

Preparing for the Next Influenza Pandemic

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Some of the challenges....

- Being in the middle of the world's 4th largest PR issue in 2005
- Dealing with media "sensationalism"
- Dealing with massive ignorance about influenza, pandemics, treatments, short-term government (politician) thinking...
- Gearing up demand/ investing ahead of orders
- Corporate responsibility to the community, investors, employees
- Preparing Roche around the world as a first step
- Building the brand TAMIFLU for "normal influenza" seasonal use
- Maintaining the focus and interest when the media is quiet

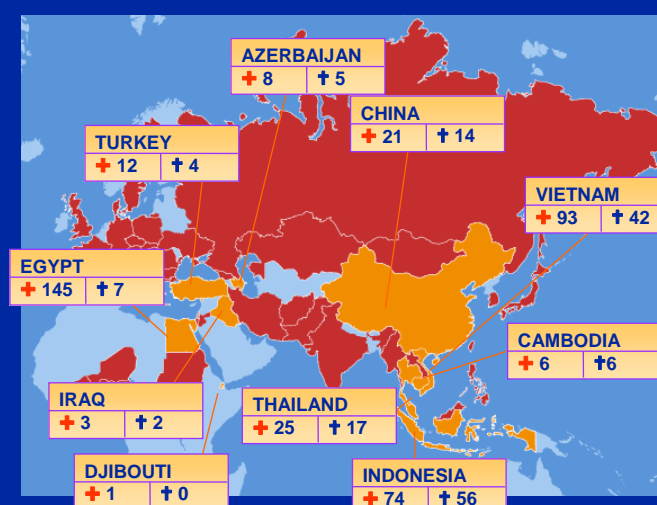
FACT: Pandemics result in significant morbidity and mortality

- A pandemic is the widespread occurrence of an infectious disease appearing for a limited time on several continents.
- Influenza pandemics are characterized by the spread of a novel type of influenza virus to many parts of the world, causing unusually high morbidity (illness), an excess mortality.
- **FACT: There will be another pandemic.....**
- 3 major influenza pandemics in the 20th century*:

		Deaths	Virus
1918-1919	Spanish influenza	40–50 Mio	H1N1
1957-1958	Asian influenza	2 Mio	H2N2
1968-1969	Hong Kong influenza	1 Mio	H3N2

*Ten things you need to know about pandemic influenza. WHO October 2005

Countries with H5N1 Infections in Birds & Humans since December 2003



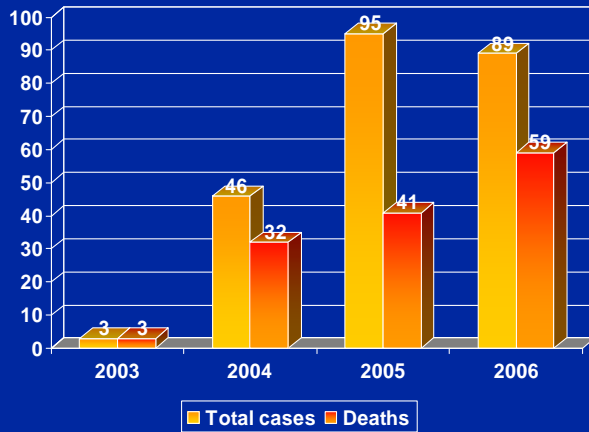
Human cases as of August 7, 2006.

- 10 countries with H5N1 infection in humans
- 233 lab confirmed cases – 135 deaths
- Almost 60% mortality
- Spanish flu 2.5% mortality

■ H5N1 in Birds
■ H5N1 in Humans



Confirmed Human Cases of H5N1 Reported to WHO Cumulative Number (as of August 7, 2006)



- Incidence of infections and deaths is accelerating
- Over a third of these cases have occurred in the first 7 months of 2006

Total number of cases includes number of deaths.
WHO reports only laboratory-confirmed cases.

