



## 2004 Request for Proposals (August 16, 2004)

### APUA and the ROAR Project

The Alliance for the Prudent Use of Antibiotics (APUA) is an independent non-profit organization dedicated to curbing antibiotic resistance through education and research activities (see [www.apua.org](http://www.apua.org)).

Under the leadership of Dr. Stuart Levy, the President of APUA, and Dr. Abigail Salyers of the University of Illinois, the first phase of the Reservoirs<sup>1</sup> of Antibiotic Resistance (ROAR) Project was initiated in 1997 to encourage global research and assemble information on the genotypes and phenotypes of commensal bacteria that serve as reservoirs of antibiotic resistance determinants for human pathogens. The central hypothesis of the ROAR Project is that resistance genes are flowing from commensals to pathogens; and that characterizing and tracking resistance genes in commensal bacteria could help to predict the emergence of new forms of resistance genes before they gain ascendancy in pathogenic bacteria. The ROAR Project is the first systematic effort to compile and disseminate information on resistance in reservoir bacteria and is developing the foundation of an international database as a centralized resource for investigators.

Monitoring resistance patterns in commensal and soil bacteria could also provide valuable clues about non-antibiotic selection pressures. For example, screening for integron- and plasmid-mediated clusters of antimicrobial resistance genes may reveal gene combinations that are co-selected by non-antibiotic pressures. Additionally, monitoring resistance gene distribution and diversity in commensal bacteria will provide information essential for public officials charged with assessing risks associated with antibiotic use in human medicine, food production and agricultural practices.

To better understand the role of commensals as reservoirs of antibiotic resistance, APUA has launched the ROAR II project, a five year Cooperative Agreement formed with the National Institute of Allergy and Infectious Disease (NIAID/NIH). Now in its third year, the ROAR II Project has already awarded three research sub-grants addressing crucial aspects of the flow of antibiotic resistance genes from commensal to disease-associated bacteria. The intent is to use these studies to populate the ROAR database and to conduct selected analyses.

### **Goal/Objectives**

ROAR is requesting proposals for pilot projects that address the association of antibiotic resistance genes among commensal bacteria and disease-associated bacterial populations. The funded research studies, which may form the basis of further fundable study, should aim to provide data appropriate to add to an APUA-curated database of the genes and the isolates from which they are described. Funded studies will address the concepts that commensal bacteria serve as reservoirs for the emergence and continued proliferation of antibiotic resistance genes in disease-associated bacteria, and that commensal bacteria can donate antibiotic resistance elements to disease-associated bacteria. Preference will be given to prospective studies of resistance determinants in different microbial communities or environments. The data produced from these

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<sup>1</sup> The ROAR Project defines an antibiotic resistance reservoir as a population of bacteria that have acquired resistance genes that have the capability of being transferred to other bacteria, especially human pathogens.

studies will provide for the development of more substantive research projects, in addition to providing a basis for ROAR’s quantitative assessment of the relationship between resistance in commensals and emerging resistance in human pathogens.

To maximize the value of the data produced, the ROAR Project will only consider as responsive those proposals that include studies of resistance genes at the molecular level; for example, by gene probes, by sequence typing, by microarrays, etc. . Furthermore, the ROAR Project plans to widen its impact through the inclusion of projects that incorporate multi-locus sequence typing (MLST) data. Future ROAR plans include expansion into this area, and projects utilizing this methodology are encouraged. Preference will be given to those studies which produce a volume of data sufficient to facilitate risk analysis and mathematical modeling.

### **CRITERIA FOR RESEARCH PROJECT APPROVAL<sup>2</sup>**

Under the direction of APUA’s Research Director, proposals will be evaluated by a Peer Review Committee comprised of members of the ROAR II Steering Committee and APUA’s Scientific Advisory Board. Proposals will be judged according to the criteria below. Proposal funding priority will be based on the score given using the 100-point scale described.

