Oklahoma Pandemic Influenza Management Plan

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July 1, 2005

Prepared by
Oklahoma State Department of Health
Pandemic Influenza Management Plan Committee

PUBLIC HEALTH RESPONSE TEAM

Oklahoma State Department of Health
James M. Crutcher, MD, MPH
Commissioner of Health

July 15, 2005

To Our Public Health Workforce and Partners:

Public health workers are being called on to address a seemingly increasing array of public health threats. Some are relatively contemporary concerns such as bioterrorism, whereas the impact of others is well documented in history. With influenza, we are beginning to see a merging of the two ends of the spectrum.

An epidemic of influenza predictably occurs every winter in the United States. Some influenza seasons are a little more challenging than others, but even when ample supplies of influenza vaccine are available, 25,000 – 50,000 persons die in our country each year as a result of influenza infection. Influenza is not a new problem, but the emergence of the H5N1 "bird flu" has captured many recent headlines. History has demonstrated that pandemic influenza has a cyclical occurrence, so the persisting and escalating threat of H5N1 influenza in Southeast Asia is placing new urgency on preparing for a possible influenza pandemic.

Most, if not all, of our public health infrastructure that has been bolstered through our terrorism preparedness and response efforts would be applied and tested should we need to respond to an influenza pandemic. We would institute our emergency operations procedures, enhance our epidemiologic and laboratory surveillance methods, activate plans for large-scale prophylaxis and care, and quickly and reliably provide risk communication to Oklahomans. A committee representing several program areas from the Oklahoma State Department of Health has worked to synthesize these elements and developed the *Oklahoma Pandemic Influenza Management Plan*. The Plan is intended to be a dynamic and "living" document that will be reviewed and revised on an annual basis. Please acquaint yourself and your staff with this plan as it would be "all hands on deck" should pandemic influenza become a reality.

Sincerely,

James M. Crutcher, M.D., M.P.H.
Commissioner of Health and
State Health Officer

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Executive Summary

The Oklahoma Pandemic Influenza Management Plan is intended to be dynamic and iterative. It consists of six essential elements of preparedness and response that would be integral in managing a potential influenza pandemic. The plan is designed to give a public health management response to such an event to assist and facilitate appropriate plans for a pandemic influenza at all levels. The six essential elements address: Command, Control and Management; Surveillance; Delivery of Vaccine; Delivery of Antiviral Medications; Emergency Response; and Risk Communication.

The Oklahoma Pandemic Influenza Management Plan and its appendices were developed to assist in the response to pandemic influenza. During and after an influenza pandemic, the prevention and preparedness activities facilitate the public health response and recovery components of the management plan.

The overall goal of the Oklahoma Pandemic Influenza Management Plan is to minimize serious illness and overall deaths and secondly, to minimize societal and infrastructure disruptions for the citizens of Oklahoma as a result of an influenza pandemic.

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The Pandemic Influenza Committee developed a management plan to address the public health response to a pandemic influenza event pursuant to recent novel virus alerts. In the past 300 years, there have been 10 documented pandemics of influenza A. The infamous "Spanish flu" of 1918-1919 resulted in 20 to 50 million deaths worldwide in a much less mobile society. The mortality rate during the more recent pandemics (in 1957 and 1968) was relatively low despite the high morbidity. Although supportive medical care and the availability of antibiotic therapy for secondary bacterial infections are factors to explain the "milder blow" of later pandemics, the causative influenza virus strains were less virulent. If a novel influenza strain emerges that is highly virulent, the rate of illness and death could rival previous pandemics despite modern healthcare technology. Beyond the human toll, an influenza pandemic will create significant social disruption and economic impact. The Centers for Disease Control and Prevention (CDC) estimate that the economic losses associated with future pandemics will total billions of dollars.

Influenza viruses have the ability to mutate, which can lead to genetic sequence realignment or reassortment. There are two main types of influenza virus mutation: antigenic drift and antigenic shift. Antigenic drift is a minor change that occurs frequently and causes the emergence of a new strain within a subtype. Antigenic drifts occur in both type A and B influenza viruses. The reason the composition of the annual influenza vaccine changes from year to year is due to antigenic drift. Antigenic shift is a major change caused by genetic recombination that results in the emergence of a novel virus strain that has not previously infected humans. Often, antigenic shift occurs in an animal influenza virus, which then allows the virus to be transmitted between animals and people. Antigenic shift occurs only in influenza type A viruses.

A real world threat for the next potential pandemic is the avian influenza H5N1 strain. This highly pathogenic avian influenza virus was first recognized in Hong Kong in 1997. Although aggressive measures were used in an attempt to eradicate bird reservoirs of the virus, there have been an increasing number and severity of recurrent poultry outbreaks in Asia. More troubling is the occurrence of bird-to-human transmission of the virus observed in three countries with a sobering case fatality rate of 55%. The New England Journal of Medicine recently published a report that provided strong clinical and epidemiologic evidence of H5N1 being transmitted from human-to-human in a limited familial case cluster[1]. This finding is especially alarming and fuels the global concern that the next influenza pandemic is imminent.

[1] *N Engl J Med* 2005 Jan 27; 352(4): 333-340.

If the next pandemic influenza strain mimics the virulence of the 1918 pandemic strain, the World Health Organization estimates that there could be 1.7 million deaths in the United States and 180 to 360 million deaths worldwide. These statistics seem overwhelming, but there are measures that can be taken now to mitigate the impact of the event. Public health officials at all levels of government have begun to develop strategies based on the following assumptions:

a) An effective response will require substantial emergency response interactions of agencies beyond health departments.

b) When the pandemic occurs, vaccines and antiviral medications will be in short supply and must be allocated on a priority basis.

c) Initial supplies of vaccine will be under the control of the federal government with states receiving a formula-based allotment.

d) Many geographic areas will be affected simultaneously.

e) The healthcare system will be overwhelmed to the extent that an altered standard of care will need to be temporarily adopted.

f) Secondary bacterial infections following influenza illness may stress antibiotic supplies.

g) Fear, fatigue, and psychological stress will prevent people from going to work and threaten the ability to maintain medical services and community infrastructure.

Developing this document is an important step in Oklahoma's preparation for pandemic influenza. The Oklahoma Pandemic Influenza Management Plan is intended to be a resource document for public health preparedness at the state, regional and local level. It is imperative that public health and all partners work together to define critical roles in the implementation of the state plan before the pandemic strikes. Areas addressed in this plan include disease surveillance, emergency management, vaccines and antivirals delivery, communication activities, and response coordination among multiple agencies. To the extent possible, the respective roles of the county health departments and the Oklahoma State Department of Health, Central Office will be outlined and revised as the plan evolves.

Purpose and Goals

1. Reduce morbidity and mortality among Oklahomans during a serious influenza season;
2. Minimize infrastructure disruption and subsequent economic impact caused by an influenza pandemic;
3. Assist and facilitate preparedness in the healthcare systems within our state;
4. Provide a comprehensive and dynamic plan that will be reviewed and updated on an annual basis; and
5. Assist and facilitate appropriate planning and response at the local, regional and state level.

Many factors must be considered when estimating the potential impact of the next influenza pandemic. Some of these include the virulence of the circulating virus, how rapidly the virus spreads, primary age group affected, and the effectiveness of public health intervention and response. Nonetheless, estimates of the health and economic impact can help direct medical response plans and guide public health policy decisions.

During a normal influenza season, 5-20% of the population becomes ill and the highest rates of influenza-related complications occur in very young children and the elderly. During severe epidemics, the attack rate may be as high as 30-50% with a higher proportion of serious illness and deaths occurring in adults less than 65 years old. During the 1918 pandemic, young adults had the highest mortality rates, with nearly one-half the influenza-related deaths occurring in those 20-40 years old.

An estimate of the number of deaths and hospitalizations that may occur in Oklahoma during the next influenza pandemic is provided in the following tables. The estimates were performed using the FluAid 2.0 modeling software available online through the National Vaccine Program office, http://www2a.cdc.gov/od/fluaid/default.htm. The numbers were generated using the 1999 US Bureau of Census data (state population of 3,317,091). Based on the model, using a

proportion representing 15% to 35% of the state's population clinically affected by influenza, it is projected that between 5,875 and 13,709 Oklahomans would require hospitalization and between 1,367 and 3,188 Oklahomans would die during an influenza pandemic. Local county health departments are encouraged to enter their respective county census data to provide estimates to assist with local planning efforts. It is important to note that the model does not allow for the mitigating effects of an effective vaccine or antiviral medications.

