the industry of vaccine development and manufacturing, (8) promotion of international cooperation, and (9) strengthening the monitoring system for communicable diseases. In order to implement these strategies, the government needed to establish a control tower function to formulate and implement comprehensive policies for communicable disease control that transcends the boundaries of ministries and agencies. In order to realize (2), a policy was presented to establish the Strategic Center of Biomedical Advanced Vaccine Research and Development for Preparedness and Response (SCARDA) within the Japan Agency for Medical Research and Development (AMED) as a control tower function to develop a system for the research, development, manufacture, and supply of vaccines in preparation for emergencies. Under SCARDA, industry, academia, and government are expected to work together to steadily implement the "Strategy for Strengthening Vaccine Development and Production" and establish a foundation that can respond any time, even in emergencies.

It is also essential that industry, academia, and government establish a foundation for the commercialization of various types of vaccines, including new types such as mRNA and viral vector vaccines. Since the spread of communicable diseases is unpredictable, and even if a vaccine can be commercialized, it is a great risk to companies as the marketability cannot be foreseen. Therefore, in addition to large-scale government support for R&D and capital investment, the government should also consider creating a system that increases predictability, such as buying up and stockpiling domestically produced vaccines. In preparation for contingencies, it is also essential to review regulations to speed up and streamline the review and approval process, as is the case with emergency use authorizations (EUAs) overseas in the US.

The COVID-19 pandemic has also revealed that the world is in a state of an "infodemic" where the Internet and other media are flooded with fake news, rumors, and false information, making it difficult for citizens to access and understand correct information regarding vaccines. In order for people to recognize the importance of vaccination, it is essential for stakeholders to work together not only during times of emergencies but during normal times to proactively collect data on safety and efficacy, share the data, and promote efforts to deepen understanding of vaccines through mutual communication with the public.

Special Session③ (KM Biologics / Meiji Seika Pharma Co., Ltd.)

"Japan-made inactivated COVID-19 vaccine

– positioning of the vaccine and scenario for the earliest supply – "

Meiji Seika Pharma, Meiji Group's leading manufacturer in the field of communicable diseases, and KM Biologics are developing a domestically produced inactivated vaccine (code name:

KD-414) for COVID-19.

Several new types of COVID-19 vaccines, such as mRNA vaccines and viral vector vaccines, have been commercialized and are being administered worldwide. However, these new types of vaccines are associated with adverse reactions such as pain in the injected area, fever, fatigue, headaches, muscle and joint pain, chills, and diarrhea. On the other hand, inactivated vaccines have an extensive track record and have been administered for many years to many people from children to the elderly, as seasonal influenza vaccines and 4-in-1 (DPT-IPV) vaccines for children.

Among them, KD-414 is expected to be a highly safe vaccine, using aluminum hydroxide as an adjuvant, which is used in vaccines worldwide. In the Phase I/II clinical trials of KD-414 conducted in Japan on 210 patients ages 20 to 65, the tolerability and safety of the vaccine were confirmed regardless of the dose, and a certain level of efficacy could be expected from the results. In terms of safety, the only severe adverse reaction that occurred within 28 days after vaccination was a single case of recoverable fever, which was considered to be not significantly different from other vaccines such as the seasonal influenza vaccines. Furthermore, KD-414 is easy to supply as it can be stored at temperatures ranging from 2℃ to 8℃ and does not require special facilities or equipment for storage or transportation.

KM Biologics is currently conducting Phase II/III clinical trials of KD-414 in 2,000 adults, age 18 and older in Japan. At the same time, it is stepping up its manufacturing system by utilizing existing facilities. Moreover, the company is planning to conduct clinical trials on adults receiving their booster dose, Phase III clinical trials using approved vaccine (actual drug) in Asia, and clinical trials on children. Based on the data from the Phase II/III clinical trials and the booster dose clinical trials, the company intends to obtain early approval for the booster vaccination in Japan and commercialize it by the end of 2022.

In order to control the spread of COVID-19 and resume socioeconomic activities, it is important to increase the vaccination rate as well as implement booster doses and maintain the effectivity of the vaccine. To do so, it is advisable to rapidly commercialize a domestic vaccine with a high level of safety that can be administered to people who cannot be vaccinated with previously approved vaccines due to allergies or other reasons, people who are hesitant for fear of adverse reactions, and even to children and infants.

