The Japan Pharmaceutical Manufacturers Association (JPMA) Proposal for Creation of Drugs and Vaccines for Infectious Diseases

-Facing the outbreak of a new coronavirus infection as a possible turning point-

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Japan Pharmaceutical Manufacturers Association (JPMA)

Introduction

This new coronavirus infection has spread all over the world at astounding speed, paralyzing economic and social activities around the world, and becoming a serious social problem on a global scale. Therapeutic drugs and vaccines hold the key to the early resolution of the infection and economic recovery and pharmaceutical companies are promoting research and development to create safe and effective new drugs and vaccines including the use of existing drugs for treating and preventing this infectious disease. In addition, with regard to products that are urgently requested by the government to supply to those in need, preparations have been made to give a top priority response and other arrangements have been put in place to ensure a stable supply of pharmaceuticals even under the current scale of infection spread.

As R&D-driven pharmaceutical companies, we are strongly aware of our mission to create therapeutic drugs and vaccines and to also provide a stable supply of pharmaceutical products. With renewed commitment to the future and further efforts to bring the pandemic to an end, we have to confront the challenges that need to be addressed not only in our efforts to bring the pandemic to an end, but also to prepare for unknown infectious diseases in the future. This report makes use of experience gained so far to provide recommendations for overcoming these challenges.

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Introduction

The new coronavirus infectious disease which was successively reported mainly in Wuhan City, China from the end of 2019 has since spread around the world and WHO announced it should “Be regarded as a pandemic” on March 11 this year. In Japan, infection was first confirmed in January, and then gradually spread, and on April 7 a “Declaration of New Coronavirus Infection Emergency” was issued. At present, the number of newly infected patients has started to drop due to the efforts of medical workers in the medical field as well as requests to refrain from going out and to take days off from work and now the spread of infection is showing signs of ending.

On the other hand, the government should be aware that pandemics will definitely occur in the future as well as in the second and third waves of the current infection, and should take responsibility for taking measures against infectious diseases in normal times. These measures must be taken to reduce the risk of the spread of infection. Such measures include utilizing online services for remote work and applying logistics to save manpower by using AI and/or ICT and by grasping the actual status of the epidemic in urban areas. Measures to promote the use of digital technology and deregulate it for use as a medical management system in times of emergency are also required.

The role of the government is to unify crisis management at the national level in the event of a pandemic and consolidate various research fields related to infectious disease countermeasures to make political decisions based on scientific views in the event of an emergency, and to establish a system functioning as so-called “command tower” to formulate comprehensive measures, incorporate them into national security strategies to enhance basic research of infectious diseases, and procure researchers. Furthermore, in view of the fact that infectious diseases spread beyond national borders, it is essential to take measures through international cooperation.

Chapter 1 Essential measures to promptly create and provide a stable supply of therapeutic drugs and vaccines

Infectious disease control is a crucial national strategy for public health. In Western countries in particular, drugs and vaccines for the treatment of infectious diseases are ranked as strategic commodities and a mechanism is in place for developing and supplying therapeutic drugs and vaccines as part of measures against infectious diseases based on clear national strategies and policies. Similarly, in Japan, measures against infectious diseases are a national public health strategy and therapeutic drugs and vaccines should be ranked in the same way as in other countries. However, it is difficult to say that sufficient preparations actually in place on a nation-wide level as measures to prevent infectious diseases by performing tasks such as by doing R&D activities, formulating therapeutic drugs and vaccines, production and a stable supply, and regulating them, etc.

In R&D activities and commercial production of vaccines as specific examples including the points that: (1) The private sector is reluctant to get involved because of concerns about the economic risks associated with vaccine development (2) Delays in researching new basic technologies will prevent the rapid development of vaccines against emerging and re-emerging infectious diseases. (3) Limitation of general versatility of existing facilities makes it impossible to achieve mass production of vaccines.

In Japan, the government needs to take responsibility for dealing with infectious diseases that are unpredictable and may occur at any time.

It is necessary to establish a command post function (a Japanese CDC (Centers for Disease Control and Prevention)) that oversees everything from vaccination measures during peacetime to countermeasures against infectious diseases during emergencies, authorizes long-term budgetary measures, and provides active support for domestic technical development and human resource development under the command post function, as well as the introduction of cutting-edge technology into existing facilities and the renewal of equipment.

In particular, since emerging and re-emerging infectious diseases have a cause by mutations of viruses with each outbreak, it is necessary to plan and implement measures against mutated viruses under the leadership of the command post function.

In addition, a support system should be promptly set up to minimize the economic burden and risk by allowing private companies and research institutes to develop therapeutic drugs and vaccines and to build a production system, to actively promote the development of new technologies domestically, and to promote the transfer of manufacturing technologies from foreign companies to domestic ones at the same time by deepening international cooperation, if necessary.

The most important task is to establish a command post function that can consistently implement these measures against infectious diseases from normal times to the outbreak of an epidemic.

Based on the recognition of this issue, in this chapter, we will make recommendations for the rapid and stable delivery of therapeutics and vaccines to the medical community based on the current state of affairs in the areas of basic research and infrastructure development, clinical development, manufacturing technology development and production, stable supply, regulation, and intellectual property.

