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BRITISH COLUMBIA'S H1N1 PANDEMIC INFLUENZA RESPONSE PLAN (2009)

Antibiotics for Secondary Pneumonia in Community and Acute Care Settings

October 2, 2009

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EXECUTIVE SUMMARY

With pandemic (H1N1) 2009 influenza, there is a risk of morbidity and mortality related to secondary bacterial infections such as pneumonia. The purpose of this document is to review the antibiotic drugs that may be required for treatment of secondary bacterial pneumonia during an influenza pandemic and to project the potential demand for these antibiotics in both the community and acute care settings.

This review considers many past and current experiences, including the 1918-1919 and 1957-1958 pandemics, seasonal influenza, recent pandemic experience from Mexico, Australia, and New Zealand, potential pathogens, effect of other anti-infective products, the antibiotic supply chain, recommendations from Public Health Agency of Canada (PHAC), and the current situation in Canada and in British Columbia.

While much can be learned from the past pandemics, caution should be used when extrapolating findings to the current pandemic due to differences in viral strains and the severity of resulting illness, health care systems, and availability of antivirals, vaccines, and antibiotics.

The potential effect of utilization of antivirals, pandemic vaccine, seasonal flu vaccine, pneumococcal vaccine and *Hemophilus influenzae* type b vaccine on the incidence and severity of secondary bacterial pneumonia is unknown. Depending on their availability, uptake and effectiveness, the antivirals and pandemic vaccine should have a significant impact in reducing the incidence of secondary bacterial pneumonia.

It is assumed that the total antibiotic supply chain (including active pharmaceutical ingredient suppliers, manufacturers, distributors, and pharmacies) collectively hold 10-15% inventory above monthly demands and this fluctuates based on seasonal demand adjustments. While the supply ebb and flow varies from antibiotic to antibiotic, it is expected that there will be flexibility in the antibiotic supply chain due to multiple recommended types of effective antibiotics, multiple source manufacturers, and varying regional demand.

To project the potential demand for antibiotics, a model for the British Columbia population was developed with various assumed inputs. The pandemic attack rate, defined as the number of clinical or laboratory-confirmed cases divided by the total population, was assumed to be 7.5% (sensitivity analyses examined a range between 5% and 15%). Where available, related estimates or actual figures generated by the Ministry of Health Services and Ministry of Healthy Living and Sport, British Columbia Centre for Disease Control (BCCDC), Public Health Agency of Canada (PHAC), World Health Organization (WHO), Australia, and New Zealand.

The model assumed that 10% of H1N1-infected cases in the community and 25% of H1N1-infected cases in acute care would necessitate treatment with antibiotics for presumed or confirmed secondary pneumonia. This resulted in a projection of approximately 11,000 courses of antibiotics required, with 96% and 4% requiring care in the community and acute settings, respectively. Based on this, the expected monthly antibiotic demand in the community setting is a very small incremental increase (base case projection 2.3%, range 0.8% to 7%) over baseline seasonal antibiotic utilization. While a specific demand analysis was not completed in the acute care setting (due to lack of actual antibiotic utilization data for all hospitals in British Columbia), the expected antibiotic demand is also expected to be low relative to baseline demand.

Recommendations:

Recommendation #1: Antibiotic stockpiling during the current 2009-2010 influenza season is not necessary in community and acute care settings, due to low anticipated demand relative to baseline demand and sufficient anticipated capacity in the current supply chain. With an assumed attack rate of 7.5% (5% to 15% in the sensitivity analyses) and an assumed secondary pneumonia attack rate of 10% (5 to 15% in the sensitivity analysis), a very small incremental increase in the monthly antibiotic demand (base case 2.3%, range 0.8% to 7%) is expected for the community setting. Since the current supply chain is expected to manage demand increases of 10% to 15% with seasonal adjustments, levels well above the expected demand, then antibiotic stockpiling should not be necessary. While a similar analysis was not completed for the acute care setting (due to lack of data), the projection and conclusion are expected to be similar.

This recommendation differs from the PHAC recommendation to stockpile antibiotics. This may be due to a difference of assumed pandemic attack rates and the additional assessment of supply chain capacity included in our analysis. This analysis used a 7.5% attack rate for its base case projections while PHAC proposed an attack rate of 15% to 35%. Based on a review of actual attack rates in Australia and New Zealand (where the pandemic peak has passed), as well as data in Canada and British Columbia, we believe that lower attack rate assumptions are justified. As of September 29, 2009, the attack rates in Australia and New Zealand were an estimated 5% (gross clinical attack rate) and 11% (gross attack rate), respectively.

