

**The 6th Nikkei Asia Africa Conference on  
Communicable Diseases 2019**

**‘Yokohama Communicable Diseases  
Statement 2019’**

Table of contents

1. Introduction	.....3
2. Report on Progress of Public-Private Partnership (P3) in Japan	.....5
2.1. Asia Clinical Trials Platform	
2.1. A Clinical Trials Platform and its Background	
2.1. B Status of Progress	
2.2 Malaria	
2.2. A Malaria P3 Initiative and its Background	
2.2. B Status of Progress	
2.3 Ebola	
2.3. A Ebola P3 Initiative and its Background	
2.3. B Status of Progress (incomplete)	
2.4 Tuberculosis	
2.4. A Tuberculosis P3 Initiative and its Background	
2.4. B Status of Progress	
3. New Issues and Actions Needed	.....17
3.1 Asia Clinical Trials Platform	
3.2 Malaria P3 Initiative: Issues and Actions Needed	
3.3 Ebola P3 Initiative: Issues and Actions Needed	
3.4 Tuberculosis P3 Initiative: Issues and Actions Needed	
4 New Challenges	.....21
4.1 Measures against Multidrug Resistance (AMR)	
4.2 Further Enhancement of UHC and Use of New Technologies	
4.3 Utilizing ICT to Contribute to Communicable Disease Control	
4.4 Incentives Promoting Private Sector Investment	
4.5 Deregulation and Harmonization	
4.6 Communication with Society	
4.7 Responding to New Communicable Diseases	
5. Conclusion	.....29
6. Appendix	.....31

## 1. Introduction

With the rapid advance of globalization, Japan and other countries in Asia and other parts of the world have been strengthening their already inseparable relationships at the levels of economics, society and culture. In recent years, relationships with African countries have also been actively strengthened. However, in this part of the world, in addition to the threats of emerging and re-emerging communicable diseases, such as outbreaks of Ebola virus and other communicable diseases, the spread of tuberculosis and malaria, the emergence of multidrug resistant (AMR) bacteria and epidemics due to them are still major issues. With increasing contact with people from the region, such communicable diseases have become a realistic threat for Japan too.

In response to the growing awareness of communicable diseases both in Japan and other countries as well as in the sectors of industry, academia and government, the key figures in communicable disease control in industry, academia, government and private sectors gathered from around the world for the 6<sup>th</sup> Nikkei Asia Africa Conference on Communicable Diseases held in Yokohama, Kanagawa Prefecture from August 31 to September 1 2019. The conference created opportunities to actively contribute to communicable disease control in Africa through the activities of the Malaria Working Group, and as the 7<sup>th</sup> Tokyo International Conference on African Development (TICAD 7) was to be held in Yokohama immediately before this conference, it had been decided to add Africa to the name of the conference, and to hold it in conjunction with TICAD 7. At TICAD 7, the Japanese government announced that it would conduct public health initiatives for the people of Africa, such as further promotion of UHC, through the establishment of an African health initiative.

Through open discussions, the diverse stakeholders attending the conference on communicable diseases reaffirmed the necessity and effectiveness of further promoting initiatives against communicable diseases that threaten people's health and economic activities, through public-private partnership (P3). Throughout the year, volunteers of the Nikkei Asia Africa Conference on Communicable Diseases have been organizing meetings of the Asia Africa Medical Innovation Consortium (AMIC), which consists of several working groups, for the planning and implementation of P3 projects. In the Plenary Session of the 6<sup>th</sup> conference, AMIC's Asia Clinical Trials Platform (referred as "Asian Communicable Diseases Clinical Reserch Center" till the 5<sup>th</sup> conference) Working Group reported that it had put together a proposal to the government for a clinical trials platform to be created through P3 in Thailand and Indonesia, and proposed it to the Cabinet Secretariat and the related ministries

and agencies. The report also mentioned about a program being launched to actually establish such platforms.

Among the topics also discussed were deregulation for the use of Japanese therapeutic drugs in other countries based on lessons learned from outbreaks of Ebola virus infections; the planning of P3 projects in Asia and Africa for malaria control and related issues; problems to overcome in backing the development of new drugs to combat multidrug resistance (AMR); measures for enhancing UHC and other public health issues; and the active utilization and promotion of innovations such as those based on ICT (information communications technology) and AI in the fight against communicable diseases. The necessity of innovations that contribute to communicable disease control was reaffirmed and potential sources of innovation from Japan as well as Asia and Africa were presented. The Japanese participants and their foreign counterparts expressed hopes that the conference would contribute to the development of measures against communicable diseases not only for Asia and Africa but also the whole world.

At the conclusion of the conference, the participants agreed on the “Yokohama Communicable Diseases Statement 2019”. The achievements of the current conference will be reported at related government meetings. In addition, the conference’s statement will not only be widely disseminated in Japan, but also to organizations in Asia and Africa and international organizations worldwide. Japan will be required to leverage the deeper level of international understanding thus achieved to make a stronger commitment to combatting communicable diseases worldwide. For details of the history of the Nikkei Asia Africa Conference on Communicable Diseases and the matters discussed at previous conferences, please refer to the respective statements.

[https://project.nikkeibp.co.jp/event/5thnac2018/statement2018\\_ja.pdf](https://project.nikkeibp.co.jp/event/5thnac2018/statement2018_ja.pdf)

[https://project.nikkeibp.co.jp/event/4thnac2017/okinawastatement2017\\_ja.pdf](https://project.nikkeibp.co.jp/event/4thnac2017/okinawastatement2017_ja.pdf)

[https://project.nikkeibp.co.jp/event/3rdnac2016/3rdnac\\_tokyo2016\\_statement\\_jp.pdf](https://project.nikkeibp.co.jp/event/3rdnac2016/3rdnac_tokyo2016_statement_jp.pdf)

<https://project.nikkeibp.co.jp/event/2ndnac2015/OkinawaCommunicableDiseasesStatement2015.pdf>

<https://project.nikkeibp.co.jp/event/1stnac2014/OkinawaCommunicableDiseasesStatement2014.pdf>

## **2. Report on Progress of Public-Private Partnership (P3) in Japan**

### **2.1 Asia Clinical Trials Platform**

#### **2.1.1 A Clinical Trials Platform and its Background**

For communicable diseases on which clinical trials are not conducted in Japan due to a small patient population, there is a need to create infrastructures in Asia (clinical trial platform) for conducting clinical trials essential for the development of new drugs and diagnostics. These infrastructures include a system for epidemiological surveys, medical institution networks, human resources development and formation of relationships between local government and central government.

##### **[Background]**

Tuberculosis is one of the 3 major communicable diseases in the world and Japan is considered to be a mid-incidence country for the disease. In Japan, however, there are few patients with AIDS/HIV and malaria and also few cases of other communicable diseases that are prevalent in tropical and subtropical regions. Regarding new drugs (diagnostics and therapeutic drugs) developed in Japan, there is a need to verify their efficacy by carrying out clinical trials in countries where such communicable diseases are prevalent. In 2017, AMIC established the Asian Clinical Trials Platform Working Group and has conducted repeated discussions since then. Putting the results of the discussions of the past 2 years together, AMIC submitted a plan to the government for the creation of an Asian Clinical Trials Platform through P3 (10-year plan) in June 2019. This endeavor is consistent with the Asia Health and Wellbeing Initiative that the Japanese government is promoting. The platform will not only contribute to the further development of Japanese industry, but also to strengthening collaborative relationships with the respective countries as well as the improvement of people's health and the attainment of the UN's SDGs (Sustainable Development Goals).

Through projects of Japan Initiative for Global Research Network on Infectious Diseases (JGRID) and Science and Technology Research Partnership for Sustainable Development (SATREPS), Japan has established basic research centers for communicable diseases in Asia and Africa, with universities playing a central role. Also, Japan International Cooperation Agency (JICA) and other organizations have been providing support for communicable disease research facilities in various countries. In addition, for more than 50 years, the Tuberculosis Prevention Association has been developing human resources for tuberculosis control by inviting doctors and researchers from Asia and other parts of the world. Furthermore, in 2016,

NCGM (the National Center for Global Health and Medicine) embarked on a project for the formation of a global clinical research center network and under it, clinical research and clinical trials centers are being established in Asian countries.

