

ARE YOU PREPARED?

Companies take measures in anticipation of an
event they hope will never happen:
a global flu pandemic.



Scientists are trying to predict how the next global influenza epidemic will start. Somewhere in Asia, Africa, or Eastern Europe, a deadly virus will leap from chickens or ducks to humans and spread like wildfire. Thousands, then millions of people will be stricken. Many will die. The globalized economy and high-speed jet travel will help spread the disease rapidly around the world, transforming an epidemic into a pandemic.

This alarming scenario could shake the world economy even harder than the current credit crisis. According to a World Bank estimate, a global flu epidemic could cost the world economy more than \$2 trillion, reduce GDP by 5%, and take millions of lives. Widespread illness would overwhelm medical facilities, cut supply lines, slow production, and create shortages of workers, food, fuel, and transportation.

If these numbers seem exaggerated, consider the much smaller-scale SARS

outbreak in China and Hong Kong in 2003. In a few short months, this deadly form of pneumonia took 1,000 lives. But the economic impact was estimated at \$50 billion as tourists fled, factories shut down, flights were cancelled, and government officials in Beijing closed schools, theaters, and discos.

Because of the threat that a flu pandemic poses, a broad coalition of governments, international agencies, and corporations has joined together to prepare for the disaster they hope never happens. Pandemic preparedness has been embraced by a growing roster of companies, and is often built into their existing plans for response to disasters, man-made or natural, because they believe an outbreak is inevitable. "There will be another influenza pandemic sometime in the future; we can't say when it will happen or how severe it will be," says Dr. David Nabarro, the U.N. System Influenza Coordinator.

Most public health experts agree.

There have been ten flu pandemics in the last 300 years, occurring on average every 20 or 30 years (see chart, S5). The deadliest pandemic occurred in 1918–19 and caused more than 40 million deaths worldwide, including 500,000 in the U.S. The last flu pandemic was in 1968–1969 and took 700,000 lives (34,000 in the U.S.).

Rx for the World

Anticipating the next major outbreak, the United Nations in 2005 created the role of the influenza coordinator to work with several international agencies, including the World Health Organization (WHO), the Food and Agriculture Organization (FAO), and the World Organization for Animal Health (OIE), and national governments to develop strategies to prepare for such a debacle.

One important aspect of the effort is to bring a wide range of experts together to contain outbreaks of avian flu as quickly as possible. "There is a need

Imagine $\frac{1}{3}$ of your employees absent for 3 weeks

Can you afford *not* to prepare for pandemic flu?



Protecting your employees' health is essential to productivity. Consider RELENZA as part of your pandemic stockpile. RELENZA is proven to prevent and treat seasonal flu with rapid delivery directly to the lungs, where the flu infection generally occurs.*

GlaxoSmithKline—your partner in pandemic planning—has created the **Pandemic Readiness for Employers Program (P.R.E.P.)** to help you overcome the barriers to stockpiling RELENZA. Choose from either **P.R.E.P. option[†]**: • Preferred Pricing • RELENZA: Reservation

For more information about **P.R.E.P.** and other pandemic planning solutions, visit www.pandemicplan.gsk.com or call 1-800-877-1158.

Important Safety Information about RELENZA

Some people have had bronchospasm (wheezing) or serious breathing problems when they used RELENZA. Many but not all of these people had previous asthma or other pulmonary disease. RELENZA has not been shown to shorten the time of flu in people with these diseases. Because of the risk of side effects and because it has not been shown to help them, RELENZA is not best for people with chronic respiratory disease such as asthma or chronic obstructive pulmonary disease (COPD).

If you develop symptoms such as wheezing or shortness of breath, stop using RELENZA and contact your healthcare provider right away.

If you have diseases like asthma and COPD and your healthcare provider has prescribed RELENZA, you should have a fast-acting, inhaled bronchodilator available for your use. If you are scheduled to use an inhaled bronchodilator at the same time as RELENZA, use the inhaled bronchodilator **before** using RELENZA.

Other kinds of infections can appear like influenza or occur along with influenza, and need different kinds of treatment. Contact your healthcare provider if you feel worse or develop new symptoms during or after treatment, or if your flu symptoms do not start to get better.

People with influenza may be at increased risk of seizures, confusion, or abnormal behavior early in their illness. Therefore, patients should be observed for signs of unusual behavior, and a healthcare provider contacted if needed.