Recommendation #2: Community and acute care pharmacies should check their antibiotic inventories and adequately replenish, as required, those recommended antibiotics (as per forthcoming guidance from the Clinical Care Advisory Group) **that are typically dispensed by individual pharmacies.** This recommendation is precautionary to ensure that pharmacies are prepared with their typical inventory. In consideration of Recommendation #1 and the relatively broad array of recommended antibiotics for secondary bacterial pneumonia, pharmacies are not to begin stocking recommended antibiotics that are not typically inventoried at the individual pharmacy.

Recommendation #3: Clinicians should be reminded and/or educated on the appropriate antibiotic use for secondary bacterial pneumonia (as per forthcoming guidance from the Clinical Care Advisory Group). Appropriate antibiotic use is expected to lead to optimal outcomes and lower rates of resistance.

Recommendation #4: Appropriate bacterial vaccination should be encouraged and aligned with direction from the British Columbia Centre for Disease Control. Bacterial vaccination (pneumococcal vaccine and *Hemophilus influenzae* type b vaccine) in appropriate individuals may reduce the incidence of pandemic-related secondary bacterial pneumonia.

1. INTRODUCTION

The emergence of pandemic (H1N1) 2009 influenza has necessitated health care decision makers and providers to anticipate, plan and prepare all potentially impacted areas of the healthcare sector. For anti-infectives, early attention has focused on vaccine development for disease prevention and antiviral drugs for early treatment. However, due to the risk of morbidity and mortality related to secondary bacterial infections such as pneumonia, the potential role and demand for antibiotics also requires assessment.

2. GOAL STATEMENT AND OBJECTIVES

2.1 Goal Description

The purpose of this document is to characterize the antibiotic drugs that may be required for treatment of secondary bacterial pneumonia during an influenza pandemic and to project the potential demand for these antibiotics in both the community and acute care settings.

2.2 Objective Description

This will address specific planning provisions to address the following issues regarding the treatment of secondary bacterial pneumonia in the community and acute care settings:

- **specific** antibiotic and/or **class** of antibiotics;
- **volume** of antibiotics.

3. CONSIDERATIONS AND ASSUMPTIONS

- **Experience from 1918-1919 Pandemic:** While much can be learned from the past pandemics like the 1918-19 pandemic, caution should be used when extrapolating findings to the current pandemic due to differences in viral strains and the severity of resulting illness, health care systems, and availability of antivirals, vaccines, and antibiotics. It has been estimated that during the 1918-19 pandemic, up to one-third of deaths were due to secondary bacterial pneumonia and one-third were caused by combined viral and bacterial pneumonia.[1] One study evaluating cause of death from tissue specimens of patients who died from the 1918-19 pandemic show that 92.7% of the specimens were positive for at least one organism (in other words, negative cultures were rare).[2] The predominant organism was *Streptococcus pneumoniae* (23.5%), *Streptococcus hemolyticus* (17%) or other *Streptococcus* species (21%); *Staphylococcus* species were rare, accounting for only for 8% of the pathogens.
- **Experience from 1957-1958 Pandemic:** In contrast to the pathogens in the 1918-1919 pandemic, *Staphylococcus aureus* was most commonly seen in bacterial respiratory infections.[3]

[1] Stiver, G. Use of vaccines and antiviral drugs in the next influenza pandemic. BCMJ 2007;49(5).

[2] Morens DM, Taubenberger JK, Fauci AS. Predominant role of bacterial pneumonia as a cause of death in pandemic influenza: implications for pandemic influenza preparedness. J Infect Dis 2008;198:962-70.

[3] Robertson L, Caley JP, Moore J. Importance of *Staphylococcus aureus* in pneumonia in the 1957 epidemic of influenza A. Lancet 1958;2:233-6.