However, Japan's infrastructure for clinical trials on communicable diseases is very weak, especially for rare ones. For instance, there has hardly been any follow up of cohorts of patients with subclinical malaria and tuberculosis. It was therefore proposed at the conference that a clinical trials platform be established.

### **[Meaning of clinical trial]**

Here, clinical trial is defined as an interventional clinical study conducted on humans. It is an essential step in the development of new drugs, diagnostic agents and other medical technologies. In carrying them out, it will be crucial to collaborate with organizations in areas where the communicable diseases actually occur. Also, in establishing the Asia Communicable Diseases Clinicals Trial Platform and putting it on track, it will be important to ensure that joint trials between Japan and Asian countries are carried out on an equal footing. Phase I clinical trials to confirm the safety of new Japanese drugs will be carried out in Japan. It will be necessary to further strengthen collaboration with such hub organizations as NCGM and Nagasaki University to create an all-Japan support system.

However, it will be necessary to carry out clinical research from phase II trials onwards, which assess the effects of new drugs, in collaboration with Asian countries where there are many people with the respective communicable diseases. By gaining marketing approvals in the respective countries and WHO-PQ certification using the data thus obtained, it will be possible to accelerate the diffusion of new drugs. Based on such results, it will be important to carry out phase III clinical trials to have the drugs applied in the medical care carried out in each country as well as have them included in their guidelines for controlling communicable diseases. When drafting phase II and phase III protocols, they should have a firm scientific basis and there should be collaboration and agreement among the respective countries that includes the participation of the regulatory authorities.

A forerunner of the Asian Clinical Trials Platform is SATVI under which clinical trials are conducted in South Africa, specifically on tuberculosis vaccines. All phase II and subsequent clinical trials on tuberculosis vaccines worldwide are conducted here.

## **2.1. B Status of Progress (content of the proposal to the government)**

A proposal for the creation of a clinical trials platform was made to the government in June 2019. The following are the broad details.

- 1) The platform consists of 2 organizational structures – one of them functioning as a clinical trial “control tower” established in Japan and the other consisting of clinical trials centers established locally. The control tower discusses and decides on when and how and on which new drugs clinical trials should be conducted and supervises the activities of the clinical trials centers. Accumulating the results of clinical trials and maintaining collaborative relationships with the local centers will ensure their sustainability and that a store of clinical information is built up in Japan. Keeping abreast of the latest trends in communicable disease research in the world and the development of new drugs as well as the latest actions of international organizations and NGOs, the control tower will function as the nerve center in determining directions of clinical research at the local centers.
- 2) Establish a “Science Advisory Council” for each disease. Gather experts from industry and academia from Japan and other countries to establish protocols for clinical research conducted by the local clinical trial centers as well as for non-clinical research (trials examining pharmacological actions, pharmacokinetics, toxicity, etc. using animals etc., prior to clinical trials) and determine their scientific, clinical and ethical validities.
- 3) Animal trials to observe the infection suppression and treatment effects carried out in primates according to human protocols by The Tsukuba Primate Research Center of the National Institutes of Biomedical Innovation, Health and Nutrition (TPRC-NIBIOHN) will be used as a reference in establishing a system for carrying out such animal experiments at the same time as human clinical trials. A system for compiling more appropriate clinical trial protocols through the interpretation of results and elucidation of mechanisms in human clinical trials in combination with interpretation of results of animal experiments in primates will be an essential condition for the development of new drugs for emerging and re-emerging communicable diseases around the world, and this system will ensure the global competitiveness of the platform.
- 4) With the move of Ryukyu University Hospital to Nishi Futenma, a system for supporting the Asia Clinical Trials Platform will be created through collaboration in establishing the Okinawa Communicable Diseases Research Center.
- 5) The Asian clinical trials centers in the respective countries will create and maintain systems for implementing clinical trials, support epidemiological research on

communicable diseases and form networks with medical institutions and government organizations in their countries as well as neighboring ones so that they can conduct clinical trials for new drugs. In cooperation with NCGM, universities and research organizations, Japanese experts in communicable diseases and clinical trials will be sent to such centers in order to create basic systems for the smooth conduct of clinical trials in collaboration with local staff.

- 6) Basically, one clinical trial center will manage the patient cohort for clinical trials on one particular disease. In addition, it will be necessary to strengthen functions for supporting clinical research such as those for logistics and conclusion of agreements with clinical research organizations and governments.
- 7) In the first 5 years, it is planned to establish and operate clinical research centers, respectively, to accomplish the development of a tuberculosis vaccine in Indonesia or Thailand and that of diagnostic agents and therapeutic drugs for malaria in Thailand.
- 8) For establishing above research centers in Japan and abroad, financial support in the amount of 6.04 billion yen has been requested to the government. Companies in Japan will share the burden of clinical research at two clinical research platforms at 2 places, through the provision of pharmaceuticals and diagnostic agents and dispatch of staff. In 10 years, it is aimed to have the clinical trial platforms be the basis for clinical research in Japan and other countries and make them self-sustaining organizations.
- 9) At the present conference, there was common recognition of the necessity of establishing similar clinical trial platforms not only in Asia but also in Africa.

## **2.2 Malaria**

### **2.2. A Malaria P3 Initiative and its Background**

In 2016, 200 million people were infected with malaria and there were 440,000 deaths. In particular, 5% of deaths in children up to the age of 5 were due to malaria, with the death rate rising to 7-10% in sub-Saharan Africa. In its roadmap, the Asia Pacific Leaders Malaria Alliance has set ambitious goals of eliminating malaria in 6 countries and preventing infection in 40.3 million people between 2016 and 2020 and eliminating malaria in 22 countries in Asia from 2026 to 2030.

To eliminate malaria, in the 3 areas of testing and diagnosis, drug discovery and vector control for prevention, Japan can provide comprehensive solutions integrating the technologies of private sector companies. The Global Fund and other international aid organizations will be

depended on for the procurement of required drugs and medical devices but in many cases these organizations require WHO-PQ accreditation. This will require (1) verification of efficacy and utilization based on evidence and other data, (2) gaining the nomination of the recipient country and (3) creation of enduring networks with the WHO, the Global Fund and other international organizations. Also, viewpoints of UHC and the SDGs will have to be considered in countries where solutions are to be provided. However, as this will be difficult for private sector companies to realize alone, it will be necessary to create P3 initiatives for seamless collaboration among industry, government and academia.

## **2.2. B Status of Progress**

Since its establishment in September 2016, the AMIC Malaria Working Group has engaged in numerous discussions and emphasized the importance of integrating development in the areas of testing and diagnosis, drug discovery, and vector control for prevention. Also, agreement was reached on consolidating the achievements beginning to appear in Asia and at the same time that aggressive measures were essential in areas where malaria is highly prevalent, particularly in Africa. The Asia Task Force and Africa Task Force set up in 2018 have been carrying out the respective activities. In addition, a malaria P3 project was put together in June 2018 and discussions with government officials were held. The main points are given in the following.

In Asia, focusing on measures for controlling asymptomatic malaria, the most important issue, a P3 package applying such technologies as high sensitivity testing (Eiken Chemical: ultra high sensitivity genetic test for malaria using LAMP method, Sysmex: Fully Automated Hematology Analyzer (XN30) capable of high speed testing for protozoa based on flow cytometry) and therapeutic drugs (Neopharma Japan: 5-amino levulinic acid (ALA) supplement which eliminates the protozoa and prevents reinfection afterwards) and a clinical research network led by NCGM with Mahidol University in Thailand and Institut Pasteur du Laos has been proposed. In Africa, the implementation of a P3 project, whose core elements are measures against severe malaria in children (XN-30, ALA supplement mentioned above and vector control (Sumitomo Chemical: Olyset Plus, a mosquito net with a long-acting repellent effect that keeps insecticide-resistant mosquitoes under control and Sumi Shield, an indoor long-acting insecticide spray) has been proposed.