Estimated Deaths in Oklahoma from Pandemic Influenza

		Attack rates	
0-18 years of age most likely #	14	23	32
Minimum	8	13	19
Maximum	190	317	444
19-64 years of age most likely #	624	1040	1456
Minimum	89	149	208
Maximum	1172	1953	2734
65+ years of age most likely #	729	1215	1700
Minimum	707	1178	1649
Maximum	904	1506	2109
Total: most likely	1367	2278	3188
Range:	804 -2266	1340 - 3776	1876 - 5287

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Estimated Hospitalizations in Oklahoma from Pandemic Influenza

		Attack rates	
0-18 years of age most likely #	246	410	574
Minimum	121	202	282
Maximum	1032	1720	2408
19-64 years of age most likely #	3686	6144	8601
Minimum	540	1137	1591
Maximum	4024	6707	9390
65+ years of age most likely #	1943	3238	4534
Minimum	1389	2315	3241
Maximum	2456	4094	5731
Total: most likely #	5875	9792	13709
Range:	2050 - 7512	3654 - 12521	5114 - 17529

In the event of an influenza pandemic, the Oklahoma State Department of Health (OSDH) will be the lead state agency in the response. State, regional and local organizations will initiate actions as outlined in the Oklahoma Pandemic Influenza Management Plan and the Catastrophic Health Emergency (CHE) Plan.

The Oklahoma Pandemic Influenza Management Plan contains six essential components:

1. Command, Control and Management
2. Surveillance
3. Delivery of Vaccine
4. Delivery of Antiviral Agents
5. Emergency Medical Services
6. Risk Communications

Role of the OSDH

1. The OSDH is responsible for the development, regular review and implementation of the Oklahoma Pandemic Influenza Management Plan.
2. The OSDH Laboratory is integral in surveillance activities by providing viral isolation, antigen detection, and strain identification of influenza viruses.
3. The Commissioner of Health and State Health Officer has the primary authority for direction and supervision of the implementation of the plan components, namely vaccine delivery and antiviral dispensing.

Roles of County Health Departments

Local County Health Departments (CHD) are responsible for planning and orchestrating the local response to an influenza pandemic with direction from the OSDH Central Office. Local CHDs, through existing or enhanced surveillance, may be the first to detect influenza activity in their community. County health department responsibilities include:

1. Meet with local key partners and familiarize them with the Oklahoma Pandemic Influenza Management Plan.
2. Liaison with local responders (e.g., emergency services, hospitals, and mortuary services) in advance of a pandemic to facilitate a coordinated community response.
3. Promote inter-pandemic routine influenza and pneumococcal vaccination to designated high-risk groups.
4. Develop a plan with key partners that addresses closing and re-opening of schools, businesses, and public events.
5. Assure local emergency plans are implemented during an influenza pandemic.

6. Assist with disseminating educational materials targeted towards the public regarding an influenza pandemic response.

Role of the Federal Government

1. Coordinate national and international surveillance.
2. Conduct epidemiological investigations in the U.S. and globally.
3. Develop and direct use of diagnostic laboratory tests and reagents.
4. Develop reference strains and reagents for vaccines.
5. Evaluate and license vaccines.
6. Determine population at highest risk and strategies for vaccination and antiviral use.
7. Assess and advise on measures to decrease transmission (such as travel restrictions, isolation and quarantine).
8. Deploy federally purchased vaccine.
9. Deploy antiviral agents in the Strategic National Stockpile.
10. Evaluate the efficacy of response measures.
11. Deploy the Commissioned Corps Readiness Force and Epidemic Intelligence Service Officers.
12. Develop and distribute medical and public health communications.

Pandemic Phases

National pandemic planning is categorized in several phases, from early identification of a novel virus threat to resolution and recovery from a pandemic cycle. These pandemic phases are determined and announced by the CDC in collaboration with the World Health Organization. The Oklahoma Pandemic Influenza Management Plan is structured according to guidelines, which were outlined by CDC and are listed below:

1. Pre-Event
   a. Pre-Pandemic
   b. Novel Virus Alert

2. Pandemic Response
   a. Pandemic Alert
   b. Pandemic
   c. Second Wave

3. Recovery Phase

4. Mitigation

Phases of a Pandemic as defined by The World Health Organization:

1. Inter-Pandemic Period (Pre-Pandemic)
   a. No indication of any new virus type has been reported.
   b. Influenza viruses antigenically related to those recently circulating among humans continue to evolve and cause disease.

2. Novel Virus Alert
   a. Novel virus detected in at least one human.
   b. A substantial portion of the population has little or no antibody to the novel virus, but the ability of the virus to rapidly spread person-to-person and cause multiple outbreaks of disease remains questionable.

3. Pandemic Alert
   Human transmission of the new virus sub-type has been confirmed through clear evidence of person-to-person spread in the general population, with at least one outbreak lasting over a minimum of a two-week period in one country.

4. Pandemic
   a. The new virus sub-type has been shown to cause several outbreaks in at least one country, and to spread to other countries with consistent disease patterns indicating that serious morbidity and mortality is likely in at least one segment of the population.

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b. This phase will result in influenza activity in initially affected regions until it has stopped or reversed while outbreaks of the new virus are still occurring elsewhere.

5. Second Wave

   A second outbreak of disease within the same geographic area that occurs 3-9 months after the initial wave of disease.

6. Post-Pandemic

   Indices of influenza activity have returned to essentially normal inter-pandemic levels and immunity to the new virus sub-type is widespread in the general population.

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The Oklahoma State Department of Health (OSDH) will lead the state response to an influenza pandemic. The local health departments will develop and implement a structured parallel system of pandemic influenza preparedness for their local jurisdictions. The Commissioner of Health will have primary authority for the implementation of the pandemic management plan.

I. Pre-Event

A. Pre-Pandemic

1. Ensure that the Oklahoma Pandemic Influenza Management Plan is developed and is annexed or supplemented to the Catastrophic Health Emergency (CHE) Plan.

2. Ensure collaboration with key state agencies (See Appendix A) to identify crucial gaps in the state infrastructure and work with state legislature through appropriate channels to correct the voids that may hinder an effective response.

3. Inform key government officials, legislators and various stakeholders of the need to address and resolve any gaps prior to the actual event of a pandemic influenza incident.

4. Coordinate planning activities with State, Local, Tribal and Federal agencies and non-governmental organizations.

5. Maintain standard operations of the OSDH Situation Room.

6. Train OSDH staff in the Incident Command System (ICS) according to the National Incident Management System.

7. Identify key positions of the Incident Command Organizational Structure. (See Appendix B)

8. Conduct drills and exercises with key organizations and personnel to ensure integration and interoperability during actual incident operations. The following key components will be addressed:

    a. Vaccine delivery at Mass Immunization Prophylaxis Strategy (MIPS) sites.
    b. Hospital surveillance and response.
    c. Strategic National Stockpile receipt and distribution.

9. Review and modify *Pandemic Influenza Management Plan* on an annual basis by committee.

B. Novel Virus Alert

1. Ensure OSDH Situation Room is ready and Command Staff identified to respond to the potential threat of a novel virus.

2. Develop Incident Action Plan and job action sheets for pandemic influenza response by September 1, 2005, and review quarterly.

3. Work with key agencies (See Appendix A) and organizations to pre-determine and prioritize essential employees to receive antiviral medication and/or vaccine in a pandemic event.

II. Pandemic Response

A. Pandemic Alert

1. OSDH will activate the Situation Room.

2. OSDH Command and General Staff will meet at least weekly to develop and review contingency plans for pandemic influenza.

3. OSDH will notify Oklahoma Department of Emergency Management (OEM) of potential threat and develop regularly scheduled planning meetings to address the threat.

4. The OEM will notify all necessary state government officials of the potential need for additional monetary resources in a pandemic influenza crisis.

5. OSDH will request and review priority lists of identified individuals from key agencies and organizations to receive antiviral agents and vaccine.

6. OSDH & OEM will ensure redundant communication systems are operational.

B. Pandemic

1. OSDH will coordinate resources with the State Emergency Operation Center (EOC).

2. OSDH Trauma Division and the Hospital Preparedness Division will gather data and other pertinent information from EMSystem® every 12 hours and report to key organizations or persons within local, regional and state governments.

3. OSDH will coordinate public health activities with other state, local and federal agencies.

4. OSDH will implement the State of Oklahoma Strategic National Stockpile (SNS) Plan and MIPS plans for distribution of antiviral agents and vaccine when available.

5. State OEM, local emergency management agencies, Metropolitan Medical Response System (MMRS), Regional Medical Response Systems (RMRS) county health departments and hospitals will activate their emergency response systems.

6. Office of Chief Medical Examiner and Oklahoma Funeral Directors Association will be advised to prepare for increases in the number of dead by following the Mass Fatality Plan as directed in the CHE Plan, Emergency Support Function #8.

C. Second Wave

1. OSDH Terrorism Preparedness and Response Service will assess, evaluate and modify the Oklahoma Pandemic Influenza Management Plan as indicated by epidemiologic findings and needs projections for a possible second wave of influenza transmission.

