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# AVIAN INFLUENZA

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An Analysis of the Current Status, Risks and Responses

**TABLE OF CONTENTS**

1. Overview	5
1.1 Statement of Report	5
1.2 Scope of Report	5
1.3 Objectives	5
1.4 Methodology	6
1.5 Executive Summary	6
2. The Basics of Human Influenza	9
2.1 Influenza, the Disease	9
2.1.1 Symptoms	9
2.1.2 Transmission	9
2.1.3 Public Health Factors	10
2.1.4 Influenza Diagnosis	10
2.2 Influenza Viruses	11
2.2.1 Types, Subtypes and Strains	11
2.2.1.1 Influenza Type A and its Subtypes	12
2.2.1.2 Highly Pathogenic versus Lowly Pathogenic Avian Influenza A Viruses	13
2.2.1.3 Human Influenza Viruses and Avian Influenza A Viruses	13
2.2.1.3.1 Influenza A H5	13
2.2.1.3.2 Influenza A H7	13
2.2.1.3.3 Influenza A H9	13
2.2.1.4 Influenza Type B	14
2.2.1.5 Influenza Type C	14
2.2.2 How Influenza Viruses Change: Drift and Shift	14
2.2.3 Seasons and Human Influenza	15
2.2.4 Risk Factors and Human Influenza	16
2.2.5 Human Influenza Complications, Comorbidities and Dangers	16
2.2.5.1 Flu complications in children and teenagers	17
2.2.6 Human Influenza Prognosis	17
2.3 Pandemic Influenza	18
2.4 How Influenza Viruses Change	18
3. The Basics of Avian Influenza	19
3.1 Avian Influenza in Birds	19
3.1.1 Avian Influenza Outbreaks in Poultry	20
3.1.2 More Information About Avian Influenza Viruses	21
3.2 Transmission of Influenza A Viruses between Animals and People	21
3.3 Avian Influenza Infection in Humans	22
3.3.1 Instances of Avian Influenza Infection in Humans	22
3.3.2 Symptoms of Avian Influenza in Humans	23
3.3.3 Antiviral Agents for Influenza	23
3.4 Avian Influenza (H5N1)	23
3.4.1 Avian Influenza (H5N1) Outbreaks	23
3.5 All Types of Avian Influenza Worldwide Outside of Asia	25
3.5.1 Canada	25
3.5.2 Netherlands	26
3.5.3 United States	26
3.5.3.1 Delaware	26
3.5.3.2 Texas	26
3.5.3.3 Maryland	26
3.5.3.4 International Response	27
3.5.3.5 Available Options	27
4. Epidemiology of Avian Influenza	28
4.1 Worldwide Avian Influenza	29
4.2 H5N1 Avian Influenza: Timeline	32
4.3 U.S. Avian Influenza	37
5. Influenza Diagnosis and Laboratory Issues	38
5.1 "Classic" Methods for Influenza Diagnosis	38
5.2 Example Lab: Yale New Haven Hospital (YNHH)	40
5.3 Conventional PCR Assay for Sub-typing Influenza Virus	41
5.3.1 Gel Analysis	41
5.4 Real Time TaqMan PCR	43
5.4.1 From PacMan to TaqMan-A Computer Game Revisited	43
5.4.2 The Advantages of Real-Time TaqMan PCR Over Conventional Quantitative PCR	45
5.5 Example Strategy for Avian Influenza	46