In the plan to create an Asia clinical trials platform presented to the government in June by the conference overall, the establishment of a malaria clinical research center at Thailand's Mahidol University was proposed. The collaboration of the Malaria Working Group in this malaria P3 project for Asia will be necessary. The importance of considering P3 projects for the new outbreak area of the Congo region was also recognized and there will need specific discussions in the future.

Regarding the Asia Task Force, Eiken Chemical has been carrying out AMED's research project for the commercialization of medical technologies in developing and emerging countries and in collaboration with NCGM and Sysmex, has been forging ahead with activities toward the implementation of local evaluation trials in Thailand. Also, Neo Pharma will conduct a dietary intervention trial with ALA in Laos. Regarding the Africa Task Force, Osaka City University's "Multidisciplinary Research on Community-led Integrated Strategies Aiming at Eradication of Malaria in Tropical Africa" initiative has been adopted as a SATREPS project. It aims to eliminate malaria by verifying vector control measures and effectiveness of group medication, as well as through the management of people with asymptomatic malaria and those in whom malaria has already developed.

In addition to the activities of the task forces mentioned above, new endeavors gathered speed before TICAD7 was held. In the African continent, particularly in the Central Africa region, which is known as the malaria belt, economic losses stemming from lost educational and employment opportunities due to severe malaria are huge. In order to achieve the sustained development of the countries in the Malaria Belt, achieving a stable, high quality working population by strengthening countermeasures against malaria infection is a priority issue. Therefore, in the period of the SDGs, anti-malaria measures are not just an urgent issue for those infected with malaria, particularly children, but also for corporations and nations. At the 6<sup>th</sup> Nikkei Asia Africa Conference on Communicable Diseases, with Africa Health Business (AHB), a consortium of private sector companies in Africa, as a counterpart, the African Business Consortium was established. Its purpose is to realize UHC in Africa and as a result, to bring about healthy, prosperous communities with the fight against malaria as a springboard. Also, moves toward collaboration with Health Care WG, Africa Business Council, in whose formation the Japan Association of Corporate Executives played a leading role, are now in full swing. Public-private partnerships with new awareness of the issue of maintenance and development of stable workforces and productive environments are expected to see further expansion in a form involving African stakeholders.

## 2.3 Ebola

### 2.3. A Ebola P3 Initiative and its Background

#### 1) Current situation of re-emergent Ebola outbreak

In August 2018, two-and-a-half years after WHO had declared that Ebola was contained in January 2016, the government of the Democratic Republic of Congo declared that a new outbreak of Ebola virus infection had occurred in the Northeast of the country. In July 2019, WHO declared a “public health emergency of international concern”. As of August 2019, there had been 2,822 cases, 1961 people had died, the mortality rate had reached 67%, and this has been called the “2<sup>nd</sup> largest outbreak of an communicable disease in human history”. Infection is particularly a problem for health care professionals and family members who all have frequent contact with patients. At present, no medicines (diagnostic agents, therapeutic drugs or vaccines), or medical devices, have been approved by the regulatory authorities for Ebola virus infections.

The WHO has been supplying VSV-EBOV, a product of the US-based company Merck, on a compassionate use basis (a public system enabling exceptional access to unauthorized medications) to the Congo region. WHO has been conducting the vaccination of high-risk individuals, such as health care professionals, pregnant women, infants, infection responders on site, persons who have been in contact with those infected and people who have been in contact with such persons. Up till now, more than 200,000 people have been vaccinated.

Experimental interventions with unapproved medicines have also been proceeding. Specifically, the agents under study are a mixture of 3 monoclonal antibodies “ZMAPP” (Zaire strain), a mixture of completely humanized antibodies “REGN-3B” (Zaire strain), a single antibody (Mab-114 (Zaire strain) and Remdesivir, a prodrug antiviral agent. In order to evaluate the efficacy and safety of these 4 interventions (in monotherapy or combination therapy) a randomized, controlled trial (RCT) with mortality rate at 28 days as the primary endpoint has been conducted. In this initiative, the mortality rate dropped to 30%. Doctors at the site of treatment feel that it will soon be possible to cure Ebola.

#### 2) Activities under Ebola P3 initiative up to now

The Ebola P3 initiative is a public-private collaboration project that kicked off in 2014 after receiving funding support from the Ministry of Health, Labour and Welfare in response to a request for support from the Government of Guinea, one of the countries with an Ebola

outbreak, and a request from the Institut National de la Santé et de la Recherche Médicale (INSERM), a French research organization, for collaborative research. This project has the following content.

2-1) Clinical research to verify therapeutic efficacy of favipiravir (brand name Avigan) in Ebola virus infection

In a clinical trial carried out from December 2014 to May 2015, favipiravir was administered to 126 patients. A decrease in mortality rate was seen for 55 patients with a low pre-treatment viral load and 44 patients survived. The final report on the trial was published in March 2016.

Favipiravir is expected to be effective in the treatment of viral hemorrhagic fevers such as Crimeia-Congo fever, Marburg disease and Lassa fever as well as severe febrile thrombocytopenia syndrome (SFTS), a tick-borne disease. A trial is underway in Japan for SFTS.

2-2) Confirmatory trial in Guinea for Ebola virus diagnostic agent and device system applying RT-LAMP technology developed by Canon Medical Systems (formerly Toshiba Medical) and Nagasaki University

Canon Medical Systems has provided diagnosis kits sufficient for 10,000 tests applying RT-LAMP technology and 9 diagnostic devices to the Guinea government free of charge. No sales forecast has been made for the Ebola virus diagnostic kit from 2018 onwards.

However, in January 2018, this kit has been submitted for marketing approval in Japan as a Zika fever diagnosis kit.

In Japan, a Cabinet Secretariat-led scheme for the provision of unapproved drugs in emergencies to developing countries has been established, with the Ministry of Foreign Affairs and the Ministry of Health, Labour and Welfare also collaborating.

### **2.3. B Status of Progress**

Fujifilm has provided favipiravir to the Congo region free of charge. As for specific details of usage, it is currently being preventively administered to persons suspected to be infected through contact with patients, and data concerning usefulness is being accumulated. When preventive administration of favipiravir was conducted for doctors and nurses from 2018-19, it

was observed to be effective and a final report of the results has been written.

Canon Medical Systems is ready to provide the diagnostic agent applying RT-LAMP technology when requested by a particular country.

The Japanese government has provided support to the Congo region through the provision of DENKA SEIKEN's rapid blood diagnosis device by JICA. Fujifilm will provide favipiravir free of charge. When the method of use has been determined, the government will provide appropriate support for transportation with the country. Canon Medical Systems's RT-LAMP system is also under consideration.

The Pharmaceuticals and Medical Devices Agency (PMDA) has several schemes ready for the provision of unapproved medicines to other countries. Their application to the re-emergence of Ebola is under consideration.

## **2. 4 Tuberculosis**

### **2.4. A Tuberculosis P3 Initiative and its Background**

For a single communicable disease, tuberculosis claims the greatest number of lives. In 2017, worldwide, 10 million people developed tuberculosis and 1.6 million died from it. Although the number of patients worldwide is tending to decrease, it continues to be prevalent, mainly in developing countries, and morbidity in Japan is still high. Also, in Asia and Africa, many people go undiagnosed and many cannot receive treatment. The number of difficult-to-treat patients has been increasing due to the appearance of multidrug-resistant tuberculosis bacteria stemming from the improper use of anti-tubercular drugs and major issues are that very few patients are treated and the treatment success rate is low.

In the End TB Strategy drawn up by WHO, the goals are to reduce the number of TB deaths by 95% and number of new cases by 90% by 2035 with 2015 as baseline. Also, the Stop TB Partnership and others are working on the goal of making 2020 a low prevalence year. A political declaration adopted by a high-level UN meeting on tuberculosis in 2018 included the necessity of accelerating tuberculosis countermeasures in individual countries as well as worldwide and affirmed the need to greatly increase expenditure on them.

