

National Institutes of Health National Institute of General Medical Sciences John E. Fogarty International Center



National Science Foundation Directorate for Biological Sciences Directorate for Geosciences

REVIEW OF THE JOINT NATIONAL INSTITUTES OF HEALTH / NATIONAL SCIENCE FOUNDATION ECOLOGY OF INFECTIOUS DISEASE PROGRAM

Final Report

July 18th – 20th, 2005 Fogarty International Center National Institutes of Health Bethesda, Maryland USA

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August 30, 2005

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Dear Drs. Hrynkow, Clutter, and Leinen,

Please find enclosed the final report of the panel convened to review the Ecology of Infectious Diseases Program in July of this year at the National Institutes of Health. The report reflects the findings and recommendations made by the review panel, which I had the pleasure of chairing. I hope that the report will be helpful to FIC, the NSF, and their partners as they look to strengthen the program and as they fashion the next request for applications (RFA) in 2006.

During our three-day review meeting at NIH, we spoke to many persons connected with the program and received many positive comments about the EID program as well as comments about how the program could be modified to make it even more effective. We were struck by the importance of ecological issues in prediction, prevention, and containment of newly emerging infectious disease threats. We hope that FIC and its partners will give the suggestions, contained in the report, serious consideration as they go forward.

As is evidenced in the report, the review panel was impressed by the accomplishments of the EID program and its role in furthering our knowledge of the relationships between ecological disturbances and transmission of infectious agents. I am confident that we can look forward to even greater accomplishments from the EID program in the future, particularly if FIC and its partners are able to build on our recommendations.

On a more personal note, I should add that I enjoyed very much chairing the EID review panel and working with my fellow panel members – my thanks go out to this talented group, whose diverse backgrounds and expertise allowed us to look at the program from many different perspectives. I would also like to thank Dr. Linda Kupfer of the FIC and the Abt staff, Allison Hodges Myerson, Christina Viola, and Alexis Wilson, who provided background summaries of program characteristics, helped staff the review, and turned our review notes into a clear and concise draft of this final report.

Best regards,

Donald'S Benko

Donald S. Burke, M.D. Professor, Department of International Health Associate Chair and Director, Disease Prevention and Control Program

Executive Summary

Initiated in 1999, the Ecology of Infectious Diseases (EID) initiative is a competitive research grant program administered jointly by the National Science Foundation (NSF) and the Fogarty International Center (FIC). Its purpose is to encourage development of predictive models and discovery of principles for relationships between anthropogenic environmental change and transmission of infectious agents.

In 2005, as part of its ongoing program review procedures, the Fogarty International Center (FIC) convened a panel of seven experts to review the achievements of the EID program to date and to make recommendations about its future. Fields of expertise represented on the panel included infectious diseases, epidemiology, public health, ecology, environmental science, and biostatistics. The panel met June 18th–20th, 2005, on the NIH campus in Bethesda, Maryland. Panel members conducted interviews inperson and via telephone with principal investigators on EID grants, key personnel on EID-funded projects, key staff members of NSF and NIH program partner agencies, EID program officers, and outside experts with relevant knowledge. In these interviews, the panelists explored the appropriateness of the program mission, management, partnerships, communication, and results. The Panelists also reviewed key program data including current and former Request for Applications (RFAs) and Program Solicitations, annual progress reports, funding data, publication data, key personnel data, and other historical program documents.

Overall, the panel concluded that the first five years of the EID program have been successful and productive. A total of 34 projects have been funded, and all of them have been both interdisciplinary and appropriately targeted at the development of new concepts and methods to predict and respond to emerging or re-emerging infectious diseases. In addition:

- At least 566 individuals from 123 institutions in 23 countries around the world have served as key personnel on EID-funded projects.
- Although EID is not a training program, it has considerable potential for impact with respect to capacity building, especially in the area of human capital and has helped to train at least 208 students at the undergraduate, graduate, and postdoctoral levels.
- Though it is a young program, more than 228 journal articles, 95 abstracts, and 11 book chapters already have been attributed to EID.

While the program has been effective in achieving goals, the panel made several recommendations for the program's future. This report outlines the panel's rationale and full set of recommendations based on the findings of the review. The key recommendations include:

NIH and NSF should continue and expand the Ecology of Infectious Diseases (EID) program (Recommendation 1).

In the past five years, the EID program has successfully bridged disparate scientific disciplines and institutional cultures to develop new approaches to critical environmental and health challenges. It has also played an important role in building a cadre of interdisciplinary scientists. The panel felt strongly that investment in the program should continue.

The EID program should add a special emphasis on those infectious diseases that are serious pandemic threats (Recommendation 2).

