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## The Canadian Pandemic Influenza Plan for the Health Sector

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### Annex E Planning Recommendations for the Use of Anti-Influenza (Antiviral) Drugs in Canada During a Pandemic

#### Date of Latest Version: *October 2006*

Summary of Significant Changes:

- Reflects the establishment of the National Antiviral Stockpile and provides information on the size, use and composition of the stockpile;
- Specific references to "priority groups" have been removed since they no longer are consistent with the decisions made to date regarding the use of the stockpile;
- Contains updated scientific data, regulatory information, policy decisions and knowledge based on experience, acquired since last version (2004);
- Uses new Pandemic Phase terminology.

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#### 1.0 Introduction

The purpose of this annex is to provide information and recommendations that will assist pandemic planners with the development and refinement of their respective antiviral strategies. Recommendations of the Pandemic Influenza Committee are intended to facilitate consistent use of antivirals across Canada at the time of an influenza pandemic and to form the basis for an effective, equitable, flexible and informed national antiviral strategy. It will be necessary to review all recommendations and implementation plans once a pandemic strain has emerged so that any changes in epidemiology or other data (e.g. antiviral resistance, optimal treatment course) can be accounted

for in the implemented strategy.

## 2.0 Role of Antivirals



Vaccination with an effective vaccine is the primary public health intervention during a pandemic. However, vaccine production requires the acquisition of the seed virus and therefore cannot be initiated until the pandemic virus is already infecting humans. Once a suitable vaccine seed strain is available to manufacturers, it is anticipated that vaccine production will require at least 3 to 4 months and even then the availability of doses will be staggered and limited. Furthermore, each individual may need to receive two doses of vaccine to be protected.

At this time antivirals (anti-influenza drugs) are the only specific medical intervention that targets influenza and that potentially will be available during the initial pandemic response. Antiviral drugs can be used to prevent influenza and, unlike vaccines, can also be used to treat cases that are identified early in their illness. While there is good evidence for reduction of complications of influenza, there is not evidence for reduction in influenza mortality. Protection afforded by antivirals is virtually immediate and does not interfere with the response to inactivated influenza vaccines. The strategic use of these drugs during the Pandemic Period will be critical to achieving the pandemic goals of firstly to minimize serious illness and overall deaths, and secondly to minimize societal disruption among Canadians as a result of an influenza pandemic.

Before the 1997 Hong Kong avian influenza incident, antivirals were not considered as a component of the Canadian pandemic response, in view of the costs and other factors. During the Hong Kong outbreak, several countries rapidly depleted global supplies of anti-influenza drugs. In light of the lessons learnt since 1997 and the approval for sale of new antivirals (the neuraminidase inhibitors), the Antivirals Working Group of PIC was formed to develop options, recommendations and guidelines for the use of antivirals. The key recommendation of this working group, which was subsequently endorsed by PIC, was the need to secure a supply of antiviral drugs in Canada to mitigate the consequences of an influenza pandemic.

The national antiviral stockpile was established in the fall of 2004. Outside of the current stockpiled quantities, the supply of antivirals in Canada is limited. To date there has been relatively little use of these drugs in Canada. During annual influenza seasons, they have been used primarily to control outbreaks in health care and long-term care institutions. During the 2003 domestic avian influenza outbreak in British Columbia, they were also used for prophylaxis of individuals exposed to avian influenza because of their roles in outbreak control (e.g. cullers). As a result of this history of limited demand, there has been little incentive for manufacturers to store significant amounts of these products in Canada, and there is little practitioner and public experience with these drugs.

## 3.0 Classes of Antiviral (Anti-Influenza) Drugs



Two classes of antiviral drugs are currently approved in Canada for prevention and/or treatment of influenza infection: M2 ion channel inhibitors and neuraminidase inhibitors. There are important differences in pharmacokinetics, side effects and drug resistance between these two classes of antivirals. Such performance characteristics and the costs should be considered in selecting the specific drugs to be used for prophylaxis or treatment. Summary information on these drugs is presented in the following table.