In studies, the most common side effects with RELENZA have been headaches; diarrhea; nausea; vomiting; nasal irritation; bronchitis; cough; sinusitis; ear, nose, and throat infections; and dizziness. Other side effects that have been reported, but were not as common, include rashes and allergic reactions, some of which were severe. If you develop a rash or have an allergic reaction, stop using RELENZA and contact your healthcare provider. This list of side effects is not complete. Your healthcare provider or pharmacist can discuss with you a more complete list of possible side effects with RELENZA. Talk to your healthcare provider promptly about any side effects you have.

*Clinical efficacy can only be concluded from clinical trials. No data are available on the use of RELENZA in patients infected with influenza A (H5N1). Given the difficulty of conducting clinical trials with potential pandemic flu strains, to date, no clear evidence exists to show whether RELENZA is effective for treating patients with H5N1 infection or for prophylaxis of people exposed to H5N1.

[†] Minimum purchase of 500 units.

Please see brief summary of complete Prescribing Information for RELENZA on the following pages.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

 GlaxoSmithKline

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RELENZA[®]
(ZANAMIVIR) INHALATION POWDER

RELENZA®

(ZANAMIVIR) INHALATION POWDER

RELENZA®

(zanamivir)
Inhalation Powder

The following is a brief summary only; see full prescribing information for complete product information

4 CONTRAINDICATIONS

Do not use in patients with history of allergic reaction to any ingredient of RELENZA including lactose (which contains milk proteins) [see Warnings and Precautions (5.2), Description (11)].

5 WARNINGS AND PRECAUTIONS

5.1 Bronchospasm

RELENZA is not recommended for treatment or prophylaxis of influenza in individuals with underlying airways disease (such as asthma or chronic obstructive pulmonary disease).

Serious cases of bronchospasm, including fatalities, have been reported during treatment with RELENZA in patients with and without underlying airways disease. Many of these cases were reported during postmarketing and causality was difficult to assess.

RELENZA should be discontinued in any patient who develops bronchospasm or decline in respiratory function; immediate treatment and hospitalization may be required.

Some patients without prior pulmonary disease may also have respiratory abnormalities from acute respiratory infection that could resemble adverse drug reactions or increase patient vulnerability to adverse drug reactions.

Bronchospasm was documented following administration of zanamivir in 1 of 13 patients with mild or moderate asthma (but without acute influenza-like illness) in a Phase I study. In a Phase III study in patients with acute influenza-like illness superimposed on underlying asthma or chronic obstructive pulmonary disease, 10% (24 of 244) of patients on zanamivir and 9% (22 of 237) on placebo experienced a greater than 20% decline in FEV₁ following treatment for 5 days.

If use of RELENZA is considered for a patient with underlying airways disease, the potential risks and benefits should be carefully weighed. If a decision is made to prescribe RELENZA for such a patient, this should be done only under conditions of careful monitoring of respiratory function, close observation, and appropriate supportive care including availability of fast-acting bronchodilators.

5.2 Allergic Reactions

Allergic-like reactions, including oropharyngeal edema, serious skin rashes, and anaphylaxis have been reported in postmarketing experience with RELENZA. RELENZA should be stopped and appropriate treatment instituted if an allergic reaction occurs or is suspected.

5.3 Neuropsychiatric Events

Influenza can be associated with a variety of neurologic and behavioral symptoms that can include events such as seizures, hallucinations, delirium, and abnormal behavior, in some cases resulting in fatal outcomes. These events may occur in the setting of encephalitis or encephalopathy but can occur without obvious severe disease.

There have been postmarketing reports (mostly from Japan) of delirium and abnormal behavior leading to injury in patients with influenza who were receiving neuraminidase inhibitors, including RELENZA. Because these events were reported voluntarily during clinical practice, estimates of frequency cannot be made, but they appear to be uncommon based on usage data for RELENZA. These events were reported primarily among pediatric patients and often had an abrupt onset and rapid resolution. The contribution of RELENZA to these events has not been established. Patients with influenza should be closely monitored for signs of abnormal behavior. If neuropsychiatric symptoms occur, the risks and benefits of continuing treatment should be evaluated for each patient.

5.4 Limitations of Populations Studied

Safety and efficacy have not been demonstrated in patients with high-risk underlying medical conditions. No information is available regarding treatment of influenza in patients with any medical condition sufficiently severe or unstable to be considered at imminent risk of requiring inpatient management.

5.5 Bacterial Infections

Serious bacterial infections may begin with influenza-like symptoms or may coexist with or occur as complications during the course of influenza. RELENZA has not been shown to prevent such complications.