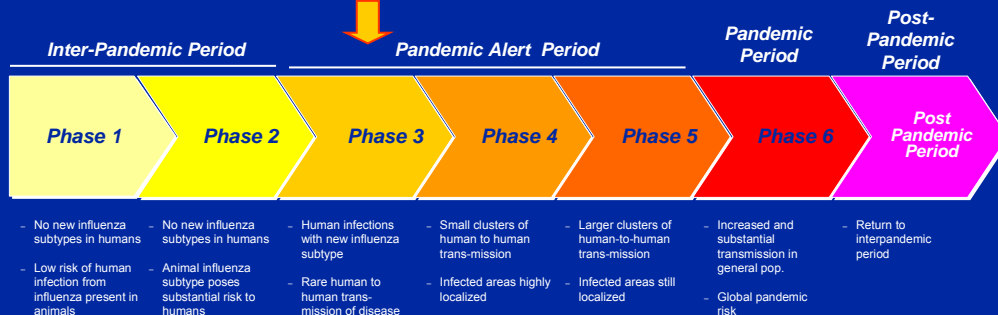


WHO Pandemic Phases

January 2005

The avian flu is in phase 3 of the WHO's monitoring system and shows signs of progression towards what has the potential of becoming a pandemic.

Estimated Current Phase of the Pandemic





Medical Interventions: Anti-virals



Role of Vaccines and Anti-virals in a Pandemic



- **Vaccines**
 - Vaccines regarded as the most important medical intervention for preventing influenza and reducing its health consequences during a pandemic.
 - Issues around the availability of matched vaccines during the first wave of a pandemic.
 - WHO panel says many years and 10 bio Dollars needed to supply anticipated demand
- **Anti-virals**
 - “Once a pandemic has been declared...the role of antiviral drugs is unquestionable”
 - “Pending the availability of vaccines, antiviral drugs will be the principle medical intervention for reducing morbidity and mortality”
 - TAMIFLU donated to WHO for “fire fighting”

Neuraminidase Inhibitors

The only anti-viral agents active against H5N1

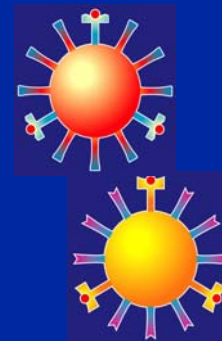


- **M2 Inhibitors**

- Block the M2 ion channel in the influenza A virus
- Amantadine and rimantadine
- Resistance of H3N2 isolates to amantadine reaches > 90% in the USA¹ and South East Asia²
- Resistance reported in currently circulating H5N1 viruses

- **Neuraminidase Inhibitors**

- Block virus replication by binding to the neuraminidase
- Oseltamivir (delivered orally, suitable for age ≥ 1 year)
- Zanamivir (delivered by inhalation, suitable for age ≥ 5 years)
- Active against H5N1 in vitro³



1. Bright et al ; JAMA Feb 2006
2. Bright et al ; Lancet 2006
3. Govorkova et al. *Antimicrob Agents Chemother* 2001

Tamiflu is not a vaccine!



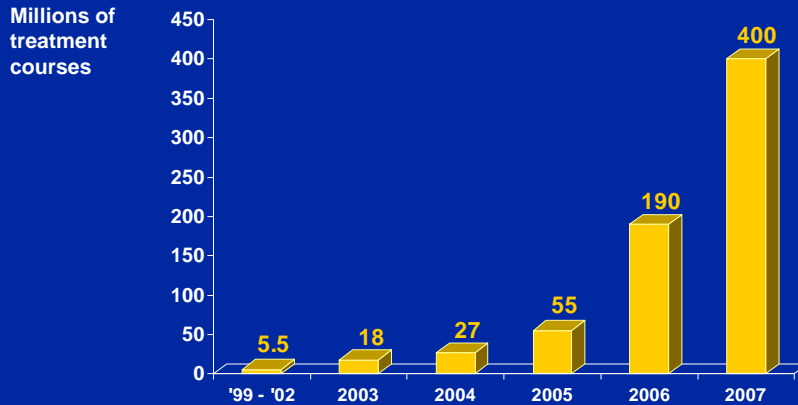
- Tamiflu is **an oral antiviral treatment**, administered as a capsule or as a liquid suspension. It is *not* a vaccine.