### 3.1 Neuraminidase Inhibitors



Oseltamivir (Tamiflu) and zanamivir (Relenza) are the two neuraminidase inhibitors that are currently approved for use in Canada. They are currently the only neuraminidase inhibitors in the global market; however, other agents such as peramivir are under development. Oseltamivir and zanamivir interfere with replication of both influenza A and B viruses in three ways: (1) they interfere with the

release of virus from infected cells, (2) they cause the aggregation of virus, and (3) they may improve the inactivation of virus by respiratory mucous secretions. The drugs are well tolerated and have been used effectively for the treatment and prophylaxis of influenza A and B infections. They are expected to be effective against pandemic viruses including H5N1. H5N1 viruses are susceptible to neuraminidase inhibitors in vitro and oseltamivir has been shown to protect mice against lethal experimental H5N1 influenza pneumonia, although at higher than usual doses.<sup>(2)</sup>

Neuraminidase inhibitors are effective when administered within 2 days of onset of illness.<sup>(3)</sup> When used in this way current estimates of the benefits of oseltamivir therapy include a 25-30% reduction in symptom duration plus a reduction in illness severity, a 59% reduction in hospitalizations (range: 30% to 70%), a 63% reduction in antimicrobial drug use (range: 40% to 80%) and a 1-day reduction in lost work days under treatment (range: 0.5 to 1.5 days).<sup>(4)</sup> No data on reductions in mortality caused by influenza due to oseltamivir treatment are currently available. In their impact analysis, Gani et al assumed that oseltamivir treatment would provide a 50% protection against death.<sup>(5)</sup> This estimate was based on the assumption that a 50% protection against the more serious outcomes of influenza would translate to equivalent protection against death.

Evidence is limited on the effects of neuraminidase inhibitors in reducing the complications of influenza in individuals with co-morbid conditions that increase their risk of these complications. The available evidence supporting such a beneficial effect derives from analyses of pooled data from multiple independent studies.<sup>(6)</sup> Both oseltamivir and zanamivir have similar effectiveness of 70-90% in preventing laboratory-confirmed influenza illness<sup>(7)</sup>.

Both oseltamivir and zanamivir were approved for use in Canada in 1999 for the treatment of infection due to influenza A or B. Since December 2003, oseltamivir has also been approved for influenza prophylaxis in Canada. Zanamivir is not currently approved for prophylaxis. Current evidence suggests that the development of resistance during treatment of influenza is less likely with neuraminidase inhibitors than with amantadine and any resistant viruses that develop are less likely to be transmissible. Neuraminidase inhibitors are more expensive than amantadine at this time.

#### Antiviral (Anti-Influenza) Drugs Currently Approved for Use in Canada

| Drug        | Trade name and Manufacturer      | Class                   | Indications  | Formulation(s)   | Shelf Life/Stability  | Expected use(s) during pandemic   |
|-------------|----------------------------------|-------------------------|--|--|---|---|
| Oseltamivir | Tamiflu®, Hoffmann-La Roche Inc. | Neuraminidase Inhibitor | <ul style="list-style-type: none"> <li>Treatment of influenza A and B in persons 1 year and older who have been symptomatic for no more than 2 days</li> </ul> | Capsules (75 mg/capsule): 10 capsules per blister pack or bottles of 10 and 100 capsules                               | Shelf life: 5 years   | Capsules for those presenting and requiring early treatment.  |
|             |                                  |                         | <ul style="list-style-type: none"> <li>Prevention of influenza A and B in persons 1 year of age and older following close contact with an infected</li> </ul>  | Powder for oral suspension (12 mg/ml when reconstituted): 900 mg per bottle (volume of 75 ml in a 100-ml glass bottle) | Shelf life: 2 years<br>Stability: Once reconstituted, 10 days in refrigerator (at 2 to 8 degrees Celcius) | Oral suspension for treatment of children weighing less than 40 kg and/or those who cannot swallow the capsules.<br><br>No decision has been made at this time to use |