Special Session④ (Fujifilm Toyama Chemical Co., Ltd.)

"COVID-19 Treatment Strategy By Antiviral Drug Early Intervention"

There are high hopes for antiviral drugs that can work effectively in the early onset of COVID-19. Once the virus infects a person, it multiplies rapidly in the body in the early stages before the symptoms appear. The amount of virus reaches its peak about one week later, then gradually declines. Therefore, it is thought that the risk of evolving into a severe case can be reduced

by administering antiviral drugs in the early onset to suppress replication of the virus in the early stages of infection. In fact, multiple animal studies and clinical trials have supported the benefit of early administration of antiviral drugs.

Antibody drugs (neutralizing antibodies) that can be administered in the early onset of COVID-19 require complicated adjustments before administration and cannot be administered easily. Moreover, the drugs are costly. On the other hand, antiviral drugs are low-molecular compounds, in which many can be administered orally, and their low cost makes it easy to administer to many patients.

In Japan, during the 5th wave of the pandemic that peaked in August 2021 becoming the largest wave so far, many individuals who tested positive but were asymptomatic or had mild symptoms, were forced to quarantine at home or receive treatment in accommodation facilities. There were also a number of people who were at risk of becoming severely ill. Under these circumstances, there is much anticipation for an antiviral drug that can be administered in the early onset to patients self-isolating at home or at accommodation facilities to reduce the risk of evolving into a severe case. If this risk can be lowered, it will help reduce the burden on the healthcare system.

COVID-19 is an acute viral infection, and it is desirable to establish comprehensive disease control measures that combine vaccines, diagnostic drugs, and therapeutic drugs.

Fujifilm Toyama Chemical's anti-influenza drug Avigan (generic name: favipiravir) is an orally administered antiviral drug that selectively inhibits RNA-dependent RNA polymerase. The drug inhibits RNA synthesis of SARS-CoV-2, an RNA virus, and has the mechanism to stop the virus from replicating. Several antiviral drugs have been developed for COVID-19, but many of them have only been administered to a limited number of patients. In contrast, it can be said that Avigan is a drug that has a fairly well-understood safety profile through its numerous clinical trials.

In Japan, Fujifilm Toyama Chemical is conducting a Phase III clinical trial involving 316 patients in the early onset who are at risk for evolving into a severe case. In this study, subjects receive oral doses of Avigan or a placebo and the rate of severe disease is compared.

It is hoped that the study will present further clinical evidence that will help the debate on antiviral drugs to proceed.

Special Session⑤ (SHIONOGI)

"Urgent need for measures against AMR threat as silent pandemics"

It is estimated that approximately 8,000 people die every year in Japan from two types of drug-resistant (AMR) bacteria alone. Compared to the total of 18,000 COVID-19 deaths, we need to place AMR as a crisis that should to be called "a silent pandemic." It is not only being brought into Japan from overseas, but there is an increasing number of cases in which drug-resistant strains of bacteria are detected in people who have no record of overseas travel.

There are two issues that make antimicrobial drugs that fight against drug-resistant bacteria difficult to develop. 1) new development is sluggish due to the high cost and low profitability and 2) the supply of the currently available antimicrobial drugs is shrinking. From the perspective of R&D, it is crucial for universities and other institutions to set the stage for basic research that turn into seeds for finding candidate substances which are effective against communicable diseases. The importance of industry-academia collaboration for conducting clinical trials was also pointed out. With regard to clinical trials, different countries and regions have different requirements. Thus, it is necessary to conduct multiple trials, leading to the issue of large R&D costs. Another hurdle pharmaceutical companies face is figuring out how to maintain and expand manufacturing facilities to ensure a stable supply of drugs for communicable diseases in which outbreaks and pandemics are difficult to predict. Specifically, 100~200 billion yen (1~2 billion USD) is required for R&D, and around 50 billion yen (500 million USD) after approval. However, sales in the first few years after approval are often less than several billion yen (less than 100 million USD), and although the "real value" is said to be several hundred billion yen (several billion USD), it is not a viable business. "Push-type incentives" that support the process of obtaining approval are being put into place at the global level, but no global "pull-type incentives" have been established to support after approval. It was voiced that the industry, government and academia should work together to realize this goal. Moreover, infections caused by resistant strains of bacteria cannot be treated properly unless they can be diagnosed rapidly. It was also expressed that the infrastructure for rapid testing such as PCR, established nationwide due to the COVID-19 outbreak, should be utilized for the diagnosis of AMR.