- 5.6 Laboratory Safety Issues for H5N1 Viruses 46
  - 5.6.1 Biosafety Level 3 46
  - 5.6.2 Biosafety Level 3-Ag 51
  - 5.6.3 CDC Criteria for Testing 52
  - 5.6.4 What Samples Are Needed? 52
- 6. Preparedness 53
  - 6.1 Education 53
  - 6.2 Ethical and Legal Issues 53
  - 6.3 Worldwide 55
    - 6.3.1 Overarching Goals, Objectives and Actions for WHO and National Authorities, by Phase 56
      - 6.3.1.1 Interpandemic Period, Phase 1-Overarching Goal 56
      - 6.3.1.2 Interpandemic Period, Phase 2-Overarching Goal 58
      - 6.3.1.3 Pandemic Alert Period, Phase 3-Overarching Goal 61
      - 6.3.1.4 Pandemic Alert Period, Phase 4-Overarching Goal 64
      - 6.3.1.5 Pandemic Alert Period, Phase 5-Overarching Goal 67
      - 6.3.1.6 Pandemic Period, Phase 6-Overarching Goal 70
    - 6.3.2 Recommendations for Non-Pharmaceutical Public Health Interventions 75
  - 6.4 U.S. 78
    - 6.4.1 U.S. National Plan 78
    - 6.4.2 U.S. Locally 87
      - 6.4.2.1 Community Preparedness Leadership and Networking 87
      - 6.4.2.2 Surveillance 88
      - 6.4.2.3 Public Health and Clinical Laboratories 88
      - 6.4.2.4 Healthcare and Public Health Partners 89
      - 6.4.2.5 Infection Control and Clinical Guidelines 90
      - 6.4.2.6 Vaccine Distribution and Use 90
      - 6.4.2.7 Antiviral Drug Distribution and Use 90
      - 6.4.2.8 Community Disease Control and Prevention 91
      - 6.4.2.9 Public Health Communications 91
      - 6.4.2.10 Workforce Support: Psychosocial Considerations and Information Needs 92
      - 6.4.2.11 State Plans 92
  - 6.5 The Hospital Response 92
    - 6.5.1 Introduction 92
    - 6.5.2 Key Assumptions 93
    - 6.5.3 Arrival 93
    - 6.5.4 Triage 94
    - 6.5.5 Isolation 95
    - 6.5.6 Patient Movement 96
    - 6.5.7 Communication 97
    - 6.5.8 Medical Evaluation 98
    - 6.5.9 Diagnosis 98
    - 6.5.10 Treatment 98
    - 6.5.11 Potential for Surge 99
  - 6.6 Business Preparedness 100
  - 6.7 School Preparedness 102
  - 6.8 Individual Preparedness 105
- 7. Economics of Avian Influenza 109
  - 7.1 Impact on Governments 109
    - 7.1.1 Worldwide Economic Impact of Avian Flu 109
    - 7.1.2 U.S. Nationally 113
  - 7.2 Impact of a Pandemic 125
    - 7.2.1 Supply Side Effect 125
    - 7.2.2 Demand Side Effect 126
- 8. Fighting the Flu 128
  - 8.1 The Worldwide Pharmaceutical Industry 128
    - 8.1.1 FDA Approved Vaccines: Tamiflu and Relenza 129
    - 8.1.2 Stockpiling 129
    - 8.1.3 Total Avian Influenza Drug Market Size and Growth 129
  - 8.2 Funding 129
  - 8.3 Antiviral Agents for Influenza: Background Information 129
    - 8.3.1 Introduction 129
      - 8.3.1.1 Antiviral Usage Recommendation-2005-06 129
      - 8.3.1.2 Neuraminidase Inhibitors (Zanamivir, Oseltamivir) 130
      - 8.3.1.3 How do the Neuraminidase Inhibitor Drugs Work? 130
      - 8.3.1.4 How Effective are the Neuraminidase Inhibitor Drugs? 130
        - 8.3.1.4.1 Treatment 130
        - 8.3.1.4.2 Chemoprophylaxis 130