5.6 Importance of Proper Use of DISKHALER

Effective and safe use of RELENZA requires proper use of the DISKHALER to inhale the drug. Prescribers should carefully evaluate the ability of young children to use the delivery system if use of RELENZA is considered [see Use in Specific Populations (8.4)].

6 ADVERSE REACTIONS

See Warnings and Precautions for information about risk of serious adverse events such as bronchospasm (5.1) and allergic-like reactions (5.2), and for safety information in patients with underlying airways disease (5.1).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The placebo used in clinical studies consisted of inhaled lactose powder, which is also the vehicle for the active drug; therefore, some adverse events occurring at similar frequencies in different treatment groups could be related to lactose vehicle inhalation.

Treatment of Influenza: *Clinical Trials in Adults and Adolescents:* Adverse events that occurred with an incidence $\geq 1.5\%$ in treatment studies are listed in Table 1. This table shows adverse events occurring in patients ≥ 12 years of age receiving RELENZA 10 mg inhaled twice daily, RELENZA in all inhalation regimens, and placebo inhaled twice daily (where placebo consisted of the same lactose vehicle used in RELENZA).

Table 1. Summary of Adverse Events $\geq 1.5\%$ Incidence During Treatment in Adults and Adolescents

Adverse Event	RELENZA		Placebo (Lactose Vehicle) (n = 1,520)
	10 mg b.i.d. Inhaled (n = 1,132)	All Dosing Regimens* (n = 2,289)	
Body as a whole			
Headaches	2%	2%	3%
Digestive			
Diarrhea	3%	3%	4%
Nausea	3%	3%	3%
Vomiting	1%	1%	2%
Respiratory			
Nasal signs and symptoms	2%	3%	3%
Bronchitis	2%	2%	3%
Cough	2%	2%	3%
Sinusitis	3%	2%	2%
Ear, nose, and throat infections	2%	1%	2%
Nervous system			
Dizziness	2%	1%	<1%

* Includes studies where RELENZA was administered intranasally (6.4 mg 2 to 4 times per day in addition to inhaled preparation) and/or inhaled more frequently (q.i.d.) than the currently recommended dose.

Additional adverse reactions occurring in less than 1.5% of patients receiving RELENZA included malaise, fatigue, fever, abdominal pain, myalgia, arthralgia, and urticaria.

The most frequent laboratory abnormalities in Phase III treatment studies included elevations of liver enzymes and CPK, lymphopenia, and neutropenia. These were reported in similar proportions of zanamivir and lactose vehicle placebo recipients with acute influenza-like illness.

Clinical Trials in Pediatric Patients: Adverse events that occurred with an incidence $\geq 1.5\%$ in children receiving treatment doses of RELENZA in 2 Phase III studies are listed in Table 2. This table shows adverse events occurring in pediatric patients 5 to 12 years old receiving RELENZA 10 mg inhaled twice daily and placebo inhaled twice daily (where placebo consisted of the same lactose vehicle used in RELENZA).

Table 2. Summary of Adverse Events $\geq 1.5\%$ Incidence During Treatment in Pediatric Patients*

Adverse Event	RELENZA		Placebo (Lactose Vehicle) (n = 318)
	10 mg b.i.d. Inhaled (n = 291)	Placebo (Lactose Vehicle) (n = 318)	
Respiratory			
Ear, nose, and throat infections	5%	5%	
Ear, nose, and throat hemorrhage	<1%	2%	
Asthma	<1%	2%	
Cough	<1%	2%	
Digestive			
Vomiting	2%	3%	
Diarrhea	2%	2%	
Nausea	<1%	2%	

* Includes a subset of patients receiving RELENZA for treatment of influenza in a prophylaxis study.

In 1 of the 2 studies described in Table 2, some additional information is available from children (5 to 12 years old) without acute influenza-like illness who received an investigational prophylaxis regimen of RELENZA: 132 children received RELENZA and 145 children received placebo. Among these children, nasal signs and symptoms (zanamivir 20%, placebo 9%), cough (zanamivir 16%, placebo 8%), and throat/tonsil discomfort and pain (zanamivir 11%, placebo 6%) were reported more frequently with RELENZA than placebo. In a subset with chronic pulmonary disease, lower respiratory adverse events (described as asthma, cough, or viral respiratory infections which could include influenza-like symptoms) were reported in 7 of 7 zanamivir recipients and 5 of 12 placebo recipients.

