



***Preparing for the Next Influenza Pandemic***  
***Roles and Responsibilities of Roche and Other Stakeholders***

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## Executive Summary

The purpose of this document is to articulate in an open and transparent manner the roles and responsibilities of Roche and other stakeholders during pre-pandemic and pandemic time periods. The audience for this document includes international agencies, governments, the business community, and any other person or organization involved or with an interest in pandemic preparedness.

Global pandemic preparedness is a critical element for the protection of global society and economy. Influenza pandemics have occurred approximately every thirty years. There have been three pandemics in the 20<sup>th</sup> century, the last of which originated in Hong Kong in 1968-1969 and resulted in 800,000 deaths. According to the World Health Organization (WHO), the next pandemic is imminent, and it is estimated that 2 to 7 million people worldwide will die during this pandemic.

Despite these facts, the issue of pandemic preparedness is not receiving the consistent attention and priority it needs from governments, international agencies, the business community, and society as a whole. In addition, while an integrated approach to pandemic planning would provide greatest benefit, agencies, governments and the business community are currently not uniformly working together across continents in a coordinated manner to prepare for this global public health threat. Pandemic influenza needs to be appreciated as not just a government public health emergency but as a potential global catastrophe and civil emergency with potentially serious impact on human health and well-being, global economy and major social infrastructure.

Roche is the manufacturer of Tamiflu (oseltamivir), an oral influenza antiviral (not a vaccine) with a unique role in the prevention and treatment of all influenza viruses, including avian H5N1 influenza.

Stockpiling antivirals is one important element of a pandemic preparedness plan. In the current pre-pandemic period, Roche has filled orders placed for Tamiflu by governments, agencies or corporations on a “first come, first served” basis. However, a stockpile alone does not ensure an adequate response to an outbreak. Comprehensive strategic pandemic preparedness plans at the global, regional and national levels must be put in place, as well as operational and logistic plans to ensure the effective implementation of these strategic plans.

It is also important to note that only 85 governments worldwide have current pandemic antiviral stockpiles and that these cumulative stockpiles are sufficient to treat less than 5% of the world’s population. Furthermore, to maximize the efficacy of Tamiflu, those infected with the pandemic influenza virus must receive Tamiflu within 48 hours.

If this cannot be achieved, much of the investment in stockpiles will not be maximized to the full benefit. The need to ensure fair and timely access will be a significant challenge to public health care systems, as well as proof of their solidity and responsiveness.

Once a pandemic is declared by the WHO, Roche will be called upon to produce more Tamiflu and upscale a complex manufacturing process. Based on current stocks, Roche could start packaging existing capsules and production of new capsules from existing API within weeks. However, since the lead time for new production is around 6 to 9 months, it will not be possible for Roche to respond immediately to a surge in demand by governments or corporations looking to purchase Tamiflu.

A further consideration regarding stockpiles is the fact that vaccines will not be available in the early stages of a pandemic, as manufacturers work to develop a vaccine matching the viral strain that has caused the pandemic. In the first few months of a declared pandemic, antivirals and social distancing will therefore represent the best tools available to treat and prevent the spread of the virus. Hence, having sufficient antiviral stockpiles in place becomes an even more stringent objective.

Therefore, in line with guidance published by the WHO, the only way to ensure that there will be sufficient supplies of antivirals at the time of the outbreak of a pandemic is to stockpile in advance.

Once a pandemic is declared by the WHO, Roche will fill orders placed for Tamiflu in the following order:

- 1) Delivery of WHO Rapid Response stockpile donated by Roche to the WHO will be the first priority.
- 2) Fulfillment of existing pandemic orders, from both government and other groups.
- 3) Increase rapid response effort for containment in collaboration with WHO and other international agencies.

## **Roche's Role**

### **1) Ensuring a Sustainable Manufacturing Supply**

#### ***Pre-Pandemic***

As the manufacturer of Tamiflu, Roche's responsibility before a pandemic is to ensure that the demand for Tamiflu for the management of seasonal influenza and for pandemic stockpiling can be met without interruption in supply.

Roche's manufacturing capacity at the end of 2004 was sufficient to produce only 28 million courses of Tamiflu treatment per year. Since that time, Roche has invested in the development of a global manufacturing network for Tamiflu that could produce 400 million courses of treatment annually if required. In addition, Roche has provided manufacturing sub-licenses to generic manufacturers in China and India allowing them to produce generic versions of oseltamivir in order to further increase the global

availability of the drug for pandemic use. Roche has also signed an agreement with a South African manufacturer to produce a generic version for the African continent.

Currently, Roche's manufacturing capacity produces a supply that significantly exceeds existing Tamiflu pandemic stockpile orders. This overcapacity of production is not sustainable from a business perspective and therefore, current production output has been modified to meet real demand.