|   |  |  |  |   |   |   |
|---|--|--|--|---|---|---|
|   |  |  | individual   |   |   | the drugs in the national stockpile for prophylaxis indications. It is recognized that outside of the national stockpile, stockpiling with the intent to use this drug for prophylaxis may have occurred                                |
| Zanamivir   | Relenza®,<br>GlaxoSmithKline   | Neuraminidase<br>Inhibitor                               | <ul style="list-style-type: none"> <li>■ Treatment of influenza A and B in persons 7 years of age and older who have been symptomatic for no more than 2 days</li> </ul> | ROTADISK® consisting of a circular foil disk with four blisters each containing 5mg of zanamivir. ADISKHALER® inhalation device is provided to administer the medication (through inhalation). One box contains 5 disks, which is equivalent to one treatment course. | Shelf life: currently 3 years (expected to be extended to 5 years on new product) | Treatment for those presenting and requiring early treatment with specific focus on pregnant and nursing women.   |
| Amantadine  | Symmetrel® and Endantadine® -Bristol Myers Squibb, <i>Generic amantadine manufacturers:</i> Dominion Pharmacal, GenPharm, Medican Pharma, Pharmel, Pharmascience | M2 Ion Channel Inhibitors (Cyclic Amines or Adamantanes) | <ul style="list-style-type: none"> <li>■ Treatment of influenza A in persons 1 year of age and older</li> </ul>  | Capsules (100 mg/capsule): bottles of 100 capsules  | Shelf life: 3 years*  | This drug has not been included in the national stockpile. It is recognized that it may be available at the time of a pandemic but should be used for prophylaxis only and only if the strain is known to be susceptible to amantadine. |
|   |  |  | <ul style="list-style-type: none"> <li>■ Prevention of influenza A in persons 1 year of age and older</li> </ul>   | Syrup (10 mg/ml): bottles of 500 ml   | Shelf life: 2 years   |   |
| <p>* Note: In one study amantadine was found to be stable after 25 years of uncontrolled storage on the shelf <sup>(1)</sup>. Stability of other antiviral drugs may also extend beyond the currently stated expiry date. If the currently stockpiled antivirals are not used by their respective expiry dates, stability testing will likely be implemented to determine whether the drugs are still expected to be effective and should be retained in the stockpile.</p> |  |  |  |   |   |   |

### 3.2 M2 Ion Channel Inhibitors (Cyclic Amines or Adamantanes)

M2 ion channel inhibitors (amantadine and rimantadine) interfere with the replication cycle of influenza A but are not effective against influenza B. Rimantadine is not currently approved for use in Canada.

Amantadine is approximately 70% to 90% effective in preventing illness from influenza A infection. When administered within 2 days of onset of illness, it can reduce the duration of uncomplicated influenza A illness by approximately 1 day, but it has not been studied as to its ability to reduce the complications of influenza. Resistance to amantadine has been shown to develop rapidly (in up to 30% of recipients) when this drug is used for treatment purposes and these resistant viruses are readily transmissible<sup>(8)</sup>.

The Antivirals Working Group has considered a potential role for amantadine or rimantadine. Their role in treatment is not supported. They could be used for prophylaxis during a domestic outbreak of avian influenza or during a pandemic if the novel virus is susceptible. However, in order to use rimantadine, which has fewer side effects than amantadine, special permission would need to be sought as it is not currently approved for use in Canada. Most of the H5N1 viruses have been found to be resistant to these drugs.

## 4.0 The National Antiviral Stockpile

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### 4.1 Size of the National Antiviral Stockpile

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Creation of a national stockpile helps ensure equitable access across Canada to a secure supply of antivirals for pandemic influenza, along with equitable access to these drugs through governmental control. The national antiviral stockpile was created in the fall of 2004 as a result of a joint federal and provincial and territorial (P/T) purchase of oseltamivir capsules. The initial quantity in the stockpile was 16 million doses, which was originally estimated to be sufficient to cover:

1. the early treatment of hospitalized patients, health care workers, public health and pandemic societal responders, key health decision makers, high-risk individuals in the community and residents of long-term care facilities experiencing outbreaks; and
2. 6 weeks of prophylaxis of one-third of all health care professionals in Canada (to cover front-line workers).

In the fall of 2005, the PIC Antivirals Working Group reviewed the assumptions used to derive the initial estimates and recommended changes to these assumptions<sup>\*</sup>. The "modified scenario" that resulted from these adjusted assumptions (including a clinical attack rate of 25%, more severe impact in terms of morbidity, higher uptake of the drugs, and 50% for the proportion of "front-line" health care workers), would require substantially more drug to cover the groups previously expected to be covered by the 16M dose stockpile. These estimates led the working group to recommend to the Pandemic Influenza Committee (PIC) that the size of the stockpile be substantially increased. The working group also recommended expansion of treatment to everyone ill enough to need care, in line with the approach being taken in many other developed countries.

At a joint meeting of the Council of Chief Medical Officers of Health (CCMOH) and the Public Health Network in February 2006, recommendations for the size, composition and use of the National Antiviral Stockpile were formalized. It was determined that the size (and diversity) of the stockpile should be increased to 55 million doses or 5.5 million treatment courses of neuraminidase inhibitors. Based on past pandemics, and reflected in the Flu-aid model developed in the U.S. by Meltzer et al, during mild-moderate pandemics approximately half of those who develop a clinical illness present for medical attention. With a clinical attack rate of 35% over the course of the pandemic, and half of the clinically ill seeking medical care, 55 million doses would be required (based on the current standard treatment course), assuming that all persons presenting for care require antivirals.