Prophylaxis of Influenza: Family/Household Prophylaxis Studies: Adverse events that occurred with an incidence of $\geq 1.5\%$ in the 2 prophylaxis studies are listed in Table 3. This table shows adverse events occurring in patients ≥ 5 years of age receiving RELENZA 10 mg inhaled once daily for 10 days.

Table 3. Summary of Adverse Events $\geq 1.5\%$ Incidence During 10-Day Prophylaxis Studies in Adults, Adolescents, and Children*

Adverse Event	Contact Cases	
	RELENZA (n = 1,068)	Placebo (n = 1,059)
Lower respiratory		
Viral respiratory infections	13%	19%
Cough	7%	9%
Neurologic		
Headaches	13%	14%
Ear, nose, and throat		
Nasal signs and symptoms	12%	12%
Throat and tonsil discomfort and pain	8%	9%
Nasal inflammation	1%	2%
Musculoskeletal		
Muscle pain	3%	3%
Endocrine and metabolic		
Feeding problems (decreased or increased appetite and anorexia)	2%	2%
Gastrointestinal		
Nausea and vomiting	1%	2%
Non-site specific		
Malaise and fatigue	5%	5%
Temperature regulation disturbances (fever and/or chills)	5%	4%

* In prophylaxis studies, symptoms associated with influenza-like illness

were captured as adverse events; subjects were enrolled during a winter respiratory season during which time any symptoms that occurred were captured as adverse events.

Community Prophylaxis Studies: Adverse events that occurred with an incidence of $\geq 1.5\%$ in 2 prophylaxis studies are listed in Table 4. This table shows adverse events occurring in patients ≥ 5 years of age receiving RELENZA 10 mg inhaled once daily for 28 days.

Table 4. Summary of Adverse Events $\geq 1.5\%$ Incidence During 28-Day Prophylaxis Studies in Adults, Adolescents, and Children*

Adverse Event	RELENZA	
	(n = 2,231)	Placebo (n = 2,239)
Neurologic		
Headaches	24%	26%
Ear, nose, and throat		
Throat and tonsil discomfort and pain	19%	20%
Nasal signs and symptoms	12%	13%
Ear, nose, and throat infections	2%	2%
Lower respiratory		
Cough	17%	18%
Viral respiratory infections	3%	4%
Musculoskeletal		
Muscle pain	8%	8%
Musculoskeletal pain	6%	6%
Arthralgia and articular rheumatism	2%	<1%
Endocrine and metabolic		
Feeding problems (decreased or increased appetite and anorexia)	4%	4%
Gastrointestinal		
Nausea and vomiting	2%	3%
Diarrhea	2%	2%
Non-site specific		
Temperature regulation disturbances (fever and/or chills)	9%	10%
Malaise & fatigue	8%	8%

* In prophylaxis studies, symptoms associated with influenza-like illness were captured as adverse events; subjects were enrolled during a winter respiratory season during which time any symptoms that occurred were captured as adverse events.

6.2 Postmarketing Experience

In addition to adverse events reported from clinical trials, the following events have been identified during postmarketing use of zanamivir (RELENZA). Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. These events have been chosen for inclusion due to a combination of their seriousness, frequency of reporting, or potential causal connection to zanamivir (RELENZA).

Allergic Reactions: Allergic or allergic-like reaction, including oropharyngeal edema [see Warnings and Precautions (5.2)].

Psychiatric: Delirium, including symptoms such as altered level of consciousness, confusion, abnormal behavior, delusions, hallucinations, agitation, anxiety, nightmares [see Warnings and Precautions (5.3)].

Cardiac: Arrhythmias, syncope.

Neurologic: Seizures.

Respiratory: Bronchospasm, dyspnea [see Warnings and Precautions (5.1)].

Skin: Facial edema; rash, including serious cutaneous reactions; urticaria [see Warnings and Precautions (5.2)].

7 DRUG INTERACTIONS

Zanamivir is not a substrate nor does it affect cytochrome P450 (CYP) isoenzymes (CYP1A1/2, 2A6, 2C9, 2C18, 2D6, 2E1, and 3A4) in human liver microsomes. No clinically significant pharmacokinetic drug interactions are predicted based on data from in vitro studies.

The concurrent use of RELENZA with live attenuated influenza vaccine (LAIV) intranasal has not been evaluated. However, because of potential interference between these products, LAIV should not be administered within 2 weeks before or 48 hours after administration of RELENZA, unless medically indicated. The concern about possible interference arises from the potential for antiviral drugs to inhibit replication of live vaccine virus.