- 8.3.4.3 Side Effects of the Neuraminidase Inhibitor Drugs 130
- 8.3.4.4 Antiviral Resistance to the Neuraminidase Inhibitor Drugs 131
- 8.3.5 Adamantane Derivatives (Amantadine, Rimantadine) 131
- 8.3.5.1 Antiviral Activity: How do the Adamantane Drugs Work? 131
- 8.3.5.2 How Effective are the Adamantane Drugs? 131
- 8.3.5.2.1 Treatment 131
- 8.3.5.2.2 Chemoprophylaxis 131
- 8.3.5.3 Side Effects of the Adamantane Drugs 132
- 8.3.5.4 Antiviral Resistance 132
- 8.3.6 Adamantanes Compared with Neuraminidase Inhibitors 132
- 8.3.7 Anti-Avian Influenza Drugs, Generics and Patents 133
- 8.3.7.1 Taiwan 133
- 8.3.7.2 India 134
- 8.3.7.3 Other Countries 135
- 8.3.8 Regulatory Issues 135
- 8.3.9 New Anti-Avian Influenza Therapy 135
- 8.3.10 Pharmaceutical Business Perspective 136
- 8.3.10.1 A Market Dominated by GSK and Roche 136
- 8.3.10.2 Generic Presence 136
- 8.3.10.3 Challenging Tamiflu 137
- 8.4 Other Treatment Requirements 137
- 8.5 Business Opportunities 138

## INDEX OF FIGURES

- Figure 2.1: Influenza Subtypes 12
- Figure 2.2: Timeline of Emergence of Influenza A Viruses in Humans 15
- Figure 2.3: Model of the Emergence of a Pandemic Virus 18
- Figure 3.1: Map of H5N1 Instances and Asian Migratory Bird Zones 24
- Figure 3.2: Map of H7N3 in British Columbia 25
- Figure 4.1: Nations with Confirmed Cases of H5N1 Avian Influenza 29
- Figure 4.2: World: Affected Areas with Confirmed Cases of H5N1 Avian Influenza Since 2003 30
- Figure 4.3: World: Affected Areas with Confirmed Cases of H5N1 Avian Influenza Since January 2006 30
- Figure 4.4: World: Areas Reporting Confirmed Occurrence of H5N1 Avian Influenza in Poultry and Wild Birds Since January 2006 31
- Figure 4.5: World: Areas Reporting Confirmed Occurrence of H5N1 Avian Influenza in Poultry and Wild Birds Since 2003 31
- Figure 4.6: Waterfowl Flyways of North America 37
- Figure 5.1: FDA-approved Kit-based Test 38
- Figure 5.2: Immunofluorescence-based Detection 39
- Figure 5.3: Uninfected and Infected Tissue Cultures 39
- Figure 5.4: TEM of Negatively Stained Influenza Virions (from Cultures) 40
- Figure 5.5: PCR Assay Graphic 41
- Figure 5.6: PCR assay 42
- Figure 5.7: "Amplicon" Generation 42
- Figure 5.8: The TaqMan 5'-3' Nuclease Assay 43
- Figure 5.9: TaqMan Amplification Plot 44
- Figure 5.10: TaqMan Fluorescent Reaction Components 45
- Figure 5.11: Biosafety Level 3-Ag-Full Tyvek Body Suit 51
- Figure 6.1: Signage: Informing Staff 93
- Figure 6.2: Signage: Informing Patients 94
- Figure 6.3: Respiratory Etiquette Kit 95
- Figure 6.4: Isolation 96
- Figure 6.5: Communication Scheme 97
- Figure 6.6: Surge 99

## INDEX OF TABLES

- Table 2.1: Probability of Influenza Diagnosis Using Office-Based Testing 11
- Table 2.2: Prescribing Guidelines for Treating Influenza 11
- Table 2.3: Influenza Virus Types 12
- Table 2.4: H5N1 Cases and Deaths, 2003-2005 15
- Table 4.1: Phase 3 is the Current WHO Phase of Alert 28
- Table 4.2: Cumulative Number of Confirmed Human Cases of Avian Influenza A/(H5N1) Reported to WHO, 2003-2006 29
- Table 4.3: Early (Pre Wave I) Events in Asia, 1996, 1997 and 2003 32
- Table 4.4: Wave I 32
- Table 4.5: Wave II 33
- Table 4.6: Wave III 34
- Table 5.1: Methods for Influenza Diagnosis 38