- **Experience and Impact of Seasonal Influenza:** The concurrent circulation of pandemic influenza and seasonal influenza further complicates the ability to project the potential incremental antibiotic demand above baseline antibiotic demand levels due to seasonal flu alone. In the modern antibiotic era, the widespread use of antibiotics, and establishment of pneumococcal and *Hemophilus influenzae* type b vaccine programs have impacted the types of organisms seen. As such, researchers have evaluated bacterial pneumonia development post-seasonal influenza. Autopsy data shows that roughly 25% of patients are co-infected with roughly 12-30% being infected with *Streptococcus pneumoniae*. A retrospective study of childhood deaths from pneumonia during the 2003-2004 season in the United States found *Staphylococcus aureus* to be the most common strain, accounting for 46% of the isolates (more than 50% of these were *methicillin-resistant Staphylococcus aureus* [MRSA]).[4] Other common organisms include *Hemophilus influenzae* (~10%) and atypicals such as *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*.
- **Experience from Pandemic in Mexico (Fall 2008/Spring 2009):** Between March 24 and April 29, 2009, the Mexico Ministry of Health reported 2,155 cases of severe pneumonia, resulting in 821 hospitalizations and 100 deaths.[5] This analysis found 87% of deaths and 71% of cases of severe pneumonia involving patients between 5 and 59 years of age (elevated from 17% and 32% respectively). A case series at a national tertiary care hospital for respiratory illnesses in Mexico City described 18 cases of pneumonia and confirmed pandemic (H1N1) 2009 influenza from March 24 through April 24, 2009.[6] Of these, 12 required mechanical ventilation, and 7 died. None of these patients had received oseltamivir prior to admission; after admission, 14 received oseltamivir. Bacterial cultures within 24 hours after admission were negative for n=6 (blood specimens), n=2 (bronchial aspirates), and n=1 (pleural fluid). Three patients had received antibiotics within 24 to 48 hours before admission. In terms of antibiotics after admission, 17 received ceftriaxone, and 10 received clarithromycin. Several patients also received other antibiotics (n=3 levofloxacin, n=7 vancomycin, n=5 cefepime, n=5 imipenem, n=2 dicloxacillin). In conclusion, it appears that secondary bacterial pneumonia was not a major cause of morbidity and mortality in these 18 cases.
- **Experience from Pandemic in Australia and New Zealand (Summer 2009):** In July 2009, the Australian government recognized that the pandemic (H1N1) 2009 is "not as severe as originally envisaged... and that the disease is mild in most cases, severe in some and moderate overall." On August 28, 2009, the WHO indicated that most countries in the Southern Hemisphere, including Australia and New Zealand, had passed their peak flu activity. As of September 7, 2009, Australia reported 35,579 confirmed cases of pandemic (H1N1) 2009 influenza and 161 associated deaths, whereas New Zealand reported 3,146 confirmed cases and 17 associated deaths (national government H1N1 news bulletins). A paper published on September 28, 2009, reported the experience in Victoria, Australia's second most populous state. With the assistance of prospective modeling tools, a 5% gross H1N1 attack rate was observed, with 0.3% of infected

[4] Bhat N, Wright JG, Broder KR, Murray EL, Greenberg ME, Glover MJ, et al. Influenza-associated deaths among children in the United States, 2003-2004. N Engl J Med 2005;353:2559-67.

[5] Chowell G, Bertozzi SM, Colchero MA, Lopez-Gatell H, Alpuche-Aranda C, Hernandez M, et al. Severe respiratory disease concurrent with the circulation of H1N1 influenza. New Engl J Med 2009;361:674-9.

[6] Perez-Padilla R, de la Rosa-Zamboni D, de Leon SP, Hernandez M, Quinones-Falconi F, Bautista E, et al. Pneumonia and respiratory failure from swine-origin Influenza A (H1N1) in Mexico. N Engl J Med 2009;361:680-9.

patients being hospitalized and 20% of hospitalized patients being admitted to intensive care.[7] Based on a review of their national government websites as well as community pharmacy guilds there does not appear to be any specific antibiotic supply preparations. Further, a search also failed to identify any news stories related to antibiotic shortages in these two countries.