Trivalent inactivated influenza vaccine can be administered at any time relative to use of RELENZA [see Clinical Pharmacology (12.4) of full prescribing information].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C. There are no adequate and well-controlled studies of zanamivir in pregnant women. Zanamivir should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Embryo/fetal development studies were conducted in rats (dosed from days 6 to 15 of pregnancy) and rabbits (dosed from days 7 to 19 of pregnancy) using the same IV doses (1, 9, and 90 mg/kg/day). Pre- and post-natal developmental studies were performed in rats (dosed from day 16 of pregnancy until litter day 21 to 23). No malformations, maternal toxicity, or embryotoxicity were observed in pregnant rats or rabbits and their fetuses. Because of insufficient blood sampling timepoints in rat and rabbit reproductive toxicity studies, AUC values were not available. In a subchronic study in rats at the 90 mg/kg/day IV dose, the AUC values were greater than 300 times the human exposure at the proposed clinical dose.

An additional embryo/fetal study, in a different strain of rat, was conducted using subcutaneous administration of zanamivir, 3 times daily, at doses of 1, 9, or 80 mg/kg during days 7 to 17 of pregnancy. There was an increase in the incidence rates of a variety of minor skeleton alterations and variants in the exposed offspring in this study. Based on AUC measurements, the 80 mg/kg dose produced an exposure greater than 1,000 times the human exposure at the proposed clinical dose. However, in most instances, the individual incidence rate of each skeletal alteration or variant remained within the background rates of the historical occurrence in the strain studied.

Zanamivir has been shown to cross the placenta in rats and rabbits. In these animals, fetal blood concentrations of zanamivir were significantly lower than zanamivir concentrations in the maternal blood.

8.3 Nursing Mothers

Studies in rats have demonstrated that zanamivir is excreted in milk. However, nursing mothers should be instructed that it is not known whether zanamivir is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when RELENZA is administered to a nursing mother.

8.4 Pediatric Use

Treatment of Influenza: Safety and effectiveness of RELENZA for treatment of influenza have not been assessed in pediatric patients less than 7 years of age, but were studied in a Phase III treatment study in pediatric patients, where 471 children 5 to 12 years of age received zanamivir or placebo [see *Clinical Studies (14.1) of full prescribing information*]. Adolescents were included in the three principal Phase III adult treatment studies. In these studies, 67 patients were 12 to 16 years of age. No definite differences in safety and efficacy were observed between these adolescent patients and young adults.

In a Phase I study of 16 children ages 6 to 12 years with signs and symptoms of respiratory disease, 4 did not produce a measurable peak inspiratory flow rate (PIFR) through the DISKHALER (3 with no adequate inhalation on request, 1 with missing data), 9 had measurable PIFR on each of 2 inhalations, and 3 achieved measurable PIFR on only 1 of 2 inhalations. Neither of two 6-year-olds and one of two 7-year-olds produced measurable PIFR. Overall, 8 of the 16 children (including all those under 8 years old) either did not produce measurable inspiratory flow through the DISKHALER or produced peak inspiratory flow rates below the 60 L/min considered optimal for the device under standardized *in vitro* testing; lack of measurable flow rate was related to low or undetectable serum concentrations [see *Clinical Pharmacology (12.3), Clinical Studies (14.1) of full prescribing information*]. Prescribers should carefully evaluate the ability of young children to use the delivery system if prescription of RELENZA is considered.

Prophylaxis of Influenza: The safety and effectiveness of RELENZA for prophylaxis of influenza have been studied in 4 Phase III studies where 273 children 5 to 11 years of age and 239 adolescents 12 to 16 years of age received RELENZA. No differences in safety and effectiveness were observed between pediatric and adult subjects [see *Clinical Studies (14.2) of full prescribing information*].

8.5 Geriatric Use

Of the total number of patients in 6 clinical studies of RELENZA for treatment of influenza, 59 patients were 65 years of age and older, while 24 patients were 75 years of age and older. Of the total number of patients in 4 clinical studies of RELENZA for prophylaxis of influenza in households and community settings, 954 patients were 65 years of age and older, while 347 patients were 75 years of age and older. No overall differences in safety or effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. Elderly patients may need assistance with use of the device.

In 2 additional studies of RELENZA for prophylaxis of influenza in the nursing home setting, efficacy was not demonstrated [see *Indications and Usage (1.3) of full prescribing information*].