To end tuberculosis, the AMIC Tuberculosis Working Group considers it essential to realize

a system of medical care under which diagnosis technologies and anti-tubercular drugs can be provided seamlessly in a package to developing countries, placing importance on (1) development of accurate tuberculosis diagnosis technologies that can be provided conveniently at low cost and (2) definitive diagnosis of multidrug-resistant tuberculosis bacteria, proper prescription of anti-tubercular drugs and good medication adherence. The Tuberculosis Working Group has achieved a certain degree of success through the MDR-TB P3 package it proposed, consisting of a convenient, high accuracy genetic test for use in screening (TB-LAMP, Eiken Chemical), multidrug resistance genetic test that can be used to definitively diagnose multidrug resistance (Genoscholar, Nipro) and a drug for treating multidrug-resistant TB (MDR-TB) (Delamanid, Otsuka Pharmaceutical). Based on this success, the individual companies are engaged in activities to promote the diffusion of the respective technologies in Asia and Africa and making efforts to have them used in the tuberculosis control measures of each country.

In recent years, new innovations that contribute to anti-tuberculosis measures have been steadily appearing in the world. Regarding new diagnosis technologies, amid the shortage of doctors who can interpret simple chest X ray images, the development of computer-assisted diagnosis (CAD) technology applying artificial intelligence (AI) to enable greater accuracy in the interpretation of simple X-ray images is in full swing around the world. Regarding such technology being developed by Fujifilm in Japan, domestic clinical trials have confirmed 100% accuracy (area under ROC curve) in the detection of tuberculosis. There is a possibility of its use in primary screening in Asia and Africa. For patients with both HIV and tuberculosis communicable diseases, Fujifilm has developed a high-speed diagnosis kit which detects Mycobacterium tuberculosis-specific LAM (lipoarabinomannan) excreted in the urine of patients. In the clinical evaluation by FIND and others in South Africa, the target for diagnostic performance was achieved and R&D is continuing with a grant from the GHIT fund.

Also, regarding diagnosis technologies for multidrug-resistant tuberculosis bacteria, efforts are being made toward the implementation of optimal treatment regimens through the comprehensive analysis of drug resistance of tuberculosis bacteria by means of whole genome sequencing (WGS) using next generation sequencers (NGS). NCGM has developed Total Genotyping Solution for TB (TGS-TB), a tool for analyzing WGS data of multidrug-resistant tuberculosis bacteria. It has been confirmed to have one of the highest levels of accuracy in the world and this is being further enhanced through the use of 4,000 strains of multidrug resistant

tuberculosis bacteria that have been collected in joint research in several countries. Also, with the Tuberculosis Prevention Society taking the lead, the development of new preprocessing technologies for WGS is also underway, which involves the extraction of high quality nucleic acids.

Furthermore, with regard to treatment technologies, the development of several anti-tubercular agents and drugs for multi-drug resistant tuberculosis bacteria is going ahead rapidly in the world. Endeavors toward universal regimens effective in all tuberculosis patients (drug-sensitive tuberculosis, multidrug-resistant tuberculosis, ultra-multidrug-resistant tuberculosis) using several anti-tuberculosis agents in combination are also being made. On the subject of prevention technologies, in a confirmatory trial conducted in Kazakhstan a few years ago, a marked preventive effect was observed for BCG vaccine (Tokyo strain). Thus, at present, major changes are happening in the area of tuberculosis, from diagnosis through treatment to prevention.

## **2. 4. B Status of Progress**

So far, Genoscholar (NTM-MDRTBII), TB-LAMP and Delamanid have all been recommended for use by WHO. Also, TB-LAMP is being provided to over 160 countries via the Stop TB Partnership's Global Drug Facility (GDF) for the procurement and provision of anti-tuberculosis drugs and the WHO's Model List of Essential In Vitro Diagnostics (EDL). Used for screening, Genoscholar (NTM-MDRTBII) will likely be adopted for competitive bidding in the GDF catalog and together with FIND, Genoscholar (PZA-TBII), which can detect resistance to pyrazinamide (PZA), is being evaluated for WHO recommendation. It is expected that the results of the evaluation will be submitted to the WHO in 2020.

As for P3 packages, in the Philippines, under JICA's Program to Expand the Use of Private Sector Technology, Nipro and Eiken Chemical have been jointly conducting primary tuberculosis screening using TB-LAMP, and a certain degree of success has been achieved in a confirmatory trial on a diagnostic algorithm for multi-drug resistant tuberculosis using Genoscholar. Based on the results of this project in the Philippines, mass screening is being carried out at national borders and in prisons.

Meanwhile, initiatives to expand the use of individual technologies constituting P3 packages are in full swing in various countries and regions. A confirmatory trial on Genoscholar is being carried out in Indonesia under JICA's Program to Expand the Use of Private Sector

Technology. The interim evaluation of this trial revealed a prevalence of around 50% for multidrug resistant tuberculosis and that there were many PZA-sensitive patients. Also, a confirmatory trial conducted on TB-LAMP in Cameroon, found that sensitivity was high and the Ministry of Health decided to use it to replace the existing method. It has been provided to smear centers all over the country, achieving rapid diagnosis. Zambia, Kenya and also Vietnam are on the point of introducing it. Negotiations are underway in 30 other countries and confirmatory trials are ongoing in 18 countries.

However, for the further diffusion of these technologies, it is not only necessary to prove usefulness regarding the effectiveness and accuracy of diagnosis and treatment technologies as well as those for prevention, but also to validate the results of medical economics analysis to show that these technologies are really needed by countries in Asia and Africa. In addition, efforts to convey such information to these countries in a respectful manner are also needed.

### **3. New Issues and Actions Needed**

#### **3.1 Asia Clinical Trials Platform**

##### **[Issues]**

So far, new technologies that have the potential to become future innovations (diagnosis technologies, therapeutic drugs, preventive drugs) have been developed by individual researchers and organization units, and they have carried out clinical trials independently. This was possible for large companies but otherwise it was difficult. Also, in Japan, the platform for clinical trials on drugs for rare communicable diseases has been particularly weak. For example, there has hardly been any follow-up of cohorts of patients with subclinical infections of such diseases as malaria and tuberculosis.

- 1) The Asia Clinical Trials Platform initiative must be implemented in the future.
- 2) Now that the P3 project has been launched with the aim to contain malaria, in Africa, where the harm done by the disease is very great, it will be necessary to consider establishing similar research centers and stepping up network creation based on the P3 concept. It was recognized that the Clinical Trials Platform should not be limited to Asia and that a future issue would be creating the ones for Africa.

##### **[Actions Needed]**

At the 6th conference, we received a basically positive response from the government regarding the Asia Clinical Trials Platform that had been proposed (refer to page 6). When an official response is received, the public and private sectors will work together on the following actions.

##### **<For Neighboring Asian Countries>**

As a collaborative project among industry, academia and government, in close collaboration with the respective countries, the process of gaining a consensus with regard to this proposal will be started. First, aiming toward the creation of a clinical trials platform in Thailand and Indonesia, relationships with local partner organizations will be developed to make a foundation of the system for implementing the platform.

##### **<For Japan>**

- 1) Establish an administrative office function for the Asia Clinical Trials Platform.

- 2) Create the control tower functions, and for the time being, recruit experts from Japan and other countries for the control tower function for malaria and tuberculosis and have them collaborate. The best and brightest people will be recruited from all over the world.
- 3) Commence negotiations with local partner organizations for the creation of a platform in Thailand and Indonesia.
- 4) Reinforce collaboration in NCGM's project to create a global network of clinical research centers as well as with Nagasaki University and others.
- 5) In collaboration with the Tsukuba Primate Research Center of the National Institutes of Biomedical Innovation, Health and Nutrition, provide a system for the simultaneous conduct of clinical trials and animal experiments on primates.
- 6) The Asia Clinical Trials Platform should be examined at an all Japan level, transcending the confines of government ministries.
- 7) The early operation of BSL4 will be required to achieve the above goals and to further enhance the foundation for research on communicable diseases in Japan.

