

# CALL FOR RESEARCH ON H1N1 INFLUENZA 09 TO INFORM PUBLIC POLICY

## **Background and NHMRC Decision to Fund Research**

Since late April 2009, there have been reports of sustained person to person infections with a new influenza A (H1N1) virus emerging in Mexico and the United States. By May 2009 the virus had spread to multiple countries in Europe, the Americas, Asia and Australia.

Given the widening risk of disease caused by this virus and its unique genetic and antigenic characteristics as an influenza A (H1N1) variant of animal origin, the World Health Organization, in accordance with established procedures, increased the influenza pandemic alert level from phase 3 to phase 4 on 27 April 2009 and to phase 5 on 29 April 2009.

The Australian Government has been actively involved in international activities to prevent and minimise the impact of a pandemic, and has developed a detailed guide for the Australian response to a pandemic influenza threat that can be found at [www.flupandemic.gov.au](http://www.flupandemic.gov.au) and [www.healthemergency.gov.au](http://www.healthemergency.gov.au).

As of May 2009, most experts predict that this strain of H1N1 will continue to infect people in the southern hemisphere over winter, and then the northern hemisphere during their winter. There is an opportunity through Australian health and medical research to learn much more about the virus during our winter. Furthermore, Australia has outstanding researchers in the necessary fields to study the virus itself and the clinical effects of infection, and to understand the public health aspects of its spread and containment.

The National Health and Medical Research Council (NHMRC), as the principal funder of public health and medical research in Australia, has developed the following criteria to take into account when assessing the need for an urgent call for research:

- immediate threat to public health;
- potential to spread, population at risk;
- unfamiliarity with the disease;
- high morbidity or mortality; and
- broad economic impact of the threat.

NHMRC has determined that influenza A H1N1 2009 meets sufficient of the above criteria to warrant issuing an urgent call for research.

## **What is the NHMRC proposing to fund?**

NHMRC is specifically calling for public health and medical research proposals that aim to rapidly inform and advance Australian strategies to prevent, prepare for and respond to a potential H1N1 Influenza pandemic and inform the development of public policy.

A total of up to **\$7 million** has been set aside by NHMRC to fund the best research that addresses needs that are not already being covered through other means.

NHMRC is therefore calling for research to be conducted over the current Australian influenza season, to better understand the biology of the virus and its impact on public health in order to inform public policy development.

## **Further targeted calls for research**

NHMRC's Research Committee will also advise in the next quarter on whether NHMRC should develop further targeted calls for research in other areas beyond the need to respond to immediate concerns with H1N1 Influenza 09 to ensure better preparedness for pandemic infections.

## **NHMRC Call for Urgent Research into H1N1 Influenza 09**

Applications are called for research of up to 12 months duration to inform public policy in the following areas:

- 1. The biology of the virus.** The NHMRC wishes to support research into all aspects of the H1N1 Influenza 09 virus. Examples of potential research areas are given below, but other relevant research aims are also encouraged.
  - a. The progress of mutations and potential of the virus to:
    1. Increase or decrease in infectivity or virulence
    2. Develop resistance to antiviral drugs
  - b. The potential for reassortment of the H1N1 virus with other human or animal influenza viruses
  
- 2. Research to ensure good decision making for the management of the influenza in the community and individual patient care.** Any research of relevance to this aim is encouraged, such as:
  - a. Evaluating the effectiveness of quarantining, including in different ages, groups and circumstances
  - b. Acquiring evidence to support the development of further policy on the most effective population-based use of antiviral drugs
  - c. Acquiring evidence to support the development of advice on public health measures such as social distancing or public health messages
  - d. Identification of co-factors placing individuals at increased risk of contracting the virus, suffering more severe effects of the infection, and at risk of rapid clinical deterioration
  - e. Modelling the progression of disease and the impact of intervention measures

## **Proposed timeline**

In order to respond to the urgent nature of the request, NHMRC has developed a rapid peer-review and administrative process. A provisional timeline for the application and selection process appears below:

<b>STEPS</b>	<b>DATE</b>
Advance notification of call for research placed on NHMRC website and sent to Research Administration Officers	FRIDAY 29 MAY 2009
Applications open	WEDNESDAY 3 JUNE 2009
Applications close	<b>5pm*</b> MONDAY 22 JUNE 2009
Peer review commences	TUESDAY 23 JUNE 2009

