



PandemicPrep.Org

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- Roche Business Continuity
- Tamiflu Production
- Vaccine Update
- H5N1 / Tamiflu
- Tamiflu Stockpiling



Roche Employee Protection Program

Why Roche Created the Employee Protection Program



- Preparing for a disaster means preparing people
- No people... no business continuity
- Having an employee protection plan can inspire confidence and can reduce absenteeism
- “In the absence of fact, people create myth”

The Elements of our Employee Protection Program



1. Hygiene
2. Social Distancing
3. Other Infection Control Measures
4. Education and Communication
5. Vaccination
6. Antiviral Program



Antiviral Distribution Program

Part 6: Antiviral Distribution Program

The Six Steps to Setting up the Program

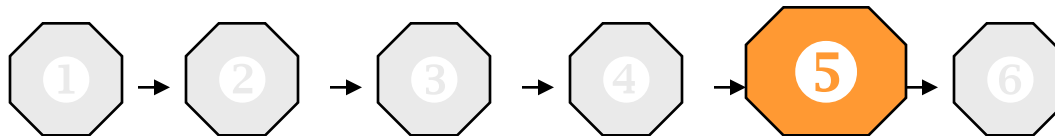


- 1** **Step 1: Determine Who to Cover**
- 2** **Step 2: Assess Number of Treatment Courses**
- 3** **Step 3: Facilitate Physician Consultations**
- 4** **Step 4: “Order” Antiviral Treatment Courses**
- 5** **Step 5: Provide Education**
- 6** **Step 6: Distribute Antivirals**

Step 5: Educate Individuals



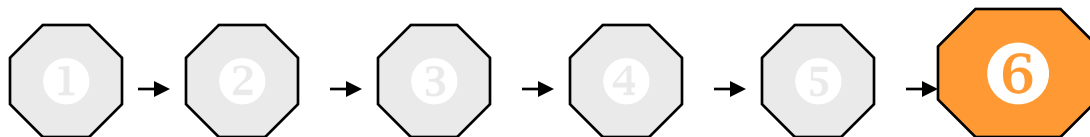
- Pandemic communication plan already coordinated in advance
- Antiviral distribution memo from the CEO to all employees
- Pandemic overview video from CEO preceding medical consultation
- Direct mailing and emailing of pandemic influenza and antiviral Q&A guide to all employees
- Mandatory web-based educational module had to be completed to participate in the program
- Employee information hot-line available during a pandemic
- Providing multiple forms of education mitigates risk of inappropriate use





Step 6: Distribute Antivirals

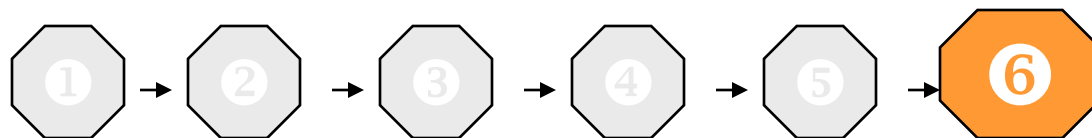
- Wrestled with the question of whether Roche should centralize or decentralize distribution
 - Will off-site employees be able to access product during a pandemic?
 - Will sick employees pose a risk of spreading infection amongst healthy individuals?
 - Does centrally storing product pose a security risk?
- Roche is using a combination of both models
 - Distribute in advance to employees at their homes – all distribution has been completed (12/06)
 - Maintain a cache of antivirals for on-site employees



Step 6: Distribute Antivirals (cont)



- Investigated numerous alternative distribution options
- Partnered with a pharmacy benefit manager (PBM) that was able to stock, secure and distribute product to individuals at home
- Sent a ‘married’ list of individuals that received an Rx and completed educational learning module
- PBMs ready to distribute product to individuals ‘before the pandemic’





Tamiflu Production Update

Roche's Organizational Commitment to Global Pandemic Planning



- Roche is a committed partner to U.S. & global health authorities; meeting with U.S. & other governments around the world
- Ramped up production of our oral antiviral more than 10 fold since '04
- Established U.S.-based supply chain, capable of producing 80 million treatment courses – part of 400 million global capacity
- This network includes eight Roche sites and 19 external manufacturing partners located in 9 different countries around the world
- Multiple donations of antivirals (5.1 million treatment courses) to WHO for regional & rapid use
- Why - Similar to finance sector, we cannot NOT be functional

Securing Product Supply



- Production is increased in response to any of the following events
 - significant additional government orders
 - the WHO declares that an influenza pandemic has evolved to phase 4 (human-to-human transmission)
 - Roche inventories of final active ingredient (oseltamivir) or key intermediates fall below target levels.
- However, if any such event occurs...
 - It will take **9 MONTHS** from start to finish to make a new batch of Tamiflu.
- We cannot guarantee availability if we reach the next phase of a pandemic!