2. OSDH will continue basic operations outlined in the Pandemic phase of the Oklahoma Pandemic Influenza Management Plan.

3. State EOC, OSDH Situation Room, MMRS and Regional Emergency Response Planners will collaborate and monitor availability of state and local resources.

III. Recovery Phase

A. OEM will assess the ability of state and local partners to resume normal services.

B. OSDH Situation Room and State EOC will return to normal operation hours.

C. OSDH will prepare After Action Reports and analyze all key components of the Pandemic Influenza Management Plan.

D. ICS Staff will de-brief and file After Action Reports from response activities.

E. The State Pandemic Influenza Management Plan will be reviewed and updated by ICS Staff to address gaps in the public health infrastructure identified during the pandemic phase.

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IV. Mitigation

A. Continue to coordinate planning activities with State, Local, Tribal and Federal agencies and non-governmental organizations.

B. Maintain standard operations of the OSDH Situation Room.

The OSDH Communicable Disease Division (CDD) in cooperation with the Public Health Laboratory (PHL) assumes primary responsibility for conducting influenza surveillance. The Oklahoma Influenza Surveillance system routinely receives information and specimens from sentinel physicians and laboratories. The PHL provides viral diagnostic testing. CDD epidemiologists provide weekly analysis and reports of surveillance data, and investigate case clusters of respiratory disease.

I. Pre-Event

A. Pre-Pandemic

1. Virologic Surveillance

   a. The PHL receives specimens from sentinel physicians, sentinel laboratories, the Office of the Chief Medical Examiner and various sources during an outbreak investigation for virus identification, typing and sub-typing. The PHL provides supplies for specimen collection, transport, shipping and testing free of charge.

   b. A network of geographically distributed sentinel laboratories voluntarily reports the proportions and types of positive influenza tests performed each week. Two of the sentinel laboratories possess the capabilities to perform viral culture and typing. Sentinel laboratories also submit specimens to the PHL for viral culture and sub-typing.

   c. Three laboratories in Oklahoma, including the PHL, participate in the WHO and National Respiratory Enteric Virus Surveillance System (NREVSS). These laboratories report the number and type of influenza viruses isolated each week. A representative sample, plus any unusual or untypable viral specimens are sent through the PHL to CDC for comparative antigenic and genetic analysis.

2. Disease-based Surveillance

   a. A voluntary network of sentinel physicians reports the number of patients presenting with influenza-like illness (ILI) per total number of patient visits by age group each week. The ratio of sentinel physicians to total Oklahoma population (currently 1:192,000) will continue to surpass the CDC recommended ratio of 1:250,000 total population. ILI data provided by participating sentinel physicians are electronically submitted to the data

repository at the CDC, as part of the U.S. Sentinel Physicians Surveillance Network. In addition, sentinel physicians obtain and submit specimens to the PHL.

b. Influenza respiratory outbreak detection in Oklahoma is a collaborative effort between County Health Department (CHD) personnel, local healthcare providers, the CDD and the PHL. Personnel in each county health department are trained in detection and investigation of outbreaks of respiratory illness in schools, nursing homes and other institutional settings. CHD personnel in conjunction with CDD epidemiologists rapidly investigate outbreaks of respiratory illness.

c. Virologic and disease-based surveillance data are compiled and analyzed by the Influenza Surveillance Coordinator, a CDD epidemiologist, in conjunction with the State Epidemiologist. The data is utilized to qualitatively assess the influenza activity each week in Oklahoma as "widespread," "regional," "sporadic" or "no activity." The influenza activity level is provided weekly to CDC through electronic communication.

d. Influenza surveillance data are distributed to laboratories, local health departments, healthcare providers, hospital infection control practitioners (ICP) and the general public by weekly data analysis reports prepared by CDD epidemiologists. These weekly data reports are accessible on the Oklahoma Influenza Surveillance website. Notifications of especially high influenza activity or unusual situations are reported to physicians, ICPs and CHD personnel through the Oklahoma Health Alert Network (RHINO).

e. Through the CDC Epi-X Exchange and other communications methods, the CDD and the PHL maintain a communication network with epidemiologists and public health laboratories in other states to share information regarding the detection and circulation of influenza viruses as well as influenza activity on a national level. CDD epidemiologists communicate regularly with surrounding states to assess regional influenza activity.

f. Occurrences of highly pathogenic avian influenza in the state or region are monitored by the State Public Health Veterinarian. The progression of these outbreaks and concurrent monitoring for potential zoonotic transmission to poultry workers is coordinated with the State Veterinarian at the Oklahoma Department of Agriculture, Food, and Forestry and the USDA Regional Veterinarian in charge.

g. Seasonal impact of influenza is also evaluated by monitoring data from volume-based surveillance systems managed by other public health partners including EMSystem®, Tulsa Area Syndromic Surveillance System (TASSS), Oklahoma County Health Alert System (OCHAS), First Watch and EMSA Medusa.

B. Novel Virus Alert

As the threat for human-to-human transmission of a novel influenza virus is raised, the activities of CDD epidemiologists and PHL staff will be intensified as follows:

1. Continue Oklahoma influenza surveillance activities as described in the Pre-Event phase.

2. Increase communications with the CDC and monitor bulletins regarding virologic, epidemiologic and clinical findings associated with the novel strain.

3. Update health care providers in the region(s) where the threat of novel influenza virus incursion is heightened and provide situation updates as needed through the RHINO system.

4. Enhance disease-based surveillance by requesting health care providers and other resources to submit respiratory specimens from patients who present with ILI, and:

   a. had recent travel to a region where the novel strain of influenza has been identified,

   b. or presented with unusually severe symptoms of ILI regardless of their travel history.

5. Enhance laboratory surveillance by obtaining the appropriate reagents from CDC to detect and identify the novel strain. If an atypical influenza virus is isolated or typed at the PHL, the results will be rapidly reported to key OSDH personnel via phone call trees and posting on the LITS database. The State Epidemiologist and State PHL Director will coordinate laboratory confirmation and any necessary epidemiologic investigations with the CDC.

II. Pandemic Response

A. Pandemic

1. Influenza surveillance activities will be modified to include the following strategic approaches. It is expected that some routine activities will need to be suspended to accommodate priority needs for information and the diminishment of resources previously available at hospitals and laboratories for reporting.

   a. Expand surveillance of hospitalized and fatal cases, and other sequelae or conditions through increased communications with hospital ICPs and the Office of the Chief Medical Examiner.

b. Facilitate rapid reporting of surveillance data relevant for use in determining prioritization for vaccine and/or antiviral medication distribution:

i. Intensify surveillance to characterize age groups most affected by the pandemic strain.
ii. Collect drug resistance data to characterize efficacy of various antiviral drugs.
iii. Devise sentinel surveillance program to estimate vaccine efficacy/failure rates.

c. Focus laboratory surveillance on detection of possible antigenic changes in the original pandemic strain.

d. Continue to monitor surveillance reports from WHO and CDC on national as well as international morbidity and mortality.

2. Enhance communication and notification of collaborating partners through additional updates utilizing the RHINO system as needed.

3. Consider collaboration with the CDC for any special studies that could be conducted without further compromise of existing limited resources.

B. Second Wave

1. Assess surveillance activities for any modifications given lessons learned in the first wave of illness.

2. Resume influenza surveillance activities as described in the pre-event phase, but implement modifications required to quickly detect respiratory disease activity indicative of a second wave of pandemic influenza.

3. Remain prepared to quickly resume pandemic response surveillance activities described above in the event of a second wave of illness.

III. Recovery Phase

A. Evaluate the strengths and weaknesses of disease-based and virologic surveillance efforts implemented during the pandemic.

B. Perform a detailed retrospective characterization of the pandemic in Oklahoma evaluating the overall morbidity and mortality.

C. Resume influenza surveillance activities as described in the pre-event phase implementing any necessary modifications.

I. Pre-Event

A. Pre-Pandemic

1. Maximize influenza vaccination rates in all high-risk populations including those for whom the rate of vaccination is low, i.e. minorities, health care workers and persons with chronic disease.

2. Maximize pneumococcal vaccination among the high-risk populations.

3. Identify occupational groups who serve the public in occupations that are critical to maintaining community services and infrastructure, but are not traditionally considered a target population for influenza immunization. (See Appendix C)

4. Assure that the SNS Plan and MIPS Guidelines and Plans are updated to address non-licensed vaccine.

5. Assure that vaccine storage and handling equipment and supplies are available for mass vaccination.

6. Assure that the Oklahoma State Immunization Information System (OSIIS) is configured to collect relevant demographic, vaccine and clinical data for inventory control and tracking. System should also be able to collect information on possible adverse events.