Many current EID projects focus on diseases and pathogens of proven public health significance for humans (*e.g.*, West Nile encephalitis, plague, malaria, Lyme disease). Other projects focus on veterinary pathogens of potential economic significance (*e.g.*, chronic wasting disease, bovine tuberculosis). Now that the program has been launched successfully, it should also seek to support research projects that focus on serious pandemic disease threats where ecological factors are known or suspected to play a crucial role in disease emergence (*e.g.*, Avian influenza, SARS).

The EID program should foster translational research in order to develop public health interventions based on research findings (Recommendation 3).

Several of the EID-funded investigators have identified opportunities to translate research findings into products that may advance surveillance, detection, control, or intervention efforts. While the program should continue to emphasize basic science questions related to the ecology of infectious diseases, opportunities for translational research should be preserved and enhanced. Additionally, assessment and evaluation of outcomes after interventions have been implemented should be promoted.

Given its inherently interdisciplinary nature, the EID program should continue to evolve as a model for interagency cooperation. Consistent with the NIH Roadmap, the EID program should pursue opportunities for substantive participation of other institutional partners across the NIH (NIAID, NIGMS, and NIEHS) and the NSF (Geosciences and Social, Behavioral, and Economic Sciences) (Recommendation 9).

The EID program mission overlaps with the missions of several of the NIH Institutes and NSF Directorates. As one of the few joint NIH-NSF programs, the EID program is also a valuable example of effective interagency cooperation. It is to the credit of the program officers and the original partner agencies that the need was recognized and the gap was effectively bridged. It is hoped that the lessons learned from the EID program can help encourage and inform future intra-agency and interagency cooperation.

The EID program should nurture the development of a community of scientists interested in the ecology of infectious diseases. Interactions between EID investigators – at all levels of training and experience – should be facilitated (Recommendation 12).

One of the major outcomes of the EID program should be the establishment of a group of investigators who are conversant in the languages of multiple disciplines related to infectious disease ecology and comfortable working across traditional disciplinary boundaries. The ultimate goal should be to nurture a united group of investigators who are equipped with the skills and the drive to address infectious disease issues through approaches that were not previously possible. The EID already advances this goal through formal networking opportunities at annual meetings. Additionally, EID should explicitly incorporate other activities that foster cross-training and capacity-building for the investigators, their students, and other collaborators. For example:

- Modelers should spend time in the field to become cognizant of the data needed to parameterize a model;
- Field biologists and lab personnel should be exposed to basic analytical methods of modeling;
- Epidemiologists should strive to understand the basic principles of the other researchers involved in their project.

Such an achievement would represent an important contribution of the EID program to both basic science and global public health.

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I. Introduction

The Ecology of Infectious Diseases (EID) program was created in 1999 as a competitive research grant initiative administered jointly by the Fogarty International Center (FIC), working in partnership with the National Institute for Environmental Health Sciences (NIEHS) and the National Institute for Allergy and Infectious Disease (NIAID), and the National Science Foundation (NSF). Its purpose is to encourage development of predictive models and discovery of principles for relationships between anthropogenic environmental change and transmission of infectious agents. Interdisciplinary by design, the program was established to fill a research need that was believed to overlap with the missions of both agencies but fell outside of the current scope of each agency's mainstream research programs.

The total annual budget for the EID program increased from about \$4 to \$5 million per year in 2000-2001 to \$14 to \$15 million per year in the most recent years. Contributing partners at NIH have included FIC, NIAID, and NIEHS. NSF partners include the Geosciences Directorate (NSF-GEO) and the Biological Sciences Directorate (NSF-BIO). Overall, more than half (56%) of the total funding contributions came from NSF and the remainder (44%) from NIH, with FIC contributing 24% of the total, NIAID contributing 16%, and NIEHS contributing 4% (Table 1).

Funding Agency	Year					Total Funding	
Funding Agency	2000	2001	2002	2003	2004	Amount (USD)	
FIC	\$1,402,000	\$1,298,102	\$2,668,129	\$2,840,592	\$3,034,460	\$11,243,283	
NIAID	\$1,238,837	\$1,178,735	\$1,041,257	\$1,310,476	\$893,264	\$5,662,569	
NIEHS	\$110,000	\$110,000	\$610,000	\$610,000	\$530,000	\$1,970,000	
NIH TOTAL	\$2,750,837	\$2,586,837	\$4,319,386	\$4,761,068	\$4,457,724	\$18,875,852	
NSF (Primary Grants Only)*	\$2,084,579	\$2,078,993	\$3,949,011	\$9,877,874	\$9,882,352	\$27,872,809	
NSF TOTAL	\$2,112,495	\$2,078,993	\$4,007,011	\$9,999,991	\$10,000,000	\$28,198,490	
Total Amount (USD)	\$4,863,332	\$4,665,830	\$8,326,397	\$14,761,059	\$14,457,724	\$47,074,342	

Table 1: Funding Sources of EID Grants by Year (2000-2004)

*Note: The NSF program officer provided annual funding information for both the primary grants, and also the "total funding" which includes the costs for running the panels, the Principal Investigator meetings, supplementary funding, workshops, etc.