Among the issues that Japan should tackle are: to promptly revise the National Action Plan on Antimicrobial Resistance developed by the government in 2016 that expires in 2020, and to incorporate AMR issues into the deepening discussion on health crisis management around the world in the wake of the COVID-19 pandemic. In anticipation of Japan becoming the host country for the upcoming G7 Summit in 2023, it was agreed that there is a need for industry, government and academia to mutually prioritize this issue so that Japan can lead the discussion and demonstrate the achievements of AMR measures, including pull-type incentives.

Special Session⑥ (Tokyo Metropolitan Government)
"COVID-19 and Risk Communication"

Risk communication is an act intended to share information and viewpoints through the exchange of information and opinions among individuals, institutions, and groups. It is easy for many people to be afraid of communicable diseases because the microorganisms that cause them are invisible to the human eye and sometimes isolation is required for infected individuals. Lack of information sharing and understanding about communicable diseases often lead to discrimination

and social division. Risk communication is important for helping individuals prevent infection and for preventing discrimination and division in society. Risk communication is essential not only in times of emergency, but also in times of normalcy.

Creating a social network on risk communication that is built upon information sharing, collaborating and cooperating among many people leads to the concept of the "human vaccine."

In October 2020, the Tokyo Metropolitan Government established the Tokyo Center for Infectious Disease Control and Prevention (Tokyo iCDC) as a permanent command center for communicable disease control. One of the eight current "expert boards" is the Risk Communication Team. It is positioned as the most basic and important team in communicable disease control.

The difficulties in risk communication during the COVID-19 pandemic can be summarized in the following 6 points. (1) The message must be delivered quickly, accurately, and plainly in a situation where knowledge is highly uncertain and often unknown. (2) Communicable disease pandemics are long-lasting and its status changes rapidly. (3) Every individual is a stakeholder in risk communication. (4) The systematic risk is high, spilling over into social, economic, political, ethical, and educational issues. (5) Making a one-way request to refrain from a certain action or to change one's behavior may lead to questions, oppositions, and distrust. It is important to acknowledge the "why"s and provide an "acceptable" explanation. (6) As the pandemic becomes more prolonged and problems more complex, it is necessary not only to educate and raise awareness about the risks and to evoke behavioral changes, but also to visualize issues and have two-way communication to build a consensus.

Compared to the 2009 H1N1 influenza pandemic, it was considered that risk communication on COVID-19 worked well in 2020. However, many people feel that was not the case in 2021. One reason for this is the fact that the prolonged period of self-restraint and the worsening economic situation led to the medical community being criticized. As a result, information sent out by the medical community had difficulty reaching the public correctly. Another reason is that there was not enough exchange in risk communication to take into account what the citizens required. Emphasis was put on one-way communication in the early stages of transmission, since the priority was to send out the latest information regarding the new virus. It took more than a year to achieve a common understanding on a virtuous cycle where policies are made based on mutual communication with the public, and then receiving feedback.

Two-way risk communication needs to be incorporated into policy decision-making not only by the national government but also by local governments. It is also essential to expand the public's understanding not only on viruses and vaccines, but also on the Japanese healthcare system, through education and media coverage. It is also advisable to take time to discuss how the restriction of general medical care can be justified.

Breakout Session A (Saraya Co., Ltd.)

"No One Left Behind: Infection Control in Nursing and Welfare Facilities in a Post-COVID World

- Thinking about the role of Industry, Government, Academia Medical and Nursing Care -"

Both nursing homes and medical facilities suffered from the COVID-19 crisis. However, unlike medical facilities, nursing homes had the disadvantage of lacking the human resources and other resources necessary for communicable disease control. Breakout Session A discussed the issues of communicable disease control specific to nursing care facilities and its countermeasures from a medical perspective and from the perspective of private suppliers of various products.

Hitomi KUROSU and her colleagues at the National Institute of Infectious Diseases (NIID) AMR Research Center, started a survey in April 2020 soon after the COVID-19 outbreak, on the infection status of the novel coronavirus in nursing homes and the countermeasures against them. As a result, the following problems were identified: the difficulty for elderly people with deteriorated cognitive functions to conduct basic infection control measures such as wearing a mask; the inability to sufficiently conduct tests to identify outbreaks in real time; the lack of human resources to play a central role in infection control; and the fact that when staff members or their family members become infected, they are required to quarantine at home, which leads to a shortage of manpower at the facility and interferes with daily operations.