1. Significance: Goal and rationale of the project; topic significance; local and regional priority; potential clinical impact, fit with ROAR’s previous granted studies	25
2. Approach: Study design, including methods, projected results, potential problems, prospective approach, innovation	30
3. Investigator: Personnel qualifications and organizational capacity, including partnerships	20
4. Environment: Generalizability of findings to other biological systems	10
5. Management plan, including timetable and plans for monitoring and evaluation	10
6. Budget rationale	5
<b>Total</b>	<b>100</b>

Reviewers will provide an evaluation of the proposal along with a numerical score. Rigorously designed project designs will be given funding priority. Identification of the specific populations and variables under study will be required, as well as specific definitions of the outcomes. In order to facilitate the development of such proposals, APUA staff will be made available for consultation during all stages of the proposal development.

### **AMOUNT/AWARDS**

- Awards for proposals are up to \$60,000 for a maximum of one year. Provision is not offered for funding of indirect costs.
- Funds may only be used for the salary and fringe benefits of faculty or study personnel and for research-related tests and supplies. No funds may be expended for equipment or travel.
- Awards will be made once per year and will be limited to one year’s duration. Awards may be renewed for a second year only under special circumstances and with approval by APUA.

### **PROPOSAL GUIDELINES**

Research proposals should carefully define the bacterial populations being sampled, with respect to the genes, resistance and environment(s) in which they are isolated. Proposals should

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<sup>2</sup> Examples of projects that ROAR has funded:

Dr. Marilyn C. Roberts *et al.* “Profiling of *mef* and *erm* Resistance Genes in Oral Pediatric Isolates”. University of Washington.

Dr. John Iredell and Dr. Ruth Hall. “Antibiotic Resistance genes and their context in commensal and disease-associated clinical isolates of gram negative bacteria”. The University of Sydney-Westmead Hospital, Australia.

Dr. James Tiedje. “Exploring transfer, diversity and distribution of antibiotic resistance genes in soil”. Michigan State University.

provide a rationale for studying specific bacterial populations, compartmentally isolated with respect to their pathogenicity and source and clinical relevance. Research proposals should carefully define the environment studied, the genes or resistances studied, and the clinical relevance of the study. Prospective studies are of particular interest.

The application should be no more than four pages, exclusive of no more than 20 references and a one-page budget justification. It should contain the following information:

1. The specific project goals and objectives. Describe specific bacterial populations of interest and associated human health implications.
2. A specific description of the methodology used for data collection, detailed data management and analysis plan, and a management plan for monitoring and evaluating the project, including a timetable for achievement of results for each step.
3. The expected sample size, and any appropriate power calculations pertinent to the hypothesis being tested.
4. The personnel and their qualifications for the research plan. Include the resume or curriculum vitae of the Project Director. Resources (human, facilities, financial, and in-kind contributions) required to achieve results. Present an itemized budget in both local currency and USD.
5. Any anticipated additional resources that could be used to contribute to the success of the proposed research plan including collaborative efforts that will enhance the proposed project's effectiveness and impact

### **PROGRESS REPORTING**

- Investigators are asked to notify the ROAR Principal Investigator in writing of significant changes in the focus of the research or allocation of funds during the project.
- APUA requests that funded investigators provide progress reports 6-months into project implementation.
- Within 60 days of completing the project, the investigator should submit a final progress report stating preliminary scientific findings, any publications that result from the research, and an accounting of unexpended funds.
- Final progress reports will also be used to evaluate extension of funding into a second year if requested by the investigators. Recipients will also be asked to report applications or publications that result from this project on an annual basis for two years after the completion of the project.

### **APPLICATION PROCEDURE**

Please submit a proposal of no more than four pages in length, exclusive of references and a one-page budget justification. Font type is to be no less than 10 points, with 1-inch page margins.

Finished proposals should be sent electronically to the email address below and are due no later than **October 31, 2004**. Alternatively, proposals may be faxed to the below individual. Questions regarding this RFP can be directed to the ROAR Program Coordinator and will be answered as soon as possible.

Kelly Chang, Program Coordinator  
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