II. Pandemic Response

A. Pandemic Alert

1. Provide pneumococcal vaccine for all high-risk groups.

2. Coordinate planning with MIPS pre- and post- vaccine availability.

3. Modify vaccination target population according to national guidance and state surveillance information. (See Appendix C)

B. Pandemic

1. Staff for data entry will be needed to assure that all influenza data is entered into OSIIS within 24 hours to facilitate vaccine inventory control. These staff

will have to be located near where the vaccine is administered. Additionally, sites that are administering influenza pandemic vaccine will be required to perform and report a daily hand count inventory of vaccine and supplies.

2. Use OSIIS to conduct recalls of individuals who need second immunizations as may be recommended by the Advisory Committee on Immunization Practices or vaccine manufacturer.

3. Assure that vaccine is securely stored at OSDH and while in transport to MIPS locations.

   a. OSDH storage has 24-hour security that can be augmented with local law enforcement. The vaccine is stored in locked rooms in refrigerators with temperature alarms that activate local and remote alarms.

   b. Security during transport will be coordinated with each MIPS site and addressed based on available security.

   c. If security is not a concern, Immunization Services staff and/or transport services may be used.

4. Vaccine Information Statements (VIS) and Influenza Vaccine Administration forms will be updated and copied for shipment with each dose of vaccine.

5. The applicable VIS will be made available on the OSDH web site.

C. Second Wave

1. All vaccine delivery-related activity conducted prior to this time will be reviewed and revised to provide better service.

2. It is anticipated that vaccine supplies will be increased by this phase and that distribution may involve the private sector. The Immunization Service will coordinate the information sharing, requisition and ordering process, and delivery of influenza vaccine to private physicians and other entities within the private sector according to guidance from CDC.

3. Inventory and restock vaccine supplies and storage equipment as needed at county health department clinic sites.

III. Recovery Phase

A. Provide pneumococcal vaccine for all high-risk groups.

B. Identify lessons learned during the first wave.

C. Assess coverage of different populations to determine who has received the vaccine and which groups still need to be targeted for receipt of vaccinations.

IV. Mitigation

A. Provide pneumococcal vaccine for all high-risk groups.

B. Maximize influenza vaccination rates in all high-risk populations including those for whom the rate of vaccination is low, i.e. minorities and persons >65 years old with chronic disease.

Currently, no national guidelines have been developed regarding the stockpiling, delivery, and use of antiviral medications to mitigate the impact of an influenza pandemic. Four antiviral agents are FDA-approved for prophylaxis or treatment of influenza A. Amantadine and rimantadine are related drugs that interfere with the replication of influenza viruses. Oseltamivir (Tamiflu®) and Zanamivir (Relenza®) are neuraminidase inhibitors that interfere with the release of viral particles from infected cells. These drugs have been shown to have an efficacy rate of 70-90% in preventing illnesses caused by naturally occurring type A influenza virus strains. To be effective for prophylaxis, the drug must be given throughout the potential period of exposure, which may be several weeks. For treatment purposes, the selected antiviral medication must be initiated within 48 hours of onset of symptoms. Treatment with an antiviral may shorten the course of illness, decrease communicability, and reduce the risk of influenza-related complications such as secondary bacterial pneumonia or sepsis. It is unknown whether these available antiviral drugs would achieve the same level of efficacy for prophylaxis or treatment of novel influenza strains. For example, amantadine and rimantadine have not been effective against the H5N1 avian influenza strain when persons are infected by direct transmission from infected poultry in Asia.

I. Pre-Event

A. Pre-Pandemic

1. In the absence of national guidelines, the OSDH will convene an Advisory Group to study the feasibility of providing an interim stockpile of antiviral medications within the state. In performing the feasibility assessment, key factors to address include:

    a. The expected supply of these drugs will be well below the anticipated demand during an influenza pandemic.

    b. The antivirals will <u>not</u> be made available for public distribution, but will be used to maintain essential medical services and community infrastructure.

    c. Adverse effects are relatively common ranging from mild gastrointestinal upset to significant neurological symptoms.

    d. The advantages of using the antiviral medications for prophylaxis will likely be outweighed by the needs for treatment use.

    e. Alternative or novel delivery mechanisms may need to be implemented to distribute medications to targeted priority groups.

f. The overall costs of maintaining a state stockpile of antivirals can be reduced by obtaining an inventory rotation plan with a large pharmaceutical wholesaler or distributor.

2. The above named Advisory Group shall consist of 11-12 members comprised of the following persons or their designees: Chief of Operations for Disease Prevention Services, State Epidemiologist, OSDH Pharmacist, TPRS Service Chief, TPRS Strategic National Stockpile Coordinator, TPRS Hospital Preparedness Division Director, Director of the Oklahoma Hospital Association, Director of the Oklahoma Pharmacy Association, an Oklahoma physician specializing in the practice of infectious diseases, a MMRS representative and OSDH Chief of Nursing Services. Panel members will be asked to submit their findings and written recommendations to the State Commissioner of Health by December 31, 2005.

3. If the Advisory Group submits a summary recommendation that affirms the need for a state stockpile, additional recommendations will be obtained regarding antiviral drug type selected, estimated number of doses requested to stockpile, and a priority group algorithm for distribution. Locations and responsible parties will need to be identified for storage, maintenance, and distribution of antiviral medications.

4. Other pre-event planning activities under the direction of the State Epidemiologist shall consist of:

   a. Determining the feasibility and logistics of creating antiviral stockpiles for front line health care workers at key hospitals in all eight homeland security regions. Funding may be available through the Health Resources and Services Administration Public Health Preparedness Cooperative Agreement as part of the hospital package plan.

   b. Estimating the amount of antiviral medications needed to maintain essential services in Oklahoma.

   c. Developing a surveillance plan for monitoring drug resistance among circulating influenza viral strains.

   d. Developing education materials for healthcare workers and the public regarding the use of antiviral medications for treatment and prophylaxis of influenza. (See Appendix D)

   e. Monitoring future federal decisions regarding influenza antivirals to modify state plan as appropriate.

II. Pandemic Response

A. Pandemic Alert

1. The Advisory Group will be reconvened to assess options for additional purchase of antivirals to augment stockpile and modify distribution algorithm based on available epidemiologic data. Current federal, state, and local supplies of antiviral medications will also be assessed:

    a. Strategic National Stockpile allocation.

    b. OSDH stockpile.

    c. Hospital stockpiles.

    d. Local pharmacies or pharmaceutical outlets.

2. Guidance will be forwarded to the State Health Officer regarding the distribution of antivirals to individuals employed in essential services:

    a. Health care workforce.

    b. Key community infrastructure (fire, police, EMSA, public utilities, government leaders, etc.).

3. Drug information sheets will be produced or revised to meet anticipated needs. Translation into other languages may be required.

4. Plans for drug distribution and administration will be finalized and communicated to key personnel at local health departments, hospitals, MMRS, OEM, and other key state agencies.

B. Pandemic

1. The antiviral drug distribution program will be fully activated and managed from the OSDH Situation Room. OSDH will also provide oversight and direction for delivery from hospital stockpiles funded through the HRSA Cooperative Agreement. Any available supply from the Strategic National Stockpile will be accessed according to the State's SNS Plan.

2. The OSDH will coordinate acquisition and delivery activities with adjoining states and public health jurisdictions:

a. Oklahoma City-County Health Department;
b. Tulsa City-County Health Department;
c. Texas;
d. Kansas;
e. Arkansas;
f. Louisiana;
g. Missouri.

III. **Recovery**

A. The OSDH will assess strengths and weaknesses of the implemented antiviral drug distribution schema. Adverse event data will be analyzed and summarized as part of the final evaluation report.

B. Any remaining antiviral medications will be inventoried and reconciled with the associated financial tracking records, under the direction of the OSDH Pharmacist.

C. The State's Pandemic Influenza Management Plan will be modified to address reported strengths and weaknesses under the direction of the State Epidemiologist. The urgency for restocking the depleted antiviral stockpile coupled with available resources will be determined.

Emergency operation plans are required by all state and local governments to address "all hazards". However, if an influenza pandemic occurs, it is likely to pose unique challenges that will overwhelm the healthcare system. Each county should incorporate a pandemic influenza management plan congruent to the state plan.

Personnel most likely to be exposed to the virus include public health workers, healthcare personnel, police, firefighters, emergency medical technicians, and other first responders. The effect of the pandemic influenza on these personnel will impact the infrastructure for critical community services through widespread absenteeism in the workforce.

I. Pre-Event

A. Pre-Pandemic

1. OSDH will work with Medical Reserve Corps to maintain a registry of volunteer healthcare personnel which include the following:

    a. Physicians;
    b. Physician Assistants;
    c. Advanced Registered Nurse Practitioners;
    d. Pharmacists;
    e. Registered Nurses;
    f. Licensed Practical Nurses;
    g. Medical Assistants;
    h. Other medical and non-medical staff that may be trained in the event of an emergency.