## **3.2 Malaria P3 Initiative: Issues and Actions Needed**

### **[Issues]**

There are four main issues in malaria control which are 1) detection and treatment of asymptomatic protozoa carriers, 2) combating multi-drug resistance/insecticide resistance, 3) securing financial resources and 4) reinforcement of health systems, and the WHO recognizes that innovations are needed in addressing them. In Japan active responses by P3 are required, particularly with respect to 1) and 2), and regarding 4), with the greater involvement of local communities, it will be essential to create a sustainable system mainly with regard to the training of medical professionals, making use of the experience gained with UHC in Japan.

### **[Actions Needed]**

<For Malaria Working Group>

To address two issues mentioned above, 1) detection and treatment of asymptomatic protozoa carriers and 2) combating multi-drug resistance/insecticide resistance, the Malaria Working Group will continue to be required to provide comprehensive solutions in the following 3 areas: highly sensitive and rapid diagnosis, creation of safe and effective drugs for drug-resistant protozoa, and highly effective vector control for insecticide resistant mosquitoes, which has been worked on for some time.

<For companies>

It will be necessary for the business consortium launched by the Malaria Working Group with the opportunity provided by TICAD7 and the Health Care Working Group of the African Business Council established by the government to promote more sustainable frameworks for P3 collaboration by further strengthening collaboration with government and health care stakeholders such as the African Union's CDC and Africa Health Business.

<For government>

In gaining WHO-PQ accreditation, P3 collaboration will be essential as there are limits on the efforts of private companies alone. Also, in order to conduct clinical trials in Africa where the harm done by malaria is the greatest, it will be crucial to create a system for implementing them, cultivate staff capable of negotiating with local medical institutions and communities, and collaborate with policy advisors. Also, at the clinical stage, a system for strengthening collaboration in the emerging Asia-Africa Clinical Trials Platform initiative will be required.

### **3.3 Ebola P3 Initiative: Issues and Actions Needed**

#### **[Issues]**

Despite the progress made in Japan and elsewhere in the development of diagnosis technologies, therapeutic drugs and vaccines for the Ebola virus infection, we have not put an end to it as we see repeated outbreaks of the disease. In addition to the lack of innovation, it is also attributed to the fact that the areas where outbreaks occur are often in conflict zones. To provide a fundamental solution, it will be necessary to provide humanitarian support and develop human resources as well as provide more basic support such as reinforcing UHC.

#### **[Actions Needed]**

<For companies>

- 1) While evidence for the preventive administration of favipiravir is being accumulated (refer to page 9), there needs to be more evidence for its effectiveness.
- 2) Regarding RT-LAMP technology and the immunochromatography technology being developed by DENKA SEIKEN, at the same time as making efforts to improve their performance in the early detection of Ebola cases, detailed studies on their superiority over other products should also be conducted.
- 3) In order to make use of excellent Japanese products and technologies in the areas of devices protecting against infection and disinfectants, study their provision in a package

with JICA's program for cultivating human resources in the health area "5S-KAIZEN-TQM"

### **3.4 Tuberculosis P3 Initiative: Issues and Actions Needed**

#### **[Issues]**

Needless to say, in order to put an end to tuberculosis, further innovation is crucial. In Japan, new innovations continue to appear and it has become clear that P3 collaboration is effective in achieving their development and diffusion. Therefore, in the process from research and development through diffusion in individual countries, seamless support matched to the development stage is needed. This will be in the form of financial support from various organizations including AMED, Global Health Innovative Technology Fund (GHIT Fund), the Bill and Melinda Gates Foundation (B&MMF) and FIND.

While efforts are being made toward diffusion in individual countries in Asia and Africa (P11; Tuberculosis; 2.4.B Status of Progress), it is not only necessary to prove the usefulness of technologies for diagnosis and treatment and prevention in terms of efficacy, safety and accuracy to the respective country, but also to validate the results of medical economics analysis to show that these technologies are really needed by countries in Asia and Africa. In addition, efforts to convey such information to these countries in a respectful manner are also needed.

#### **[Actions Needed]**

<For Companies>

- 1) TB-LAMP is one of the tuberculosis diagnosis technologies currently available. Research should be carried out on the possibility of realizing even higher accuracy tuberculosis diagnosis by combining computer-assisted diagnosis (CAD) of simple chest X-ray images with TB-LAMP.
- 2) Regarding new diagnosis technologies, in confirmatory trials in other countries, it will be necessary to conduct an evaluation not just of accuracy but also one from the viewpoint of medical economics (cost effectiveness) to gain understanding regarding the usefulness of the technology in the respective country. For instance, evaluation will be carried out for the economic benefits of CAD alongside those of TB-LAMP, which are currently being evaluated.

- 3) BCG vaccination (Tokyo strain) is only being carried out at the national level in Japan and Korea. It is necessary to carry out cohort studies to confirm the preventive effect.

<For Academia>

- 1) In order to analyze whole genome sequencing (WGS) results with high accuracy, in addition to collecting multidrug resistant bacteria strains in joint studies, it will be necessary to continue with the creation of databases and with raising the accuracy of the National Institute of Infectious Diseases' multidrug resistant tuberculosis analysis tool "TGS-TB".
- 2) Regarding the extraction of high quality nucleic acids for WGS, a schedule should be made for the development of new preprocessing technologies being carried out by the Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association.

<For Government>

- 1) In addition to the continuous support being provided by the government for endeavors such as nurturing health care professionals, the Ministry of Foreign Affairs will aid the diffusion of products and technologies constituting P3 packages via the embassy in each country.

## 4. New Challenges

### 4.1 Measures against Multidrug Resistance (AMR)

#### [Current Status and Issues]

In April 2019, in view of the worldwide crisis situation regarding drug resistance (AMR) where antibiotics are ineffective, the WHO published a report requiring individual countries to devise trans-industry countermeasures as soon as possible. According to the initial report of the Review on Microbial Resistance (O'Neil report) chaired by Jim O'Neil in the UK, the estimated number of deaths due to drug resistant microbes was at least 700,000 per year. It warns that if no measures are taken, the annual number of deaths will rise to 10 million in 2050 and the shock to the world economy will be comparable to that of the 2008 - 2009 currency crisis.

A survey conducted in Japan found that 32% of children examined at medical institutions for upper respiratory tract inflammation due to a virus had been prescribed antibiotics. In another survey, 44% of respondents stated that antibiotics were effective against colds due to viruses. This illustrates the improper use of antimicrobial agents and indicates that the risk of

drug resistant bacteria appearing is ever present. Methicillin-resistant *Staphylococcus aureus* (MRSA) and macrolide-resistant *Mycoplasma pneumonia* have been reported not only in children but also in infants and newborns, the threat of AMR has spread outside hospitals into surrounding residential areas and the difficulty of controlling communicable diseases has become much greater.

However, there has been a tremendous decrease in the development of new therapeutic drugs for AMR because of the difficulty and high cost of R&D and low profitability. While mechanisms for push incentives to support R&D funding are being established in each country, once anti-AMR drugs are launched, as their use is controlled in order to prevent new drug-resistant bacteria, not much income can be expected from their sales. In a situation in which the disadvantages exceed the advantages for pharmaceutical companies, major pharmaceutical companies have been continually withdrawing from the development of AMR agents or selling the business and there is strong concern that the same will happen to companies that have not yet reached this stage because they are already losing their staff, knowledge and expertise. Thus, the creation of pull incentive systems that guarantee profitability after launch is essential.

