

Severe H1N1 Disease: Preventing Cases, Reducing Mortality
Winnipeg, Manitoba, Sept 1-2, 2009

Breakout Session
Severe H1N1 Research Critical Questions
Antivirals and Vaccines
in the Community

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Severe H1N1 Research: Critical Questions

Antivirals and Vaccines in the Community

- **Antivirals**
 - National strategy
 - Research Issues/Questions
- **Vaccines**
 - National strategy
 - Major 'a priori' issues
 - What will be known when vaccine rolls out?
 - What postmarket studies are already planned?
 - What are the gaps?
- **Communicating Antiviral & Vaccine Strategies**

National Antiviral Pandemic Strategy

“Treat all who need it”

- ILI + otherwise healthy = supportive care
- ILI + **risk factors** OR **severity indicators** = Treat with antivirals

Limited prophylaxis

- To control outbreaks in closed facilities (e.g. long term care facilities, prisons)

Research Questions:

Are antivirals effective in infants less than 1 year?

Do antivirals decrease the rate of complications?

Is IV zanamivir effective? (available through Health Canada's Special Access Programme)

National Pandemic Vaccine Strategy

Vaccine (Annex D)

- “Immunization with a safe and effective pandemic vaccine..... the cornerstone of the response....”
- “...vaccine for every person in Canada....”
- “...available to as many people as possible as quickly as possible.”
- 2001: 10 year pandemic readiness vaccine contract established

Pandemic (H1N1) 2009 Vaccine

Major 'a priori' issues

BECAUSE IT IS A PANDEMIC

- Much less safety, immunogenicity data than usual
- No efficacy data

BECAUSE IT IS H1N1 OF SWINE ORIGIN

- 1976 'swine flu' H1N1 vaccine: attributable risk of Guillain Barre Syndrome about 1/100,000 dose
- All other seasonal flu vaccines: $\leq 1/100,000$ doses

BECAUSE IT CONTAINS A NOVEL ADJUVANT

- ASO3: oil-in-water emulsion with squalene (shark liver oil)
 - No marketed product experience anywhere
 - limited safety profile based on:
 - ~ 12,000 in H5N1 trials (3yr - 65+)
 - ~ 30,000 older adults in studies of ASO3 adjuvanted seasonal TIV
- MF59 also oil-in-water shark derived adjuvant
 - Novartis pandemic vaccine
 - Licensed influenza vaccine for elderly since 1997 in Europe; > 40million doses distributed - no proven risk; limited experience in younger adults/children

Pandemic (H1N1) 2009 Vaccine

What will be known when vaccine rolls out?

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Pandemic (H1N1) 2009 Vaccine

What will be known when vaccine rolls out?

- Immunogenicity of a single dose of unadjuvanted vaccine (15 or 30 ug)
 - mid to late September (CSL product)
- GSK first dose comparative immunogenicity data available by late October/early November
- Safety data on adjuvanted and unadjuvanted vaccine from global experience will be shared - primarily will inform common (0.5-1%) reactions and possibly some lower risk events (1/1000)
- GSK clinical development - much planned but takes time (well into 2010)
 - Near simultaneous adult (>4000) and pediatric(1800) evaluations
 - Confirm benefit of adding ASO3 to H1N1
 - Antigen sparing
 - Superior immunogenicity versus plain antigen
 - Cross-reactive immunity against drift variants
 - 1-visit schedule (2 doses simultaneously)
 - Assess interference between TIV and H1N1 (sequential or co-ad)
 - Can ASO3 overcome interference if any?
- Pandemic Vaccine Task Group will make specific recommendations on vaccine use in October - based on whatever data is available

Pandemic (H1N1) 2009 Vaccine

What postmarket studies are already planned?

PHAC-CIHR Influenza Research network (PCIRN)

- Rapid clinical trials
- Special populations
- Active/stimulated passive surveillance of large cohort of first vaccinees (likely HCWs; >100,000)
- Active surveillance for Adverse events of special importance (AESI)
 - Pediatric and adult acute care settings

Health-Portfolio newly supported research

- National surveillance for all GBS cases (not just those following vaccine)
 - Use self-controlled case series analysis to assess if increased risk or not

F/P/T Immunization program planning

Pandemic (H1N1) 2009 Vaccine

What are the research gaps?

- Many of the populations at risk for severe disease regarding specific vaccine safety, immunogenicity, effectiveness data
 - Pregnant women
 - Immunocompromised hosts
 - Individuals with chronic medical conditions
 - Young children
 - Aboriginal populations
- Interaction between seasonal and pandemic vaccine

Communicating Antiviral & Vaccine Strategies

PANDEMIC GOAL	Strategy	Vaccinate		Antivirals	
	Target Group	Target	Contacts	Treat	Prophylaxis

Communicating Antiviral & Vaccine Strategies

PANDEMIC GOAL	Strategy	Vaccinate		Antivirals	
	Target Group	Target	Contacts	Treat	Prophylaxis
Reduce severe disease & deaths	Pregnant women				
	Infants <6mos				
	Children 6-<24 mos				
	Immunocompromised				
	Chronic disease <50yr				
	Chronic disease ≥50yr				
	Morbid obesity				
	Healthy Adults 18to<50				
	Healthy Adults 50+ years				
Maintain critical infrastructure reduce societal disruption	'health care workers'				
	pandemic responders				
	Critical infrastructure workers				
Reduce viral transmission	Preschoolers ≥24 mos				
	Schoolage				

National Antiviral Pandemic Strategy

Upcoming Issues

Accessing antivirals from National Antiviral Stockpile

- AVs generally available through retail pharmacies
- Each province/territory working out best way to mobilize AVs from the National Antiviral Stockpile
 - pharmacies
 - P/T run health centres
 - local public health

What to do when/if oseltamivir resistance develops?

- 80% stockpile is oseltamivir
- Severe shortage scenario will mean limited use.
- Allocation framework has been developed; need for professional/public consultation

Canada's Pandemic Vaccine: **Where are we now?**

Vaccine Production Events	Pandemic H1N1 2009
Strain Selection	May 2009
Reassortant 'seed'	June 2009
Antigen production	Start July
Clinical studies	Sept 09
Formulation	Start Sept
Filling activities	Start sept/oct
Regulatory authorization	± mid-Nov
Vaccine distribution	mid-late Nov
Vaccine administration	late Nov-Dec

- 50+ million doses ordered
- Flexibility in final formulation(s) remains, with at least 1 million doses being unadjuvanted
- Meeting on prioritization for the earliest rounds of immunization held and recommendations will soon be announced
- F/P/T meeting on vaccine distribution later in Sept.
- Immunization program planning in progress
- Expanded capacity in place for post-market assessment of pandemic vaccine (PHAC-CIHR Influenza Research Network + expanded health portfolio surveillance)