Production Capacity for Tamiflu



FACT: It takes many months to produce TAMIFLU!



- Based on the current orders we have received from governments around the world, our capacity to produce 400 million treatments by 2007 is significantly ahead of demand.

Efficacy of Tamiflu against H5N1



FACT: Tamiflu can prevent mortality in mammals

- No one knows which strain of influenza will cause the next influenza pandemic
- Tamiflu and Relenza are both active against H5N1 *in vitro*¹
- **Tamiflu is active against H5N1 *in vivo*** (mice² and ferrets³)
 - Significantly reduced the mortality rate of mice and ferrets infected with a lethal dose of H5N1
 - Significantly reduced viral titre levels in GI and lung tissue
 - Increasingly virulent strains may require higher doses of Tamiflu for effective treatment particularly under conditions of delayed initiation of therapy.



1. Govorkova et al. *Antimicrob Agents Chemother* 2001
2. Yen et al. *J Infect Dis* 2005;192:665
3. Govorkova et al. *Lancet Asia Medical Forum*, May 2006

Tamiflu in the treatment of H5N1-infected humans

Tamiflu is active in reducing levels of the H5N1 virus



- No controlled clinical studies (human cases rare and geographically dispersed)
- Case reports from Turkey¹
 - 10 individuals infected with H5N1 were given Tamiflu at various times following onset of symptoms at the approved treatment dose of 75mg twice daily
 - 4 patients died – they received Tamiflu after ~8.5 days after onset of symptoms
 - 6 patients survived – they received Tamiflu after ~3.5 days after onset of symptoms
- Available clinical information on H5N1 infected individuals suggests that
 - Tamiflu is active in reducing levels of the H5N1 virus and that,
 - in line with controlled data from the use of Tamiflu in seasonal influenza, the early administration of Tamiflu to H5N1 infected individuals is critical for achieving optimal clinical outcome.

1. Avian Influenza Outbreak Report of Turkey
Presentation by Assoc. Prof. Huseyin Avni Sahin
New-Fields Bird 'Flu Summit', Washington DC, 27th February, 2006

WHO Rapid Advice Guidelines



FACT: *Tamiflu recommended for treatment and prophylaxis by WHO*

- **Treatment (5 days)**
 - Oseltamivir treatment (strong recommendation)
 - Zanamivir as an alternative (weak recommendation)
 - **NO** amantadine or rimantadine alone (strong recommendation)
- **Post-exposure prophylaxis (10 days)**
 - In high risk exposure groups oseltamivir as PEP (strong recomm.)
 - High risk exposure groups = household or close family contacts of a strongly suspected or confirmed H5N1 patient
- **Supported by Ferguson et al:** treatment of infected individuals and post exposure prophylaxis of household contacts could reduce attack rates by 50%



WHO Rapid Advice Guidelines on pharmacological management of humans infected with avian influenza A (H5N1) virus, *WHO, May 2006*