Research and development of therapeutic drugs and vaccines

Enhancement of research infrastructure and basic research

From the perspective of earnings predictability, R&D of drugs and vaccines for treatment of infectious diseases has become an area difficult for pharmaceutical companies to enter. In Japan, the number of enterprises engaging in this field is dropping year by year. This has led to fewer researchers in the field of infectious diseases in the private sector and a weakening of the foundation for new technology development. Responding quickly to emerging and reemerging infectious diseases in the future, requires making the following efforts to promote the research infrastructure in the fields of infectious disease and immunology in cooperation with the public and private sectors during normal times and to upgrade the nation's R&D capability.

1) Active collaboration among industry, academia, and government in technological fields to foster innovation

・Collaboration among industry, academia, and government is essential for rapid commercialization of new technologies that lead to innovative breakthroughs such as DNA vaccines, RNA vaccines, and adjuvants. It is also necessary to work on the development of guidance and guidelines with the aim of achieving a level of practical application that can rapidly respond to emerging and reemerging infectious diseases. Also necessary is providing political support, such as continuing financial assistance and human resource development for R&D based on such new technologies.

・Also it is essential to discuss introduction of legislation to protect health care providers and vaccine developers from claims for health injury and to achieve prompt recognition of compensation coverage for those who suffered health injury caused by vaccines produced and administered in an appropriate manner, assuming that their emergency use may be allowed by special provisional approval in the future, which legislation may include establishing a vaccine health injury compensation system based on a no-fault basis.

・Further, promoting industry-academia-government collaboration for infectious diseases in Japan, requires collaborating with all stakeholders. To this end, a task force should be established under the leadership of the so-called command tower function, with the participation of the Japan Agency for Medical Research and Development (AMED), the National Institute of Infectious Diseases (Infectious Diseases Research Center), the National International Medical Research Center, the Japan Society of Pharmaceutical Manufacturers, the Japan Pharmaceutical Manufacturers Association, and the Cabinet Secretariat's Office for Measures against New Coronavirus Infectious Diseases. Efforts should be made to coordinate R&D activities specializing in measures against new coronavirus infections and medical systems developmental strategies to promote

harmonization among the different stakeholders.

2) Development of new drug discovery and treatment methods by unlocking the mechanisms of onset and severity

・Various factors, including age and the presence of underlying diseases may be involved in the onset and progression of infectious diseases so as much data as possible must be collected and analyzed in order to clarify these factors. Also essential is developing a system that can construct and analyze a database that integrates clinical information such as treatment history, lifestyle habits, and medication history (including drugs taken regularly) as well as genome information, other omics information, the results of immune system analysis of persons who have been cured without exhibiting symptoms, those whose condition has aggravated to a serious stage (cytokine storm complications, etc.) and those who have suffered a relapse.

3) Establishment of a library type public institution to pool existing drugs, etc.

・Public institutions should form and manage libraries in advance based on various information provided by each company and the various drugs, compounds. Moreover, public research institutions such as the National Institute of Infectious Diseases which have facilities higher than Biosafety Level 3 (BSL-3) should promptly establish appropriate evaluation systems and conduct screening in case of emergencies.

・At this time, it is necessary to establish rules for the provision of drugs, to secure library storage areas and to establish rules for drug management, to select research institutes that have at least BSL-3 facilities where screening is possible, to establish a system that enables the prompt implementation of clinical trials after the selection of compounds, etc., and to secure annual budgets for continuous maintenance.

4) Expansion of laboratories essential for infectious disease research in public institutions and promotion of joint use with pharmaceutical companies

・When handling pathogens, laboratories and production facilities that can be sealed at appropriate biosafety level (BSL) grades are required. It is difficult for private companies to develop new non-basic containment laboratories such as at the BSL-3 level. It is also difficult for private enterprises to conduct experiments and other tasks dealing with pathogens without cooperation with public research institutes. In order to promote public-private partnerships to this end, it is important for public research institutions to expand the number of BSL-3 and 4 facilities and equip them with the required equipment for infectious disease research such as supercomputers and cryo-electron microscopes. In addition, in order to develop human resources proficient in manipulating these technologies and to create drugs and vaccines for treating emerging and reemerging infectious diseases, a system must be established that utilizes these locations as avenues for

industry-academic-government collaboration.

5) Establish a system to quickly share throughout the world the latest epidemiological information and news on strains and viruses

・To anticipate and respond to potential outbreaks and pandemics, appropriate storage of pathogen samples and genomic information in national biobanks is required to enable timely sharing. A system should also be established to collect and share detailed epidemiological information for public health and R&D purposes. To this end, it is necessary to unify the management of information from domestic and overseas research institutes and experts during normal times, establish a mechanism to share the latest information in Japan under international cooperation with WHO and the CDC in the United States, etc., and develop vaccines and therapeutic drugs in advance of a pandemic.