Between 1999 and 2004, a total of 34 research awards were made under the EID program¹ (for a complete list of awards by investigator and title, please see Appendix D, Table D1). Of these, 11 (32%) were funded by NIH and 23 (64%) were funded by NSF. Overall, 41% of the grants involve field research conducted at study sites outside of the United States (US); these international grants comprise a large majority (81%) of the NIH-funded awards (Appendix D, Table D2).

To date, at least 566 individuals have been listed by name and title as key personnel on EID proposals or progress reports, but it should be noted that this is likely to be a drastic

¹ One additional award was initiated in 2000, but it was withdrawn before a substantial portion of the proposed research had been completed.

underestimate of the total number of people involved in the 34 projects because of incomplete records and inconsistent definitions of "key personnel" between NIH and NSF. Of these, at least 208 were undergraduate, graduate, or post-doctoral students or fellows who received training and research experience through the program. Key personnel on EID projects are located in at least 123 different institutions in 23 countries around the world. Of the 31 projects for which full or partial key personnel information was available, only 9 were limited to key personnel from US-based academic institutions only; all others had at least one participant from a non-profit organization, government agency, or an academic institution located outside of the US.

In 2005, as part of its ongoing program review procedures, FIC convened a panel of seven experts to review the achievements of the EID program's first 5 years and to make recommendations for its future. Fields of expertise represented on the panel included infectious diseases, epidemiology, public health, ecology, environmental science, and biostatistics. The panel met on June 18-20, 2005, on the campus of the National Institutes of Health in Bethesda, Maryland. Panelists conducted interviews via phone or in person with 14 Principal Investigators or key Personnel on EID grants, 12 representatives of the NSF and NIH program Partners, 5 outside experts with knowledge of the field, and the relevant program officers at NSF and FIC. A letter to the panel chair can be found in Appendix A, the biographical sketches of the review panel in Appendix B and a complete list of recommendations in Appendix C. The review was conducted following the FIC Framework for Evaluation.²

II. Overall Assessment

A deeper understanding of the ecology of infectious diseases is critical for improving global public health. Without such an understanding, it will be impossible to anticipate and respond quickly to the effects of environmental changes on human, animal, and environmental health. As the pace of anthropogenic change continues to accelerate, basic research will be essential to anticipating impacts and potential management or policy interventions. Whether the relevant questions concern long-range impacts of global climate change, more effective control of familiar pandemic diseases with animal vectors and reservoirs, or securing our food supply against the increasing threat of bioterrorism, the ecological dimensions of infectious disease are fundamental and poorly understood.

Despite increasing recognition in the international community of the need for a robust understanding of the ecology of infectious

"EID is one of the few programs that values unique, interdisciplinary nature of science. It facilitates putting together things that aren't intuitively obvious and opens bridges for collaboration like no other program – really, it opens everyone's eyes to opportunities we don't ordinarily see and teaches us to think in a different way. This is always positive for science." -EID Principal Investigator

² Fogarty International Center, "Framework for Program Assessment (Evaluation and Review): A Performance-based Review Process," National Institutes of Health, December 2002 (updated April 2005). Available at <u>www.fic.nih.gov/about/eval_framework.pdf</u> (accessed August 11,2005).

diseases,³ research funding in this area remains scarce. In part, the lack of funding opportunities is likely due to the inherently interdisciplinary nature of the research. Many infectious disease processes are best understood when studied in their natural setting where factors that may impede or accelerate their spread within an environment can be understood, and there are well-developed principles from ecology that can provide a framework in which the interaction of pathogens and their hosts can best be understood. As illustrated in Figure 1, many of the relevant questions simply do not fall neatly under traditional fields of research areas such as vector biology and epidemiology.



Figure 1: Schematic representation of hypothetical plague transmission cycle. The area highlighted in blue corresponds to the part of the cycle that is usually included in traditional vector biology and epidemiology research. Figure provided by the EID program officers and adapted from EID Principal Investigators S. Collinge and M. Kosoy.

Clearly, therefore, research initiatives to address the ecology of infectious diseases cannot effectively be conducted in isolation; EID research spans the boundaries of many traditional scientific disciplines and areas of expertise, and its practical applications are relevant to a variety of agency mission and mandates. However, EID research does not fall under the traditional purview of biomedical research funding agencies such as NIH. NIH has a vested interest in infectious disease research with an emphasis on diagnosis and treatment of disease and studies of the epidemiology of human pathogens and select animal pathogens, but it has no vested interest in the study of ecology *per se*, as this is the usual domain of NSF. At NSF, however, ecological research funds are administered by the Biological Sciences

³ For example, see Grand Challenges in Environmental Sciences, 2001, Committee on Grand Challenges in Environmental Biology, National Research Council, National Academy Press, Washington, D.C. Available online at http://www.nap.edu/books/0309072549/html, accessed 8/2/05.