2. OSDH will maintain an inventory or appropriate listing of the following items:

    a. Estimated hospital bed capacity;
    b. ICU/CCU capability;
    c. Emergency room status;
    d. Negative pressure isolation rooms;
    e. Estimated amounts of available personal protective equipment;
    f. Potential alternate care sites.

3. OSDH will ensure MIPS Plans are exercised at the local, regional and state level.

4. OSDH will develop contingency plans to address any of the items which may be considered inadequate:
    a. Ready supplies of antibiotics used to treat secondary bacterial pneumonia.

b. Ready supplies of antiviral agents for treatment of ill patients and chemoprophylaxis of healthcare workers.
c. Adequacy of contingency alternate medical care facilities in "All Hazards Emergency Response Plan".
d. Adequacy of social and psychological services for families of victims.

5. Develop and conduct appropriate training/exercises for the public health work force to respond to a pandemic influenza event.

6. Develop a list of essential community services.

7. Develop strategies for identifying and prioritizing groups for distribution of antiviral medications and vaccines. (See Appendix C).

B. Novel Virus Alert

1. Meet with key partners to review major elements of response plans.

2. Implement contingency plans for obtaining critical equipment such as ventilators and other necessary medical supplies to respond to a pandemic influenza event.

II. Pandemic Response

A. Pandemic Alert

1. Ensure that resources and logistics are in place to provide a public health response to a pandemic influenza event.

2. Ensure coordination with Medical Emergency Response Center (MERC) to assess the impact of the healthcare system within their jurisdictions.

3. Assess the healthcare system in areas which currently do not have a MERC.

B. Pandemic

1. Activate CHE Plan.

2. Monitor status of emergency facilities, hospital beds, emergency medical services, other treatment facilities and medical equipment through the OSDH network systems.

3. Monitor healthcare system to determine need of secondary care facilities. These secondary facilities could include but are not limited to the following:

a. Nursing Homes;
b. Specialty Hospitals;
c. Ambulatory Surgery centers;
d. Urgent Care Facilities;
e. School Gymnasiums;

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f. Auditoriums;
g. Community Centers.

C. Second Wave

OSDH will continue pandemic phase operations of the Oklahoma Pandemic Influenza Management Plan.

III. Recovery Phase

Demobilization efforts will be implemented in order to provide systematic, timely and orderly release of resources, personnel and agencies that have responded to the pandemic events.

IV. Mitigation

Evaluation of the pandemic response as determined by the Terrorism Preparedness and Response Service.

Our primary objective will be to provide a timely, accurate and persuasive flow of information to the public, health care providers and government leaders to keep them appropriately informed through each stage of the pandemic. The OSDH will utilize the *Crisis and Emergency Risk Communications Plan* (CERC) and the Reportable Health Information and Notification in Oklahoma (RHINO) as important tools to help achieve this goal.

I. Pre-Event

A. Pre-event messaging will focus on preparing the public psychologically and emotionally to be ready for a pandemic.

1. An influenza pandemic is very likely in the next few years, and when it occurs, significant lifestyle changes will be required.

2. Many people may die.

3. Messages employed in this phase will include the following:

   a. Medically high-risk groups should obtain routine influenza vaccination.

   b. Medically high-risk groups should obtain pneumococcal vaccination to reduce risk of bacterial pneumonia.

   c. Critical decisions regarding who gets vaccine or antivirals – and who will be unprotected – must be made wisely. These decisions will not be based on fairness issues but rather on who must be protected to ensure essential services are maintained for society to function (vaccine to those in critical occupations vs. those most vulnerable). These decisions could be unpopular.

   d. We must begin preparing now – local planning is vital: businesses, hospitals and schools should begin to consider how and if they would operate during a pandemic.

   e. Isolation, quarantine and travel advisories will become commonplace.

   f. Families must begin to practice hand and respiratory hygiene habits that can reduce the chance of catching germs and passing them on to others:

      i. frequent hand washing with soap and water or 60 % alcohol-based hand sanitizer;
      ii. covering your cough; and

iii. staying home from work or school when sick.

g. Wearing masks may become necessary under certain circumstances.

h. We must support government efforts to acquire and stockpile when possible, vaccines and antiviral medications.

4. Using CERC Plan, the OSDH Office of Communications will assess communications needs, capacities and any obstacles to reach the general public, health care providers, key policy makers and government leaders during a pandemic, and adapt as necessary.

II. Pandemic Response

A. Event messaging will focus on the pandemic as a very real threat to the health and safety of Oklahomans.

1. Critical workers must be protected (vaccines, if available, or antivirals).

2. Other persons must take extreme hygiene precautions.

3. Communities must employ their emergency response plans.

4. Public involvement, including mobilization of volunteers, is essential.

B. The OSDH Office of Communications will employ the CERC plan, including the establishment of a Joint Information Center (JIC), to handle the surge of media requests and public inquiries generated by the pandemic and provide guidance regarding disease susceptibility, diagnosis and management.

C. The OSDH CDD will use RHINO to alert health care providers of public health recommendations.

III. Recovery Phase

A. Post-event messaging will focus on the following:

1. Directions to lift any community or individual public health restrictions that have been imposed.

2. Cautions that a “second wave” of infection could occur.

3. Possible need for mental health counseling.

4. If vaccines are available, potential for vaccinating high priority groups that did not receive vaccination in the first wave.

B. The OSDH Office of Communications will continue to employ its CERC plan, however, the JIC may be allowed to stand down.

C. The OSDH Communicable Disease Division will continue to use RHINO to alert health care providers of any updates to public health recommendations.

IV. Mitigation

A. Messages employed in this phase will include the following:

1. Medically high-risk groups should obtain routine influenza vaccination.

2. Medically high-risk groups should obtain pneumococcal vaccination to reduce risk of bacterial pneumonia.

B. The Oklahoma State Department of Health will review “lessons learned” from communications strategies employed in the first wave and adjust its CERC plan accordingly.