10 OVERDOSAGE

There have been no reports of overdose from administration of RELENZA.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis: In 2-year carcinogenicity studies conducted in rats and mice using a powder formulation administered through inhalation, zanamivir induced no statistically significant increases in tumors over controls. The maximum daily exposures in rats and mice were approximately 23 to 25 and 20 to 22 times, respectively, greater than those in humans at the proposed clinical dose based on AUC comparisons.

Mutagenesis: Zanamivir was not mutagenic in *in vitro* and *in vivo* genotoxicity assays which included bacterial mutation assays in *S. typhimurium* and *E. coli*, mammalian mutation assays in mouse lymphoma, chromosomal aberration assays in human peripheral blood lymphocytes, and the *in vivo* mouse bone marrow micronucleus assay.

Impairment of Fertility: The effects of zanamivir on fertility and general reproductive performance were investigated in male (dosed for 10 weeks prior to mating, and throughout mating, gestation/lactation, and shortly after weaning) and female rats (dosed for 3 weeks prior to mating through Day 19 of pregnancy, or Day 21 post partum) at IV doses 1, 9, and 90 mg/kg/day. Zanamivir did not impair mating or fertility of male or female rats, and did not affect the sperm of treated male rats. The reproductive performance of the F1 generation born to female rats given zanamivir was not affected. Based on a subchronic study in rats at a 90 mg/kg/day IV dose, AUC values ranged between 142 and 199 mcg•hr/mL (>300 times the human exposure at the proposed clinical dose).

17 PATIENT COUNSELING INFORMATION

See *FDA-Approved Patient Labeling (17.6)*.

17.1 Bronchospasm

Patients should be advised of the risk of bronchospasm, especially in the setting of underlying airways disease, and should stop RELENZA and contact their physician if they experience increased respiratory symptoms during treatment such as worsening wheezing, shortness of breath, or other signs or symptoms of bronchospasm [see *Warnings and Precautions (5.1)*]. If a decision is made to prescribe RELENZA for a patient with asthma or chronic obstructive pulmonary disease, the patient should be made aware of the risks and should have a fast-acting bronchodilator available.

17.2 Concomitant Bronchodilator Use

Patients scheduled to take inhaled bronchodilators at the same time as RELENZA should be advised to use their bronchodilators before taking RELENZA.

17.3 Neuropsychiatric Events

Patients with influenza (the flu), particularly children and adolescents, may be at an increased risk of seizures, confusion, or abnormal behavior early in their illness. These events may occur after beginning RELENZA or may occur when flu is not treated. These events are uncommon but may result in accidental injury to the patient. Therefore, patients should be observed for signs of unusual behavior and a healthcare professional should be contacted immediately if the patient shows any signs of unusual behavior [see *Warnings and Precautions (5.3)*].

17.4 Instructions for Use

Patients should be instructed in use of the delivery system. Instructions should include a demonstration whenever possible. For the proper use of RELENZA, the patient should read and follow carefully the accompanying Patient Instructions for Use.

If RELENZA is prescribed for children, it should be used only under adult supervision and instruction, and the supervising adult should first be instructed by a healthcare professional [see *Dosage and Administration (2.1) of full prescribing information*].

17.5 Risk of Influenza Transmission to Others

Patients should be advised that the use of RELENZA for treatment of influenza has not been shown to reduce the risk of transmission of influenza to others.

17.6 FDA-Approved Patient Labeling and Instructions for Use

See separate leaflet.

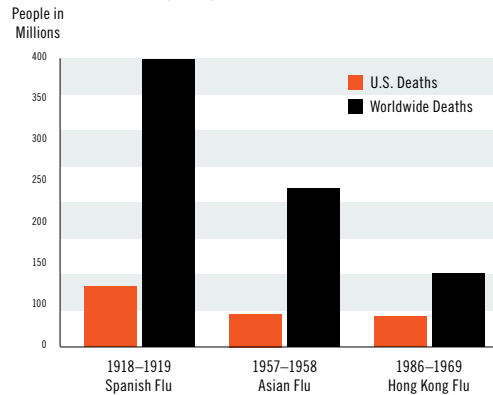
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VIRAL CATASTROPHES

Major flu pandemics since 1900



Source: Hoffman-La Roche

for professionals who work on animal and human health, environmental health, food safety, and crisis management to work together so as to ensure the world is better prepared for diseases that threaten the security of the human race," says Dr. Nabarro.