6) Promoting R&D through global collaboration and industry-academic-government collaboration

・As a global countermeasure against new coronavirus infectious disease, "Access to COVID-19 Tools (ACT) Accelerator" was established under the initiative of EU in May this year. Under the scope of this international framework, international efforts are being made toward R&D activities vaccines, therapeutic agents, and test agents needed for control of infection from the new coronavirus as well for their rapid application in developing countries. Within this framework, the Government of Japan has provided funds to the CEPI (Infectious Disease Epidemic Prevention Innovation Alliance), which is responsible for R&D of vaccines, but has not taken part in projects such as dispatching human resources. It is necessary for Japan to actively participate in these efforts in order to efficiently and timely grasp R&D trends related to countermeasures against new coronavirus infections in the world, and to coordinate the establishment and implementation of strategies through industry-academic-government collaboration aiming at early development of seeds to nurture domestic R&D activities.

Acceleration of clinical development

The development of vaccines, antiviral drugs and drugs to prevent a disease from aggravation must be promoted promptly. In response to the recent outbreak of COVID-19, public institutions and domestic pharmaceutical companies are making strenuous efforts to develop therapeutic agents and vaccines in Japan. As of May 24, there were nine cases of vaccine development and 21 cases of therapeutic agent and therapy development in Japan. However, since general clinical development requires three to seven years and even just a phase III trial alone requires two to three years, it is extremely important to rapidly extend the indications (drug re-ranking) of existing drugs for the infectious disease to prevent serious infections in affected patients until vaccines and therapeutic drugs are put

into practical use. In response to COVID-19, pharmaceutical companies are currently undertaking domestic development of antiviral drugs and therapeutic drugs to prevent serious infections as described above. However, in order to ensure safety and promptly evaluate the efficacy of drugs and vaccines, the following efforts are required.

1) Promotion of clinical development support to expand the indications for existing drugs to prevent serious infections etc.

・The safety and effectiveness in an emergency must be verified from the early stages of infection through to the epidemic period. To achieve this, it is necessary to prepare data, information, clinical evaluation guidelines, guidance and other documents that companies and other institutions should submit in normal times for evaluating safety and efficacy.

・In order to facilitate clinical trials in times of emergency, it is important to coordinate clinical trials such as patient recruitment, to interpret the results of clinical trials in cooperation with the authorities, to conduct multinational clinical trials, and to cooperate internationally by way of the data obtained. The so-called command tower function is essential for taking control of these matters and coordinating them as a whole.

・From a long-term perspective, it is essential to further promote basic and applied research by industry, academia, and the government in order to further improve the level of research in the fields of infectious diseases and immunology and to serve as a world leader in this area. For this reason, it is even more vital that the government provide one-stop support from the basics to practical application, such as strengthening academic basic research through Grant-in-Aid for Scientific Research, supporting research and development in AMED, and accelerating research activities to serve as a link to private enterprises.

2) Accelerate clinical development with Real World Data (RWD) and Real World Evidence (RWE)

・In phase III trials comparisons should be made with existing treatments or placebo controls. However, problems include impediments to accessing the study drug when assigned to the placebo group, a larger size due to aligning the control and test groups, and a longer length of time that serve as bottlenecks to rapid development. To address these bottlenecks, the use of RWD and RWE in the control group is expected to improve patient access and clinical trial efficiency. To accomplish these goals, the following measures are specifically required.

・While protecting personal information, medical information such as electronic medical record information should be consolidated into a database of high-quality RWD that can be applied to approval applications while maintaining connectivity through the use of pseudonyms. Legislation should be drawn up to allow secondary use for the purpose of developing new therapies and expanding indications.

・It is necessary to establish rules for more finely defined electronic medical record input and a standardized data format for medical institutions, and to also establish a system to support electronic medical record input in medical institutions (medical clerks, AI support, etc.).
・It is necessary to build up an ecosystem with a view to international cooperation to make the above system sustainable, including through private participation, and to develop an environment in which patient information can be quickly shared between domestic and foreign medical institutions and authorities.
・International cooperation and standardization are required for the study design and judgement standards of the clinical trial using RWD and/or RWE.

Improvements in manufacturing technology and expansion of production capacity

This section describes the challenges of vaccine production and their solutions that have been recognized anew in terms of production technology and commercial production in the current COVID-19 epidemic.
Regarding the development and production of vaccine manufacturing technology, the vaccine business in the private sector has a large economic risk not only in Japan but also in other countries. Vaccines require both manufacturing technology development and production facility investment almost simultaneously from the development stage, but it is difficult for private companies to bear the investment risk alone when the success or failure of vaccine development is uncertain. In each country, efforts are being made to stabilize the vaccine business by ensuring these risks within a public framework. Production facility for pandemic vaccines is generally not flexible enough for multiple uses and a lack of government support for the cost of equipment and facility maintenance and management and the cost of training production personnel is also a major challenge. In the future, the following efforts will be required to achieve both rapid and ample commercial production of vaccines that conform to new technologies.
On June 1 of this year, the Ministry of Health, Labour and Welfare released its "accelerated parallel plan" aimed at the early commercialization of a new coronavirus vaccine, in which the nation's government indicated it would support the acceleration of the process from basic research to pharmaceutical approval and production, and that the development of a production system in particular would be undertaken in advance by the government utilizing funds established in the second supplementary budget for FY 2020. We welcome this initiative and look forward to its implementation.