Table 5.2: Summary of Current Clinical Virology Laboratory Tests for Influenza	40
Table 6.1: Interpandemic Period, Phase 1-Planning and Coordination	56
Table 6.2: Interpandemic Period, Phase 1-Prevention and Containment	56
Table 6.3: Interpandemic Period, Phase 1-Health System Response	57
Table 6.4: Interpandemic Period, Phase 1-Communications	58
Table 6.5: Interpandemic Period, Phase 2-Planning and Coordination	58
Table 6.6: Interpandemic Period, Phase 2-Situation Monitoring and Assessment	59
Table 6.7: Interpandemic Period, Phase 2-Prevention and Containment	59
Table 6.8: Interpandemic Period, Phase 2-Health System Response	60
Table 6.9: Interpandemic Period, Phase 2-Communications	61
Table 6.10: Pandemic Alert Period, Phase 3 - Planning and Coordination	61
Table 6.11: Pandemic Alert Period, Phase 3-Situation Monitoring and Assessment	62
Table 6.12: Pandemic Alert Period, Phase 3-Prevention and Containment	62
Table 6.13: Pandemic Alert Period, Phase 3-Health System Response	63
Table 6.14: Pandemic Alert Period, Phase 3-Communications	64
Table 6.15: Pandemic Alert Period, Phase 4-Planning and Coordination	64
Table 6.16: Pandemic Alert Period, Phase 4-Situation Monitoring and Assessment	65
Table 6.17: Pandemic Alert Period, Phase 4-Prevention and Containment	65
Table 6.18: Pandemic Alert Period, Phase 4-Health System Response	66
Table 6.19: Pandemic Alert Period, Phase 4-Communications	67
Table 6.20: Pandemic Alert Period, Phase 5-Planning and Coordination	67
Table 6.21: Pandemic Alert Period, Phase 5-Situation Monitoring and Assessment	68
Table 6.22: Pandemic Alert Period, Phase 5-Prevention and Containment	68
Table 6.23: Pandemic Alert Period, Phase 5-Health System Response	69
Table 6.24: Pandemic Alert Period, Phase 5-Communications	70
Table 6.25: Pandemic Period, Phase 6-Planning and Coordination	70
Table 6.26: Pandemic Period, Phase 6-Situation Monitoring and Assessment	71
Table 6.27: Pandemic Period, Phase 6-Prevention and Containment	72
Table 6.28: Pandemic Period, Phase 6-Health System Response	73
Table 6.29: Pandemic Period, Phase 6-Communications	74
Table 6.30: National Measures (Living or Traveling Within an Affected Country)	75
Table 6.31: International Measures (for Entering or Exiting a Country)	77
Table 6.32: State and Local Planning Checklist-Community Preparedness Leadership and Networking	87
Table 6.33: State and Local Planning Checklist-Surveillance	88
Table 6.34: State and Local Planning Checklist-Public Health and Clinical Laboratories	89
Table 6.35: State and Local Planning Checklist-Healthcare and Public Health Partners	89
Table 6.36: State and Local Planning Checklist-Healthcare and Public Health Partners	90
Table 6.37: State and Local Planning Checklist-Vaccine Distribution and Use	90
Table 6.38: State and Local Planning Checklist-Antiviral Drug Distribution and Use	91
Table 6.39: State and Local Planning Checklist-Community Disease Control and Prevention	91
Table 6.40: State and Local Planning Checklist-Public Health Communications	91
Table 6.41: State and Local Planning Checklist-Workforce Support: Psychosocial Considerations and Information Needs	92
Table 6.42: Arrival	93
Table 6.43: Triage	94
Table 6.44: Isolation	95
Table 6.45: Patient Movement	96
Table 6.46: Communication	97
Table 6.47: Medical Evaluation	98
Table 6.48: Diagnosis	98
Table 6.49: Treatment	98
Table 6.50: Surge	99
Table 6.51: Plan for the Impact of a Pandemic on Your Business	100
Table 6.52: Plan for the Impact of a Pandemic on Your Employees and Customers	101
Table 6.53: Establish Policies to be Implemented During a Pandemic	101
Table 6.54: Allocate Resources to Protect Your Employees and Customers During a Pandemic	101
Table 6.55: Communicate to and Educate Your Employees	102
Table 6.56: Coordinate with External Organizations and Help Your Community	102
Table 6.57: Planning and Coordination:	103
Table 6.58: Continuity of Student Learning and Core Operations	104
Table 6.59: Infection Control Policies and Procedures	104
Table 6.60: Communications Planning	104
Table 6.61: Items to have on Hand for an Extended Stay at Home	107
Table 6.62: Immunizations FAQ	107
Table 6.63: WHO Global Plan for Pandemic Preparedness	110
Table 7.1: Assumptions Underlying Estimates of the Supply-Side Impact of an Avian Flu Pandemic	126
Table 7.2: Assumed Declines in Demand, by Industry, in the Event of an Avian Flu Pandemic	127
Table 8.1: Top 30 Pharmaceutical and Biotech Companies Ranked by Healthcare Revenue ("Big Pharma")	128
Table 8.2: Recommended Daily Dosage of Influenza Antiviral Medications for Treatment and Prophylaxis	133
Table 8.3: Examples of Preparedness Supplies	138