H5N1 Vaccine - Update

Potential Role of Vaccines and Antivirals in an Influenza Pandemic



- Vaccines are the first line of defense against any Influenza virus but a truly effective vaccine can only be made when the next pandemic occurs (vaccines need to be matched against the specific viral strain causing the pandemic)
 - **How close are we to developing the ideal pandemic influenza vaccine?**
An ideal influenza vaccine that would protect against all strains of influenza is still very much upstream in the pipeline, and might not be available in the next five to 10 years.
 - **How long will it take to produce the first doses of pandemic influenza vaccine in the event of a pandemic?**
If production of a vaccine starts on the day a pandemic is declared, it is thought that at least four to six months will be necessary to produce the first doses of vaccine.
 - **Who will have access to the vaccine?**
Vaccine for H5N1 will not be sold commercially but is being stockpiled by the government
- Antivirals: Neuraminidase Inhibitors (NAIs) works to inhibit a protein found on all Influenza A viral strains (all past pandemics have been Influenza A viruses)
- NAIs are currently being stockpiled as part of the federal government's pandemic preparedness plan
 - The WHO recommends NAIs for treatment and prevention of the spread of pandemic influenza disease through household contacts



H5N1 and Tamiflu

Current Human Morbidity and Mortality due to H5N1 Influenza



- Summary of cases and deaths through May 15, 2009.

Country	2003		2004		2005		2006		2007		2008		2009		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	0	0	0	0	0	0	8	5	0	0	0	0	0	0	8	5
Bangladesh	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0
Cambodia	0	0	0	0	4	4	2	2	1	1	1	0	0	0	8	7
China	1	1	0	0	8	5	13	8	5	3	4	4	7	4	38	25
Djibouti	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0
Egypt	0	0	0	0	0	0	18	10	25	9	8	4	13	0	69	26
Indonesia	0	0	0	0	20	13	55	45	42	37	24	20	0	0	141	115
Iraq	0	0	0	0	0	0	3	2	0	0	0	0	0	0	3	2
Lao PDR	0	0	0	0	0	0	0	0	2	2	0	0	0	0	2	2
Myanmar	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0
Nigeria	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	1
Pakistan	0	0	0	0	0	0	0	0	3	1	0	0	0	0	3	1
Thailand	0	0	17	12	5	2	3	3	0	0	0	0	0	0	25	17
Turkey	0	0	0	0	0	0	12	4	0	0	0	0	0	0	12	4
Viet Nam	3	3	29	20	61	19	0	0	8	5	6	5	3	3	111	56
Total	4	4	46	32	98	43	115	79	88	59	44	33	29	11	424	261

The total case fatality (CFR) rate is 62%.

Source: WHO 5/15/09



Non-human data does not necessarily indicate clinical activity in humans. To date, results from clinical studies in humans are not available.

- **Both influenza A and B (H5N1 is A strain) can survive up to 17 days on banknotes**
- **Economic analysis shows Tamiflu use in a pandemic could halve the death toll versus no intervention**
 - Modeling research conducted at the University of Toronto showed that the treatment of infected and the prophylaxis of those exposed could be one of the most effective strategies in reducing illness and death during an influenza pandemic
- **Efficacy of oseltamivir therapy in ferrets inoculated with different clades of H5N1 influenza virus**
 - Designed to determine the efficacy of oseltamivir for post-exposure prophylaxis and for delayed treatment
 - Shows efficacy against two currently circulating stains of H5N1...preventing death if administered within 24 hours of exposure, along with an immune response for subsequent infections

Source: B Sander et al. Economic Evaluation of Influenza Pandemic Mitigation Strategies in the US Using a Stochastic Microsimulation Influenza Model. Data presented at OPTIONS VI 2007

Source: Antimicrobial Agents and Chemotherapy (April 2007)