Directorate, which does not have a mandate to study infectious diseases in humans. In serving as a unique source of basic research funds for this important emerging field, the EID program fills a critical gap within the federal research funding system in the area of ecology of infectious diseases.

Since its inception, the EID program has been highly successful in bridging both scientific disciplines and institutional cultures to develop an innovative approach to some of the 21st century's most critical environmental and health challenges. It also serves a key function in helping build a cadre of interdisciplinary scientists versed, or acquiring fluency, in the multiple scientific disciplines. Interdisciplinary programs are, by definition, capacity building in terms of integrating scientific disciplines. In this regard, the EID program plays a key role in fostering a combination of research, training, and capacity building. Therefore:

Recommendation 1: NIH and NSF should continue and expand the EID program.

III. Program Mission

As stated in the most recent Program Solicitation, the EID program supports "development of predictive models and discovery of principles for relationships between anthropogenic environmental change and transmission of infectious agents." ⁴ Substantial progress has already been made towards achieving this mission. Thus far the EID program has supported a broad array of studies on a variety of infectious diseases. Thirty-five percent of the grants are focused on prions and/or viral pathogens, 27% on pathogenic bacteria, and 27% on protists or multi-cellular parasites (Appendix D, Table D3). The program supports projects in terrestrial, freshwater, and marine field sites (Appendix D, Table D4). Study designs and research topics range from the abstract (*e.g.,* investigations of the impact of social behavior on spheroid transfer processes among honeybees) to more classical epidemiology-oriented studies focused on zoonotic or vector-borne diseases with environmentally-mediated risk factors. Virtually all of the funded projects to date have been both interdisciplinary and targeted at the development of new concepts and methods to predict and prevent infectious diseases.

While the EID program has been successful, its current mission could be improved in several ways:

Recommendation 2: The EID program should add a special emphasis on those infectious diseases that are serious pandemic threats.

Epidemic diseases that are zoonotic, vector borne, water borne, or emerge from animal reservoirs continue to pose serious threats to human health. Some recently emerged examples include SARS and West Nile Virus; others, like avian influenza, seem poised to emerge as major public health threats. Still others, such as plague, anthrax, and tularemia, are considered potential agents of bioterrorism. Meanwhile, pandemics such as malaria

⁴ "Ecology of Infections Disease Program Solicitation", NSF 03-507, 2003. Available online at <u>http://www.nsf.gov/pubs/2003/nsf03507/nsf03507.html</u>, accessed 8/2/05.

continue to claim lives at a pace that may well be affected by ongoing anthropogenic environmental change, even as existing treatments become less effective.

An understanding of how these and other diseases emerge, adapt, and spread through ecosystems is essential in order to predict, manage, and prevent them. The relevant science cannot be conducted solely in the laboratory or the clinical environment; it must also include field ecology and epidemiology in the relevant ecosystems and communities. Similarly, this research cannot be conducted effectively by scientists who are conversant in the language of a single discipline only.

Together, these attributes of the EID program will enable it to improve the readiness of the US to counter the threat of epidemic infectious diseases in several important ways:

- (1) New scientific principles, concepts, and methods will be generated;
- (2) Expert academics and professionals will be better trained and more prepared to respond to threats;
- (3) Predictive models will help direct resources towards early detection of emerging or re-emerging disease threats, facilitating early intervention and rapid response; and
- (4) Specific microbes that are known to have epidemic potential will be studied in detail.

Diseases and pathogens of proven public health significance that are currently the focus of EID projects include: West Nile encephalitis, plague, malaria, rabies, Chagas disease, Lyme disease, hantaviruses, cholera, human alveolar echinococcosis, and schistosomiasis, (for full list, please see Appendix D, Table D1). Several projects also focus on veterinary pathogens of potential economic significance such as chronic wasting disease and bovine tuberculosis. Now that the program is fully launched, the program should expand to target those diseases known or expected to pose critical threats to human health, such as SARS, Avian influenza, and others.

While the primary goal of the EID program should continue to emphasize basic science questions related to the ecology of infectious diseases, some of the current projects have already identified potential opportunities to translate their research findings into products that could be exploited for improving disease surveillance, diagnosis, and control. This aspect of the program should be preserved and enhanced:

Recommendation 3: The EID program should foster translational research in order to develop public health interventions based on research findings.

The interdisciplinary nature of EID research provides unique opportunities to identify novel strategies for disease detection and control. As much as possible, attempts to translate predictive models into instruments for assessing and measuring disease risk, disease incidence and trend (*e.g.*, epidemics and pandemics), and evaluation of outcome after intervention should be encouraged. Whenever possible, epidemiologic and microbiologic observations made in the field also should be translated into products such as, new diagnostic tests, vaccines, drugs, vector control agents, or surveillance devices that could be

used to improve human as well as nonhuman infectious disease treatment, prevention, and control.