\* Australian Eastern Standard Time

## Considerations for Applicants

- This is an urgent call for research and it is expected that only projects of up to twelve months duration will be funded.
- Applicants should particularly note that the NHMRC will conduct a confidential workshop in December 2009 with a requirement that researchers will report their findings to that time. This workshop will be attended by researchers funded under this program, other researchers with related existing grants and public health officials. The aim of this workshop will be to ensure that NHMRC funded researchers can help policy makers better plan for the future. For information, Appendix 1 lists questions that the Department of Health and Ageing have identified as important in responding to the H1N1 Influenza 09 virus.
- Proposals should draw on established Australian research expertise (international partnerships are encouraged) and focus on outcomes that will contribute to public policy development aimed at minimising the risk or impact of a pandemic in Australia.
- Applicants who are current holders of other research grants are eligible to apply for funding under this Program; however, applicants must be able to demonstrate that:
  - the research team is able to meet the agreed research deliverables within the timeframes indicated above [Note that these timeframes will be specified in a Schedule to the Deed of Agreement with your Administering Institution]
  - the proposed research does not duplicate work already funded (either by the NHMRC or from another source)
- Collaborative research, including with industry or international partners, is encouraged, as are applications from investigators and organisations that do not normally apply for NHMRC funds, such as veterinary researchers.
- NHMRC's intention is to fully fund the direct research costs of proposals. However, researchers will be free to obtain supplementary research funding from other sources. If this occurs, NHMRC funded research should continue to be identifiable, with the capacity for discrete reporting.
- NHMRC reserves the right to broker collaborations to conduct the proposed research, and to negotiate with other funding organisations to increase the total funding that is awarded through this process.
- NHMRC is committed to fast-tracking the peer-review and approval process for this urgent call for research.
- Potential researchers and Administering Institutions will need to give consideration as to how they fast-track their approval processes.

## Budgets

Successful proposals will receive one line funding, paid in accordance with normal NHMRC payment procedures.

The budget parameters that apply to Project Grants funded in 2009 (PSPs etc) should be used in framing the budget.

Please note that NHMRC will only pay funds to an NHMRC registered Administering Institution, and NHMRC will recognise only one institution per application as the Administering Institution.

The Administering Institution must have in place policies and procedures for the management of public funds and the proper conduct of research in relation to human and animal ethics and scientific conduct in accordance with NHMRC Codes of Practice. Further information on is available at: <http://www.nhmrc.gov.au/funding/policy/admininst.htm>

Administrative costs will not be payable under these grants and therefore should not be included in the budget.

### Intellectual Property

Applicants in receipt of funding under this urgent call for research must agree to comply with the Interim Guidelines for Intellectual Property Management for Health and Medical Research available at: <http://www.nhmrc.gov.au/funding/policy/ipmanage.htm>

Consortia must ensure that there is a written agreement between participating organisations on the ownership of intellectual property and associated rights in relation to the research supported by this grant.

### **Application Process**

Applicants should use the CALL FOR URGENT RESEARCH ON H1N1 INFLUENZA 09 TO INFORM PUBLIC POLICY *Application Form* which is available from the NHMRC's website – <http://www.nhmrc.gov.au>.

### **Selection Process**

Applications will be considered against the following criteria:

1. Relevance to the aims of this Urgent Call for Research
2. Scientific quality/merit and/or innovation
3. Qualifications and evidence of experience of investigator/s in the use of proposed research techniques
4. Overall project design, method and feasibility
5. Strength of the proposed research team/consortium
6. Ability to commence and complete the proposed research within the given timeframe
7. Value for money

NOTE: The Assessment of the applications and finalising of funding recommendations will be conducted by a peer review committee to be appointed by the NHMRC. The peer review committee will operate under the auspices of NHMRC's Research Committee, which in turn will provide a recommendation for funding to the CEO of the NHMRC. The CEO of the NHMRC will seek the advice of Council prior to providing a recommendation to the Commonwealth Minister for Health and Ageing for the release of funds from the Medical Research Endowment Account.