### ***Pandemic***

Upon the declaration of a pandemic by the WHO, Roche will immediately upscale the complex manufacturing process for Tamiflu to fully use its total annual production capacity of up to 400 million treatments. Based on current stocks, Roche could start packaging existing capsules and production of new capsules from existing API within weeks. However, it will take 6 to 9 months before additional supply from the enhanced manufacturing process is available.

## **2) Filling Orders for Stockpiles**

During an influenza pandemic, resources will be in short supply. For this reason, Roche, in line with WHO recommendations, advocates advance stockpiling of antivirals by governments and the private sector as a key pandemic preparedness measure.

Roche, supported by a network of partners, has established an infrastructure capable of producing 400 million courses of Tamiflu treatment per year. However, global stockpiles of Tamiflu currently secured by governments are sufficient to treat less than 5% of the world's population. As a result, Roche anticipates that demand for the drug will greatly outstrip production capacity in the event of a pandemic and will therefore be faced with the challenge of how to allocate a critical but scarce resource.

### **Objective**

Roche has determined that its policy for allocating Tamiflu during a pandemic should be consistent with the recent WHO publication, "Ethical considerations in developing a public health response to pandemic influenza", whereby "resources should be used to provide the maximum possible health benefit".

### **Principles**

As a global company, recognizing the role Tamiflu will play in the event of a pandemic, Roche's policy regarding the decision on the allocation of Tamiflu during a pandemic is guided by the following key principles:

- Maximize the health benefit to society during a pandemic, by supporting WHO's and national governments' containment, treatment and transmission reduction efforts.
- Balance the needs of Roche's shareholders, employees and society as a whole.
- Base decisions on the strength and integrity of the scientific and medical information available.
- Communicate Roche's approach in a transparent manner.

- Maintain a dialogue with the WHO and other international agencies regarding the areas and populations in need of antiviral allocation

Roche respects the role of international agencies and experts regarding pandemic preparedness. In addressing the question of how to allocate Tamiflu during a pandemic, Roche has sought input from a variety of stakeholders representing different interests including ethicists, physicians, government and non-governmental organizations, policymakers and the private sector.

### **Policy for the Allocation of Tamiflu**

In alignment with the overall objective “to provide maximum possible health benefit”, the priorities for the allocation and delivery of Tamiflu are as follows. The principles will apply to the extent permitted under local emergency legislation affecting Roche’s manufacturing and supply capabilities.

#### *Phase III – Focus on pandemic preparedness and prevention*

- WHO stockpiles – 5 million packs of Tamiflu donated by Roche established for rapid containment and for management of current outbreaks as a preventative measure.
- Governments will be prioritized over the private sector.
- Any further orders will be fulfilled on a “first come, first served” basis.

#### *Phase IV – Focus on implementation of pandemic containment measures*

- Delivery of WHO Rapid Response stockpile (3 million packs, currently stored at Roche US and Europe).
- Fulfillment of existing pandemic orders, from both governments and other groups.
- Increase rapid response effort for containment in collaboration with WHO and other international agencies.

It is important to note that Roche will prioritize new WHO and government orders over those from other groups. Roche will suspend supplying new corporate orders and normal retail sales until the requirements of the WHO and governments are met.

#### *Phase V/VI – Containment measures have failed*

- Roche will continue to seek the input of international agencies such as the WHO as well as other advisors to meet the objective “to provide maximum possible health benefit” in the allocation of Tamiflu.
- In the absence of international input and advice, and where clear priorities for allocation cannot be developed and agreed upon, Roche will consider the “first come, first served” principle for fulfilling government orders.

### **3) Donations**

#### ***Pre-Pandemic***

During discussions with the WHO in this pre-pandemic phase, it became clear that developing countries needed additional attention regarding pandemic preparedness. As a result, Roche has donated a total of 5.125 million treatments to the WHO for distribution at the discretion of the WHO to countries in need. These donations include:

- 2004 – Donation of 125,000 treatments which were used by the WHO in affected countries (Asia and Eastern Europe).
- 2005 – Donation of a rapid response stockpile of 3 million treatments – 1.5 million treatments being stored in Switzerland and another 1.5 million treatments being stored in the United States. In both cases, these stockpiles are ready to go immediately to the airport closest to the outbreak and to be used as a fire blanket to contain the pandemic at the place of outbreak.
- 2006 – Donation of 2 million treatments to the WHO as regional stockpiles for use in those developing countries which are most likely to be affected by avian influenza in humans and are unable to purchase the drug for economic reasons. These treatments are stored by the WHO in the regions.