Kanagawa Prefecture has taken a policy of compensating for the lack of personnel with specialized knowledge by dispatching special teams. The Corona Cluster Attack Team (C-CAT) was established in May 2020 to be able to intervene quickly in case of cluster outbreaks in medical health and welfare facilities. Takayuki OHISHI, deputy director of the Infection Control Office at the TQM Center of the Kanagawa Saiseikai Yokohamashi Tobu Hospital and a member of the C-CAT, stated, "Leadership by people with expertise is essential for preventing the outbreak of clusters, and we will promote the development of human resources for this purpose."

The sudden outbreak of the pandemic also had a profound impact on the supply chain for disinfectants and PPE (personal protective equipment). Yoko YOSHIDA, managing director of the Medical Business Division of Saraya, a major player in the industry, recalled, "The volume of product shipments reached five times the normal level at hospitals during the peak period, and ten times the normal level at nursing homes. Compared to medical facilities, the number of orders from nursing homes fluctuated dramatically. The price hike put a heavy burden on the nursing homes." Since PPE and other products are manufactured overseas, there is inevitably a large time gap between supply and demand. She added that the global shortage of shipping containers for imports and the priority given to supply Europe and the US have combined to "disrupt the supply chain." As a lesson from this experience, she said, "It is important to be able to share information with users on a regular basis so that we can respond to sudden changes in demand, and to comply with infection control measures daily."

Michikazu KOSHIBA, the general manager of the Social Impact Partnership Business Department at Mitsubishi UFJ Research and Consulting, who moderated Breakout Session A, concluded, "This pandemic was an unprecedented event for which we could not prepare adequately in advance, but it was also an opportunity to learn. It is important to share what each of us has learned in order to use it as wisdom to prepare for the next pandemic."

Breakout Session B (FUMAKILLA LIMITED)

"Problems with insecticide resistance development: How to use the discovery of mutant mosquitoes to vector control"

In order to overcome malaria and dengue fever, it is essential to control the mosquitoes that transmit these diseases, but the emergence of insecticide-resistant mosquitoes has become a major problem worldwide. The National Institute of Infectious Diseases (NIID) has developed a technology to analyze the emergence and mechanism of resistance by analyzing mosquito genomes. Fumakilla, which has been working on detecting insecticide-resistant mosquitoes around the world, used this technology to discover and report on a highly resistant Culex quinquefasciatus mosquito in Brazil.

Pyrethroid is a widely used insecticide proven to be safe and effective. However, genetic mutation of the sodium channels which are the point of action, increased metabolic activity due to induction of detoxification enzymes, and mechanisms such as decreased skin permeability has led to the emergence of pyrethroid-resistant mosquitos in various parts of the world causing a threat to public health. Fumakilla, a manufacturer of insecticides, has been quick in identifying the emergence of such resistant mosquitoes, and has been developing and providing insecticides in roughly 70 countries around the world.

Dr. Shinji KASAI, Director of the Department of Entomology at the National Institute of Infectious Diseases, and his colleagues have been developing a capture probe method, a next-generation sequencer, and a technology to search for genetic mutations in the sodium channels of insecticide resistant mosquitoes using newly created analysis software. Dr. Kasai commented "This technology will enable us to quickly understand the correlation between genetic changes in sodium channels and resistance. However, presently we lack the data necessary for analysis, so we need to build a database of genetic and phenotypic information on mosquitoes around the world."

Fumiko KIMOTO, researcher at the Research & Development Department, R&D Division of Fumakilla, analyzed the sodium channel gene of the Culex quinquefasciatus mosquito captured in Brazil with the cooperation of Dr. Kasai, and confirmed that the mosquito was a resistant type with two genetic mutations that had never been reported before. These results were then published.

Fumakilla has been developing new insecticides that are effective against such resistant mosquitoes, but regulations in various countries have become a hindrance to their widespread use.

Tomonori SASAKI, Office Manager at the Research & Development Department of Fumakilla said, "In Brazil, mosquito coils that are ineffective against resistant mosquitoes are currently being sold. This is because there is a strict limit to the types of pyrethroids and the amount allowed to be used in mosquito coils. Efforts by manufacturers alone cannot change this situation. Academic societies, NGOs, and governments must also work together to prompt organizations such the World Health Organization (WHO)."