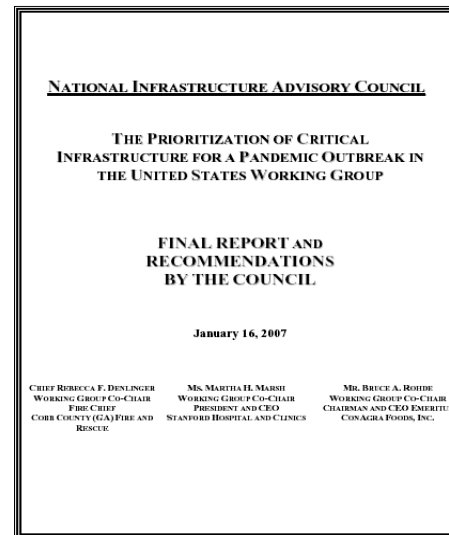
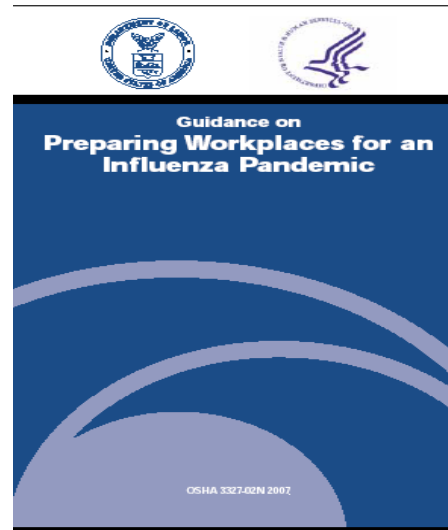
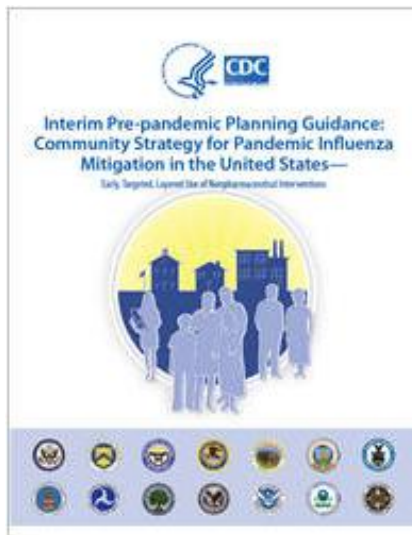


Tamiflu Stockpiling



Why should Corporations prepare?

- The US Government, CDC, OSHA, and the FDA have advised businesses to prepare for pandemic...



FDA Pandemic Influenza Preparedness Strategic Plan
United States Department of Health and Human Services
Food and Drug Administration
Rockville, MD
March 14, 2007



- Contingency plans will help minimize a pandemic's impact on businesses

Recent CDC Guidance on Antiviral Stockpiling*



- "Planning and preparing for a pandemic influenza requires action by every part of society, including individuals and families, communities, and private sector employers as well as all levels of government.
- "Employers will play a key role in protecting employees' health and safety, which in turn reduces the impact of a pandemic on the nation's health, the economy and society."
- "Businesses should have a plan in place for responding immediately at the first sign a pandemic to be sure the business can protect the health of the workforce and continue to operate."
"Employers may want to consider stockpiling antiviral drugs as one part of that plan."



About Tamiflu

TAMIFLU – Treatment



- Indicated for children and adults (≥ 1 years of age)
- Treatment should begin within 2 days of symptom onset
- Oral dosing – Adults (≥ 13 years of age): 75 mg capsule twice daily for 5 days
 - Dose reductions recommended for patients with renal impairment
- Oral dosing – Children (< 13 years of age): 30/45/60 or 75 mg (based on weight) twice daily for 5 days
 - Each bottle of oral suspension is supplied with a bottle adapter and oral dispenser

TAMIFLU – Treatment



- TAMIFLU significantly reduces duration of influenza^{a,b}
- When initiated within 48 hours, TAMIFLU significantly reduced flu duration by 1.3 days (30%) versus placebo ($P < 0.001$)^a
- Symptom relief was defined as the first 24-hour period in which all influenza symptoms were described as mild or none^a

a. Tamiflu® (oseltamivir phosphate) package insert. Nutley, NJ: Roche Laboratories Inc.; November 2006.

b. Nicholson KG, Aoki FY, Osterhaus ADME, et al. Efficacy and safety of oseltamivir in treatment of acute influenza: a randomised controlled trial. *Lancet*. 2000; 355:1845-1850.