It is essential to realize that, in a pandemic situation, Roche has a responsibility to ensure that the donated supply of Tamiflu as per above reaches the WHO for delivery to the countries in need. However, Roche is not responsible for the subsequent delivery of donated Tamiflu to patients in the countries affected. The responsibility for decisions regarding which country will be offered Tamiflu and regarding distribution within the respective countries rests with the WHO and national governments receiving the donation.

#### **4) Tamiflu Pandemic Pricing Policy**

Roche has offered Tamiflu at a reduced price for government orders, with further reduced pricing offered to developing countries, since stockpiling efforts began in 2004. This will not change during a pandemic. However, if the costs for raw materials, contract manufacturing, transportation and applicable taxes and duties are raised during a pandemic, the company may be forced to review its current policy.

## **5) Data Collection on Real-Life Utilization of Tamiflu**

### ***Pre-Pandemic***

Roche has entered into collaboration with a clinical research organization for the development of a patient registry in order to collect clinical and virology information from people infected with the currently circulating H5N1 virus. The purpose of this registry is to better understand the clinical course of the disease and whether changes in treatment duration and dosing of Tamiflu are warranted in the management of these cases, based on different strain virulence. Roche wishes to ensure appropriate use of Tamiflu and this data collection will provide valuable insight into real-life use.

### ***Pandemic***

Roche already has a pharmacovigilance process for Tamiflu in place and, in a pandemic, will adapt it to collect data on the use of Tamiflu in a pandemic situation.

## **6) Company Pandemic Preparedness**

Roche has developed a company pandemic preparedness plan to enable Roche to fulfill its obligations during a pandemic. This plan includes prioritizing products and services to be maintained during a pandemic, such as the supply of previously specified life-saving medicines, but also identifying medical and non-medical interventions to minimize the risk of spread of the virus at the workplace, including the provision of Tamiflu to Roche employees and their families for pandemic use.

## **The Role of Governments, International Agencies and Corporations**

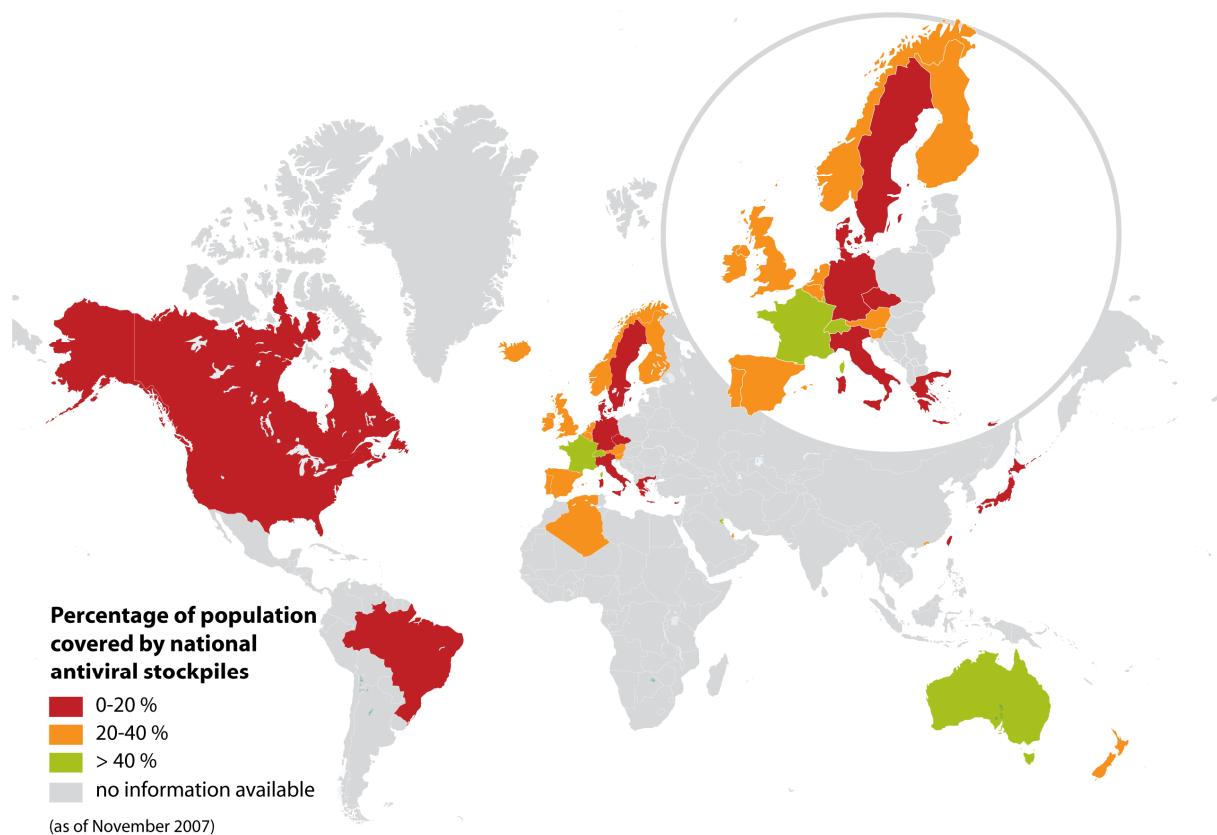
### **1) Respective Responsibilities regarding Pandemic Preparedness**