The national stockpile was distributed on a per capita basis to each of the P/Ts. Some P/Ts have chosen to purchase additional quantities of antivirals. At the time of publication, it is estimated that approximately 39 million doses (including the 16 million in the national stockpile) of oseltamivir have been stockpiled by the federal and P/T governments in Canada. If the government stockpiles that currently exist outside of the national stockpile are incorporated into the national stockpile, the target of 55 million doses could be achieved as early as spring 2007.

The content of the stockpile (i.e. number of doses and drugs) will be assessed on an ongoing basis as planning activities continue and additional science and resources (including drug supply) become available to further inform the antiviral strategy. The latest set of recommendations, specifically

regarding the size of the National Antiviral Stockpile, are intended to assist planning and should not be interpreted as establishing the absolute requirements for an influenza pandemic.

\* Original assumptions used for antivirals needs estimate: Mild-moderate severity, 20% clinical attack rate, 6 weeks pandemic wave, 33% of health care workers are "front-line".

## 4.2 Use of the National Antiviral Stockpile

Use of the initial 16 million dose national stockpile was originally anticipated to be a combination of treatment and prophylaxis indications which would have covered a limited number of the nationally agreed upon priority groups. With the expansion of the stockpile to 55 million doses, the strategy has been revised and is described below.

### **Early Treatment (i.e., treatment within 48 hours of symptom onset)**

The National Antiviral Stockpile should be used at the time of a pandemic for early treatment of all persons with influenza-like illness (presumed pandemic influenza) who are ill enough to need care, and who are assessed within 48 hours of the onset of symptoms. At the time of implementation of the antiviral strategy prioritization may still be necessary, for example if treatment is found to require more than 10 doses or the stockpile is not yet completely built up. If prioritization for treatment is recommended at that time then the doses from the national stockpile would be used for those with ILI who are deemed to be most at risk of serious morbidity and mortality based on the available data.

There has been an accumulation of literature and modeling studies, particularly in the past year, to support a focus on early treatment (in contrast to prophylaxis) as the most efficient way to prevent hospitalizations and death in both high risk individuals and the general public. Based on the estimated impact of a pandemic, treatment with antivirals is expected to be cost-saving to the economy under several treatment strategies. One recent international study has shown therapeutic treatment and post-exposure prophylaxis both to be cost-saving, with a cost-benefit ratio of 2.44-3.68<sup>(4)</sup>. Canadian modeling is underway and early indications are that a treatment-focused strategy is the most cost-effective strategy.

There are ethical obligations to provide effective treatment to persons who can benefit, through the timely administration of a safe and effective treatment that keeps harm (in this situation, the risk of complications of influenza), if not fully avoidable, at the lowest possible level. The principle challenge of a treatment-focused strategy is ability to deliver drugs in a timely manner to ill individuals. To be effective, neuraminidase inhibitors must be administered as early as possible, ideally within 12 hours after the start of illness but definitely within 48 hours. Delivery of the drugs is primarily the responsibility of the respective P/T and local governments. Since the current antiviral supplies have been allocated on a per capita basis, treatment courses should be provided through the local distribution point regardless of whether the individual has any ties to the federal system (e.g., lives on a First Nations reserve or is a federal government employee).

### **Prophylaxis**

Both the Antivirals Working Group and PIC recognize that prophylaxis of health care workers, key decision makers and public health and societal responders (see Glossary for definitions) could contribute to the Canadian pandemic goals of minimizing serious illness and death, and societal disruption. Prophylaxis of health care workers could help keep the health care work force in place at a time of greatly increased need and help maintain an effective early treatment strategy for the general public. Unlike the situation during SARS, it is unclear whether health care workers will be at increased risk in the health care setting because of their use of infection control precautions and personal protective equipment. Health care workers are as likely as anyone else to be exposed in the community. Should their onset of illness occur while at work in the health care setting, they could expose vulnerable patients and residents in closed units, which could in turn lead to outbreaks. Control of influenza outbreaks in health care facilities is usually (during the annual influenza season)

swiftly accomplished by antiviral prophylaxis of all residents and unvaccinated staff. During a pandemic similar availability of antivirals for outbreak control in these facilities would also be of value, likely providing significant benefits in terms of hospitalizations averted and lives saved.