A key goal of the international efforts is to reduce the presence of the virus in developing countries. One way to do that is to encourage local authorities to cull poultry from domestic flocks that are infected with H5N1, the virulent strain of avian flu that experts fear will be transmitted to humans. United Nations System Influenza Coordination (UNSIC) has reported some success, with a reduction of avian flu outbreaks in poultry and, as a result, in humans. However bird flu remains a constant presence in some countries and sporadic cases of human infection occur. Since 2003, 387 people have been sickened by avian flu around the world; 245 have died, mostly young adults and children, says Nabarro.

Preparation for pandemics has not been limited to the developing world, and much has been done by governments in advanced economies to find and fix vulnerabilities. In the fall of 2007, the U.S. Treasury Department and some 2,700 financial firms in the United States, including banks and insurance companies, joined a three-week exercise to see how well global financial systems would handle a pandemic. In the simulation, the flu quickly spread out of Nigeria on daily international flights; it was soon reported in Asia, Europe, and the U.S. As it spread, absenteeism soared to 49%. Stock markets declined; supplies became scarce. In the fictional scenario more than nine million are hospitalized in the U.S and nearly two million die.

Before the simulation, 63% of the participants said they had already made pandemic flu preparations. Afterward, 91% said the exercise had provided them with information they would use to strengthen and refine their disaster planning efforts.



A BROAD COALITION OF PUBLIC AND PRIVATE SECTOR ORGANIZATIONS ARE WORKING TO DEVELOP A PLAN TO PREPARE FOR A DISASTER THEY HOPE NEVER HAPPENS.

A Twist in Crisis Management

Companies that have embraced modern techniques may find themselves especially vulnerable because of practices like just-in-time manufacturing, which reduces the amount of inventory a company keeps at hand and depends on a constant stream of deliveries to keep functioning. "People say we have better technology, but we don't necessarily have the production capacity," says Aaron Desmond, director of licensing and new business development at the University of Minnesota's Center for Infectious Disease Research & Policy (CIDRAP), which has developed a ten-point framework to help companies plan for a pandemic. "We need to be prepared for when it happens, whether it is tomorrow, five years, or ten years from now," says Desmond. CIDRAP (www.cidrapsource.com) offers companies a

full range of seminars, web lectures, and newsletters to help businesses allocate resources and set their priorities for the duration of a pandemic.

CIDRAP urges companies to make pandemic planning an integral part of their crisis management and disaster plans; to focus on employee safety by considering stockpiling antiviral products and protective clothing; to identify critical functions; and to ensure that their supply chains will remain in place to deliver necessary components or ingredients. (For the entire list see sidebar, right.) "The collateral damage may have more impact than the pandemic itself," says Desmond.

The Right Prescription

Producing and delivering critical products during a pandemic carries a special urgency for pharmaceutical companies like Roche, whose U.S. operations are based in Nutley, N.J. For Roche, pandemic preparedness is twofold. In addition to providing essential medicines to patients, Roche expects that there will be considerable demand for its antiviral medication, Tamiflu, which will be used to help quell a pandemic flu while a vaccine for the specific virus strain that triggers the pandemic is being developed and distributed.

A TEN-STEP ACTION PLAN

- ✓ Create an emergency operations team for pandemic response, with redundancy for team members.
- ✓ Focus on employee safety, plan evacuation procedures, educate your workforce, and stockpile protective clothing and antiviral drugs.
- ✓ Design an emergency communications plan that will utilize call centers, hotlines, e-mail, and instant messaging to keep employees informed.
- ✓ Plan to add security at key sites and warehouses, and consider the impact of reduced staffing.
- ✓ Ensure that your information systems will continue to operate and can handle a surge of remote workers.
- ✓ Strengthen core components of your supply chain and create a plan to operate with shortages.
- ✓ Identify key spokespersons and develop plans to inform the public in an emergency.
- ✓ Identify legal and liability issues that could affect your operations during a pandemic.
- ✓ List key government contacts you will need in an emergency.
- ✓ Prioritize your operations and ensure that succession planning for key executives, and a business recovery plan, are in place.

Source: CIDRAP Business Source, University of Minnesota (www.cidrapsource.com/framework)



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CEO

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Business
Continuity

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The **Roche Antiviral Protection Program** helps your company prepare your people for a flu pandemic.

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The company has developed an extensive plan to cope with a pandemic. In analyzing how it would handle a full-scale outbreak, Roche is determined to ensure that its supply lines continue to operate. Last year, the company brought together more than 200 of its suppliers and business partners to assist in the advancement of their pandemic planning and to enhance coordination.