## 1. Overview

### 1.1 Statement of Report

The purpose of this report is to understand the current status of avian influenza: its progress, the risks to human populations and the public health response to the crisis. The specific objectives of this analysis are to:

- Examine the epidemiology of avian influenza.
- Describe the diagnosis and treatments available for influenza.
- Discuss preparedness for a worldwide pandemic.
- Evaluate the world economic impact of an influenza epidemic.

### 1.2 Scope of Report

The U.S., Asia and Europe are the focus of this study. Primary attention is paid to the clinical market segment and, separately, to the medical procedures and supplies for the influenza infection control market. An analysis of the technology trends and developing areas of influenza infection science is provided, along with a review of the market for pharmaceutical agents, vaccines and hospital supplies in clinical use. Activity in research—including the factors that influence infection control—are addressed in this review. Also discussed are changes that have stimulated this disease and patterns of information processing in assessing its spread. Several subjects related to the major elements of influenza treatment such as disposable plastic supplies, needles and lancets are discussed only briefly because they are considered entirely different fields or markets. Fuller explorations of these areas of interest can be found in other TriMark Publications reports such as *Disposable Syringe Markets*, *Disposable Medical Supplies* and *Molecular Diagnostics Markets* at <http://www.trimarkpublications.com>.

### 1.3 Objectives

The goal of this report is to review the potential threat of a human influenza pandemic resulting from the avian flu virus. It defines the responses that are now being undertaken worldwide by governmental authorities to contain the spreading bird flu. Specifically, this study contains:

- A comprehensive overview of the several categories of anti-influenza technology platforms that are or will be revolutionizing flu related healthcare in hospitals.
- Full descriptions of the public health measures involved in controlling the spread of avian influenza and the prevention of cross infection to humans.
- Analysis of the technological approaches undertaken by various world governments, as well as industry and end-user response to these ideas.
- Regulatory issues and legislation affecting use and marketing of influenza prevention and treatment products.
- Forecasts for each category of infection control.

The analysis will allow the reader to:

- Evaluate the effect of strategic factors and technology driven measures for controlling avian flu and subsequent human infections.
- Investigate how cost-constraints and technological advances are driving change in the influenza market.
- Examine the structure of the avian flu response across the world and learn how to respond successfully to this challenge to human health.
- Assess the growth opportunities in all influenza-related treatments and preventative measures.
- Review the main approaches in each sector and plan a strategy in line with the strengths and weaknesses of the infection control measures.

## 1.4 Methodology

The information made available in this report is based upon a collection of government data made publicly available, as well as trade association reviews and company data. Additional data was obtained from proprietary databases. Moreover, this review is based upon interviews with medical professionals in the infectious disease field. They were queried, some several times, about healthcare strategies as well as their overall thoughts about the possible responses to a flu pandemic. Descriptions of the laboratories and patient facilities were derived from interviews with laboratory directors and medical technologists in these areas. Clinical aspects of influenza treatment and diagnosis were discussed with physicians and clinicians directly involved with patient care.