Hajime INOUE, Assistant Minister for Global Health and Welfare of the Ministry of Health, Labour and Welfare said, "It was reaffirmed that the increment of insecticide resistance in mosquitoes is a major public health crisis. We must keep in view that international cooperation is necessary." The moderator, Professor Noboru MINAKAWA of the Institute of Tropical Medicine, Nagasaki University said, "Malaria kills 400,000 people each year. The situation is improving with the spread of pyrethroid-treated mosquito nets and other measures, but recently, the rate of decline in the number of victims has been slowing down. There is an urgent need for countermeasures against insecticide-resistant mosquitoes."

Breakout Session C (The Research Foundation for Microbial Diseases of Osaka University) "From Risk Management to Health and Productivity: Infectious Disease Control in Companies for After-Pandemic"

If an employee becomes infected with the novel coronavirus, he or she must leave the workplace, and if the number of infected employees increases, it will inevitably have a significant impact on the company's business. Clearly, communicable diseases are a management risk, and it is necessary for each workplace to work on maintaining employee health and preventing communicable diseases.

The Tokyo Metropolitan Government is recommending that companies set up a business continuity plan (BCP) to deal with communicable diseases as part of its "Infectious Disease Preparedness Improvement Project". The Tokyo Metropolitan Government, the Tokyo Chamber of Commerce and Industry (TCCI), and the Tokyo Medical Association are collaborating on this project to support corporate countermeasures against communicable diseases.

Aya KAYEBETA, Director of the Tokyo Metropolitan Government's Disease Prevention and Information/Data Management Section, Infectious Disease Control Division, Bureau of Social Welfare and Public Health said, "You can choose from three courses that should be practiced, such as acquisition of necessary knowledge and measures to prevent rubella. We hope many companies will participate in this program." The three courses are "Training Employees to Understand Communicable Diseases", "Creating BCP for Communicable Diseases", and "Promoting Measures to Prevent Rubella". As of October 2021, 1,569 companies have applied to participate in the program and 434 companies have achieved the course standards.

Dr. Kayebeta said, "There are far more cases of rubella in adults than in children. There is also concern about congenital rubella syndrome (CRS), which can be transmitted to the fetus and cause hearing loss and other disabilities to the newborn, so I hope companies will take proactive measures to combat rubella."

"COVID-19 has changed not only people's lives, but also companies and the way they work." said Kunio OKADA, president of Kenkokeiei, a non-profit organization. "Maintaining the health of employees leads to stable management. The recent pandemic has increased this awareness among management." he stresses. According to Dr. Okada, if there are problems in the way employees work or in their work environment, they will be overworked and accumulate stress, which will lower their immunity and make them more susceptible to communicable diseases, resulting in a decline in labor productivity.

The legally mandated periodic health checkups also include tests for communicable diseases such as tuberculosis, hepatitis virus, Helicobacter pylori, and HPV (human papillomavirus). Okada says "There is a growing trend to analyze the results of periodic health checkups and reflect them in employee health management. If the company focuses on employee health management, this will lead to employee loyalty, and as a result, labor productivity is expected to rise." He emphasizes that improving health management is a management investment.

The moderator, Hisahiko YANO, senior staff writer at the Editional Bureau of Nikkei Inc., summed up the session by saying, "COVID-19 has brought a whole new perspective to health management, making employees rethink the way they work and managers renew their awareness of health investment. COVID-19 has brought a whole new perspective to health management."

Breakout Session D (Sysmex Corporation)

"Innovation in Diagnostics for Emerging and Reemerging Communicable Diseases"

For COVID-19, an emerging communicable disease, and malaria, one of the re-emerging communicable diseases, innovation in diagnostics can play a significant role in preventing serious illness and the spread of infection. In COVID-19 testing, Kobe City in Hyogo Prefecture has achieved great results in preventing the spread of the disease by leading the nation in establishing a PCR testing system through a public-private partnership, and quickly establishing a system for monitoring the prevalence of the disease using epidemiological surveys and genome network analysis. They are also leading the world in the development of testing methods using fluid-based predictors associated with severe cases. Sysmex has developed a test kit using this factor in collaboration with the National Center for Global Health and Medicine and Shionogi. It is said that by picking out patients who are at risk of becoming severely ill, it will be possible to intervene early and prevent them from becoming severely ill, leading to the proper allocation of limited medical resources. In antibody testing, it is important to use diagnostic reagents according to the purpose of

the test, such as for vaccine recipients or for those with previous infections. However, the antibody titer and the criteria for testing positive (cut-off value) differ between kits from different companies, and it is necessary to have a standardized antibody titer using WHO standard products and IVDs to ensure the quality of diagnostic reagents.