During a pandemic, the company may have to narrow its operations. For example, explains Mike McGuire, vice president of anti-infective drugs at Roche, instead of making 20 to 30 products, Roche might produce just five or six of the most critical drugs. One of those products would be Tamiflu.

Roche has also been working as a collaborative partner with governments and businesses to help make Tamiflu accessible prior to a pandemic outbreak. For example, while the U.S. government encourages companies to consider stockpiling antivirals, McGuire says some planners have told Roche that they lack the logistical resources and capabilities to store the medication. In response, the company designed the Roche Antiviral Protection Program (RAPP), whereby companies can reserve their own stockpile of Tamiflu capsules at a nominal fee, to be stored by Roche and delivered upon full purchase in a crisis. Since the announcement of this program, many companies have taken an interest in this stockpiling solution. Roche has distributed Tamiflu to all of its employees around the globe to be used in the event of a pandemic.

Ensuring Business Continuity

Employee health has also been a high priority for another pharmaceutical company, GlaxoSmithKline, headquartered in London. With expectations that companies may suffer 30% to 40% absenteeism, GSK has focused on keeping employees healthy and working during a pandemic. In formulating its plan, GSK realized it had to provide for the families of its employees, as well. "If your child gets pan-



THE NEXT FLU PANDEMIC COULD SHAKE THE WORLD ECONOMY HARDER THAN THE CURRENT CREDIT CRISIS.

demic flu and you have antiviral medicine from your employer, you're going to give it to your child," says Dr. Ron Joines, director of employee health and performance at GSK. The result is a plan to make antiviral medicines such as Relenza available to all 435,000 employees and dependents in more than 130 countries, he says. GSK has also created a storage program for corporate customers in the U.S.

Based on its experience in creating its own preparedness plan, GSK is now sharing its expertise with other companies. GSK has posted a series of videos on its website that feature Joines speaking about the steps needed to develop an effective pandemic plan (www.pandemic-plan.gsk.com). "The message is to build

real capability, not just plans on paper," says Joines. "If your company has a business continuity program, leverage that to deliver a health-care message." But he admits that the best-laid plans may go astray. "There are many unknown questions about a pandemic. You have to plan for the most likely failures."

While humanitarian issues are a strong motivation for companies to embrace pandemic planning, Dr. Joines says companies cannot overlook the business impact if they fail to perform well during such an event. "If a company that plays a critical role in the fabric of American society doesn't deliver and its rivals do, how will people view them on the other side of the pandemic?" he asks. The bottom line always gets the attention of companies, and is another reason for them to plan for an event they hope never happens. ●

To advertise in our Pandemic Preparedness sections, contact Laurie Evans at 212.522.0767. For reprints, call Jo Mattern at 212.522.2582.

IS THERE SOMETHING IN THE AIR?

Many experts agree that a global pandemic could involve infectious agents that are spread through the air we breathe. Vaccines exist for some infectious diseases and some medicines are useful treatments. However, "prevention is the best medicine". Hand washing and avoiding close contact with others who may be sick are always recommended to help prevent illness. An additional way to help reduce exposure to airborne germs is through the proper use of NIOSH-approved (i.e. N95) respirators.

Although other masks may look similar, NIOSH-approved N95 respirators, like those from 3M, contain special filters, fit tightly to the face, and, when properly used in a workplace setting, help reduce exposure to hazardous particles in the air. During an outbreak of infectious disease, such as avian flu, they can help reduce the inhalation of airborne germs.



During the 2003 SARS outbreak, respirator availability became limited due to very high demand. To be prepared, businesses, communities and families should consider stockpiling in advance to ensure respiratory protection is available when they need it.

Businesses, community leaders, and families can look to government agencies for guidance (i.e. OSHA, CDC, etc.) about the use of respirators. Careful product selection, and training on how to use and put the respirators on properly, are essential. Members of the general public planning to use them should look for respirators specifically marked "FDA-cleared for use by the general public," read and follow all directions, and practice putting on the respirators. Employers providing respirators should implement a respiratory protection program as required by OSHA. 3M has extensive experience with respirators and can help you select the right product and quantity to meet your needs.

 A man in a dark blue shirt is wearing a white 3M N95 respirator mask. He is holding a white sign with the word "OPEN" written on it in large, dark letters. The background is blurred, showing other people in a public setting.

**Be Prepared.
Move Forward.**

3M can help.

During a public health emergency, wearing respiratory protection can help reduce worker exposures to airborne germs.

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The 3M logo, consisting of the letters "3M" in a bold, red, sans-serif font.