- **Potential Pathogens:** The most common organisms in secondary bacterial pneumonias are *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Hemophilus influenzae*, as confirmed by a recent American analysis.[8] It is assumed that current antibiotic sensitivities will remain stable during a pandemic.
- **Effect of Other Anti-Infective Products:** The potential effect of utilization of antivirals, pandemic vaccine, seasonal flu vaccine, pneumococcal vaccine and *Hemophilus influenzae* type b vaccine on the incidence and severity of secondary bacterial pneumonia is unknown. Depending on their availability, uptake and effectiveness, the antivirals and pandemic vaccine should have a significant impact in reducing the incidence of secondary bacterial pneumonia. The antivirals will be made available via the provincial pandemic stockpile as of October 1, 2009. The pandemic vaccine is expected to be available in November 2009. The seasonal flu vaccine will also be available in November 2009. The pneumococcal vaccine has historically had poor uptake in British Columbia; this level of utilization is not expected to increase significantly in the short to medium term.
- **Antibiotic Supply Chain:** It is assumed that the total antibiotic supply chain (including active pharmaceutical ingredient suppliers, manufacturers, distributors, and pharmacies) collectively hold 10-15% inventory above monthly demands and this fluctuates based on seasonal demand adjustments. While the supply ebb and flow varies from antibiotic to antibiotic, it is expected that there will be flexibility in the antibiotic supply chain because there are multiple antibiotics that are effective against potential pathogens (see section on specific antibiotics and/or class of antibiotic), and many of these antibiotics are off-patent and thus available from multiple manufacturers. Multi-source products (i.e., antibiotics with more than one manufacturer) include: amoxicillin, amoxicillin-clavulanate, azithromycin, cefuroxime, ceftriaxone, ciprofloxacin, clarithromycin, doxycycline, erythromycin, gentamicin, levofloxacin, piperacillin-tazobactam, tobramycin, and vancomycin. Single-source products (i.e., antibiotics with only one manufacturer) include: aztreonam, cefepime, cefotaxime, imipenem, linezolid, meropenem, and moxifloxacin. The overall incremental supply demand pressures above baseline demand will depend upon the region of demand, (municipality, provincial, versus national), increased consumption rate, and the duration of increased demand.
- **Recommendation from Public Health Agency of Canada (PHAC):** In Annex G Health Services: Clinical Care Guidelines and Tools, PHAC made the following recommendation: *Health planners need to consider stockpiling medications and supplies to address treatment. This includes both antibiotics and supplies for sputum and blood cultures, as well as Gram stains. Stockpiling of antibiotics should be based on the most recent consensus guidelines for the management of community-acquired pneumonia in adults.* See Appendix A for PHAC clinical

[7] Lum ME, McMillan AJ, Brook CW, Lester R, Piers LS. Impact of pandemic (H1N1) 2009 influenza on critical care capacity in Victoria. Med J Austr 2009. Available online at: http://www.mja.com.au/public/issues/191_09_021109/lum10916_fm.html. Accessed Sept 29, 2009.

[8] CDC. Bacterial coinfections in lung tissue specimens from fatal cases of 2009 Pandemic Influenza A (H1N1) – United States, May-August 2009. MMWR September 29, 2009;58(Early Release):1-4. Available online at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm58e0929a1.htm?s_cid=rr58e092. Accessed Sept 30, 2009.

care guidelines. In arriving at its recommendation, it is unclear whether PHAC included into their evaluation all of the considerations and uncertainties highlighted in this review, including supply chain capacity. Based upon the recently observed trends, PHAC is reviewing this recommendation.[9]

[9] Personal communication with Marra F, British Columbia Centre for Disease Control. Received September 24, 2009.

4. SPECIFIC ANTIBIOTICS AND/OR CLASS OF ANTIBIOTIC FOR SECONDARY BACTERIAL PNEUMONIA

The most common organisms in secondary bacterial pneumonias are expected to be *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Hemophilus influenzae*. These organisms are expected to be sensitive to the drug therapy guidance described in Table 1. Two primary sources were considered in developing the draft drug therapy guidance: (1) PHAC guidelines and (2) January 2009 clinical guidance for community-acquired pneumonia developed by Pharmaceutical Services Division (PSD) of the Ministry of Health Services in consultation with external partners. The consulted partners was a multidisciplinary working group comprising of hospital-based infectious disease physician and pharmacist specialists, medical microbiologists, general physician practitioners, the British Columbia Centre for Disease Control, Do Bugs Need Drugs®, and the Guidelines and Protocols Advisory Committee, PSD developed coverage recommendations for fluoroquinolone antibiotics. Antibiotics or antibiotics classes recommended for the appropriate management of bacterial pneumonia are summarized in this document (Table 1) are in **DRAFT form for projection purposes only**, and will be finalized by an infectious diseases working subgroup of the Clinical Care Advisory Group..