#### ***Pre-Pandemic - Governments***

Governments have a responsibility to deliver public health care to their citizens. Governments therefore have the responsibility to plan for a pandemic, to put strategic and operational pandemic plans in place, to ensure adequate stockpiles of antivirals, to prioritize patients (if needed), and to set up systems and measures ensuring rapid distribution and effective delivery in order to guarantee urgent and timely access to antiviral treatment for their populations.

To date, only 85 governments worldwide have stockpiled antivirals for pandemic use. According to recent statistics, stockpile levels show wide variability, with some governments having sufficient stockpiles to treat up to 50% of their national population, while others will only be able to cover a much smaller fraction. Currently,

the total stockpile by governments around the world will provide treatment for less than 5% of the world's population.



Strong advance planning in terms of logistics and operations will also be essential, not only because of the added pressure that a pandemic will impose on healthcare systems as a whole, but also because of the need to deliver Tamiflu to patients within 48 hours for maximum efficacy.

### ***Pre-Pandemic – International Agencies***

International agencies also have a responsibility to put pandemic plans for their employees in place. The World Health Organization (WHO) has been the most active international agency in this regard.

The WHO has urged all countries to develop pandemic preparedness plans and has developed a checklist to assist governments in their preparations. In the face of a pandemic threat, the WHO stated in January 2005 that “stockpiling antiviral drugs in advance is presently the only way to ensure that sufficient supplies are available at the start of a pandemic.” The WHO has also issued guidance on the management of patients with H5N1 and has strongly recommended oseltamivir for the treatment and prevention of H5N1.

Roche has already delivered the donation of 2 million treatments of Tamiflu to the WHO. It is now the responsibility of the WHO to deliver that donation as needed. Furthermore, as soon as a pandemic breaks out, Roche's responsibility will be to deliver to the WHO the donation of 3 million treatments of Tamiflu in stockpiles for the countries in need. It is the WHO's role to deliver and supply this donated stock to countries. Once donated stockpiles reach these countries, the distribution of Tamiflu to individuals and groups affected will become the sole responsibility of the WHO and of the national governments concerned. The importance of timely delivery (within two days) to ensure maximum efficacy of Tamiflu needs to be considered in the planning for delivery.

### ***Pre-Pandemic – Corporations***

Corporations must also consider the impact of a pandemic on the continuity of their business operations, both on the short and on the long term, in order to appropriately assess and manage the risk of a pandemic. For instance, some corporations are currently preparing for a pandemic by establishing pandemic planning committees to combine strategic planning, operational continuity procedures, human resources and stockpiling of antivirals, so that the impact of a pandemic on their employees, products and/or services can be contained or even reduced.

## ***2) The Need for Interaction and Cooperation***

In this pre-pandemic phase, governments, international agencies and corporations must work together to plan and prepare in order to ensure that they can cooperate effectively for the good of society and the global economy once a pandemic is declared. Current pandemic preparedness efforts and initiatives still lack interaction between these sectors and amongst the actors at the international, national and regional/local levels. Most countries do not provide specific government guidance on pandemic preparedness for corporations, in particular with regard to medical interventions and antiviral stockpiling. This lack of guidance severely hampers the establishment and implementation of an integrated and coordinated national response.

Realistically, no sector on its own can protect the whole of society adequately. Furthermore, with current government stockpiles worldwide ensuring protection of less than 5% of the global population, there is much more to be done.

### ***Pandemic – Governments, International Agencies and Corporations***

Once a pandemic is declared, all elements of society must come together. Strategic pandemic preparedness plans will need to become operational. Stockpiles of Tamiflu will need to be distributed and reach patients within two days. Resources will be stretched and cooperation between sectors at the international, national and regional levels will be critical.

## **Conclusion**

This position paper describes Roche's roles, responsibilities and contributions, both in a pre-pandemic and a pandemic setting, and addresses the expectations of the community.

Responsibility for pandemic preparedness has to be shared between governments, international agencies/non-governmental organizations (NGOs), corporations as well as manufacturers of antivirals and vaccines.

**In this respect, Roche calls upon all stakeholders involved to understand their responsibility and take appropriate action. Roche strongly believes that there is now, before a pandemic, a unique window of opportunity for all of us to fulfill our roles and ensure that adequate preparations are made for the protection of society. Once a pandemic is declared, this opportunity will be gone.**