The interdisciplinary nature of the EID program and particularly the cross-training opportunities it provides may help to facilitate translational research. For example, ecologists who have worked with local public health officials may be quicker to recognize and more likely to include local needs in their research design, while public health officials with a more in-depth understanding of science are likely to apply research findings to their work more quickly.

There is some evidence that translational research is already taking place under the auspices of the EID program in the form of new interventions identified and implemented by research teams. For instance, one Principal Investigator conducting research on malaria transmission in Belize described working with local officials to improve wastewater management practices in an effort to reduce malaria transmission. Another was sharing his results with local fishermen on Lake Malawi to limit exposure to schistosomaisis transmission through the food supply, and yet another had demonstrated that imposing strict controls on placement of fruit trees near pig farms limited exposure to Nipah virus.

Overall, most of the current programmatic elements are appropriate. However, in addition to incorporating an emphasis on pandemic threats and translational research, there is room to include additional fields such as evolutionary ecology and genetics under the EID umbrella:

Recommendation 4: Key programmatic elements that should be continued include: ecology, epidemiology, field studies, dynamics in reservoir species, modeling, and public health. A new emphasis should be put on evolutionary ecology and microbial genomics. The EID program should encourage but not require an emphasis on anthropogenic change.

When asked whether the modeling component should continue to be required or strongly encouraged, the majority of interviewees stated that it should. Several Principal Investigators mentioned that the modeling component had forced them to diversify the expertise on their project teams, increasing interdisciplinarity and introducing them to researchers they would not otherwise have contacted. In one case, a Principal Investigator claimed that the relationship she developed with the modeling experts on her project team helped to launch a campus-wide interdisciplinary working group. Others simply expressed appreciation for the opportunity to learn more about modeling as a valuable tool for integrating research. One Principal Investigator whose project was funded in the earliest round (when modeling was not yet a required component) mentioned that she had voluntarily added a modeling component at the end of her project in the hope of further integrating the results. She cautioned that the process has been less efficient than it could have been if modeling had been incorporated into the initial project design.

While modeling should continue to be an important component of the EID program, there may not presently be sufficient emphasis on testing and validating the models that are

developed. Validation of infectious disease models is an important issue, but no clear consensus has yet been reached on how this concern might be translated into operational advice for the program at this stage. As the program matures, however, dialog on this issue should continue.

Multiple program stakeholders also indicated that the EID program should seek to engage researchers interested in evolutionary ecology and genomics. There are a number of important and relevant questions that might be explored concerning the interplay of ecology and evolution in the emergence and spread of infectious disease – one example might be in understanding the dynamics of pathogen-host-reservoir co-evolution. In future versions of the Program Solicitation, the program officers should consider adding language that encourages (but does not necessarily require) the integration of these disciplines. However, the reviewers should be careful to distinguish evolutionary ecology projects from projects that focus on the evolution of infectious disease (for which there is a separate program at NIH); all projects funded under this program should continue to have a significant ecological component.

While the current focus on anthropogenic change is appropriate, it should not necessarily be required for EID program proposals. The majority of interviewees expressed a similar view, with several arguing that the environmental phenomena of interest are best determined by the disease processes and ecosystem dynamics rather than the other way around. Others pointed out that the boundaries of "anthropogenic change" are difficult to define, as human activity has to some extent influenced every ecosystem. There should be room for flexibility with respect to interesting and innovative proposals focused on the disease implications of "natural" environmental phenomena. Examples of appropriate topics might include the effects of El Nino-Southern Oscillation; local or regional climatic phenomena such as hurricanes, droughts, and tornados; geological events such as earthquakes, tsunamis, or volcanic eruptions; and random effects such as genetic bottlenecks.

IV. Program Management

The EID program leadership was found to be highly enthusiastic and invested in the success of the program despite the inherent difficulties of cross-agency work. Differences in application and review procedures, reporting systems, and institutional culture between NIH and NSF have created significant obstacles for cross-agency collaboration efforts, but the goodwill and dedication of the program officers in particular seems to have helped to mitigate these operational difficulties. While the EID program management appears to have been adept at bridging the gap between NIH and NSF administrative processes, additional efforts should be made to streamline the application and review processes:

Recommendation 5: Proposal application and review should be streamlined into a single process for interagency submissions.