Table 1: Recommended specific antibiotics and/or class of antibiotic by care setting – DRAFT – for projections only

Care Setting		Recommended Specific Antibiotic and/or Class of Antibiotic*
Community	Previously healthy, no antimicrobials in previous 3 months	• Macrolide** • Doxycycline
	Comorbidities or antimicrobials in previous 3 months or residential care	• Beta-lactam (amoxicillin high-dose, amoxicillin-clavulanate, or cefuroxime) + macrolide** • Beta-lactam (amoxicillin high-dose, amoxicillin-clavulanate, or cefuroxime) + doxycycline • levofloxacin or moxifloxacin
Acute	Non-intensive care unit (ICU)	• Beta-lactam (amoxicillin high-dose, amoxicillin-clavulanate, or cefuroxime) + macrolide** • levofloxacin or moxifloxacin
	ICU	• Beta-lactam (cefotaxime, ceftriaxone, ampcillin-sulbactam) + azithromycin intravenous OR + levofloxacin or moxifloxacin • If penicillin-allergic, levofloxacin or moxifloxacin + aztreonam • If *Pseudomonas aeruginosa,* piperacillin-tazobactam, cefepime, imipenem or meropenem) + levofloxacin or moxifloxacin OR aminoglycoside + azithromycin IV • If *methicillin-resistant Staphylococcus aureus,* + vancomycin or linezolid

* For more details of specific antibiotics included in each class, please refer to forthcoming guidance from the Clinical Care Advisory Group.

** Use of azithromycin alone promotes resistance with *Streptococcus pneumoniae.*

5. PROJECTED ANTIBIOTIC DEMAND

To project the potential demand for antibiotics, a model for the British Columbia population was developed with various assumed inputs. Where available, related estimates or actual figures generated by the Ministry of Health Services and Ministry of Healthy Living and Sport,[10] British Columbia Centre for Disease Control,[11] PHAC,[12-13] World Health Organization (WHO), Australia[14-15] and New Zealand[16] were considered (please refer to Table 2).

Table 2: Comparison of rates of pandemic attack and hospitalizations by jurisdiction, as of September 2009

Jurisdiction	Pandemic (H1N1) 2009 Influenza Attack Rate	Hospitalization Rate
Australia (Victoria)	5%	0.3%
New Zealand	11%	0.2%
Projection model for British Columbia	**7.5%**	**0.5%**

[10] H1N1 flu virus (human swine flu) under surveillance, update 12pm PDT, 15 Sept 2009. Available online: http://www2.news.gov.bc.ca/news_releases_2009-2013/2009HSERV0001-000004.htm. Accessed September 21, 2009.

[11] Influenza & Emerging Respiratory Pathogens Team, British Columbia Centre for Disease Control. Novel pandemic H1N1 virus (nH1N1) surveillance update: British Columbia, 14 Sept 2009. Available online: http://www.bccdc.ca/NR/rdonlyres/EB9B5651-1251-4E16-8AFE-D4819DADBEB2/0/BC_nH1N1_Surveillance_Update.pdf. Access September 21, 2009.

[12] Bi-weekly and cumulative number of deaths due to Pandemic (H1N1) 2009, by province/territory, Canada, as of 17 September, 2009, 11h00 EDT. Available online: http://www.phac-aspc.gc.ca/alert-alerte/h1n1/surveillance-eng.php. Accessed September 21, 2009.

[13] FluWatch August 23, 2009 to August 29, 2009 (Week 34). Available online: http://www.phac-aspc.gc.ca/fluwatch/08-09/w34_09/index-eng.php#t1. Accessed September 21, 2009.

[14] National tally of confirmed cases of H1N1 Influenza 09 (Human Swine Influenza) as of 12pm, September 9, 2009. Department of Health and Ageing. Available online at: http://www.healthemergency.gov.au/internet/healthemergency/publishing.nsf/Content/2FBF38115CD98BB7CA25762A00121475/$File/090909.pdf. Accessed Sept 9, 2009.

[15] Lum ME, McMillan AJ, Brook CW, Lester R, Piers LS. Impact of pandemic (H1N1) 2009 influenza on critical care capacity in Victoria. Med J Austr 2009. Available online at: http://www.mja.com.au/public/issues/191_09_021109/lum10916_fm.html. Accessed Sept 29, 2009.