<u>1) Active support for vaccine technology development and human resource development</u>

・In the future, with the aim of being able to respond quickly to all emerging and re-emerging infectious diseases, it is essential to foster human resources and

provide financial support through more active cooperation with overseas organizations and cooperation among industry, academia, and the government with the goal of improving vaccine manufacturing technologies and the capabilities of researchers and engineers mainly in those technological fields where innovation is expected.

2) Development of production facilities compatible with new technologies

・When handling highly pathogenic pathogens such as the Ebola virus, it is necessary to handle them at biosafety level BSL-4. However, production using existing facilities and equipment is also possible by attenuating pathogens using genetic recombination technology. If cell culturing is not an option, recombinant DNA and RNA vaccines offer possibilities. In the case of private companies, there is a concern that investment in new manufacturing facilities for these new technologies might not be collected as initially expected. In order for private companies and research institutes to start developing vaccines and building production facilities for emerging and reemerging infectious diseases, it is necessary to establish a system that allows the nation's government to promptly provide support systems to minimize economic burdens and risks.

3) National government support for vaccine production

・Annual public support is also required to cover the cost of introducing technologies to improve the versatility or flexibility of current facilities for cell culture production facilities built for the production of H1N1 influenza vaccines as part of national crisis management measures so that these facilities can respond to emerging and reemerging infectious diseases other than H1N1, as well as for the cost of updating production facilities, readiness (Stocking of raw materials, basic and CMC (Chemistry, Manufacturing and Control) research, securing of production personnel and education), and maintenance (Regular operation of production facilities).

Achieving a stable and persistent supply

Drug substances (API: Active Pharmaceutical Ingredient) utilized as active ingredients in drugs are often manufactured and imported overseas such as in China and India, and much of the raw materials for APIs come from China. In addition, the respective manufacturing processes from raw materials through intermediates and APIs to drug products are often conducted in multiple countries.

As for vaccines, only a few companies are able to produce them in Japan and the current production facilities are designed specifically for egg and cell cultures. Therefore, it is difficult to significantly increase production in response to an outbreak of a sudden infection.

As described above, the production of drugs for infectious diseases in Japan is highly dependent on foreign countries and there is a certain limit to the amount of

vaccine that can be produced. Therefore, in order to establish a system that can respond to the stable supply of drugs and vaccines even in the event of a pandemic, the following measures should be taken during normal times.

1) Stable supply of drugs and vaccines for infectious diseases

・In order to provide a stable supply of drugs for the treatment of infectious diseases; raw materials, intermediates, and APIs must be persistently secured. For this purpose, it is necessary to establish a system of public support for the procurement and storage of raw materials needed for manufacturing by clarifying the priority of therapeutic drugs in view of the risk of infection spread and the necessity for public health through industry-academia-government cooperation.

・It is also necessary to consider domestic production of raw materials which until now have relied on foreign imports. In consideration of manufacturing risks such as the degree of oligopoly, production capacity, and quality of the production of high-priority raw materials for drugs by region, and also the lead time for the preparation of drug products with consideration given to an emergency response, it is important to determine what new raw materials to produce domestically and their processes, and to install joint manufacturing facilities with public support.

・Changing the source of raw materials in the manufacture of drugs and vaccines for infectious diseases requires a variety of regulatory changes. When there is a problem in the stable supply of drugs in an emergency or even in normal times, a flexible response to these regulations is required.

2) Guidance to expedite the development of blood products in Japan

・Promising agents for the treatment of COVID-19 include blood-derived products, such as hyperimmunoglobulins which are plasma fractions. Blood products are manufactured using donated plasma as a raw material. In Japan however, only blood from healthy people is allowed to be collected based on the standard stipulated in the "Ordinance for Enforcement of the Act on Securing a Stable Supply of Safe Blood Products."

On the other hand, plasma used as a raw material for COVID-19 therapeutics is obtained from convalescent patients with COVID-19 and is fractionated from blood. At present in Japan, the possibility of blood collection from COVID-19 patients in the recovery period is not specified for the purpose of using it as a manufacturing raw material, and blood collection from a person with a history of SARS infection was prohibited in past cases. Plasma fractionated products may be allocated preferentially to the country from which the blood raw material is collected, and in order to ensure the stable distribution of these products in Japan, guidance should be provided to ensure that plasma is domestically available.

3) Securing a stable supply of drugs and vaccines essential for treatment of

infectious diseases

・Simultaneous with the ending of an epidemic, the demand for the drugs and vaccines used to treat the infectious diseases rapidly declines and decreases While it is the mission of pharmaceutical companies to provide the necessary drugs and vaccines in a stable manner, this poses a significant risk to the business continuity of private companies under the current system, and it is difficult for them to bear developmental costs and manufacturing costs (including waste loss) alone. Therefore, in order to ensure these economic risks, the following systems should be introduced and expanded.