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APPENDICES

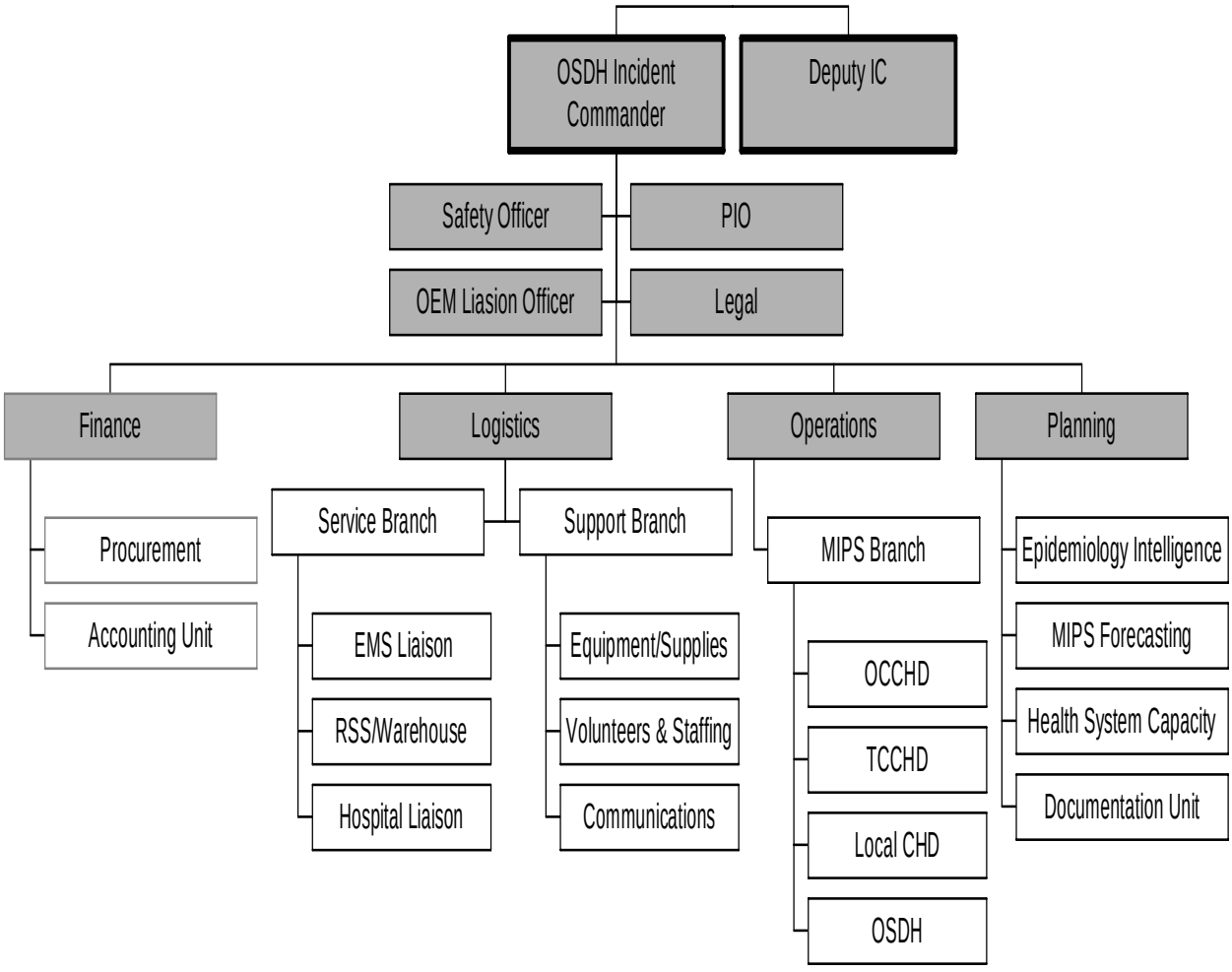
Appendix A

Key Agencies

OK Department of Emergency Management
OK Office of Homeland Security
OK Department of Public Safety
OK Military Department
OK Department of Mental Health and Substance Abuse Services
OK Department of Agriculture, Food and Forestry
OK State Bureau of Investigation
OK Department of Transportation
OK Attorney General's Office

Appendix B

Pandemic Influenza Management ICS Organizational Chart



Appendix C

Strategies for Distribution of Vaccine and Antiviral Medications

Vaccine availability will be limited due to the time required to produce vaccine and the number of individuals who need to be vaccinated. The health care infrastructure as well as those at high risk for complications related to contracting influenza must address prioritization of those to be vaccinated.

The essential services personnel listed in the following priority categories can be further lengthened by referring to Homeland Security Presidential Directive 7 Titled: Critical Infrastructure, Prioritization, and Protection.

Priority 1. Health care workers and public health personnel involved in the distribution of vaccine.

Rationale: The first line of defense during a pandemic will be the healthcare and public health sectors. These sectors are crucial components in the execution of a pandemic response plan. Maintaining the healthcare infrastructure during a pandemic is essential for reducing the morbidity and mortality. Healthcare workers in the following settings should be considered a priority for vaccine or antiviral medication distribution:

1. Personnel involved in the distribution of vaccine;
2. Long term care facilities/nursing homes (OSDH Protective Health Services will identify facilities and doses needed);
3. Acute care hospitals (OSDH Office of Medical Facilities will identify facilities and doses needed);
4. Public health offices (OSDH Community Health will identify facilities and doses needed);
5. Pharmacies (Oklahoma Board of Pharmacy will identify facilities and doses needed);
6. Laboratories (OSDH PHL will identify facilities and doses needed);
7. Field epidemiologists and investigators (Acute Disease Service will identify individuals and doses needed);-
8. Private physicians and others who come in contact with patients/clients (Oklahoma State Medical Board will assist with identifying facilities and doses needed).

Priority 2: Persons responsible for community safety and security.

Rationale: The community safety and security sectors are a vital component to the pandemic response plan. In order to assure an effective response to the demand placed on the healthcare community as well as ensuring the safety of the public, the following group of people will need to be vaccinated or prophylaxed. This priority group may include the following but are not limited to:

1. Police;
2. Firefighters;
3. Paramedics / EMTs;
4. Military/National Guard;
5. Local responders not included in the first priority group.

Priority 3: Other persons with specialized skills that provide essential community services.

Rationale: Individuals whose absence would either pose a significant hazard to public safety or severely disrupt the pandemic response effort. Members of these groups are likely to vary widely from community to community and are highly influenced by local circumstances; however, those considered in this priority group may include the following but are not limited to:

1. Key emergency response decision makers (e.g. elected officials, essential government workers, public works, and disaster services personnel).

Priority 4: Persons traditionally considered being at increased risk of severe influenza illness and mortality.

Rationale: The ability to reduce the morbidity and mortality caused by a pandemic is contingent on protecting those persons most likely to experience severe complications or death. The following is a list of priority groups based on the current definitions by the Advisory Committee on Immunization Practices:

1. Persons of any age with high-risk medical conditions;
2. Pregnant women;
3. Persons in nursing homes and other long-term care facilities;
4. Persons age 65 or older without high-risk medical conditions;
5. Infants between the ages of 6 to 12 months, if supported by epidemiological and clinical data.

Priority 5: Persons who, in the judgment of state and local health officials, provide critical community services.

Rationale: Individuals that provide the services that are essential to the response plan as well as to maintaining key community services. Members of these groups are likely to vary widely from community to community and are highly influenced by local circumstances; however, those considered in this priority group may include the following but are not limited to:

1. Utility workers;
2. Funeral services personnel;
3. Persons involved in the transport of essential goods or provision of essential services (e.g. food/water and sanitation/waste disposal).

Priority 6: Household contacts of persons with high-risk medical conditions and household contacts of persons in the first three groups.

Rationale: Household contacts of the person in the first three groups are a potential source of infection for these individuals.

Priority 7: Pre-school age children (especially those attending daycare centers).

Rationale: Daycare centers and those attending these facilities contribute to the spread of diseases. While pre-school children are not considered to be at high risk for complications from influenza, they are considered vessels through which the spread of diseases can be perpetuated, especially those attending large-group care facilities.

Priority 8: Healthy persons between the ages of 18 to 64.

Rationale: Even though this group is at low risk for complications from influenza, they are the majority of the working class and therefore an increase in morbidity and mortality would lead to a significant impact on the economy. Simultaneous absence of large numbers of individuals from this priority group could lead to a disruption in the community even if they are not considered essential personnel.

Priority 9: School age children (the population least likely to have severe illness).

Rationale: While this group is at the lowest risk for developing severe complications from influenza during annual epidemics, they do play a major role in the spread of the disease. Simultaneous absenteeism from school may not have any direct financial or disruptive effects in the community; however, it may effect the adult population since care for ill children would be of concern.

Regional Distribution of vaccine will be tailored to meet the needs of the threat in three separate but unique and scalable phases:

> ***Phase I:*** Fewer and larger sites countywide for infectious cases with limited threat or low transmissibility hazard; and two weeks or more timing to complete effective vaccination or prophylaxis of the general public.

Phase II: Additional but smaller sites countywide for infectious cases with a higher extent of release or higher transmissibility hazard; and 7 to 14 days timing to complete effective vaccination or prophylaxis of the general public.

Phase III: Represents a maximal deployment of all pre-identified primary and secondary immunization sites throughout the State for infectious cases which pose an extreme transmissibility hazard; or less than 4 days to complete effective vaccination of the general public. Phase III will only be utilized in the event there is an unlimited supply of vaccine to treat entire state population. Strike Teams should be utilized at this phase to meet the needs of special populations, which are incapable of mobility to immunization sites.

Appendix D

Antiviral Agents for Planning and Response

The following is excerpted from an informal background document prepared by the National Vaccine Program Office and the Centers for Disease Control and Prevention (CDC). This appendix is intended to provide background information and stimulate discussion for planning purposes. It does not imply endorsement by any federal agency.

Introduction

There are currently four approved medications in the United States that have antiviral activity against influenza A viruses. They fall into two drug classes, namely adamantane derivatives and neuraminidase inhibitors. All four medications are prescription drugs meaning they must be prescribed by a physician. Since a pandemic is expected to occur with the emergence of a novel human influenza A subtype virus from an animal reservoir or through reassortment of influenza A viruses, this document will focus upon antiviral treatment and chemoprophylaxis of influenza type A.

Background

1. Adamantane derivatives

The adamantane derivatives, amantadine and rimantadine, are chemically related, orally administered drugs that are approved for treatment and chemoprophylaxis of influenza A. Amantadine and rimantadine specifically inhibit replication of influenza A viruses, but not influenza B viruses. When administered for treatment within 48 hours of illness onset, controlled studies have found that both drugs are effective in decreasing viral shedding and reducing the duration of illness of influenza A by approximately one day compared to a placebo. The recommended duration of treatment is usually five days. When used for chemoprophylaxis, amantadine and rimantadine are approximately 70 - 90% effective in preventing symptoms of illness resulting from influenza A infection. The efficacy and effectiveness of amantadine and rimantadine to prevent complications of influenza are unknown. Amantadine and rimantadine are commonly used in the U.S. for chemoprophylaxis of influenza A during institutional outbreaks such as in nursing homes. Amantadine is approved for the treatment of influenza A in children aged one year and older and in adults. Rimantadine is approved for treatment of influenza A in adults. Both drugs are approved for chemoprophylactic use for influenza A in children aged one year and older.