TAMIFLU – Prophylaxis In Adults



- For postexposure prophylaxis:
 - 75 mg capsule once daily for 10 days
 - Administration should begin within 2 days of exposure to an infected close contact during a seasonal outbreak
- For seasonal prophylaxis:
 - 75 mg capsule once daily during a seasonal outbreak for up to 6 weeks
 - Adverse events were qualitatively very similar to those seen in the treatment studies, despite a longer duration of dosing
 - Duration of protection lasts for as long as dosing is continued

TAMIFLU – Pediatric Postexposure Prophylaxis



- Oral dosing: 30/45/60/or 75 mg (based on weight) once daily for 10 days
- The safety and efficacy of TAMIFLU for prophylaxis of influenza in pediatric patients younger than 1 year of age has not been established
- Prophylaxis in patients 1 to 12 years of age has not been evaluated longer than 10 days' duration
- Prophylaxis therapy should begin within 2 days of exposure

Safety of Neuraminidase Inhibitors: Oseltamivir



- Clinical trials show oseltamivir to be safe and well tolerated in most populations^a
- Prior to its launch, TAMIFLU was studied in more than 4,000 patients in clinical trial settings. In adult prevention trials, some patients were on TAMIFLU for up to six weeks^b
- In treatment studies of TAMIFLU in adult patients, the most frequently reported adverse events were mild to moderate transient nausea or vomiting^c
 - Premature discontinuation of TAMIFLU use in clinical trials due to nausea or vomiting occurred in less than 1% of patients^c

Refer to the full product information for complete indications and precautions before prescribing.

a. Nicholson KG, Aoki FY, Osterhaus ADME, et al. Efficacy and safety of oseltamivir in treatment of acute influenza: a randomised controlled trial. *Lancet*. 2000; 355:1845-1850. **b.** Roche Pandemic Planning Toolkit Web site. What is the efficacy and safety profile on TAMIFLU? Available at: <http://www.pandemictoolkit.com/about-tamiflu/about-efficacyoftamiflu.aspx>. Accessed October 10, 2006. **c.** Harper SA, Fukuda K, Uyeki TM, Cox NJ, Bridges CB. Centers for Disease Control and Prevention. Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR*. 2005;54(RR-8):1-40.

Important Safety Information for TAMIFLU[®] (oseltamivir phosphate)



● Treatment

- Adult patients: ($\geq 1\%$): nausea, vomiting and other events (bronchitis, insomnia and vertigo) reported more frequently compared with placebo
- Pediatric patients (1-12 yo): ($\geq 1\%$): vomiting and other events (abdominal pain, epistaxis, ear disorder, conjunctivitis)
- Self-injury and delirium reported, mostly from Japan, and primarily among pediatric patients
 - TAMIFLU's contribution to these events is unknown
 - Patients should be monitored throughout treatment period

● Prophylaxis

- Adult patients: ($\geq 1\%$): nausea, vomiting, diarrhea, abdominal pain, dizziness, headache, insomnia. AEs similar to treatment
- Pediatric patients (1-12 yo): ($\geq 1\%$): AEs consistent with treatment studies; GI most frequent

Refer to the full product information for complete indications and precautions before prescribing.
Tamiflu[®] (oseltamivir phosphate) package insert. Nutley, NJ: Roche Laboratories Inc.; November 2006.

Important Safety Information for TAMIFLU[®] (oseltamivir phosphate) (cont.)



- No evidence for efficacy of TAMIFLU in any other illness than influenza A and B
- Treatment patients should be 1 year and older; symptomatic for no more than 2 days
- TAMIFLU is not a substitution for vaccination; early, annual vaccination is recommended
 - Treatment efficacy in high-risk patients not established (chronic cardiac, respiratory disease)
- No differences in incidence of complications between treatment and placebo groups in this population
- Safety and efficacy of repeated treatment of prophylaxis courses not studied
- Rare cases of anaphylaxis and serious skin reactions, including toxic epidermal necrolysis, Stevens-Johnson syndrome and erythema multiforme, have been reported post-marketing
- Concurrent use of TAMIFLU with live attenuated influenza vaccine (LAIV) intranasal has not been evaluated
 - LAIV should not be administered 2 weeks prior or 48 hours after TAMIFLU administration
 - Trivalent inactivated influenza vaccine can be administered any time relative to the use of TAMIFLU

Refer to the full product information for complete indications and precautions before prescribing.
Tamiflu[®] (oseltamivir phosphate) package insert. Nutley, NJ: Roche Laboratories Inc.; November 2006.

