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Issue Brief

Innovation and Collaboration: The Backbone to Preparing for and Responding to Global Pandemic Threats

The Research-Based Pharmaceutical Industry's Role

Overview

Earlier this year, signs of an influenza pandemic emerged and took many by surprise. Not because it was unexpected, but because it was a different virus than many had anticipated to emerge as the next global influenza crisis.

A quick and effective response to this emerging pandemic health threat was critical. The global pharmaceutical industry played an important role in achieving that response -- through breakthrough scientific innovation and collaboration with other stakeholders to help patients.

Complex challenges in public health also require intensive planning and extensive partnerships. Coordinated collaboration within the pharmaceutical industry, as well as with government leaders and public health officials have endeavored to ensure that the global community will quickly receive the pandemic influenza vaccine and medicines necessary to help protect against this growing threat.

Background

Typical seasonal influenza outbreaks are caused by subtypes of influenza viruses that have previously circulated among the general public. Because of this previous exposure, many people are able to mount at least a partial immune response against the illness. Despite this, between 250,000 to 500,000 people die each year worldwide due to influenza.

By contrast, about once every 30-40 years, pandemic influenza occurs when a strain of influenza virus that has never circulated among people emerges in the population. There is little or no pre-existing natural immunity to these viruses. Thus, pandemic influenza can quickly spread around the world and lead to high morbidity and mortality.¹

Prior to 2009, the most recent influenza pandemic was in 1968. That flu contained a combination of genes from avian and human influenza strains.² It spread from Asia to Europe and North America within three months and ultimately killed an estimated 1 million people worldwide.³

But since 1997, global health authorities have watched influenza strain A/H5N1 – otherwise known as “avian flu” – with caution. The assessment was that it posed the greatest potential to become the next pandemic due to sporadic outbreaks of avian flu in Asia and an observed mortality rate of 60 percent.

Nevertheless, a different strain – A/H1N1 – emerged in April 2009 in Mexico. Called “swine flu” because of its genetic similarity to the influenza virus that occurs in pigs, this strain proved capable of human-to-human transmission. By April 23, 2009, the virus had spread into the United States. On April 25, 2009, the World Health Organization (WHO) raised the pandemic alert level to Phase 5, defined by the human-to-human spread of a virus in at least two countries in one region, such as the Americas. By June 11, 2009, the virus had spread beyond the Americas to Asia, Europe and Oceania, prompting WHO officials to declare Phase 6, the highest pandemic alert level. A/H1N1 was considered a global threat.

Industry Action

Pharmaceutical and vaccine manufacturers were prepared to respond rapidly to the newly identified virus -- because the research-based industry sees innovation, investment, and planning to tackle such threats a core part of its business. Industry, through the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), approached WHO requesting regular meetings to facilitate clear and concise communications to support rapid development of a targeted pandemic vaccine. The virus strain was identified and quickly distributed to manufacturers so they could begin to develop a vaccine to help protect against the pandemic.

Five main initiatives have enabled the industry to respond effectively to this potential global health crisis:

1. *Technology & Innovation*
2. *Industry Investment to Overcome Challenges and Improve Pandemic Preparation*
3. *Collaboration*
4. *Access*
5. *Pharmaceutical Industry Business Continuity Planning*

1. Technology & Innovation

Innovation is the lifeblood of the pharmaceutical industry. Science-centered, research-based companies succeed by making huge and risky investments to create new, innovative treatments for unmet medical needs and to solve urgent public health problems.

Understanding the unpredictable nature of infectious diseases, the industry has made significant investments in research and development to advance vaccine technology. For several years, companies have focused on designing faster, more scalable manufacturing techniques. In late May, when the wild-type virus became available, MedImmune (AstraZeneca) began developing its own strain for H1N1 vaccine development using its unique "cold-adapted" technology. Both Baxter and Novartis Vaccines announced on June 12, 2009, that their cell culture-based technology yielded A/H1N1 antigen – just one day after the Phase 6 pandemic was declared and about 16 days after the U.S. Centers for Disease Control and Prevention distributed A/H1N1 seed samples to manufacturers. In July, the vaccine manufacturers CSL (Australia) and Sinovac (China) began clinical trial testing with their pandemic H1N1 vaccines. Baxter, GSK Bio, MedImmune, Novartis Vaccines and Sanofi Pasteur quickly followed with their own clinical trials.

Companies have also developed a new generation of 'adjuvants' to help extend the supply of antigen – the active component in a vaccine. Adjuvants are added to vaccines to enhance the body's immune response to immunization. By utilizing adjuvants, less antigen is needed in each vaccine dose to develop protective immunity. This allows more doses to be made using existing production capacity, meaning that more people can be immunized. For example, one of the first H5N1 pandemic influenza vaccines developed utilized 90 micrograms of antigen per dose. By applying new adjuvant technology, one vaccine manufacturer was able to reduce the amount of antigen required for protective immunity against the disease to 3.8 micrograms per dose.

Antiviral manufacturers have also committed to defending the population by ramping up production of medicines to treat patients who contract the illness before they can be immunized. Both Roche, maker of oseltamivir (Tamiflu®), and GlaxoSmithKline, manufacturer of zanamivir (Relenza®), have increased production of these antivirals that have shown efficacy against the A/H1N1 influenza virus strain.

2. Industry Investment to Overcome Challenges and Improve Pandemic Preparation

The vaccine industry has invested over \$4 billion to protect society against pandemic influenza. This investment covers a broad range of activities, including vaccine R&D, clinical studies and

facilities modification and expansion to incorporate biosafety measures required to produce pandemic vaccines, as well as new manufacturing technologies such as cell culture.