Ferguson et al. Strategies for mitigating an influenza pandemic, *Nature 2006*



Influenza Pandemic Preparedness Plan



National Preparedness



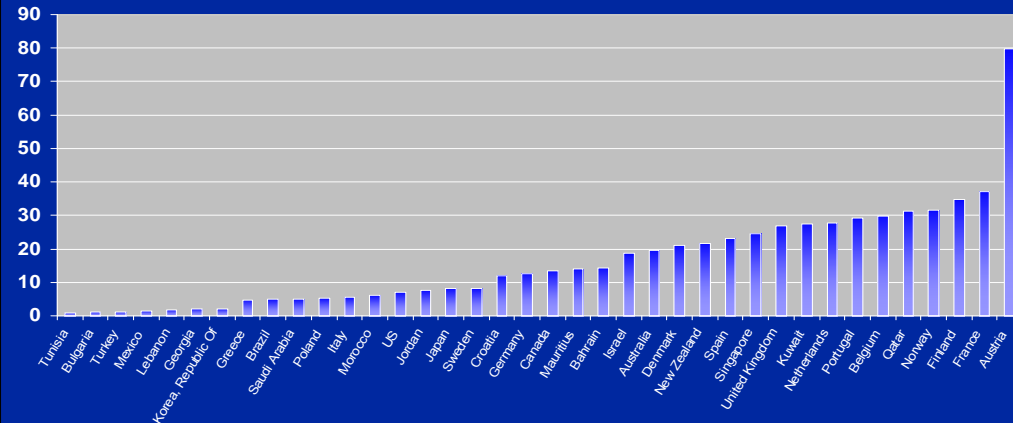
FACTS:

- Governments cannot effectively close their borders!
- Government anti-viral stockpiles are limited- Denmark's "19%" is actually about 2% of the normal population
- Most plans do not clearly address treatment vs prophylaxis
- Plans for transportation to areas of outbreak and from there to those infected or those requiring prophylaxis are lacking
- Few plans acknowledge potential bottle-necks with existing systems during a pandemic
- Most plans do not identify priority e.g. DK does not include GPs!
- The impact on "normal businesses" is not considered in any plan
- The reaction to a Pandemic will be extreme!

Current Tamiflu stockpiles by governments



% coverage



Roche's Business Continuity Plan



Objectives

- To ensure that business activities do not inappropriately increase the infection risk of employees or third parties
- To ensure that Roche employees and their families will have TAMIFLU in their medicine cupboard just before the pandemic hits
- To ensure that Roche sites pose no danger to people or the environment in the event of a pandemic
- To ensure that life-saving medicines, including Tamiflu and other anti-infectives, continue to be manufactured and distributed.
- To give Roche the best chance of a rapid return to business

Our Corporate Strategy

Medical Interventions



Key questions	Consideration
Who will receive Tamiflu	All Roche employees Their close family contacts sharing the same household , in a manner permissible according to local laws and regulations
Treatment vs. prophylaxis	Treatment of infected employees: treatment twice daily for 5 days Prophylaxis for essential pandemic phase workers (on site): once daily up to 6 weeks
Timing of supply	During Phase 5, the last phase of pandemic alert period During Phase 4, if country is affected by human-to-human transmission
Mechanism of supply	Distribution to employees together with solid educational material to ensure appropriate use of drug and how to act in the event of a pandemic
What about vaccines	Employees should be encouraged to get vaccinated as soon as vaccines become available

Our Corporate Strategy

Non-Medical Interventions



Intervention	Implementation
Avoid social contact	Upon alert from Roche and/or local government, employees should be encouraged to work from home and to divert their office phone to their company mobile phone. Only "essential pandemic phase workers" will be asked to ensure continuity of the business at the Roche premises. Gathering of people (meetings, elevators, cafeterias, ...) Travel policies
Hygienic measures	Personal hygiene (wash hands, cover mouth, not shake hands, ...) Workplace cleaning Air conditioning
Personal protective equipment	Respirators (face masks) Personal protective equipment (for health care workers)

Anti-viral agents are only one component of a pandemic response plan

Roche's Corporate Template Plan

A working document & its elements



- 1 EXECUTIVE SUMMARY
- 2 OBJECTIVE
- 3 DEFINITIONS
- 4 INFECTION CONTROL GUIDELINES
 - 4.1 Medical Interventions
 - 4.1.1 Vaccines
 - 4.1.2 Antivirals
 - 4.1.3 Tamiflu
 - 4.2 Non-Medical Interventions
 - 4.2.1 Avoiding Social Contact
 - 4.2.2 Hygienic Measures
 - 4.2.3 Personal Protective Equipment
- 5 IMPACT ON BUSINESS
 - 5.1 Effect on Staffing Levels
 - 5.2 Other Impact on Business
 - 5.3 Business Continuity Plans – Objectives
 - 5.4 Essential Functions
- 6 INFLUENZA PANDEMIC PREPAREDNESS & BUSINESS CONTINUITY PLAN
- 7 KEY ACTIONS AND TRIGGERS
- 8 ROLES & RESPONSIBILITIES
- 9 APPENDICES