TAMIFLU Shelf Life and Storage



- Product shelf life is 5 years^a
- TAMIFLU capsules are supplied in blister packages of 10 (NDC 0004-0800-85)^b
 - They are 75 mg grey/light yellow hard gelatin capsules. "Roche" is printed in blue ink on the grey body, and "75 mg" is printed in blue ink on the light yellow cap^b
- TAMIFLU capsules must be stored at 25° Celsius (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F)^b
- Storage of TAMIFLU must adhere to storage guidelines of United States Pharmacopeia (USP)^b

a. The Threat of and Planning for Pandemic Flu: *Hearings Before the Subcommittee on Health of the House Committee on Energy and Commerce*. 109th Cong. 1st Sess. (2005) (statement of Dominick A. Iacuzio, Ph.D. Medical Director, Hoffmann-La Roche Inc.)

b. Tamiflu® (oseltamivir phosphate) package insert. Nutley, NJ: Roche Laboratories Inc.; November 2006.



Roche Antiviral Protection Program For Corporate Stockpiling

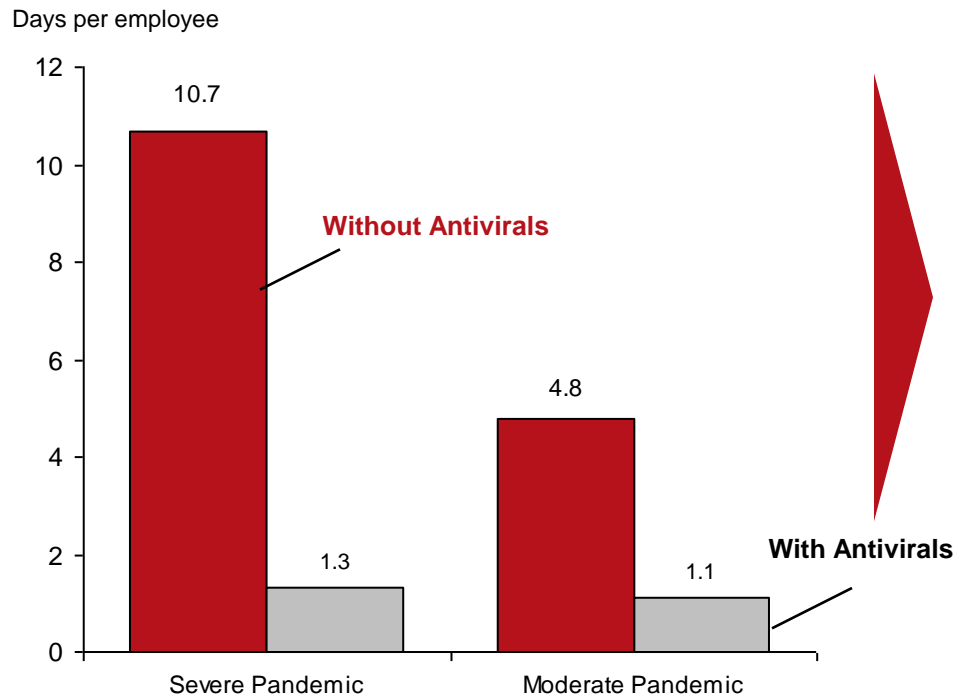
Potential Impact of Antivirals: Average U.S. Firm