[16] Baker MG, Wilson N, Huang QS, Paine S, Lopez L, Bandaranayake D, et al. Pandemic Influenza A (H1N1)V in New Zealand: the experience from April to August 2009. Euro Surveill 2009;34:pii=19319. Available online at: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19319. Accessed September 24, 2009.

The model included the following key assumptions:

- pandemic attack rate, defined as the number of clinical or laboratory-confirmed cases divided by the total population (**assumed to be 7.5%; sensitivity analyses 5% to 15%**);
- hospitalization rate, which was defined as the number of hospitalizations divided by the number of cases (**assumed to be 0.5%**);
- treatment setting: community (**assumed to be 96%**) and acute care (**assumed to be 4%**);
- antibiotic demand rate for presumed (empiric therapy) or confirmed (treatment therapy) secondary bacterial pneumonia rate: community (**assumed to be 10%; sensitivity analyses 5% to 15%**) and acute care (**assumed to be 25%; sensitivity analysis 15% to 40%**). The acute care rate includes antibiotic courses for community-acquired pneumonia and hospital-acquired pneumonia.
- antibiotic class selection for the cost projection (see Table 1);
- antibiotic costs based on typical treatment regimens and dispensing fees (in the community setting only);
- consumption time period (**assumed to be 4 months**) and rate (**assumed to be equal rate for each month**)

Based on the above assumptions, the model projects approximately 104,000 community clinical presentations and 1,600 hospitalizations due to H1N1. Of these, approximately **11,000 courses of antibiotics are expected to be required**, with 96% and 4% required in the community and acute settings, respectively. For key assumptions like pandemic attack rate and rate of antibiotic demand, sensitivity analyses were conducted around base case assumptions (Appendix A). The lowest and highest assumptions in the sensitivity analysis projects approximately 3,600 to 32,600 courses of antibiotics required.

Based on the projections, **the expected antibiotic demand is low relative to the baseline demand in the community care setting.** In the community setting, the average projected monthly increase in antibiotic demand due to pandemic-related secondary bacterial pneumonia is a 2.3% (0.8% to 7%) during the months of November through to February (Appendix B).

While this analysis was not completed for the acute care setting (due to lack of actual antibiotic utilization data for all hospitals in British Columbia), **the expected antibiotic demand is also expected to be low relative to baseline demand.**

6. ANTIBIOTIC SUPPLY RECOMMENDATIONS

Recommendation #1: Antibiotic stockpiling during the current 2009-2010 influenza season is not necessary, due to low anticipated demand relative to baseline demand and sufficient anticipated capacity in the current supply chain.

Rationale: With an assumed attack rate of 7.5% (5% to 15% in the sensitivity analyses) and an assumed secondary pneumonia attack rate of 10% (5 to 15% in the sensitivity analysis), a very small incremental increase in the monthly antibiotic demand (base case 2.3%, range 0.8% to 7%) is expected for the community setting. Since the current supply chain is expected to manage demand increases of 10% to 15% with seasonal adjustments, levels well above the expected demand, then antibiotic stockpiling should not be necessary. While a similar analysis was not completed for the acute care setting (due to lack of data), the projection and conclusion are expected to be similar.

This recommendation differs from the PHAC recommendation to stockpile antibiotics. This may be due to a difference of assumed pandemic attack rates and the additional assessment of supply chain capacity included in our analysis. This analysis used a 7.5% attack rate for its base case projections while PHAC proposed an attack rate of 15% to 35%. Based on a review of actual attack rates in Australia and New Zealand (where the pandemic peak has passed), as well as data in Canada and British Columbia, we believe that lower attack rate assumptions are justified. As of September 29, 2009, the attack rates in Australia and New Zealand were an estimated 5% (gross clinical attack rate) and 11% (gross attack rate), respectively.

Recommendation #2: Community and acute care pharmacies should check their antibiotic inventories and adequately replenish, as required, those recommended antibiotics (as per forthcoming guidance from the Clinical Care Advisory Group**) that are typically dispensed by individual pharmacies.**

Rationale: This recommendation is precautionary to ensure that pharmacies are prepared with their typical inventory. In consideration of Recommendation #1 and the relatively broad array of recommended antibiotics for secondary bacterial pneumonia, pharmacies are not to begin stocking recommended antibiotics that are not typically inventoried at the individual pharmacy.

Recommendation #3: Clinicians should be reminded and/or educated on the appropriate antibiotic use for secondary bacterial pneumonia (as per forthcoming guidance from the Clinical Care Advisory Group**).**

Rationale: Appropriate antibiotic use will lead to optimal outcomes and lower rates of resistance.

