

Continuation awards within an approved project period will be made on the basis of satisfactory progress as evidenced by required reports and the availability of funds.

Recipient Financial Participation

Matching funds are not required for this program.

Funding Preferences

Applications for new studies are encouraged, however, funding preference may be given to the competing continuation application over applications for programs not already receiving support under the existing program. The current awardee has implemented vaccine research that requires continued support to become fully developed and to realize the benefits of an improved vaccine.

E. Program Requirements

In conducting activities to achieve the purpose of this program, the recipient will be responsible for the activities listed in 1. Recipient Activities, and CDC will be responsible for the activities listed in 2. CDC Activities.

1. Recipient Activities

(a) Develop a study design to accomplish the following research goals:

(1) Use the rhesus macaque as a primate model for measles infections. These studies which produce disease in rhesus that closely resembles measles in humans will describe the pathogenesis of measles in the primate model.

(2) Characterize the immune response to natural measles disease and measles vaccination. Studies should attempt to measure differences between the immune response in animals receiving measles vaccines to those experiencing infection with a virulent strain. Efforts should be aimed at providing a complete description of the humoral, and especially, the cellular immune responses. These studies should include and broaden our understanding of cell mediated immunity by mapping CD4 and CD8 T-cell reactive epitopes on measles antigens and by measuring the cytokine/chemokine responses following infection or vaccination.

(3) Develop improved measles vaccines. Research efforts should be directed at developing, testing and optimizing novel vaccine formulations that could be used to stimulate an immune response in the presence of maternal antibody. Such vaccines would be used to protect newborn humans from measles infection or disease during their first year of life. In addition, subunit or DNA vaccines that could be used to stimulate or boost

immunity in immunocompromized individuals should also be considered. Using recombinant measles viruses as a vector to present other antigens should also be considered.

(4) Conduct studies to evaluate the safety and efficacy of standard measles vaccines given by alternate routes. In particular, studies to evaluate the safety and efficacy of measles vaccines given as aerosols or dry powders via the intranasal route should be conducted in normal and immunosuppressed animals. Evaluation of immune response to individual measles virus antigens.

(5) Conduct studies to determine the genetic basis for virulence of measles virus in the rhesus macaque. Studies should include experimental infections with recombinant measles viruses that have defined genetic characteristics. Another important goal will be the maintenance and genetic characterization of viral stocks which can reliably produce disease in rhesus by the intranasal route. Conduct detailed analysis of these stocks to help understand the genetic basis for the pathogenesis of measles virus.

(b) Perform all inoculations of research animals. Maintain records of clinical observations and obtain samples for laboratory analysis.

(c) Perform specialized tests on specimens obtained from study animals and coordinate shipment of specimens to CDC for additional testing.

(d) Provide routine veterinary care, housing and other support for rhesus macaques to be used in experiments. Comply fully with PHS policies regarding research on animal subjects.

(e) Maintain sufficient numbers of rhesus macaques so that experiments can be completed in a timely manner.

(f) Develop experimental measles vaccines and evaluate them in the animal model.

(g) Analyze data and manuscripts describing results of research investigations.

2. CDC Activities

(a) Collaborate on the design and conduct of the research.

(b) Collaborate in the development of various preparations of measles virus antigens, recombinant viruses, rescued viruses or complementary DNA (cDNA) clones for use as experimental vaccines.

(c) Provide Direct Assistance for specialty reagents, such as monoclonal and polyclonal antiserum, and PCR primers as needed.

(d) Conduct specialized analysis of samples obtained from test animals and assist with genetic characterization of viruses used in the study.

(e) Collaborate in data analysis, manuscript preparation and presentation.

F. Content

Letter of Intent (LOI)

An LOI is optional for this program. The Program Announcement title and number must appear in the LOI. The narrative should be no more than two pages, single-spaced, printed on one side, with one-inch margins, and unreduced 12-point font. Your letter of intent will be used to enable CDC to determine the level of interest in the announcement and should include the following information, a brief description of the proposed study, the business address of the organization, and the name and phone number of the Principal Investigator.

Applications

The Program Announcement title and number must appear in the application. Use the information in the Program Requirements, Other Requirements, and Evaluation Criteria sections to develop the application content. Your application will be evaluated on the criteria listed, so it is important to follow them in laying out your program plan. The narrative should be no more than ten pages, double-spaced, printed on one side, with one-inch margins, and unreduced 12-point font.

The narrative should consist of Background and Need, Capacity, Objectives and Technical Approach, Measures of Effectiveness, Budget, and Animal Subjects.

G. Submission and Deadline

Letter of Intent (LOI) Submission

On or before May 22, 2003, submit the LOI to the Grants Management Specialist identified in the "Where to Obtain Additional Information" section of this announcement.

Application Forms

Submit the signed original and two copies of PHS 398 (OMB Number 0920-0001). Adhere to the instructions on the Errata Instruction Sheet (posted on the CDC website) for PHS 398. Forms are available at the following Internet address: www.cdc.gov/od/pgo/forminfo.htm

If you do not have access to the Internet, or if you have difficulty accessing the forms on-line, you may contact the CDC Procurement and Grants Office Technical Information Management Section (PGO-TIM) at: 770-488-2700. Application forms can be mailed to you.