In response to the adoption of the Global Action Plan for AMR at the WHO's annual general meeting in 2015, Japan drew up the Drug Resistance Measures Action Plan (2016-2021) in 2016. It is appearing to be effective in reducing the improper use of antimicrobial agents. Also, with 8 Japanese communicable diseases related societies as major players, industry, government, academia, and private sectors collaborated to establish AMR Alliance Japan in November 2018. In addition, a government declaration on the promotion of AMR countermeasures that included putting AMR on the agenda of G20 Summit in Osaka in June this year was made. As a result, the G20 Osaka Leaders Declaration adopted by the G20 included AMR-related items and mentioned that further efforts toward promoting the proper use of antibacterial drugs and access to them were required. It required analysis on and reporting of the results for incentive systems for the R&D of AMR agents in the countries comprising G20 and AMR R&D hubs. While industry-government-academia-private sector partnerships have been gaining momentum, stronger collaboration is required to produce more robust results from their activities.

#### **[Actions Needed]**

At the 6<sup>th</sup> Nikkei Asia Africa Conference on Communicable Diseases, it was decided to

establish a 5<sup>th</sup> working group, one concerning AMR, in the Asia Africa Medical Innovation Consortium (AMIC). The working group will study specific methodologies and strategies for pull incentives to sustainably support the R&D of AMR drugs with industry, academia and government. Regarding the threat of AMR and the risk of improper use of antibacterial agents, the themes of the working group will be educational activities to enhance awareness not only among health care professionals but also the public, and surveillance.

## **4.2 Further Enhancement of UHC and Use of New Technologies**

### **[Current Status and Issues]**

Universal Health Coverage (UHC) means a system under which all people can access services for health improvement, prevention and treatment of diseases and recovery of function at an affordable cost, so communicable diseases are very closely connected with UHC. The Japanese government is actively making provisions for health crises as a major component of UHC. In order to fully realize UHC, in addition to reinforcing health systems in terms of governance, finance and service delivery, in making provisions for health crises, it is important to adopt a multifaceted preventive approach when things are normal. For this purpose, endeavors from a broad field of view including that of human resources development are necessary. However, adopting a cross-functional paradigm in efforts is difficult and there has been insufficient discussion regarding the lack of coordinating roles that bring together individual aspects and make them function as a whole or regarding the appearance of new technologies. Investment in health not only contributes to the quality of life of the individual, it is also essential for creating a sustainable society.

### **[Actions Needed]**

- 1) Greater use of digital health and other new technologies
- 2) In view of the shortage of health care professionals and insufficient training on site, make use of mobile apps
- 3) Develop new technologies that contribute to “last one mile” strategies for remote areas and achieve their diffusion.
- 4) Study collaboration in private sector investment to support and expand grant-based funding for technology ideas until they lead to confirmatory projects.
- 5) Promote regulatory harmonization for products and services that include new technologies.

New possibilities include initiatives in the following areas:

- Development and support of diffusion for technologies related to UHC (delivery, last one mile strategies, training of personnel in remote areas, etc.)
- Study impact on health and economy of supply chain reform and expanded computerization in public procurement systems
- Promotion of “data health” (design of systems that achieve collaboration among countries)
- Examination of innovative mechanisms for funding through government-private sector collaboration

[List of New Technologies Presented at Conference]

- Last Mile Delivery by motorcycle and boat (Yamaha Motor Co., Ltd.)
- Last Mile Delivery to multiple locations using drones capable of 2-way flight (Terra Drone Corporation)
- Remote training support app for health care personnel using ICT (Kyoto University/Castalia)

### **4.3 Utilizing ICT to Contribute to Infection Control**

#### **[Current Status and Issues]**

Following its reorganization in January 2019, the WHO announced the Global Strategy on Digital Health 2020-2024 in April, which stated that, under the supervision of Director General Tedros Adhanom, future efforts would be directed at promoting digital health and accelerating investment in innovation. In line with this, the use of ICT and big data in communicable disease control is increasing worldwide.

Also as shown in the “eHealth Strategy building blocks” of the WHO and the International Telecommunication Union (ITU), through cooperative investment by donor countries, including Japan, and investment organizations, it is important to create environments facilitating the promotion of digital health.

In Japan, various initiatives are underway. They include apps that use input from users and information released by local governments to help visualize the situation of communicable disease outbreaks and prediction of communicable disease outbreaks using mathematical models. In Japan and other countries, companies, organizations, and researchers all act separately so human, physical and financial resources are not being used effectively, meaning that resources are only being used from the narrowest sense.

### **[Actions needed]**

With an overall view of technologies being developed in Japan, discuss at greater depth how they can contribute in a global framework. Ensuring that personal information is protected, efforts toward the sharing of high quality data will be needed.

### **[List of New Technologies Presented at Conference]**

- Prediction, evaluation and monitoring in communicable disease control measures using weather and traveler data (WHO).
- Mathematical model of communicable diseases (Hokkaido University)
- Community platform for health care professionals (PATH)
- Use of open frequency bands (white spaces) to support remote diagnosis and adherence (encourage patients to take an active part in their treatment, including medication) Kgakalolo Project (Ultimate Informatics)
- “Warning”: app based on user votes and information available from local governments
- “MYDAWA”: Platform facilitating purchase of prescription drugs
- “Flare”: Private sector ambulance service
- DentaCarts: E-commerce for dentists
- RecoMed: Doctor appointment service
- IFA: Micro insurance
- Ozone disinfectants (E Tec)
- Vaccine development platform (Takeda Pharmaceutical)

## **4-4 Incentives Promoting Private Sector Investment**

### **[Current Status and Issues]**

In order to achieve further progress in private sector investment in R&D for new technologies that contribute to communicable disease control, incentives that stimulate investment by companies are necessary. To solve the issue of drug resistant (AMR) bacteria, it is crucial to ensure the proper use of antibacterial agents and develop new antibacterial agents. However, pharmaceutical companies continue to be reluctant to carry out the R&D required for new antibacterial agents.

As reasons, the development of antibacterial agents against resistant bacteria is difficult and companies cannot expect large sales for drugs that are developed. At 0.03%, the success rate in the development of new drugs in general is not high and the success rate in developing antibacterial agents against resistant bacteria is even lower so this is clearly a very difficult situation. In addition, even if success is achieved in the development of a new antibacterial drug and it has been launched, its use will be restricted to prevent the new appearance of resistant bacteria. Also, the business model for regular new drugs of growing sales and investing the income will not work. Thus, the disadvantages of R&D on antibacterial agents for pharmaceutical companies exceed the advantages.

Also, in the case of using ICT in communicable disease control, since there is no past experience of its use in the development and commercialization of similar products and no markets exist, R&D is not without risks. If there are local needs and there is further investment, development will proceed.

#### **[Actions Needed]**

It will be necessary to study the introduction of a system of incentives for private sector companies with particular focus on pull incentives. Specifically, consideration should be given to such programs as a marketing entry reward (MER) system that rewards pharmaceutical companies when their antibacterial agents are approved, and a Transferable Exclusivity Extensions (TEE) system that gives pharmaceutical companies the right to the extension of marketing exclusivity for another drug desired by the company when marketing approval for an antibacterial agent is received. At the time of introducing such systems similar systems in force in other countries will be used as a reference.

In order to press forward with R&D on ICT and AI that will contribute to communicable disease control, it will be necessary to consider establishing funds in which corporations and other stakeholders play a pump-priming role. In addition to funding, it will be important to design programs as global accelerator programs that are aligned with development.

## **4.5 Deregulation and Harmonization**

#### **[Current Status and Issues]**

In order to be able to use drugs that are not approved in the respective countries or regions as soon as possible for Ebola hemorrhagic fever and other serious communicable diseases,

deregulation and harmonization between Japan and the other countries will be crucial. Deregulation achieved in some Asian, Middle Eastern and South American countries allows drugs approved by the Ministry of Health, Labour and Welfare to be endorsed or their examination periods shortened. Also, in Korea and China, deregulation is proceeding to adopt new drugs supported by Japanese data based on the perception that there is no ethnic difference between two peoples.

#### **[Actions needed]**

Efforts in deregulation and harmonization that have already succeeded need to be expanded to many more countries, including those in Africa.