The first round of EID application and review occurred at NIH, and the most recent four rounds have occurred at NSF. The NSF FastLane electronic submission process is widely

admired for its speed and efficiency, while the NIH application system remains paperbased. For the most part, initial review of EID applications has adhered to the rules of the agency where the review was held, with the NIH reviews scoring proposals numerically by priority for funding and the NSF reviews assigning proposals to appropriate "bins." Under NSF rules, proposals that are considered "highly competitive" are recommended for funding, and more power rests with the program officer to make the final decision regarding which proposals are awarded. However, to retroactively satisfy NIH review requirements, the EID proposals rated "highly competitive" under NSF rules that are candidates for NIH funding must then be resubmitted by the Principal Investigator in NIH format, at which time they are assigned a standard NIH priority review score. This need for double scoring creates unnecessary work for the program officers and staff at NIH and NSF. Based on interviews with program partners at NIH in particular, it can also generate concern about a lack of transparency on the part of the agency that was not responsible for conducting the particular round of review in question. The burden placed on Principal Investigators who are asked to convert proposals from one format to another can be significant. A more standardized system and format for application and review would be greatly appreciated by everyone involved with the EID program.

Similarly, once proposals are funded, there is currently no common reporting system used between NIH and NSF to track program accomplishments. NIH requires all Principal Investigators to submit annual progress reports, while continued NSF funding is not necessarily contingent on the receipt of an annual report. The content of the progress reports to both agencies can also vary in quality and detail, with more emphasis often given to reporting on use of funds than documentation of scientific and other accomplishments. As progress reports can be an extremely rich source of information for program planning, they should be standardized and expanded:

Recommendation 6: The EID program should require standardized, annual progress reports that include scientific progress and metrics of success.

Again, while standardization of reporting procedures across agencies would involve a great deal of effort and approval at a very high level, this is a goal towards which the agencies should aspire. In the meantime, the program officers could collect or standardize certain program-specific data. For instance, under the current reporting system, information regarding key personnel is collected in a disparate manner from NIH and NSF Principal Investigators. NSF has a clear definition as to what constitutes "key personnel," whereas NIH has no specific definition, making it difficult to collect consistent, program-wide information about exactly who works on EID projects. In order to document the achievements and to further encourage a unified, cohesive program, an EID-specific set of data should be systematically collected. At a minimum, metrics such as program accomplishments and success stories, number of publications attributable to the grant, number of students involved, breadth and depth of disciplines represented, and translational impacts should be reported for all EID projects.

In addition to a unified reporting system, the program officers should consider promoting data and sample sharing between all EID projects:

Recommendation 7: The EID program should develop procedures that promote data and sample sharing. At a minimum, proposals should provide plans for how data and samples will be shared and stored.

As discussed at the May 17, 2005, Heads of International Research Organizations (HIRO) Brainstorming Meeting on the Ecology of Infectious Diseases, high-quality human and animal population and epidemiologic data are scarce and insufficiently shared. It is not entirely clear to what extent this scarcity results from unwillingness to share data or a lack of opportunity to do so, although Principal Investigators interviewed during this review seemed generally amenable to data sharing. While the EID program does not currently have sufficient resources to facilitate data sharing itself, requiring applicants to present plans for data and sample sharing might help to institutionalize data sharing into the culture of an emerging field of interdisciplinary research. Additionally, both NIH and NSF currently have some data-sharing mechanisms in place; it might be possible to tie in EIDrelated data-sharing with existing efforts.

Finally, in the interest of providing Principal Investigators with the resources they need to adequately identify opportunities, assemble interdisciplinary teams, and collect preliminary data, additional funds should be available for planning:

Recommendation 8: Planning Grant opportunities should be available.

Several of the Principal Investigators interviewed mentioned that they were initially unsuccessful in their application to the EID program because the reviewers felt that they did not have any preliminary data from which to begin or they did not yet have all of the members of an appropriate interdisciplinary team assembled. In special cases, NSF has made small planning grants available to prospective EID Principal Investigators that enabled them to collect preliminary data and begin building a team. This practice has helped to develop and nurture particularly innovative projects that would not otherwise have been funded, and the results have been well worth the relatively small cost.

V. Partnerships

The EID program is a valuable model for interagency cooperation. EID research questions are situated at the intersection of agency missions, and it is very much to the credit of the program officers and the original partner agencies that they were able to recognize the need and find a way to bridge the gap. In fact, in part as a result of this success, the FIC program officer has recently been named to lead an NIH working group on interagency collaboration. As one of the first examples of successful interagency collaboration, it is hoped that the lessons learned from the EID program can help smooth the way for future cooperation.

However, while the spirit of collegiality and goodwill that was apparent among all of the past and present program partners interviewed at NIH and NSF was impressive, it was

clear that some of the partnerships were not as strong as they could have been, whereas other partnerships that could potentially yield mutual benefits had not yet been explored:

Recommendation 9: Given its inherently interdisciplinary nature, the EID program should continue to evolve as a model for interagency cooperation. Consistent with the NIH Roadmap, the EID program should pursue opportunities for substantive participation of other institutional partners across the NIH (NIAID, NIGMS, and NIEHS) and the NSF (Geosciences and Social, Behavioral, and Economic Sciences).