Model is customizable to specific industry or employer

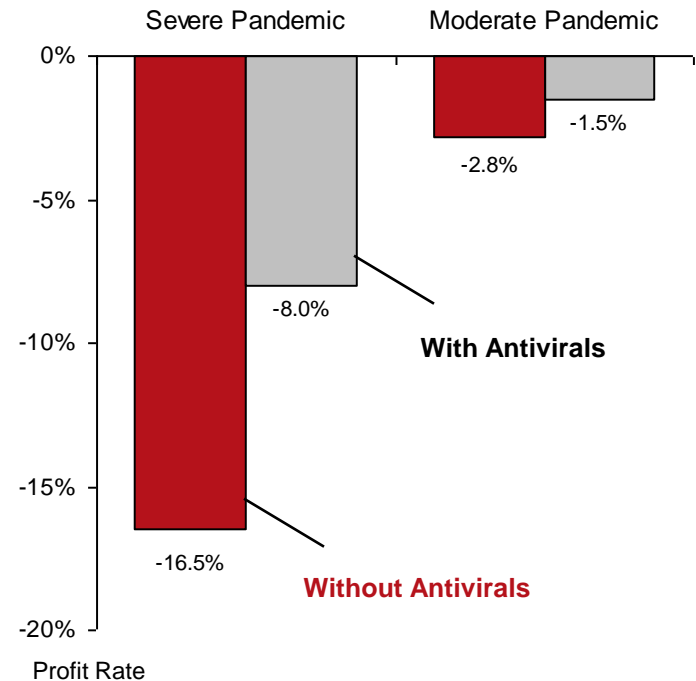


Antivirals may significantly reduce the severity of an influenza pandemic

Estimated Absenteeism in a Pandemic¹



Estimated Profitability in a Pandemic²



Disclaimer: Estimates provided by pandemic specialists at Surveillance Data Inc.;
To date, results from clinical studies in humans are not available

1. Pandemic Influenza Planning Model; SDI, February 2008 (Average firm)

2. "Pandemic Influenza Risk Management for Employers", Milliman Consultants and Actuaries, May 2007 (Average firm)

Roche Antiviral Protection Program: Overview

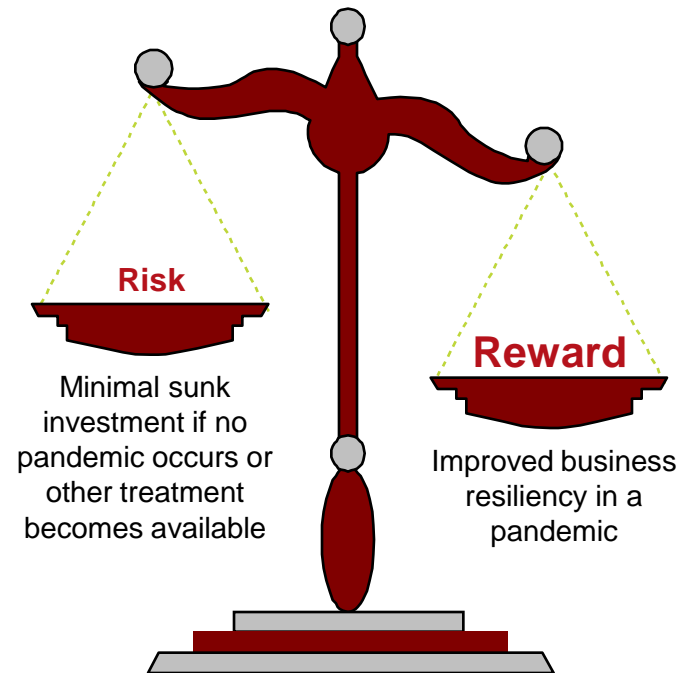


To address the risk reward trade off, Roche has developed a cost effective offering allowing greater access to antivirals