・Under the Advanced Purchase Guarantee Program (stockpiling), the government is responsible for purchasing a certain amount of drugs and vaccines for infectious diseases for which marketing approval has been obtained. The government allocates the purchased drugs to the core organizations in each prefecture and asks them to stockpile them. In this case, the government will purchase the drugs according to the expiration date and will not return them to the company. Stockpiles are determined by the government, but transaction prices need to be determined as transparently as possible between the government and the company in question, depending on the stockpiles

・The Marketing Authorization Reward System (MER: Market Entry Rewards) allows companies to receive appropriate rewards (compensation) from the government or appropriate public authorities so that they can get appropriate benefits when new therapeutic agents or vaccines to treat high-priority pathogens are finally approved for marketing through research and development. From the viewpoint of rewards for contributions to new development, this system should be operated separately from the ordinary medical fee system. Remuneration (financial compensation) amounts and payment methods (lump sum, split, etc.) should be determined in a transparent manner between the government and the enterprise concerned.

Regulations in the event of an epidemic

In Japan, regulatory authorities have issued notices regarding the handling of clinical trial protocol notifications and approval reviews and some regulations allow taking exceptional measures to promptly create drugs and vaccines to treat new coronavirus infections. However, in order to prevent the spread of infection, it is necessary to develop therapeutic drugs and vaccines promptly and further deregulation and harmonization of regulations are necessary together with COVID-19 in view of new infectious diseases that will occur in the future. For this reason, it is necessary to establish clear guidelines for the prompt approval of new technologies, such as the establishment of evaluation items, in order to quickly deliver the results of innovations from Japan to patients, and to establish in advance regulatory measures for the prompt approval of new technologies, while taking safety, quality and efficacy into consideration.

1) Introduction of a new system to promptly provide emergency drugs and vaccines

・In the United States, the EUA (Emergency Use Authorization) has been passed into law allowing prompt delivery of unapproved drugs and vaccines to the public under certain rules with a view to prioritizing lifesaving. In Japan on the other hand, although a special approval system has been established, this system applies only to products that have already been approved for sale overseas, and does not enable the use of drugs and vaccines that have not yet been approved in overseas countries.

A system that enables the early administration of therapeutic drugs and vaccines developed for emerging and reemerging infectious diseases must be formulated, and it is necessary to respond flexibly to various situations that might occur in the future. Therefore in Japan, apart from pharmaceutical approval, it is necessary to introduce a system that enables prompt supply of therapeutic drugs and vaccines to medical institutions.

2) International regulatory harmonization as an international measure to prevent the spread of infection

・If the spread of an infectious disease expands to a worldwide scale then simultaneous development and approval of drugs and vaccines will be urgently needed to prevent its further spread. However, this issue cannot be resolved only by the efforts of individual governments and individual companies. Besides sharing scientific evidence on emerging and reemerging infectious diseases among countries, a system must be established that enables Japan, the United States, and Europe to conduct reviews in a unified manner and to implement relevant regulations in a unified manner to the greatest extent possible.

Achieving prompt approval of COVID-19 drugs and vaccines and prompt approval of drugs and vaccines for emerging and re-emerging infectious diseases in the future, requires that the so-called command tower function serve as a contact point for cooperation and negotiation with various stakeholders such as foreign governments, review organizations, and research institutes, and also that international adjustment of the mutual regulations be promoted in the event of a pandemic.

3) Flexible regulatory response to expedite vaccine research and development in emergencies

・There is a high possibility that an application for approval based on regulatory measures for the use of living modified organisms “Law Concerning the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms” will be required for the development and manufacture of vaccines. Confirmation by the Minister of Education, Culture, Sports, Science and Technology for research purposes and the Minister of Health, Labour and Welfare for development purposes is required. It has been pointed

out that valuable time needed to start research and development is lost due to this complicated application procedure and the long time required for approval. In the event of an emergency, it will prove necessary to reduce this time loss before starting research and development and to respond flexibly to regulations so that research and development can start promptly.

4) Acceleration of national examination of vaccines

・In order to promptly supply vaccines to treat new infectious diseases such as the new coronavirus vaccine, it will prove necessary to significantly shorten the national examination which usually requires several months, and complete it in cooperation with the Ministry of Health, Labour and Welfare and the National Institute of Infectious Diseases. Special measures should therefore be taken, such as allowing batch release only through the reviewing of abstracts of manufacturing and assay records (SPL: Summary Lot Protocol) based on quality tests conducted by private companies.

Intellectual property

1) Importance of patents in drug discovery innovation

・In the pharmaceutical industry, the patent system is an important system that supports a series of long-term and extremely costly R&D activities in which the cost of R&D is recovered by allowing the patentee to monopolize the patent rights for a certain period of time and then invest in the next R&D activities. Under this patent system, pharmaceutical companies have contributed to the welfare of mankind by developing and providing many medicines and vaccines.

2) Ensuring access to drugs and vaccines in the event of a pandemic and promoting research and development

・In the event of an emergency such as a pandemic, making a flexible response that is not bound by existing frameworks including patent rights may be required in some cases. In the first place however, no case has been recognized in which patent rights are an impediment to COVID-19 responses. If access to pharmaceuticals is hindered by a COVID-19 pandemic, then the delay is not a matter of patents but rather more likely to be caused by various disruptions such as distribution delays due to the pandemic, and the pharmaceutical industry is making every effort to prevent such problems from occurring.