Industry's pandemic vaccine production capacity is estimated to have expanded by 300% in recent years, to between 2.5 and 7.7 billion doses annually.

Vaccine production is complicated and capital intensive. Manufacture utilizing disease-causing pathogens requires specialist facilities, which often cannot be used for other products. Producing safe, high quality vaccines requires many stages of processing and purifying. Quality testing against strict standards is undertaken throughout the process, for every batch, to avoid contamination or the introduction of even small deviations in manufacture. Further testing of each batch after the vaccine is packed into sterile containers ensures a further level of quality assurance. Unsurprisingly, production using these stringent processes under strict regulatory oversight requires expensive manufacturing facilities, highly skilled employees and time: manufacture of each vaccine batch can take many months or even, in some cases, more than a year.

3. Collaboration

Vaccine manufacturers received the seed virus and necessary information to meet the rapid timelines required to respond to the pandemic influenza. This was aided by a well-orchestrated communication and virus-sharing program coordinated by the WHO and its collaborating centers. In addition, the IFPMA initiated regular technical information exchanges between its influenza vaccine member companies the WHO and its Global Influenza Surveillance Network.

Timely exchange of critical information between the WHO, national health bodies in key countries and vaccine manufacturers is essential for the speedy development, testing and production of a targeted influenza pandemic vaccine. The industry's rapid response to the A/H1N1 influenza virus strain is proof that the current system is functioning well. Recent efforts to change this system raise troubling questions, as they could delay the availability of vaccines to millions of people around the world.

4. Access

The health impact of the pandemic is likely to be greatest in low-income countries. They will be hit by an overload on already strained healthcare resources and lack of preparedness for the pandemic, including inadequate healthcare system infrastructure.

The pharmaceutical industry has a strong history of helping to address developing world health needs, especially in times of crisis, and the current H1N1 outbreak has been no exception. IFPMA member companies have donated antibiotics, painkillers, nutritional supplements and antivirals, as well as thousands of doses of seasonal influenza and pneumococcal vaccines to countries in need. Companies have also created tiered pricing programs for medicines, so that developing countries can stretch their healthcare resources even further. Industry-developed virus testing technology is facilitating authorities' monitoring of the outbreak, determining rapidly which of the many clinical samples collected by hospitals and other health facilities contain the pandemic H1N1 influenza strain.

5. Pharmaceutical Industry Business Continuity Planning

Research-based pharmaceutical manufacturers play an important role in improving global health. Like other organizations, the industry is vulnerable to external crises that can interrupt business operations and impact its capacity to deliver medicines. An influenza pandemic, which could result in a peak employee absenteeism rate of 30 to 50 percent and may last for an extended period of time, has long been considered a significant risk.

Therefore, pharmaceutical manufacturers have proactively adapted their business continuity plans to focus on maintaining the manufacture and supply of essential medicines to patients and communities around the world during influenza pandemics and other natural disasters.

Through the IFPMA, the industry has developed the *Pandemic Influenza Preparedness: Business Continuity Planning for the Global Healthcare Industry*, which outlines key areas that company plans should address. These include developing detailed continuity plans and publishing a non-confidential overview on company Web sites. This should enhance confidence and demonstrate preparedness to key stakeholders, such as employees, government officials, suppliers, customers, healthcare professionals and local communities. As a result, many companies already had pandemic business continuity plans in place prior to the WHO declaration of a pandemic, and some had even started to put their plans in to action.

Conclusion

New threats, like the recent emergence of an H1N1 pandemic, underscore the importance of innovation and collaboration by the global pharmaceutical industry in addressing global public health crises.

Improvements in global public health depend on the innovations that flow from the laboratories of research-based industry. New medicines and vaccines can advance health quickly and efficiently. But this innovation does not come easily, and it must be nurtured with the right incentives to drive the most creative science to address new health threats.

By focusing on improving key technologies and collaborating with the WHO, the industry has been able to move swiftly to help advance the health of people around the world.

As the H1N1 example shows, threats to global health are not solved by pronouncements, but through a steady flow of medical innovations and collaborative work to get those medicines to the patients who need them.

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¹ CDC Pandemic Influenza, Pandemic Flu Questions and Answers, January 17, 2006. Available at: <http://www.cdc.gov/flu/pandemic/pdf/pandemicfluQandA.pdf>¹.

² World Health Organization, Influenza (Seasonal) Factsheet, April 2009. Available at: <http://www.who.int/mediacentre/factsheets/fs211/en/>

³ World Health Organization, Influenza (Seasonal) Factsheet, April 2009. Available at: <http://www.who.int/mediacentre/factsheets/fs211/en/>.

About the IFPMA:

The International Federation of Pharmaceutical Manufacturers & Associations is the global non-profit NGO representing the research-based pharmaceutical, biotech and vaccine sectors. Its members comprise 27 leading international companies and 44 national and regional industry associations covering developed and developing countries. The industry's R&D pipeline contains hundreds of new medicines and vaccines being developed to address global disease threats, including cancer, heart disease, HIV/AIDS and malaria. The IFPMA Clinical Trials Portal (www.ifpma.org/ClinicalTrials), the IFPMA's Ethical Promotion online resource (www.ifpma.org/EthicalPromotion/) and its Health Partnerships information (www.ifpma.org/HealthPartnerships/) – Developing World) help make the industry's activities more transparent. The IFPMA strengthens patient safety by improving risk assessment of medicines and combating their counterfeiting. It also provides the secretariat for the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).