Pandemic Preparedness & Business Continuity Plan

12 Steps



- **Step 1: Local Emergency Management Team**
Establish a pandemic emergency management team.
- **Step 2: Key Activities**
to be maintained in your department to ensure business continuity in a pandemic case and the human/other resource requirements (assume different levels of absenteeism (10% 25%, 50%) of essential pandemic phase workers).
- **Step 3: Essential Employees**
Identify by name “essential pandemic phase workers” whose uninterrupted presence is required on a day to day basis to ensure business continuity.
- **Step 4: Key Suppliers and Distributors**
Determine key suppliers and distributors to protect upstream and downstream activities related to manufacturing and distribution of services/products.

Pandemic Preparedness & Business Continuity Plan



12 Steps

- **Step 5: Define Work Related Risk Groups**
Define risk groups for work-related infection for all employees remaining on site and measures to be taken to reduce risk.
- **Step 6: Infected Employees**
Decide on how to deal with infected employees (e.g. those who show first symptoms of illness while at work and those who have had close contact with influenza patients).
- **Step 7: Medical and Non-Medical Resources**
Calculate the amount of Tamiflu required.
Calculate the amount of personal protective equipment. required.
- **Step 8: Storage and Distribution**
Develop a plan for the storage and distribution of Tamiflu and protective equipment in case of a pandemic.

Pandemic Preparedness & Business Continuity Plan



12 Steps

- **Step 9: Reduction of Activities**
Set up a plan for the stepwise reduction of activities at your sites. Further develop this plan to the point where only basic safety and security functions will be maintained.
- **Step 10: Communication**
Decide on responsibilities for and appropriate ways of communication in case of a pandemic.
- **Step 11: Business Recovery**
Establish criteria and process for agreeing to return to business as normal.
- **Step 12: Test your Plans**
Set up scenarios/assumptions, test your plan and revise regularly.

What is Roche doing?



- Proactively contacting the Fortune 500 companies
- Adding local personnel for Corporate and Pandemic activities
- Building regional account management to better co-ordinate activities e.g. supply of stock, central contact point, accurate records of who has stock
- Working to change legislation where needed to allow companies to stockpile
- Refining the manufacturing process to anticipate demand and speed the process
- Clinical testing to try to estimate efficacy against Avian flu strains

What should Corporations do?



- **Consider their responsibility for the welfare of their employees**
- **Recognise that the government is not thinking about business**
- **Recognise that government plans are basic and may fall to pieces under the pressure of a pandemic**
- **Recognise that it is essential to act sooner rather than wait for impending disaster**
- **Consider how a business decimated by a pandemic will avoid bankruptcy**
- **Balance the cost versus the consequences and/ or benefits!**

The cost calculation



- 1 Pack = 1 treatment (2 capsules for 5 days)
- 5 Packs = 1 Prophylactic Treatment (6 weeks @ 1 capsule per day)
- Shelf life of 5 years
- Masks, disinfectants, gloves etc for 56 days

Cost for 100 Employees

- 100 Employees = 100 treatments
- 150 "Households" = 150 packs
- 10 employees on prophylaxis = 50 packs
- **TOTAL PACKS = 300**
- 1 Rx for all packs to a pharmacy
- 1 pack: DKK 244.50
- **300 packs: DKK 73,350.00**
- Pharmacy discount of 5% > DKK 60,000
- 300 packs @ 232.28 = **DKK 69,684**
- **Cost per employee: DKK 697 (139.4/ year)**
- **Approx cost of masks, disinfectants, gloves etc DKK 2200 per employee**

TAMIFLU



- Please contact your doctor for further information



We Innovate Healthcare