・Compulsory patent licenses and other patent pool efforts have already been employed in countries around the world in response to the COVID-19 pandemic. Under the current system, implementation of these systems in line with the TRIPS agreement may be an option. However, these systems alone do not create new vaccines or therapeutics, increase production, provide rapid access to people in need, or adequately respond to the COVID-19 outbreak emergency. These systems should be implemented so as not to impede the promotion of R&D activities for required vaccines and therapeutic agents.

・Regarding the handling of patents, in order to supply vaccines and therapeutic drugs to the people who need them as soon as possible, it is important to have a mechanism that supports the efforts of companies such as public-private partnership, while relying on the individual discretion of each company handling products related to the patents.

・Similar arguments were made in the IFPMA Statement on the "Solidarity Call to Action to realize equitable global access to COVID-19 health technologies through reporting of knowledge, intellectual property and data" (https://www.ifpma.org/resource-centre/ifpma statement on the solidarity call to action to realize equitable global access to covid 19 health technologies through pooling of knowledge intellectual property and data/), published by the IFPMA on May 28, 2020, and this proposal has the same intent and direction as the IFPMA.

Chapter 2 JPMA activities other than drug discovery

In Chapter 1, recommendations were made mainly on R&D, clinical development, manufacturing technology and production, stable supply, and regulation as measures needed to promptly create and provide a stable supply of therapeutic drugs and vaccines. In addition to the recommendations in Chapter 1, this chapter provides recommendations for actions and measures considered necessary to ensure that therapeutic drugs and vaccines are provided to those patients and citizens who need them by way of healthcare professionals.
In addition, as a medical-related industry, the pharmaceutical industry has the resources and know-how to contribute to the fight against infectious disease, and it is also important to make use of these resources to contribute to medical care in our country and to the health of the people and fulfill its social mission. From this point of view, those issues that the industry should address are also proposed here.

Initiatives and policy proposals needed for the stable supply of pharmaceuticals

Logistics and distribution

In order to secure a stable supply of drug substances, therapeutic drugs, vaccines, etc., it is necessary to preferentially secure a shipping means such as airmail to foreign countries that functions even in cases of emergency.

It is necessary to establish a system for early communication of information and prompt response in order to minimize the impact on medical institutions, etc., even in the event of supply concerns or other issues encountered by each company engaging in the “Pharmaceutical Supply Adjustment Scheme” formulated by the Federation of Pharmaceutical Manufacturers Associations of Japan.

Drug price system

It is necessary to establish a new evaluation of the drug price due to an additional indication causing the re-ranking of an existing drug.
There is a need for a pricing structure that will cover the investments and costs associated with domestic production of drug substances, secure multiple procurement routes, and that will also not prove unprofitable.

Provision of Pull type incentives and institutional development in the international framework

In addition to the measures proposed in Chapter 1, as a Pull type incentive, the introduction of (i) a subscription system, (ii) a system to extend the market monopoly period applicable to other products, and (iii) a system to review drug prices in advance based on the drug profile and other items can be considered including cases being evaluated in other countries.

Since it is difficult to predict when and how much new drugs and vaccines for emerging and reemerging infectious diseases will be needed; their marketability and predictability to profitability are low. This is a major factor that hampers active R&D and capital investment. As a direct solution to this problem, the incentive system for obtaining marketing approval (MER: Market Entry Rewards) and the subscription method described in Chapter 1 are desirable Pull incentives. In addition, since pharmaceuticals are researched and developed globally, it is necessary to establish a system within an international framework for these Pull type incentive measures along with establishing a system suited to the situation of each country.

Social responsibility and contribution as a pharmaceutical industry
Reconstruction and expansion of initiatives within the JPMA and the pharmaceutical industry

The existing committees have been working on infectious disease issues and in order to strongly promote these recommendations, a cross-sectional organization will be established to deal with issues related to infectious diseases in an integrated manner, thereby reinforcing the efforts of pharmaceutical cooperatives on infectious diseases.

The organization will examine the impact of COVID-19 and issues of member companies on their business activities and the medical environment and work with related parties to develop and compile measures to address infectious diseases and issue in the event of an infectious disease outbreak.

Measures during normal times

While the situation of people infected with COVID-19 is stabilizing for the time being, we will consider measures that should be taken by the pharmaceutical industry during normal times by focusing on the following items and will implement them based on items that have already been prepared, while also anticipating the outbreak of second wave, third wave, and other emerging and reemerging infectious diseases.

1) Support for volunteer activities of current and former employees at each company for local medical care, etc.

The fact that healthcare professionals (physicians, nurses, pharmacists, clinical laboratory technicians, etc.) of each company take part as volunteers in local medical care, and that employees and former employees of each company take part as volunteers in consultation services and public health centers dealing with infectious diseases in the local area is highly significant. To support these efforts, developing standard training programs and providing training opportunities should be considered.