Other sources of information included trade association publications and meetings, product brochures and catalogs, and company literature. Approaches for responding to an influenza epidemic threat were adapted from recommendations of the World Health Organization (WHO), and guidelines published by the American Family Physicians, and the *Journal of the American Academy of Family Physicians*. Annual reports, 10k filings and financial reports were used as the basis for data reported on publicly held companies.

Finally, some of the information was taken from Biotechnology Associates' databases and from TriMark's private data stores. The information set forth in this study was obtained from sources that we believe to be reliable, but we do not guarantee the accuracy, adequacy or completeness of any information, omission or for the results obtained by the use of such information. TriMark does not guarantee its accuracy, adequacy or completeness of any information, omission or for the results obtained by the use of such information.

## 1.5 Executive Summary

Influenza, commonly known as the flu, is an infectious disease that infects birds and mammals (primarily of the upper airways and lungs in mammals) and is caused by an RNA virus. Flu rapidly spreads around the world in seasonal epidemics, killing millions of people in pandemic years and hundreds of thousands in non-pandemic years. Three influenza pandemics in the 20th century—each following a major genetic change in the virus—killed millions of people all over the world. The world's current major influenza pandemic threat is H5N1; but it is at present mostly in birds, not in people.

Only influenza A viruses infect birds, and all known subtypes of influenza A viruses can infect birds. However, there are substantial genetic differences between the influenza A subtypes that typically infect birds and those that infect both people and birds. Three prominent subtypes of the avian influenza A viruses that are known to infect both birds and people are H5, H7 and H9.

Influenza viruses are dynamic and are continuously evolving. Influenza viruses can change in two different ways: antigenic drift and antigenic shift. Influenza viruses are changing by antigenic drift all the time, but antigenic shift happens only occasionally. Influenza type A viruses undergo both kinds of changes; influenza type B viruses change only by the more gradual process of antigenic drift. Some relevant facts include:

- Influenza has been causing recurrent epidemics of febrile respiratory disease every █ to █ years for at least █ years.
- Over █ deaths in U.S. per epidemic.
- Over █% of mortality is in persons aged █ and older.
- Attack rates of █% to █% in general population.
- Nursing home attack rates of █%.
- There is always the potential for pandemics.

During the winter months, influenza is one of the most common illnesses among patients of primary care physicians, with as many as █ in █ adults infected each year. The prevalence of influenza is an important factor to consider. Prevalence varies from less than █% among patients with febrile respiratory illness before or after the influenza season, to approximately █% to █% during the early and late influenza season ("shoulder" season), to █% or more during the peak of influenza season. The proportion of patients with influenza A versus influenza B varies each year, as does the seasonal peak. For example, in the 2004-2005 flu season, the peak occurred in mid-February; █% of patients with suspected influenza were diagnosed with the illness, and approximately one third of these patients had

influenza B. During the 2003-2004 flu season, however, the peak occurred in mid-December, and although █% of patients with suspected influenza were diagnosed with the disease, only █% had influenza B.

The U.S. Centers for Disease Control and Prevention (CDC) releases annual guidelines for the prevention of influenza and the appropriate use of antiviral agents. The cost-effectiveness of empiric treatment with antiviral agents for appropriate patients with influenza is high. Oseltamivir (Tamiflu) therapy is recommended for all patients during a regional epidemic when the probability of influenza is over █%. Treatment is also recommended with amantadine (Symmetrel), rimantadine (Flumadine), or oseltamivir when the likelihood of influenza is high.

Domesticated birds may become infected with avian influenza virus through direct contact with infected waterfowl or other infected poultry, or through contact with surfaces (such as dirt or cages) or materials (such as water or feed) that have been contaminated with virus. People, as well as inanimate objects such as vehicles and bird cages, can be vectors for the spread of influenza virus from one farm to another. When this happens, avian influenza outbreaks can occur among poultry.