Recommendation #4: Appropriate bacterial vaccination should be encouraged and aligned with direction from the British Columbia Centre for Disease Control.

Rationale: Bacterial vaccination (pneumococcal vaccine and *Hemophilus influenzae* type b vaccine) in appropriate individuals may reduce the incidence of pandemic-related secondary bacterial pneumonia.

7. OPERATIONAL CONSIDERATIONS

Recommendation # 1 (No antibiotic stockpiling): Develop core messages and communication plan. Communicate to key stakeholders. No other action required.

Recommendation #2 (Check and replenish antibiotic inventories): Develop core messages and communication plan. Communicate to key stakeholders. Community and acute care pharmacies should be advised to check and adequately replenish their antibiotic inventories as required.

Recommendation #3 (Remind and/or educate clinicians on appropriate antibiotic use): Develop core messages and communication plan. Communicate to key stakeholders. Where applicable, consider local drug formularies and related prescribing policies and utilize existing medical educational channels wherever possible.

Recommendation #4 (Bacterial vaccination): BC Centre for Disease Control (BCCDC) and Provincial Health Officer (PHO) to consider with their other vaccination initiatives.

8. ROLES AND RESPONSIBILITIES

Table 3 summarizes the proposed roles and responsibilities to be finalized pending consultation and/engagement with the appropriate stakeholder. Stakeholders may include:

- College of Pharmacists of British Columbia (CoPBC)
- British Columbia Pharmacy Association (BCPhA)
- College of Physicians and Surgeons of British Columbia (CoPSBC)
- British Columbia Medical Association (BCMA)
- British Columbia Centre for Disease Control (BCCDC)
- Provincial Health Officer (PHO)
- British Columbia Health Authorities (BC HA)
- Health Authorities Division (HAD)
- Pharmaceutical Services Division (PSD)
- Pandemic Influenza Operational Planning Project Clinical Care Advisory Group (CCAG)

Table 3: Proposed roles and responsibilities to implement recommendations

	Action	Lead(s)	Collaboration
Recommendation # 1 (No antibiotic stockpiling)	Develop core messages and communication plan	PSD BCCDC	PHO CCAG BC HA HAD
	Communicate to key stakeholders	PSD BCCDC HAD	CoPBC BCPhA BC HA Pharmacies
Recommendation #2 (Check and replenish antibiotic inventories)	Develop core messages and communication plan *(to be informed by outputs from Recommendation #3)*	PSD BCCDC	PHO CCAG BC HA HAD
	Communicate to stakeholders	PSD BCCDC HAD	CoPBC BCPhA BC HA Pharmacies
Recommendation #3 (Remind and/or educate clinicians on appropriate antibiotic use)	Develop core messaging and communication plan	PSD BCCDC CCAG	PHO
	Communicate to stakeholders	PSD BCCDC PHO CCAG	CoPBC BCPhA CoPSBC BCMA BC HA HAD
Recommendation #4 (Bacterial vaccination)	To be determined	BCCDC PHO	To be determined

9. Next Steps or Future Recommendations

The Clinical Care Advisory Group has identified an infectious diseases working subgroup that will finalize the clinical guidance on recommended antibiotics for bacterial pneumonia. As many of the sub-plans that form part of the Ministry's overall plan will be evergreen, the content in this sub-plan will evolve, or be expanded on in the future. Next steps and future recommendations will be updated as new information becomes available.

APPENDICES

Appendix A: Sensitivity Analyses for BC Antibiotic Demand Projection for Pandemic-Related Secondary Pneumonia (shaded cell = base case projection)