2) Future medical information provision system and environmental improvement

In response to requests from medical institutions, medical information is provided and collected appropriately under the guidance of each company and the actual conditions and issues of these are verified. In addition to grasping the needs of healthcare professionals and the general public, and in view of the utilization of

various IT tools and the current state of E-promotions being developed by different industries, etc., future approaches to the collection of drug safety information and information providing activities as well as the development of the environment for such activities, will be examined.

3) Promotion and enhancement of public awareness activities concerning infectious diseases and public health

Public awareness campaigns on infectious diseases and public health are socially expected efforts in the pharmaceutical industry. In order to contribute to the prevention and early treatment of infectious diseases, besides providing information on the activities of each member company that started on the JPMA website, we will also consider measures to enhance awareness-raising activities.

[Examples of Initiatives]

・Creation of COVID-19 Memorial Day/week/month and implementation of public health education and infectious disease prevention activities

・Expansion of existing activities to promote proper use (Polypharmacy, AMR, etc.) and promotion of educational activities to prevent and combat infectious diseases

・Creation of educational and awareness-raising videos on infectious diseases (for patients and doctors), public lectures and school education courses on the Internet, provision of learning materials for school education

・Provision of online health promotion programs

・Awareness-raising activities in cooperation with digital media, etc.

(3) Emergency measures

It is the role of pharmaceutical companies to promote research and development of effective drugs and vaccines and to secure a stable supply of necessary drugs in the event of an outbreak of a new or reemerging infectious diseases, but it is also important to fulfill a social mission as an industry involved in medical care. Based on this understanding, pharmaceutical companies are making various related efforts. In order to further promote the efforts of the industry as a whole, the following items will be studied and necessary measures will be taken in consideration of the situation in the medical field during emergencies.

1) Providing information on pharmaceutical companies' initiatives

In the event of a pandemic, it is important to provide information on research and development efforts for these drugs, as expectations grow for effective therapeutic agents and vaccines. Since the new coronavirus infection is spreading, information on R&D activities of member companies has been transmitted through our association's website. In regard to this activity, we will consider further enhancing the content of information and intensifying the prompt and accurate provision of information in emergencies.

2) Support for students studying medicine, pharmacology, public health, etc.

The development of human resources for future infectious disease

countermeasures and medical jobs is closely related to the business of the pharmaceutical industry and has great social significance. For example, providing financial support to students in these fields who need economic support through funding to third-party organizations should be considered.

3) Utilizing resources of JPMA member companies

In regard to each company’s facilities, after building a cooperative system with local governments during normal times, we will consider the effective use of existing facilities in the region, such as the provision of space as an emergency evacuation area and the opening of company daycare facilities to the local community.

In addition, we will consider social solidarity through simultaneous illuminating (lighting up) each company's business sites and activities to honor healthcare professionals.

Appendix

Japanese response system for infectious diseases in the event of a pandemic

Public health (prevention and diagnosis)

Early sharing of epidemiological information and specimens at the outbreak source of emerging infectious diseases is the key to establishing an initial response and testing regime in the health care setting. International cooperation is of course essential and it is also necessary to establish a system in Japan to identify signs of a pandemic at an early stage and take countermeasures.

In regard to infection with the new coronavirus in Japan, aggressive epidemiological studies such as cluster countermeasures in the initial stage of infection were considered effective in controlling infection in a limited examination system. On the other hand, there is a concern that the public health center which is the main body of the survey might lack sufficient resources. Therefore, it is necessary not only to take measures against the new coronavirus infection, but also to increase the resources available for epidemiological surveys and enhance the inspection system in preparation for future pandemics. Epidemiological information is also very important in the research and development of vaccines, so a more powerful investigative system is preferable[*1]. In Singapore and South Korea, where SARS/MERS caused the spread of infection in the past, the inspection system has been bolstered as a lesson gained from that experience. The international community has evaluated the new coronavirus infection countermeasures from the viewpoint of transparency. In order to recover from this pandemic, it will prove essential to strengthen the inspection system[*2], and it is also essential to develop an appropriate inspection system in Japan.

*1. https://www.mhlw.go.jp/stf/shingi/2r98520000036w4i-att/2r98520000036w9p.pdf

*2. https://www.pandemictesting.org/whitepapers/toward-global-pandemic-resistance

2. Medical delivery system

The spread of the new coronavirus has led to disruption of medical services in some Western countries. On the other hand, a declaration of a state of emergency based on the Act on Special Measures Concerning Countermeasures against Novel Influenza was issued because of the possibility that medical care could collapse before the explosive increase in infections after the outbreak of the pandemic. Since then, the number of newly infected patients has decreased due to voluntary curfews and requests for work leave. Subsequently, the number of beds for patients infected with the new coronavirus has increased, and hotels for patients with mild symptoms or no symptoms have been secured. As a result, the collapse of medical care has been avoided. However, even though this is due to the efforts of medical professionals in the medical field, it is still necessary to rebuild the medical supply system with infectious disease countermeasures in mind for the future.