Influenza A viruses have infected many different animals, including ducks, chickens, pigs, whales, horses and seals. However, certain subtypes of influenza A virus are specific to certain species—except for birds—which are hosts to all known subtypes of influenza A. Subtypes that have caused widespread illness in people either in the past or currently are H3N2, H2N2, H1N1 and H1N2. H1N1 and H3N2 subtypes also have caused outbreaks in pigs, and H7N7 and H3N8 viruses have caused outbreaks in horses. Although avian influenza A viruses usually do not infect humans, the WHO reports more than █ confirmed cases of human infection with avian influenza viruses since █. However, experts at WHO and elsewhere believe that the world is now closer to another influenza pandemic than at any time since █, when the last of the previous century's three pandemics occurred.

A practical strategy for avian influenza involves using parallel assays:

- Influenza A/B real-time assay (M1 and NS1 targets).
- CDC subtype-specific real-time assays, H1, H3, H5 and H7 (HA target).
- Conventional PCR sub-typing assay (H1, H3, H5).
- Culture when H5N1 ruled-out.

Preparing for a pandemic requires the leveraging of all instruments of national power, as well as coordinated action by all segments of government and society. Influenza viruses do not respect the distinctions of race, sex, age, profession or nationality, and are not constrained by geographic boundaries. The next pandemic is likely to come in waves, each lasting months, and pass through communities of all size across the world.

U.S. national strategy will provide a framework for future U.S. government planning efforts that is consistent with the national security strategy and the national strategy for homeland security. It recognizes that preparing for and responding to a pandemic cannot be viewed as a purely federal responsibility, and that the nation must have a system of plans at all levels of government and in all sectors outside of government that can be integrated to address the pandemic threat.

The continuing outbreaks that began in late 2003 and early 2004 have been disastrous for the poultry industry in Asia; by mid-2005, more than █ birds had died or been destroyed and losses to the poultry industry are estimated to be in excess of USD \$█. There are two main categories of economic impacts associated with outbreaks of infectious diseases such as HPAI in poultry and a potential human influenza pandemic:

- Costs of sickness or death resulting from the disease outbreaks.
- Costs associated with public and private efforts to prevent the emergence or spread of the disease and to treat its effects.

The most direct impact on output would be through the effect of increased illness and mortality on the size and productivity of the world labor force. In addition, there will also be a general decline in labor productivity due to illness and sick leave among the labor force at large. Such productivity losses due to illness during normal annual influenza episodes are estimated to be ten times as large as all other flu-related costs combined. Other long-term impacts would play out as the increased costs of preventing and treating disease reduced savings and investment.



The impact on output at the national level would vary widely, depending on the extent of the epidemic, the country's demographic structure, the extent of unemployed resources and other key variables.

A severe pandemic would reduce the labor force. In [REDACTED], the U.S. labor force totaled [REDACTED] people. Under the assumption of an attack rate of [REDACTED]% and a case fatality rate of [REDACTED]—the same assumptions applied to the population as a whole—a severe pandemic would cause the deaths of more than one million labor force participants, or about [REDACTED]% of the labor force. Since growth in the labor force averaged [REDACTED]% during the 1948-2005 period, losing [REDACTED]% of the labor force would be equivalent to a pause of [REDACTED] year in the growth of the U.S. workforce. Under the assumptions for infection and mortality associated with the mild-pandemic scenario—an attack rate of [REDACTED]% and a fatality rate of just over [REDACTED]—the number of workers killed would be [REDACTED], or [REDACTED]% of the labor force.

Only two antiviral drugs, oseltamivir and zanamivir, have shown promise in treating avian influenza. Oseltamivir is licensed as Tamiflu and manufactured under patent by the Swiss firm Roche Laboratories in tablet form. A treatment course for Tamiflu includes ten pills taken over five days. Zanamivir is licensed as Relenza and manufactured by GlaxoSmithKline. Relenza is administered by oral inhalation and is not recommended for people with chronic lung problems. The U.S. Food and Drug Administration (FDA) has approved both antiviral drugs for treating influenza. Tamiflu has also been approved to prevent influenza infection.

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