Gastrointestinal and central nervous system (CNS) adverse effects have been reported during controlled chemoprophylaxis studies of amantadine and rimantadine in healthy adults and

elderly nursing home residents. Chemoprophylactic use of both drugs has been associated with CNS toxicity such as lightheadedness, difficulty concentrating, nervousness, insomnia, and seizures in patients with pre-existing seizure disorders. Rimantadine use has been associated with fewer CNS side effects than amantadine. Amantadine is teratogenic and embryo toxic in animals. Rimantadine has not been found to be mutagenic. The safety of amantadine and rimantadine has not been established in pregnancy.

The use of amantadine and rimantadine has been associated with the rapid selection and development of resistant viruses. Drug-resistant viruses can be spread to contacts of treated individuals, including persons receiving chemoprophylaxis. Since the mechanism of resistance is the same for both adamantane derivatives, influenza A viruses resistant to one adamantane drug are also resistant to the other. There is no evidence that adamantane-resistant viruses are more transmissible or more virulent than adamantane sensitive viruses. Resistance to adamantanes does not affect susceptibility to neuraminidase inhibitors. The percentage of influenza viral isolates from the general population exhibiting resistance to amantadine or rimantadine has remained low.

*During 1999-2000, approximately 88.5 million dose-equivalents (100 mg/dose) of amantadine and rimantadine were produced in the U.S. (combined tablet/capsule and syrup). Manufacturers have estimated that up to 310 million doses (100 mg/dose) of amantadine and rimantadine could be produced each year if needed. However, this would only treat 31 million persons for five days, or provide chemoprophylaxis against influenza A for 22.1 million adults for 14 days.

There are several U.S. manufacturers of amantadine, but currently only one manufacturer of rimantadine (manufacture of rimantadine is protected by a process patent). Both drugs are produced from similar raw materials supplied by different sources in Europe. Key issues related to antiviral supply during a pandemic include the conversion time from raw material to final drug product, excess capacity for production of raw materials, capacity to stockpile both raw materials and finished product, and shelf life of raw materials and finished drug.

[*Preliminary results of unpublished CDC survey data; not all manufacturers responded to the survey. Note that amantadine is also used for treatment of Parkinson's Disease.]

2. Neuraminidase inhibitors

The neuraminidase inhibitors, zanamivir and oseltamivir, are chemically related members of a new class of antiviral drugs for influenza that have activity against both influenza A and B viruses. When treatment is initiated within 48 hours of illness onset, both drugs are effective in decreasing shedding and reducing the duration of symptoms of influenza by approximately one day compared to placebo. Zanamivir is an orally inhaled powdered drug that is approved for treatment of influenza in persons aged 7 years and older. Oseltamivir is an orally administered capsule or oral suspension that is approved for treatment of influenza in persons older than 1 year. For both drugs, the recommended duration of treatment is five days. Oseltamivir is also approved for chemoprophylaxis of influenza in persons aged 13 years and older. Zanamivir is not currently approved for chemoprophylaxis of influenza. However,

controlled studies have demonstrated the efficacy of both drugs for prevention of symptoms of illness resulting from influenza infection in adults and adolescents compared to placebo. The efficacy and effectiveness of neuraminidase inhibitors to prevent complications of influenza are unknown. Since zanamivir and oseltamivir were approved in 1999, there is limited clinical experience to assess adverse effects. Oseltamivir use has been associated with nausea and vomiting during controlled treatment studies compared to placebo. Nausea, diarrhea, dizziness, headache, and cough have been reported during zanamivir treatment, but the frequencies of adverse events were similar to inhaled powered placebo drug. Few serious CNS adverse effects have been reported for the neuraminidase inhibitor drugs; however, no controlled studies allow for conclusions regarding a direct comparison with the adamantane drugs. Zanamivir is not generally recommended for use in persons with underlying respiratory disease because of the risk of precipitating bronchospasm.

There are limited data on antiviral resistance to the neuraminidase inhibitor drugs. Studies have identified some evidence for the development of neuraminidase inhibitor-resistant influenza virus strains, but surveillance has been limited by the short time period that the neuraminidase inhibitors have been available for clinical use and by the lack of optimal methodology to detect viral resistance to these drugs. In vitro studies have found that cross-resistance occurs between the neuraminidase inhibitor drugs, but does not affect susceptibility to adamantane drugs.

*During 1999-2000, the quantity of neuraminidase inhibitor drugs produced for the U.S. market was estimated to be less than sufficient to treat 2 million adults for five days. The quantity of both zanamivir and oseltamivir produced for the U.S. market during 2005-06 is expected to be higher than during 1999-2000 and to increase in the future. The estimated surge capacity is unknown.

[*Crude estimate based upon incomplete responses to CDC inquiries, unpublished data.]

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Comparison of antiviral drugs for influenza

INDICATOR	ADAMANTANE DERIVATIVES			NEURAMINIDASE INHIBITORS
	Amantadine	Rimantadine	Zanamivir	Oseltamivir
Type of Influenza virus infection indicated for use	Influenza A	Influenza A	Influenza A Influenza B	Influenza A Influenza B
Administration	Oral	Oral	Inhalation	Oral
Ages approved for treatment of flu	≥ 1 year	Adults	≥ 7 years	> 1 year
Ages approved for prevention of flu	≥ 1 year	≥ 1 year	not approved	≥ 13 years
Cost per 5 day treatment*	$9.82 $1.73 - generic	$18.87	$44.40	$53.00

* Cost to the pharmacist for the lowest recommended dosage for a 70-kg patient. The Medical Letter 1999; 41(1067): 113-120.

Options for the recommended use of antiviral drugs during an influenza pandemic

A. Treatment only

The recommended use of antiviral drugs would be directed toward early treatment (within 24-48 hours of illness onset) of suspected or confirmed influenza cases. This strategy would also address the relative roles of all four antiviral agents (e.g., use of only one class of antiviral drugs versus all four drugs for treatment of illness resulting from infection with a pandemic influenza A strain). Issues to be considered include specifying which patients should be treated (e.g., high-risk populations, core infrastructure, etc.), the definition of suspected and confirmed cases, when treatment should be initiated, duration of treatment, and guidelines for patient evaluation.

DRUG-RESISTANCE: Drug-resistant viruses can appear in up to approximately one third of patients when either amantadine or rimantadine is used for therapy. During the course of therapy, antiviral-resistant influenza strains can replace sensitive strains within 2-3 days of starting therapy (Houck, 1995; Hayden, 1991). Emergence of amantadine- and rimantadine-

resistant influenza A viruses in symptomatic immunocompromised adults has been reported (Englund, 1998).

ANTIVIRALS FOR TREATMENT: SUMMARY

Antiviral agents shorten clinical course and accelerate return to normal functioning; work best if given within 2 days of symptom onset. Symptomatic measures include bed rest, antipyretics, antitussives, nasal sprays/drops, and adequate fluid intake. Early immunization is prophylactic method of choice.

When administered within 2 days of illness onset to otherwise healthy adults, antiviral drugs can reduce the duration of uncomplicated influenza illness. None of the available agents has been demonstrated to be effective in preventing serious influenza-related complications (e.g., bacterial or viral pneumonia or exacerbation of chronic diseases).

To reduce the emergence of antiviral drug-resistant viruses, treatment of persons who have influenza-like illness should be discontinued as soon as clinically warranted, generally after 3 to 5 days of treatment or within 24 to 48 h after the disappearance of signs and symptoms, depending on the agent used.

AMANTADINE: For treatment of influenza A in adults and children. Start within 24 to 48 h after symptom onset and continue for 48 h after disappearance of symptoms (usually 5 to 7 d).

(1) 1 TO 9 YEARS: 5 mg/kg/d (up to 150 mg) PO in 2 divided doses.

(2) 10 TO 12 YEARS: 100 mg PO BID (children over 10 yr who weigh less than 40 kg: 5 mg/kg/d).

(3) 13 TO 64 YEARS: 100 mg PO BID.

(4) OVER 64 YEARS: Up to 100 mg PO once daily.

RIMANTADINE: For treatment of influenza A in adults and adolescents. Start within 24 to 48 h after symptom onset and continue for 48 h after disappearance of symptoms (usually 5 to 7 d).

(1) 13 TO 64 YEARS: 100 mg PO BID.

(2) OVER 64 YEARS: 50 to 100 mg PO BID.

ZANAMIVIR: For treatment of influenza A or B in adults and children 7 years and older who have been symptomatic for no more than 2 days.

(1) 7 YEARS AND OLDER: Two inhalations (one 5-mg blister per inhalation for total dose of 10 mg) BID for 5 days via a hand-held, breath-activated plastic inhaler device.

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OSELTAMIVIR: For treatment of influenza in adults and children who have been symptomatic for no more than 2 days.