## **4.6 Communication with Society**

#### **[Current Status and Issues]**

Communication with society is needed in response to vaccine hesitancy and drug resistant (AMR) bacteria, which are threats to public health worldwide. Vaccine hesitancy is an attitude of refusing vaccination or avoiding it from various reasons when it is readily available, and it has become a global problem. Regarding AMR, efforts to increase the understanding of ordinary people and to ensure that many more people have the correct perception of the proper use of drugs are a long way from being sufficient. In addition, little progress has been made in improving the understanding of doctors and other health care professionals.

#### **[Actions Needed]**

For vaccine hesitancy, in addition to raising the awareness of ordinary people, we need to carry out education programs directed at health care professionals. It will also be necessary for industry, government and academia as well as the media to come together in ensuring that the correct information is communicated to ordinary people.

## **4.7 Responding to New Communicable diseases**

#### **[Current Status and Issues]**

Owing to climate change and greatly increased movements of people and goods on a global scale, there is a growing need for a response not only with respect to endemic communicable diseases but also communicable disease epidemics. Apart from the communicable diseases taken up by the conference, there are many others that require a response. For these diseases, too, it is our responsibility to research and develop new vaccines, medications, diagnostic

technologies and treatment technologies. It is also important to create a system for the diffusion of these technologies in a form with no barriers to access for anyone in many countries including those in Asia and Africa.

**[Actions Needed]**

- 1) Future conferences should continually examine whether the diagnosis technologies, prevention and treatment technologies and digital and information technologies currently under development may be put to use in future P3 packages for new communicable diseases that appear.
- 2) For severe fever with thrombocytopenia syndrome (SFTS), the safety and efficacy of favipiravir have already been confirmed so further development is required. Also, the efficacy of favipiravir has been observed for the viral communicable diseases of Lassa fever, Crimean-Congo hemorrhagic fever (CCHF) at the experimental level so clinical trials are now required in other countries.

## 5. Conclusion

The 6<sup>th</sup> conference was held in conjunction with the 7<sup>th</sup> Tokyo International Conference on African Development (TICAD 7). This provided the opportunity for discussions on expanding various scopes of collaboration beyond Asia to include Africa, and with UHC among the themes, the contribution to the health care systems of many African countries that have many issues was also discussed. Also, regarding the creation of the Asia Clinical Trials Platform that has been proposed by the Nikkei Asia Africa Conference on Communicable Diseases, agreement of the conference participants was unanimous. Furthermore, measures against AMR were launched as a new P3 project. The endeavors to tackle communicable diseases (tuberculosis, malaria, Ebola, etc.) through P3 projects presented by the conference had produced some good results in a short period of time, which confirmed that infection control measures by P3 are effective.

However, there are still issues that have to be overcome in measures against communicable diseases carried out by P3. If Africa is included in the field of view regarding the risks and importance of measures against neglected tropical diseases (NTDs) which have not yet occurred in Japan, as communicable diseases know no borders, it is essential to raise public awareness in Japan and by doing so raise political attention. Through further strengthening collaboration among stakeholders in Japan and other countries, through P3 efforts, concrete progress is expected to be made by the time of the 7<sup>th</sup> conference in various actions included in the current statement that need to be acted on (Details of discussions made by the breakout sessions are included at the end of this statement as an Appendix).

[6<sup>th</sup> Nikkei Asia Africa Conference on Communicable Diseases 2019]

- Organizer: Nikkei Inc., The Financial Times Ltd.
- Special Supporters: Kanagawa Prefecture, Yokohama City
- Supporters: Cabinet Office, Ministry of Foreign Affairs, Ministry of Economy, Trade and Industry, Ministry of Health, Labour and Welfare, Ministry of Education, Culture, Sports, Science and Technology
- In Association with: Mitsubishi UFJ Research and Consulting Co., Ltd, Africa Health Business, Japan International Cooperation Agency (JICA), Nikkei Business Publications, Inc.

- Administration Office: Nikkei Medical Publishing, Inc.
- Special Sponsors: DAIICHI SANKYO CO., LTD., FUJIFILM Toyama Chemical Co., Ltd., Nippon Trading EST, FUMAKILLA LIMITED, Meiji Seika Pharma Co., Ltd., KM Biologics Co., Ltd., MSD K.K., Saraya Co., Ltd., SHIONOGI, Sumitomo Chemical Co., Ltd., SYSMEX CORPORATION
- Sponsors: Asia Africa Investment and Consulting, Eiken Chemical Co., Ltd., Global Health Innovative Technology Fund (GHIT Fund), Mitsubishi Tanabe Pharma Corporation, NIPRO CORPORATION, Sumitomo Dainippon Pharma Co., Ltd., Takeda Pharmaceutical Company Limited

<Appendix>

## **Content of the 6<sup>th</sup> Nikkei Asia Africa Conference on Communicable Diseases Luncheon Sessions and Breakout Sessions**

Lunch Session 1 (Meiji Seika Pharma, KM Biologics)

“From Prevention to Treatment – Issues in Asia and Japan’s contribution to their solution”

Dengue fever is a mosquito-borne communicable disease and 4 billion people in 128 countries are at risk. In 2014, Japan saw its first cases in 70 years and there have been many cases of people who were infected overseas before returning to Japan. The mechanism of infection by the Dengue virus is complicated due to the presence of multiple virus types and other factors. The world’s first Dengue fever vaccine was developed by the major French Pharmaceutical company Sanofi. However, regarding cases where someone with no history of infection is infected after vaccination, the risk of serious disease has been demonstrated. At present, potential vaccines based on various scientific concepts are under development and a Phase I trial on the vaccine of KM Biologics is underway in Australia.

Currently, carbapenem antibiotics are available for serious bacterial communicable diseases but drug resistant (AMR) bacteria producing an enzyme called carbapenemase, which degrades carbapenem, have become prevalent in the world. There are 4 classes of carbapenemase (Class A, B, C, D) which differ greatly by region. Development of antibacterial agents against these classes as well as inhibitors of  $\beta$  lactamase, which produces carbapenemase, is underway in the world and a combination drug containing Meiji Seika Pharma’s new  $\beta$  lactamase inhibitor has been found to improve the action of various antibacterial agents. As a measure against drug resistant bacteria, it is essential to promote the proper use of antibacterial drugs.

Lunch Session 2 (Kanagawa Prefecture)

“Innovative Development of Pandemic Influenza Control Strategy”

With Kanagawa Prefecture embarking on the formulation of an action plan to control new strains of influenza virus, measures against them are proceeding at both national and local government levels. Hopes are pinned on innovative measures that include the launching of confirmatory trials focusing on the containment of new types of influenza virus in the home through the use of such new technologies as telemedicine and remote monitoring; new strain influenza virus detection kits and rapid diagnosis based on gene amplification; and consultation systems combining diagnosis kits and online treatment. For the commercialization of these innovations, it will be necessary to create a system that goes beyond existing systems

and regulatory frameworks.

#### Breakout Session A-1, 2 (MSD, SHIONOGI)

“Efforts to realize the sustainable development and access of novel treatments for AMR”

In Japan, the number of community-acquired communicable diseases due to such bacteria as methicillin resistant *Staphylococcus aureus* (MRSA) is increasing and in other countries, particularly in Asia, bacteria with resistance to carbapenem antibiotics appear with high frequency. Despite the need to continually develop new antibacterial agents against the increasing risk of infection by drug resistant bacteria (AMR), there has been a tremendous decrease in the development of new drugs due to the difficulty and high cost of R&D and low profitability. Major pharmaceutical companies continue to withdraw from or transfer their business.

Owing to the peculiarity of antibacterial drugs that their use has to be restricted in order to prevent the occurrence of resistant bacteria, pull incentive mechanisms under which compensation can be received after launch are required. Two types of pull incentive are Market Entry Reward (MER) and Transferable Exclusivity Extensions (TEE) and in the UK in July, a trial on a subscription model that allows compensation to be received not on the sales volume of a new drug but on value was announced. While push incentives to support R&D funding are expanding in individual countries, no systems of pull incentives have yet been established so it is necessary for industry government and academia to continue discussions on the research and development of systems. From the viewpoint of the fiscal authorities, information on the magnitude of the risks of communicable diseases due to drug resistant bacteria in comparison with other diseases, such as death rates and economic losses, will be material for making decisions.