In our country, due to its historical background, the medical care system is centered on the private sector, and it is pointed out that the number of acute-phase hospital beds per population is larger than that in Western countries, and the number of sophisticated medical equipment devices such as CT is also larger. At present, based on the regional medical care plan formulated by each prefecture, the number of hospital beds required in 2025 is estimated for each medical function, and efforts are being made to attain an efficient medical care provision system by promoting the differentiation of hospital bed functions and cooperation through consultation among local medical professionals. In light of the recent outbreak of a new coronavirus infection, it is necessary to not only expand the infectious disease ward but also to secure the medical supply system in the whole region to cope with the outbreak of the pandemic. In particular, a system should be established to share medical data and other information so that information on transportation of infected patients can be shared quickly and reliably when transfer to another hospital is required. In addition, due to the spread of infection by the new coronavirus, online medical care was utilized in view of the exceptional circumstances but having a "primary care physician" which plays an important role in regional medicine should be promoted while verifying the effects.

3. Universal health insurance

Our country has achieved the world's highest levels of life expectancy and health care standards through its universal healthcare system. Under the universal health insurance system, citizens are basically free to choose medical institutions and receive necessary medical care by making a co-payment. The new coronavirus infection is suspected in the recent spread of infection, and medical insurance is also provided when the patient visits the outpatient clinic while consulting with the health center and the family doctor. In March, PCR testing was covered by insurance, and in principle, the cost of the testing and treatment of patients confirmed to be infected are covered by public funds.

In our country, the universal health insurance system encourages people to seek medical care if they suspect they have a disease. While this has been criticized as causing an increase in medical costs, it has also contributed to the prevention of serious cases. Although the relationship between the low number of deaths caused by the new coronavirus infection and the existence of universal health insurance in Japan is uncertain, good access to medical care at least render a positive effect on preventing the disease from becoming more serious. While there is no objection to the need for fundamental reforms to maintain universal health insurance as the population ages, careful consideration should be given to the current epidemic caused by the new coronavirus infection and the role played by the universal health insurance system.

4. Securing and stable supply of medical supplies and pharmaceuticals

As new coronavirus infections spread rapidly in Japan, the shortage of medical supplies such as masks and protective clothing has become a problem. In regard

to pharmaceuticals, each company is making use of the Business Continuity Plan*3 that it formulated when the new influenza pandemic occurred, and is striving to maintain as appropriate an amount of stock as possible of pharmaceuticals and vaccines in view of reasons including: "There is a high urgency matter." "Directly life-threatening" "There is no substitute." and "public health problems may result from the lack of supplies". Top priority is also being given to products that are urgently required to be supplied by the government. On the other hand, China has imposed export restrictions on medical supplies. The current infectious disease is considered to be a long-term battle. In order to respond to future pandemics, pharmaceuticals, medical devices, and health care providers supplies should be ranked as nationally strategic items from the viewpoint of security and these items should be shifted to domestic production and stockpiled.

*3. http://www.jpma.or.jp/about/basis/guide/influenza.html

5. The way people live, work, and socioeconomic activities

In order to prevent the spread of new coronavirus infection, a new way of life is required in which people are aware of the need for social distancing and avoid closed, crowded and close "3 dense" situations. While the spread of remote work and the creation of new business practices such as digital transactions between companies are expected to increase productivity, measures against information leakage associated with cyber attacks are still required. Measures and investments for strengthening cyber security measures are necessary.

In addition, medical workers and other essential workers are engaged in their daily work tasks while also fighting the risk of infection. In order to reduce the risk of the spread of infection, measures should be taken to promote the use of digital technology and to ease regulations to allow its use as an emergency management system such as by the use of online systems and the use of drones to save manpower during logistics and distribution work.

6. Role of national and local governments

The "Act for Partial Revision of the Act on Special Measures Concerning Countermeasures for Novel Influenza" was enacted on March 14 while the number of people infected with the new coronavirus was increasing in Japan. As a result of this revision, the new coronavirus infectious disease also became subject to this law making it possible to issue a "Declaration of Emergency" that allows a "Request for self-restraint on unnecessary and non-urgent outings", "Request for delivery of pharmaceuticals", "Requests for the sale, securing, and storage of pharmaceuticals, etc. by pharmaceutical companies and owners" based on the law. On April 7, the "Declaration of New Coronavirus Infection Emergency" was issued because of the rapid increase in the number of cases in which the route of infection could not be identified and the tightly stretched medical care system.

Based on this, it has now become possible to issue the above request or

instruction with the authority of the prefectural governor in the area where the declaration of emergency had been issued. Yet it has been pointed out that the effect is limited because it is only a request and has no legal enforceability. Based on the recent spread of infection with the new coronavirus, the issues under the current law should be sorted out, and measures against infectious diseases should be carefully considered after holding a national discussion.

The role of the government is also expected to include the establishment of a system that can integrate various research fields relating to infectious disease countermeasures and formulate comprehensive measures, the enhancement of basic research in the field of infectious diseases, and the procurement of researchers in order to unify crisis management at the national level in the event of a pandemic and to make political decisions based on scientific views in emergencies. Furthermore, in view of the fact that infectious diseases spread beyond national borders, it is essential that measures be taken in a spirit of international cooperation.