(1) ADULTS & ADOLESCENTS 13 YEARS AND OLDER: 75 milligrams orally twice a day for 5 days.

(2) CHILDREN 1 YEAR AND OLDER: Under 15 kilograms, 30 milligrams orally twice a day for five days; 15-23 kilograms, 45 milligrams orally twice a day for 5 days; 24-40 kilograms, 60 milligrams orally twice daily for 5 days; over 40 kilograms, 75 milligrams orally twice a day for five days.

B. Chemoprophylaxis Only

The recommended use of antiviral drugs would be focused upon chemoprophylaxis to prevent symptoms of illness resulting from infection with a pandemic influenza A strain. This strategy would direct antiviral usage toward chemoprophylaxis of specific groups (e.g., persons at high- risk for complications from influenza and other groups such as health care workers - to be identified). This strategy would also address the relative roles of all four antiviral agents (e.g., use of only one class of antiviral drugs versus three drugs for chemo-prophylaxis of influenza A; zanamivir is not currently approved for chemoprophylactic use). This strategy should also address chemoprophylaxis of persons who are targeted to receive vaccination against the pandemic strain, when available. Recommendations for priority groups for antiviral chemotherapy could be modified based upon the evolving epidemiology of the pandemic. Clinical care would be focused upon management of complications of influenza such as antibiotic treatment of patients with secondary bacterial pneumonia, but would not utilize antiviral treatment. Issues to be considered include which persons should receive chemoprophylaxis, and the duration of chemoprophylaxis.

GENERAL: Factors such as cost, compliance, and potential side effects should be considered when determining the period of prophylaxis. For maximal effectiveness, the drug must be taken each day for the duration of influenza activity in the community; however, to be most cost effective, antiviral prophylaxis should be taken only during the period of peak influenza activity in a community.

HIGH-RISK PERSONS: Still can be vaccinated after an outbreak of influenza A has begun in a community; however, the development of antibodies in adults after vaccination usually takes 2 weeks, during which time chemoprophylaxis should be considered. Children who receive influenza vaccine for the first time can require up to 6 weeks of prophylaxis (i.e., for 2 weeks after the second dose of vaccine has been received). Chemoprophylaxis does not interfere with the antibody response to the vaccine.

CARE PROVIDERS OF HIGH-RISK PERSONS: During community or institutional outbreaks, chemoprophylaxis during peak influenza activity can be considered for unvaccinated persons who have frequent contact with persons at high risk to reduce the spread of virus to persons at high risk. Persons with frequent contact include household members, visiting nurses, volunteer workers, and employees of hospitals, clinics, and chronic-care facilities.

IMMUNODEFICIENCY: Chemoprophylaxis may be indicated for high-risk persons who are expected to have an inadequate antibody response to influenza vaccine, including persons with HIV infection, especially those with advanced disease. No data are available concerning possible interactions with other drugs used in the management of patients with HIV infection. Such patients must be monitored closely if chemoprophylaxis is used.

OTHER PERSONS: Chemoprophylaxis throughout the influenza season or during peak influenza activity might be appropriate for persons at high risk who should not be vaccinated.

Antiviral Agents for Influenza Prophylaxis

RECOMMENDATIONS: To be effective as chemoprophylaxis, antiviral medication must be taken each day for the duration of influenza A activity in the community (generally 6 to 12 weeks).

AMANTADINE:

(1) 1 TO 9 YEARS: 5 milligrams/kilogram/day (up to 150 mg) orally in 2 divided doses (NOTE: 5mg/kg of amantadine syrup = 1 tsp/22 lb).

(2) 10 TO 12 YEARS: 100 milligrams orally twice daily (children over 10 yr who weigh less than 40 kg: 5 mg/kg/d).

(3) 13 TO 64 YEARS: 100 milligrams orally twice daily.

(4) OVER 64 YEARS: 100 milligrams orally once daily.

(5) Available Forms: Symmetrel® syrup; Symadine® capsules; Amantadine-HCl syrup, capsules

RIMANTADINE:

(1) 1 TO 9 YEARS: 5 milligrams/kilogram/day (up to 150 mg) orally in 2 divided doses (NOTE: 5mg/kg of rimantadine syrup = 1 tsp/22 lb).

(2) 10 TO 12 YEARS: 100 milligrams orally twice daily (children over 10 yr who weigh less than 40 kg: 5 mg/kg/d).

(3) 13 TO 64 YEARS: 100 milligrams twice daily.

(4) OVER 64 YEARS: 50 to 100 milligrams orally twice daily (NOTE: Elderly nursing home residents should be administered only 100 mg/day; a reduction in dose to 100 mg/dy should be considered for all persons ≥65 years of age if they experience possible side effects when taking 200 mg/d).

(5) Available Forms: Flumadine® tablets, syrup

OSELTAMIVIR:

(1) ADULTS & ADOLESCENTS 13 YEARS AND OLDER: 75 milligrams orally twice a day for 5 days

(2) Available Forms: Tamiflu® capsules, oral suspension

Package label information for the four currently approved antiviral medications in the United States can be found at: www.fda.gov/cder/drug/antivirals/influenza/default.htm

C. Treatment and targeted chemoprophylaxis

Under this option, the recommended use of antiviral drugs would be for both treatment of ill patients and chemoprophylaxis against illness resulting from infection with the pandemic strain. ***Given the expected demand and need for antiviral drugs in this strategy, rationing or specific targeting of priority groups for chemoprophylaxis should be addressed.*** Chemoprophylaxis would not be recommended for widespread use and would only be recommended for specific categories of individuals (e.g., laboratory workers with direct contact with pandemic virus strains in a containment facility, health care workers in direct contact with confirmed cases, and for outbreak control in closed populations). This strategy would also address the relative roles of all four antiviral agents (e.g., which drugs should be used for treatment and which should be used for chemoprophylaxis; zanamivir is not currently approved for chemoprophylactic use.). This strategy should address the issues listed above under options A and B.

D. Targeted vaccination, targeted chemoprophylaxis, treatment

This strategy would recommend use of antiviral drugs for the highest priority groups for influenza vaccination until a vaccine-induced immune response is expected (e.g., duration until fourteen days post-vaccination). Unvaccinated high-risk persons and others could receive chemoprophylaxis against the pandemic strain for an unknown period - to be specified. Confirmed and suspected influenza cases would receive treatment within 48 hours of illness onset. Given the expected demand and need for antiviral drugs in this strategy, rationing or specific targeting of priority groups for chemoprophylaxis would need to be employed.

E. Other options

OUTBREAK CONTROL: Use of antiviral drugs for treatment and prophylaxis of influenza is an important component of institutional outbreak control (CDC, 2003):

(a) When institutional outbreaks occur, chemoprophylaxis should be administered to all residents and should continue for at least 2 weeks or until approximately 1 week after the end of the outbreak. Chemoprophylaxis can also be offered to unvaccinated staff that provides care to persons at high risk. Prophylaxis should be considered for all employees, regardless of their vaccination status, if the outbreak is caused by a variant strain of influenza that is not well-matched by the vaccine.

(b) Can also be considered for controlling influenza outbreaks in other closed or semiclosed settings such as dormitories or other settings where persons live in close proximity.

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PREGNANCY: Because of the unknown effects of influenza antiviral drugs on pregnant women and their fetuses, these agents should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus (CDC, 2003).

List of Commonly Used Acronyms

CDC	Centers for Disease Control and Prevention
CDD	Communicable Disease Division
CDN	Communicable Disease Nurse
CERC	Crisis and Emergency Risk Communication Plan
CERT	Community Emergency Response Teams
CHD	County Health Department
CHE	Catastrophic Health Emergency Act
ED	Emergency Department
EMS	Emergency Medical System
EOC	Emergency Operation Center
HAN	Health Alert Network
HRSA	Health Resource Services Administration and Services
ICP	Infection Control Practitioner
ICU	Intensive Care Unit
ILI	Influenza-like Illness
JIC	Joint Information Center
LHD	Local Health Department
MERC	Medical Emergency Response Center
MIPS	Mass Immunization Prophylaxis Strategy
MMRS	Metropolitan Medical Response System
MRC	Medical Reserve Corps
MOU	Memorandum of Understanding
NEDSS	National Electronic Disease Surveillance System
NVPO	National Vaccine Program Office
OEM	Office of Emergency Management
OSDH	Oklahoma State Department of Health
PHIDDO	Public Health Information & Disease Detection in OK
PHL	Public Health Laboratory
PIO	Public Information Officer
RHINO	The Reportable Health Information & Notification in OK
RMPG	Regional Medical Planning Group
RMRS	Regional Medical Response System
SNS	Strategic National Stockpile
TPRS	Terrorism Preparedness and Response Service
WHO	World Health Organization

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