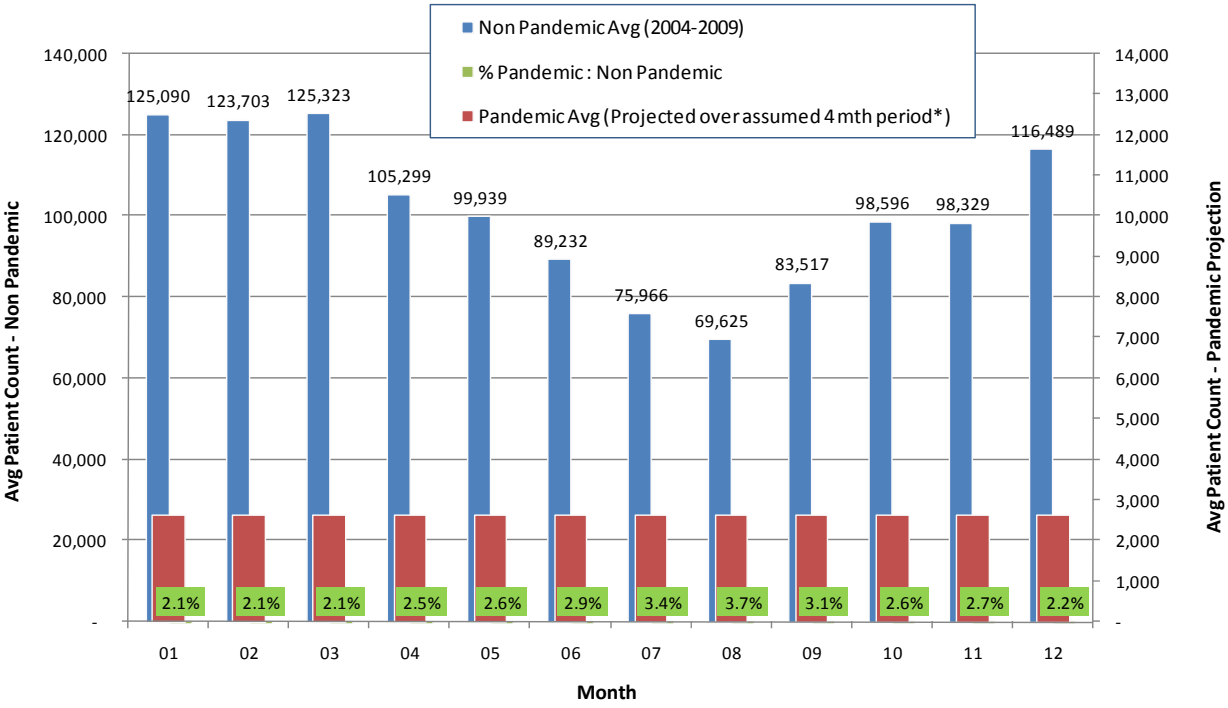
A. Community Antibiotic Demand (Antibiotic Courses)

Community Antibiotic Demand	H1N1 Attack Rate					
	5.0%	**6.6%**	**7.5%**	**10.0%**	**12.5%**	**15.0%**
5.0%	3,480	4,594	5,221	6,961	8,701	10,441
7.5%	5,221	6,891	7,831	10,441	13,051	15,662
10.0%	6,961	9,188	10,441	13,921	17,402	20,882
12.5%	8,701	11,485	13,051	17,402	21,752	26,103
15.0%	10,441	13,782	15,662	20,882	26,103	31,323

B. Acute Care Antibiotic Demand (Antibiotic Courses)

Acute Care Antibiotic Demand	H1N1 Attack Rate					
	5.0%	**6.6%**	**7.5%**	**10.0%**	**12.5%**	**15.0%**
15.0%	163	215	244	325	407	488
20.0%	217	286	325	434	542	651
25.0%	271	358	407	542	678	813
33.0%	358	472	537	716	895	1,074
40.0%	434	573	651	868	1,085	1,302

Appendix B. Projected Monthly Demand for Antibiotics in the Community Care Setting During a Pandemic



* Notes on Pandemic Avg Projection: (1) Based upon avg. monthly use over a 4 month period. (2) While a pandemic is expected to last approximately 4 months, use is documented monthly in this chart ifor llustrative purposes since it is unknown when the pandemic will occur.

Sensitivity Analysis: Percent Projected Pandemic Demand to Avg Actual Seasonal Use (Nov to Feb) in Community Setting

		H1N1 Attack Rate					
		5.0%	**6.6%**	**7.5%**	**10.0%**	**12.5%**	**15.0%**
Community Antibiotic Demand	**5.0%**	0.8%	1.0%	1.2%	1.5%	1.9%	2.3%
	7.5%	1.2%	1.5%	1.7%	2.3%	2.9%	3.5%
	10.0%	1.5%	2.0%	2.3%	3.1%	3.9%	4.6%
	12.5%	1.9%	2.6%	2.9%	3.9%	4.8%	5.8%
	15.0%	2.3%	3.1%	3.5%	4.6%	5.8%	7.0%