FIC was clearly instrumental in the creation of the EID program and continues to serve as the program's primary administrator and advocate at NIH. Other current partners at NIH include NIAID and NIEHS, while NIGMS had a role in the creation of the program but has not contributed funding. Several of the NIH partners interviewed mentioned that FIC has long been a leader at NIH in terms of building partnerships Across NIH Institutes. In light of the NIH Roadmap's emphasis on interdisciplinary research and the considerable overlap between the mission of the EID program and several of the NIH Institutes, efforts should be made to overcome any existing administrative and cultural barriers to collaboration.⁵ Furthermore, as noted elsewhere in the report, the EID program has not yet managed to fully engage the biomedical community. Expanded support from institutes at NIH that typically support such research could

"There is a need for the ecology community to be involved in biodefense, but there are some cultural gaps that need to be closed before it can happen. Specifically, the ecological community has to have more direct involvement with the public health community." -EID Expert

potentially help to increase its visibility and desirability in the biomedical research community.

At NSF, the current partners are the Biological Sciences Directorate and the Geosciences Directorate. While continued interest in participation by the Biological Sciences Directorate appears to be strong, continued support from the Geosciences Directorate is less certain. In part, this appears to be due to a perceived lack of a component to the EID research projects that advances cutting edge research in geoscience disciplines; one interviewee described the role of the geoscientists on existing EID projects as supportive rather than substantive. Encouragingly, however, the same interviewee stated that there were many unexploited opportunities for EID research in the geosciences that would be innovative and might move the field forward. Examples of related topics given included:

- The dynamics of airborne and waterborne transport of pathogens;
- The implications for infectious disease of changes in geomorphology and land surface;
- Paleogeology and environmental history as they relate to disease evolution;
- Soils as substrates for microbial ecology associated with infectious disease; and
- The effect of climate change on movement or migration of vector and host populations.

⁵ For details on the NIH Roadmap, see: http://nihroadmap.nih.gov/

This interviewee believed that more outreach to the geosciences community might raise interest and awareness of these opportunities and encourage them to develop projects directed or significantly influenced by questions of fundamental importance to geoscience.

In addition to strengthening existing partnerships and exploring new ones within NIH and NSF, there is a need for outreach to other federal agencies with research, surveillance, or regulatory mandates that may complement the needs of the EID program:

Recommendation 10: The EID program should facilitate opportunities for coordination and collaboration with federal agencies with capacity for prediction and prevention of epidemic diseases including: Centers for Disease Control and Prevention (CDC), Department of Defense (DoD), Department of Agriculture (USDA), National Oceanic and Atmospheric Administration (NOAA), United States Geological Survey (USGS), National Atmospheric and Space Administration (NASA), United States Environmental Protection Agency (EPA), and Department of Homeland Security (DHS).

While most of these agencies have limited funding available for extramural research on this topic, there are opportunities for synergy in data and resource sharing, translational research, and exchange of expertise. Several of the EID projects already involve key personnel from CDC and USGS, and there is evidence that the collaborations have been fruitful. In the case of three EID projects focused on pathogens considered to be high risk for bioterrorism, a CDC laboratory has been extensively involved because it was the only lab that was certified to handle the agents in question at the time of the award. An interviewee from CDC also described one instance where EID research on hantavirus ecology has had a significant impact on helping the agency to allocate scarce surveillance resources.

It should also be noted that USGS, USDA and NASA have all been listed as collaborators in earlier versions of the EID program Solicitation and Requests for Applications. The extent to which these agencies are willing to participate at an institutional level is unclear. However, it was believed that a renewed emphasis on officially sanctioned collaboration might help to spark additional interest among current program participants, new applicants, and agency personnel.

VI. Communication

As the program is still relatively new, additional efforts should be made to increase awareness of and communication about the EID program. In particular, outreach efforts are needed to potential partners at NIH and NSF; relevant scientific communities; and to local health officials. Increased visibility for the program might potentially help to bring in new funding sources and talent pools while simultaneously magnifying the impact of the program. As one Principal Investigator interviewee put it, awareness "is like an infection – it is starting out slowly, but will eventually snowball – we need to get the key players involved early in the game." "I am a community ecologist and I'm having the opportunity to work with medical entomologists and microbial biologists – these interdisciplinary interactions between disparate areas are extremely valuable. Some of the technology that was once intimidating to an ecologist now becomes much more comfortable on a day-to-day basis. This type of interaction should be encouraged further"

-EID Principal Investigator

Recommendation 11: As an especially creative new program, the visibility of the EID program and the discipline of infectious disease ecology should be raised in relevant scientific communities.

Of particular concern is that the EID program may not be engaging the relevant biomedical communities to the fullest extent possible. Although there are exceptions, an imbalance was noticed between the quality of key personnel involved on the ecology end as opposed to the biomedical researchers. In general, the ecologists

are more likely to be experienced investigators with outstanding credentials while the biomedical researchers tend to be capable but less experienced. It would be beneficial for NIH and NSF to find ways to bridge the gap between the two communities and facilitate interactions, perhaps by funding meetings or symposia. To some extent, NSF is already attempting to do this, but interdisciplinary symposia on EID issues remain scarce.