It also must be recognized that beyond the goal of the Plan, there is also the goal of business continuity and optimal personal protection. Coupled with the efforts of governments and the private sector to build appropriate business continuity plans, the issue of supplying antivirals for prophylaxis has also been raised in this context.

Antiviral prophylaxis requires considerably more drug than early treatment. Four to five individuals could be treated with the amount of drug required to provide prophylaxis for one individual for a 6 week period. Implementation of a prophylaxis strategy has several challenges, including identification of eligible personnel, the need to adjust timing to local epidemiology, compliance, potential for drug diversion (e.g., to family members), and the requirement for off-label use of the drug (in the case of zanamivir).

At this time the recommended use of the National Antiviral Stockpile is for treatment only. However, a national process including citizen and stakeholder dialogue, is underway in order to inform future policy decisions regarding whether antivirals provided through the National Antiviral Stockpile should be used for prophylaxis and to whom, during the pandemic period. There are health care system, scientific, economic, societal/ethical, legal and policy considerations that must be explored. Any decision to include prophylaxis indications would require F/P/T consensus on whether the existing stockpile should be expanded for this purpose.

### **Containment**

The role and impact of antivirals in preventing transmission and slowing down the spread of a novel influenza virus is unknown. The use of antivirals for this purpose is under discussion as part of containment measures during the Pandemic Alert Period.

## **4.3 Composition of the National Antiviral Stockpile**



It is expected that when the 55 million dose stockpile is completed, it will be composed of approximately:

- 90% oseltamivir (2 million doses as oseltamivir solution)
- 10% zanamivir

Adding zanamivir to the stockpile provides an option against oseltamivir-resistant strains, allows for a more optimal treatment option for pregnant and nursing women and enhances security against supply disruptions by supporting two manufacturers. Oral oseltamivir suspension would be used for the treatment of children and adults or intubated patients that cannot swallow capsules. Although oral oseltamivir suspension has a relatively limited shelf-life (2 years from date of manufacture), at this time data are lacking on the effectiveness of oseltamivir capsules that have been opened and mixed with another substance (e.g., applesauce) to facilitate administration to children or adults that cannot swallow capsules. The decision to stock oral oseltamivir suspension on an ongoing basis will be reviewed pending the availability of data on alternative antiviral treatment options for children or individuals that cannot swallow capsules.

At this time there are no plans to include adamantanes in the national stockpile. Compared to the neuraminidase inhibitors, there is an increased likelihood of resistance to adamantanes from the outset. Ongoing monitoring of antiviral drug resistance suggests that there is no role for M2 inhibitors in the stockpile but that diversification within the NAI drug class would be beneficial.

## **5.0 Planning Principles and Key Recommendations**



The Antivirals Working Group and PIC have made a number of recommendations regarding the antiviral strategy. The following list summarizes principles and key recommendations for planning purposes.

**1. The use of antivirals should be consistent with the goal or objective of the pandemic period (e.g., Interpandemic Period, Pandemic Alert Period, Pandemic Period).**

Recommendations regarding the use of antiviral drugs during the different Canadian pandemic phases are included in the Public Health Measures annex ([Annex M](#)) and in the [Response](#) Section of the Plan. Use of these drugs during the Pandemic Alert Period is to support the objective of containment during this period. This includes treatment of cases and prophylaxis of close contacts when human to human transmission is occurring. During the pandemic period, antiviral use is intended to support the overall pandemic goals of minimizing serious illness and overall deaths, and secondly minimizing societal disruption among Canadians. Therefore antiviral drug use during the Pandemic Period is expected to follow the nationally-agreed strategy which currently focuses on early treatment.

**2. Neuraminidase inhibitors can be used for either treatment or prophylaxis of influenza. M2 ion channel inhibitors (e.g. amantadine) should be used only for prophylaxis and only if the strain is known to be susceptible.**

The antiviral strategy focuses on the use of neuraminidase inhibitors as the drugs of choice for the treatment and prophylaxis of novel influenza viruses with pandemic potential and for the pandemic virus. When used for treatment, the neuraminidase inhibitors have been shown to be effective in preventing complications and hospitalization. They are also effective in preventing influenza. The emergence of drug resistance during treatment is less likely to occur than with amantadine where emergence of resistance occurs rapidly (and is already widespread among the H5N1 viruses). In addition, neuraminidase inhibitors are associated with fewer side effects than amantadine, thus facilitating compliance.