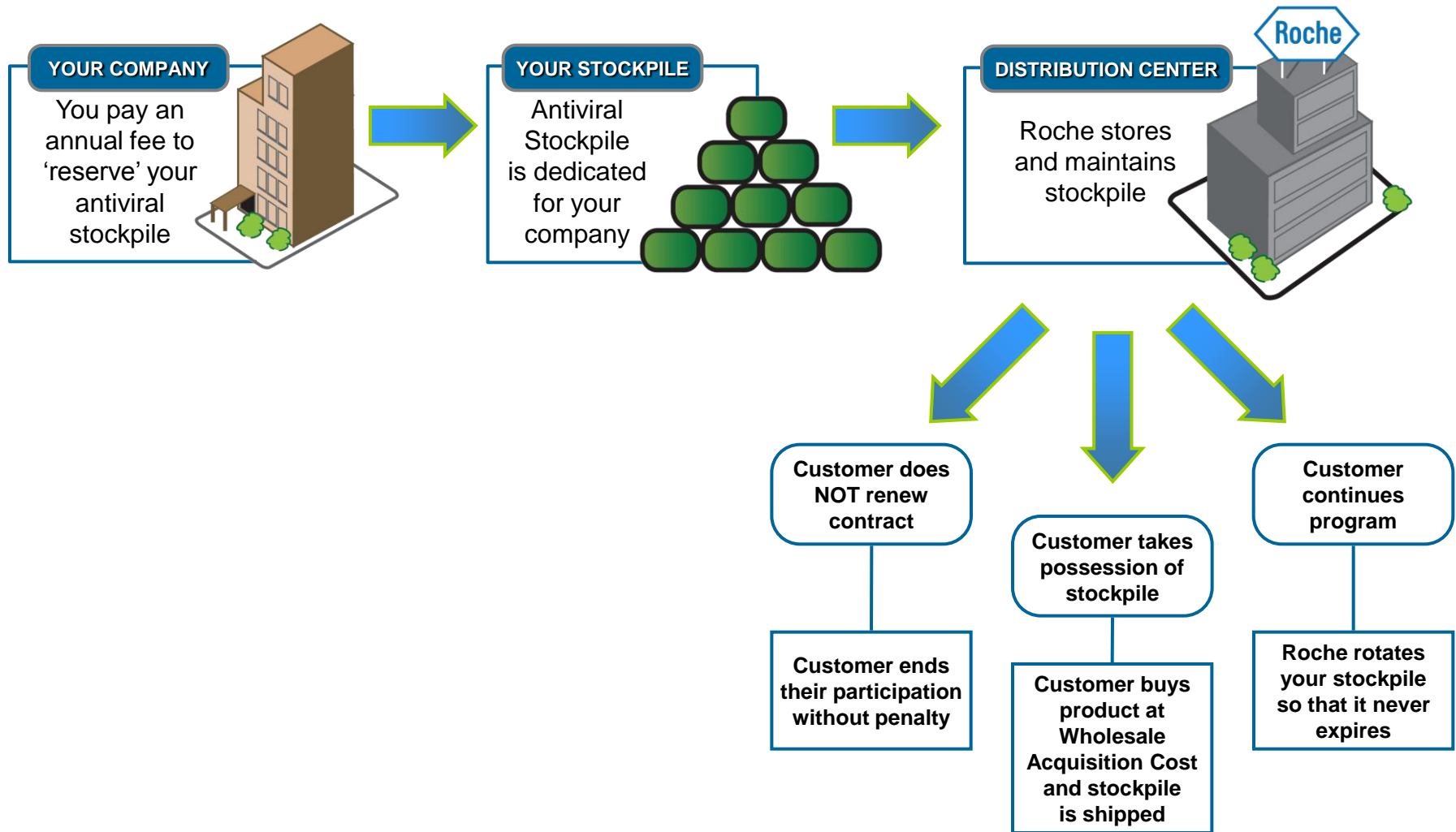
Roche Antiviral Protection Program

- The customer agrees to an annual contract that dedicates a Roche maintained stockpile for the corporation
- Low annual fee with the option to renew at the end of each year¹ for corporations enrolling in the program by 6/30/09.
- A usage fee is charged if the corporation takes possession of the product
- The customer has the right to terminate the contract at any time for no additional fee
- Stock is rotated as the product reaches expiry for no additional fee

The New Risk-Reward Tradeoff



RAPP Process Flowchart



Program Details



ROCHE ANTIVIRAL PROTECTION PROGRAM

1. Product

NDC	DESCRIPTION	UNIT OF MEASURE
0004-0800-80	Antiviral Capsules, 75 mg, Blister Pack 10	NDC

2. Pricing and Quantity

Customers will be eligible to receive pricing on product

NDC	DESCRIPTION	Program Fees
0004-0800-80	Antiviral Capsules, 75 mg, Blister Pack 10	Annual Fee: \$6 Usage Fee: WAC ¹ at time of delivery to corporation

3. Additional Purchase Conditions

- At contract initiation, the customer pays the “annual fee” and gains dedicated stockpile
- Roche maintains and rotates dedicated stockpile
- If the corporation decides to opt out, there are no further obligations
- If the corporation decides to continue, they will pay an annual fee yearly
- If corporation takes delivery of product, they will be billed the “usage fee”
- The product will have a minimum of 1 year remaining when shipped to corporation
- The terms of this document are valid **only** for the period ending June 30, 2009

1. “Wholesale Acquisition Cost” or “WAC” is the Roche published list price to Wholesalers and is subject to change by Roche. Sept. 2008 WAC is \$81.36 per unit of sale.



Thank You



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