While malaria requires a comprehensive response from prevention to treatment in moderate to high endemic regions, the detection of infected individuals is important for its eradication in low endemic areas. Ever since the start of the COVID-19 pandemic, it has become necessary to rapidly differentiate between Malaria and COVID-19 as the symptoms of the two are similar. Under these circumstances, in addition to conventional tests, such as microscopic tests to visually check for malaria parasites infecting red blood cells and simple test kits using antigen-antibody reactions, there is an urgent need for the widespread use of new test methods that excel in accuracy and speed. The technology developed by Sysmex to detect red blood cells infected with Plasmodium falciparum through "flow cytometry" is one of the new testing methods. The adoption of this method, particularly in Africa, is expected to spur the progress of eradicating malaria by 2030, the target of the Sustainable Development Goals (SDGs).

Breakout Session E (Pfizer)

"The Economic Value of AMR Countermeasures and the Need for New Antimicrobials"

It is estimated that about 8,000 people in Japan and at least 700,000 people worldwide die annually from bacteremia caused by two types of drug-resistant (AMR) bacteria. The resistant bacteria issue is also directly related to medical costs. In an example overseas, the cost of treatment for "Methicillin-sensitive Staphylococcus Aureus (MSSA)" is $16,000, compared to an estimated $35,000 for the resistant strain, "Methicillin-resistant Staphylococcus Aureus (MRSA)". It has been pointed out that in the US, the societal costs and the economic impact of resistant bacteria is 55 billion yen (US$550 million). On the other hand, a Japanese study has recently shown that a 50% reduction in the current rate of drug resistance in the three most common types of "gram-negative" bacteria would result in an annual reduction in hospitalization costs by 2.5 billion yen (US$25 million) to 6.4 billion yen (US$64 million). Decreasing the rate of drug resistance could have a positive impact clinically and on health care economics.

The issues in drug development and R&D, one of the measures for AMR, was also a topic of discussion. Due to the high cost and low profitability of antimicrobial drug development, it is necessary to have not only "push-type incentives" prior to approval, but also "pull-type incentives" to support the development after approval. As called for in the proposal compiled by the AMR consortium of the AMIC (Asia Africa Medical Innovation Consortium), derived from the Nikkei FT Communicable Diseases Conference, the amount of money required for the "subscription model" (SM), a fixed amount of money paid periodically regardless of the amount used, is approximately 2-

8 billion yen (US$20-80 million) per drug per year. Even in the case where the Market Entry Reward (MER) system is adopted, which guarantees an adequate return on investment in addition to sales based on the volume of antimicrobial use, the amount of money is not large, ranging from 10 to 30 billion yen (US$100-300 million). Financial resource is one of the issues, however, through the COVID-19 pandemic we have learned the importance of advanced investment in countermeasures against the threat communicable diseases have on the economy. It is critical to think of it, not as a cost, but as an investment against future threats. It will also be important to "select and focus" or narrow down the target pathogens and candidate substances. It will also be necessary to have rapid diagnostic techniques for appropriate treatment and to develop oral antimicrobials that do not require hospitalization.

The COVID-19 disaster has raised public awareness of the value of pharmaceutical innovation in combating the threat of communicable diseases, and the Basic Policy on Economic and Fiscal Management and Reform for 2021 and the Pharmaceutical Industry Vision 2021 include content that will lead to further promotion of AMR measures. The G7 summit held in the UK discussed AMR measures, and the momentum for international cooperation to achieve this goal is growing. Given the characteristics of communicable diseases which spread across international borders, Japan taking measures alone would be insufficient. It is essential to promote countermeasures based on international cooperation. Considering the level of basic research and other aspects, this is an important opportunity for Japan to take a leadership role in this area. It is necessary to share successful examples with the rest of the world and change the behavior of the world as a whole.