Zanamivir may be used as an alternative to oseltamivir, although it is not yet approved for prophylaxis in Canada. As the drug is inhaled, little is systemically absorbed; thus it may be preferred for pregnant and nursing mothers in order to minimize exposure of the fetus or young infant. Zanamivir may also remain effective should resistance develop to oseltamivir. One limitation, however, is that not all persons will be able to use the inhalation device successfully. Another limitation is that inhaled zanamivir would not be expected to be effective for treatment if the pandemic virus replicates systemically instead of just in the respiratory tract.

**3. Treatment with neuraminidase inhibitors should be initiated within 48 hours of symptom onset.**

Since replication of influenza virus in the respiratory tract peaks between 24 and 72 hours after the onset of the illness, neuraminidase inhibitors (which act at the stage of viral replication) must be administered as early as possible. This is ideally within 12 hours after the start of illness but definitely within 48 hours. Because of the lack of evidence for benefit when antiviral drugs are started more than 48 hours from onset of illness, treatment should generally be restricted to those presenting within that time frame unless experience with the pandemic virus suggests otherwise. Due to the importance of early antiviral treatment in Canada's pandemic plan, clinical planning groups should consider ways to implement this strategy at a time of high numbers of clinically symptomatic individuals.

**4. The susceptibility of the novel strain to antiviral drugs (both during the Pandemic Alert Period and the Pandemic Period) should be monitored.**

Monitoring for drug resistance is essential to ensuring that the antiviral drugs will have the desired effect and that resources are optimized. This will be carried out at the National

Microbiology Laboratory. Detailed protocols are under development.

## 6.0 Outstanding Issues



There are a number of antiviral issues still to be addressed including:

- F/P/T consensus on inclusion or exclusion of prophylactic indications.
- Updating the clinical guidelines for the use of antivirals
- Development of communication materials for health care providers and the public on the appropriate use of antiviral drugs, for circulation prior to a pandemic
- Guidelines for delivery and administration of antivirals including security, monitoring of drug distribution, uptake and wastage (mainly a P/T level activity)
- Use of diagnostic tests in guiding antiviral treatment
- Protocol for monitoring antiviral drug resistance
- Review of the adverse reaction reporting and monitoring system to identify the need for any pandemic enhancements, such as timeliness and capacity for rapid analysis, investigation and dissemination of information
- Modeling the impact and cost benefit of different strategies for the use of antiviral drugs
- Ongoing considerations of the optimal antiviral strategy and deployment based on new scientific developments (including modeling studies)
- Protocols for monitoring the shelf life of the antiviral stockpiles
- Considerations of potential off-label use of antivirals

There are also outstanding research issues including:

- Safety and effectiveness of antivirals for the treatment and prophylaxis of children under the age of 1 year and select high-risk groups, such as pregnant women, immunocompromised persons, elderly with underlying disease
- Safety and effectiveness of prolonged prophylaxis
- More robust data for effectiveness of neuraminidase inhibitors in reducing complications, hospitalization and mortality
- Minimum effective dose and duration of treatment for complicated and uncomplicated influenza caused by the pandemic strain
- Use of combination therapy in different populations
- Improved diagnostic tests
- Effect of antiviral administration on the response to live attenuated influenza vaccines
- Mechanism for resistance to both classes of antivirals and assessment of the biological consequences (e.g. infectiousness, virulence) of resistance
- Development of new antiviral drugs

At a national Influenza Research Priorities Workshop held in the summer of 2005, research aimed at the development and use of antivirals in the treatment of individuals with influenza and in the prevention of infection was identified as a priority. This included studies of novel approaches with existing antiviral medications as well as research aimed at the development and evaluation of new antiviral agents. The Public Health Agency of Canada and the Canadian Institutes of Health Research

will be holding follow-up consultations on how best to coordinate and fund this research. Other countries have held similar influenza research priority meetings and recently the World Health Organization has indicated its intent to map out a global strategy and work plan for coordinating antiviral and vaccine research.

Some of the important questions about effective treatment protocols can only be answered when the pandemic strain emerges. Rapid clinical trials will be critical to guide the most appropriate use of antiviral drugs. In Canada, an Emerging Infectious Diseases Research Network has been established to bring together government and University researchers ahead of a mass emergency so that research studies can be launched rapidly during a pandemic. As its work progresses, the advance development of research protocols and mechanisms for rapid ethical approval will help address these concerns.

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