Applications will be ranked and both successful and non-successful applicants notified of the outcome immediately following approval of the funding recommendations by the Minister for Health and Ageing.

Inquiries regarding administrative issues that have not already been addressed by the supporting documentation should be directed to Dr Greg Ash ([greg.ash@nhmrc.gov.au](mailto:greg.ash@nhmrc.gov.au)) or by phone to (02) 6217 9010.

Applications should be lodged by email to [H1N1@nhmrc.gov.au](mailto:H1N1@nhmrc.gov.au) no later than 5pm Australian Eastern Standard time on Monday 22 June 2009.

**Successful applicants will need to note:**

- Once funded, the research must commence, and be completed, within agreed specified timeframes.
- The conditions of award for funding will be set out in a Deed of Agreement between the Commonwealth and the Administering Institution and also in a Letter of Offer to the researcher.
- A program may not commence, nor grant funds be expended, prior to:
  - the Deed of Agreement being in place;
  - the appropriate Schedule being signed; and
  - all required ethics clearances and approvals having been obtained.
- Applicants and their institutions are requested to understand that this research is urgent and must take all necessary steps to expedite obtaining the relevant clearances.

### Virus Questions:

Has the virus changed genetically?

Do isolates in Australia show resistance to oseltamvir and zanamivir?

If the virus develops resistance:

- will it be fit enough to circulate?
- How has resistance developed, reassortment or mutation?

Has the virus reassorted with other seasonal viruses ?

Has the virus displaced other seasonal viruses?

How long does the virus survive on surfaces and how effective is cleaning, disinfection?

### Laboratory Diagnosis:

What is the cost benefit of laboratory investigations at different stages of the epidemic?

Is laboratory screening for influenza cost effective?

### Epidemiology Questions:

What are the epidemiological and clinical characteristics of the first few hundred cases?

What is the population attack rate?

How severe is the disease?

What is the efficacy, cost benefit of school closures?

What is the efficacy, cost benefit of other intervention measures, social distancing, cancelling mass gatherings?

What is the level of absenteeism?

How much herd immunity to H1N1 09 is developed over 3 months of winter?

### Clinical Questions:

What are the transmission mechanisms? (For instance, large particle droplet, small particle aerosol, faecal, oral)

Over what distance does the virus transmit to others?

What masks provide protection, protective effect of P2 and surgical masks?

Does in vitro resistance correlate with clinical non response to therapy?

How effective is post exposure prophylaxis when given within 48 hours or after 48 hours?

How effective and safe is long term pre-exposure prophylaxis?

How effective is treatment when initiated within 48 hours of onset or 48 hours of onset?

Does the viral load correlate with outcomes?

What is causing secondary infections and co-infections (including co infection with seasonal viruses) and what are the impacts on host outcomes?

Does natural infection confer immunity and how long does this last?

What are the transmission parameters of the disease, serial interval, reproductive number, incubation period?

What is the period of communicability?

Shedding studies - how long and how much live virus is shed by patients, by age group and does this correlate with symptoms?

Does vertical, oral, faecal or blood borne transmission occur?

Over what distance can the virus transmit to others?

Are asymptomatic people shedding virus?

#### Vaccine Questions:

What is the appropriate dose of vaccine, and what adjuvants should be used?

What is the Vaccine Effectiveness, how well does it work in the field?

What is the appropriate dose and vaccination schedule for pregnant women, other special risk groups?

What adverse events are associated with the vaccine?

What is the association between autoimmune events, including GBS, with vaccination?

Does seasonal vaccine provide any protection in any age groups?

Baseline studies on cross-reactive antibodies in sera of different age groups +/- seasonal vaccination

Baseline studies on cross-reactive T cells in peripheral blood mononuclear cells: frequencies specific for known conserved epitopes

What in vitro level correlates with in vivo protection from illness?

Correlated clinical and serological studies, Acute and convalescent sera (and PBMC) to evaluate levels and specificities associated with recovery

How long is immunity maintained?

In vitro vaccine efficacy - Post-vaccination sera

#### Other Questions and Follow-up:

What are the community concerns about equity of access to antiviral medication, vaccine?

Evaluation measures - would anything be done differently?