#### Breakout Session B1 (FUJIFILM Toyama Chemical)

“Current landscape and future prospects of antiviral treatment for SFTS (severe fever with thrombocytopenia syndrome)”

Severe fever with thrombocytopenia syndrome (SFTS) was first reported in China in April 2011. It is a severe arthropod-borne infection with a mortality rate of around 30% and in recent years around 90 cases have been diagnosed in Japan annually. At present, its prevalence in Asia is likely to be widespread.

In Japan, the safety and efficacy of the existing treatment for SFTS, favipiravir (FUJIFILM Toyama Chemical), have been confirmed in an investigator-initiated trial. Currently, Fujifilm and Toyama Chemical are conducting a company-initiated trial for the purpose of filing for

approval. At the same time, the companies are developing an injection for patients with difficulty in taking oral medication, whose commercialization is expected at an early date.

In order to use existing drugs for a new communicable disease like SFTS, deregulation and harmonization between Japan and other countries is very important. In some countries in Asia, the Middle East and South America, deregulation has been achieved in terms of endorsing drugs approved by the Ministry of Health, Labour and Welfare or shortening the examination periods for them. Also, in Korea and China, deregulation is proceeding with regard to considering that there are no ethnic differences when Japanese data is submitted. There is a need to further expand such deregulation to many more countries, including those in Africa. In addition, in order to be able to use new technologies swiftly for serious communicable diseases in Japan and other countries in the medium-long term, it will be crucial to create systems enabling randomized controlled trials to be conducted swiftly both in Japan and other countries.

#### Breakout Session B-2(DAIICHI SANKYO)

“Vaccine hesitancy: A global threat to fighting against communicable diseases, which can be prevented by vaccines”

Vaccine hesitancy (VH) is now a problem in many parts of the world. VH means despite the availability of preventive vaccination, people put it off or refuse it. Various factors are involved in the cause in a complicated way, such as risk/benefit of the vaccine, religious and cultural aspects and incorrect knowledge. VH is considered to be one of the causes of recent outbreak of measles and the WHO cited VH as one of the top ten threats to world public health in 2019. In Japan, a high vaccination rate is being maintained for measles-rubella vaccine for children who are subjected to regular vaccination. However, if VH should increase, the risk of outbreaks will increase greatly.

In order to protect individuals against communicable diseases and protect populations as well by maintaining a high vaccination rate, it is necessary to promote attitude changes that have people who are against vaccination or hesitant to have it accept the need for vaccination. To this end, it will be crucial to carry out initiatives in such areas as (1) communication, (2) creation of evidence for quality, safety and efficacy, (3) improving safety, efficacy and convenience and (4) behavioral economics perspective. Among them, communication is very important in enhancing understanding of vaccines through experts sharing their knowledge with the general public. In this, the collaboration of various stakeholders, including governments, academia, health care professionals, companies, the media and civil society, collaborate is very important.

#### Breakout Session C-1 (Sumitomo Chemical)

##### “Japan’s initiatives for malaria elimination in Africa”

In Africa, where the harm done by malaria is the most serious, Japan is conducting a P3 initiative whose main components are measures against severe pediatric malaria and vector control. The key project, Osaka City University’s Interdisciplinary Research for Community-led Integrated Strategies to Eradicate Malaria in Tropical Africa, has been adopted as a SATREPS project. Under it, a plan for the management of asymptomatic persons and those who already have malaria has commenced, with vector mosquito measures and group medication as core elements. Some new technologies for vector control (mosquito nets with long-lasting mosquito repellent effect, sustained effect indoor sprays, mosquito larvicides) have already received WHO PQ and should be effective in local anti-malaria measures. Continuing responses to new resistance, an integrated approach comprising the further diffusion of measures through the efforts of international organizations and products incorporating new technologies will be the key to success. However, for the purpose of eliminating malaria, a package integrating diagnosis and treatment with vector control will be required. Also, in order to achieve effectiveness in the medium- to long-term, it will be essential to bring in communities and foster a sense of ownership.

#### Breakout Session C-2 (SYSMEX)

##### “Malaria-free continent: Africa and Japan working together for sustainable growth”

In Africa, economic losses due to lost educational and employment opportunities are huge, and achieving a stable, high quality working population through anti-malaria measures is a top priority for the sustainable development of Africa. The new technology applied in fully-automated hematology analyzers using flow cytometry, which can test for plasmodium at high speed, is expected to make a major contribution to eliminating malaria and in order to achieve their effective introduction locally, capacity building will be essential. Sustainability will be ensured not only by improving access and ensuring quality but also by training local technicians and building cooperative relationships involving industry, government, and academia, where Ministries of Health and research institutes are also involved.

#### Breakout Session D-1(Saraya)

##### “Jigger Infestation in Africa Sub Sahara Regions; Current status and issues”

Tungiasis is prevalent in tropical and subtropical regions of Africa. The parasite that causes

the disease is the female jigger, a type of flea that burrows into the skin and lays eggs in it, in particular in the toes, soles of the feet, rim of the feet and heels, which causes itchiness and inflammation of the affected part. When the inflammation is severe, it may be difficult to walk. While the WHO has not recognized it as a neglected tropical disease (NTDs), 1.4 million people are thought to have the disease in Kenya and the WHO estimates that 20 million people are at risk of infection in North and South America. It has been pointed out that people living in poverty repeatedly contract tungiasis and this leads to a “chain of poverty across generations.”

Metrifonate, an insecticide, and thiobendazole, a fungicide, and ivermectin, a treatment for intestinal nematode disease have been used for tungiasis but are ineffective. While it has been demonstrated that applying coconut oil twice daily for 8-10 weeks reduced incidence, a proper method of treatment has still to be established. Saraya has developed a gel for this purpose.

In countermeasures, it will be crucial to continually collect data to keep abreast of the current situation. Nagasaki University is already planning research. In addition to funding support for the diffusion of products to combat the disease, it will also be necessary to improve sanitation. The Kenya government has designated March 3 as National Jiggers Day and momentum to make this International Jiggers Day is growing. Global level educational and awareness increasing activities are essential. In addition, people are infected because they do not wear shoes so shoes will be a means of prevention. Results Japan has been working on the eradication of jigger since 2016 and by March 2019 had provided 13,000 pairs of washed, used sports shoes.

#### Breakout Session D-2 (FUMAKILLA)

“Development of Mosquito Killer Products in Asia and Its Application to Malaria Control in Africa”

FUMAKILLA has a high market share for vector control products such as insecticides and mosquito coils in Southeast Asia. In addition to marketing activities involving regular visits to small shops in each country, the company is aiming to enhance awareness by holding symposiums on Dengue fever prevention and distributing consumer pamphlets. FUMAKILLA wants to develop a market in Africa for its insecticides and mosquito coils to contribute to malaria prevention.

In the prevention of malaria in Africa, Sumitomo Chemical’s Olyset Net, a mosquito net incorporating an insect repellent, has been effective in vector control. Sumitomo Chemical developed Olyset Net in the 1980s and started selling it in the 1990s. The recommendation of the WHO in 2001 has greatly contributed to its diffusion. As a result, it is in the procurement

lists of the Global Fund, UNICEF and other international organizations.

However, there are limitations on a mosquito net containing an anti-mosquito ingredient. One of them is people being bitten by mosquitoes in places not covered by the net and another is the appearance of mosquitoes with resistance to pyrethroid, the anti-mosquito ingredient used.

Therefore, there is demand for the use of mosquito coils to prevent malaria in Africa. There are 2 possible marketing strategies for anti-malaria products. One strategy is having products procured by international organizations as in the case of Sumitomo Chemical's Olyset Net and the other conducting marketing activities directed at small shops, as FUMAKILLA has done in Asia. As evidence is crucial for gaining a WHO recommendation for use and accumulating it takes time, the marketing strategy for mosquito coils directed at small, local shops can be effective.