In addition to increasing outreach to communities and investigators who currently do not participate, there is also a need to improve communication among researchers within the EID program. In particular, communication should also be facilitated between researchers working on different projects:

Recommendation 12: The EID program should nurture the development of a community of scientists interested in the ecology of infectious diseases. Interactions between EID investigators – at all levels of training and experience – should be facilitated.

Many grantees interviewed conveyed considerable satisfaction with their participation in the annual EID program meeting. Some interviewees stated that they particularly benefited from the formal training they received during these meetings in subject areas such as modeling, while others described the connections they made with other investigators as beneficial. In one case, a Principal Investigator working on schistosome-related illness in one area of the world described explicitly exchanging data and ideas with EID researchers at the meeting that were working on the same disease in a different location. These researchers continue to communicate regularly, with apparent mutual benefit to both projects.

When asked whether the annual meetings could be improved, however, some Principal Investigators expressed a desire that more time should be scheduled for informal discussion. Increased informal discussion is likely to benefit all program participants, but the potential benefit to students and junior scientists might be the greatest. In particular, given the importance of training truly interdisciplinary professionals, young scientists should be encouraged to attend. One suggestion was that the EID program might sponsor a competition each year with travel awards for 6 to 10 undergraduates, graduate students, and post-doctoral researchers. The successful applicants would have submitted abstracts for presentations/posters at the meeting, and could be judged by a panel of rotating membership consisting of program Principal Investigators.

In addition to informal networking opportunities, EID should explicitly incorporate activities that foster cross-training and capacity-building for the investigators, their students, and other collaborators. For example:

- Modelers should spend time in the field in order to become intimately familiar with the data s/he inputs into a model;
- Field biologists and lab personnel should be exposed to the basic analytical methods of modeling; and
- Epidemiologists should be encouraged to understand the basic principles of the other disciplines represented in the research project.

In other words, one of the major outcomes of the program should be the creation of a cadre of investigators who are well-versed in the language of the different disciplines that define infectious disease ecology. The ultimate aim should be to integrate several disciplines and establish the ecology of infectious diseases as a transdisciplinary research area that can address the issues of infectious diseases in ways that were not previously possible. Such an achievement would represent one important measure of success of the EID program.

Facilitating such cooperation between interdisciplinary and multi-national teams takes a considerable amount of time. Based on interviews with program participants, a minimum of five years is required to get all participants to "speak the same language," cooperate as a team, and to collect the necessary data to parameterize the models:

Recommendation 13: Because interdisciplinary and international studies often require a substantial start up time and long-term follow up, a longer funding period is essential to maximize productivity and return on investment.

Finally, there should be increased communication with the local governments and health agencies. Potential benefits include increased opportunity for rapid adoption of interventions, increased access to study sites and populations of interest, and increased capacity to tap into local knowledge about ecologies and disease dynamics that may be useful in generating hypotheses. In order to facilitate public health impacts, it is crucial to get buy-in from local government agencies. Where possible, EID Principal Investigators should make an effort to involve local stakeholders in the project planning and implementation stages. The potential for tangible public health impacts increases markedly when research is not conducted in isolation. While these opportunities may be most critical for the projects with international field sites, they apply to US research as well.

Recommendation 14: Where possible, projects should be developed in cooperation with local health agencies.

It should be noted that collaboration with local officials and/or populations is already taking place in several EID projects. One Principal Investigator has already begun transitioning the work he initiated under the EID program to the local government in South

Africa. This involvement of local officials has increased the impact of the project and has ingrained the project within the community. At least 3 other Principal Investigators working in Belize, Malaysia, and on Lake Malawi also described interaction with local populations and public health officials.

"This program has given me a boost in terms of my own research activities, interests, and enthusiasm – it has also broadened my horizons in terms of what journals I read. This is one of the most important and innovative projects to come down the pipeline at NIH or NSF for a very long time. This program has the potential for a very high level of productivity to really lead the field for the next 10-15 years."

-EID Principal Investigator

VII. Results

With just over four years of research completed as part of the EID program, it is too early to expect outcomes and impacts on par with more established research programs. Nevertheless, initial evidence of progress was found in the areas of scientific accomplishments, capacity building, and public policy. For the most part, this evidence is drawn from two sources: analysis of publications and anecdotal evidence from the interviews conducted by the panel.

Evidence for Scientific Outputs

Initial publication information was provided by the program officers at NIH and NSF in the form of database of publications from 2000-2003 and was supplemented with information from annual program progress reports. Because complete information was not available for all projects, the publication data almost certainly underestimates the actual research output. The 27 projects for which publication information was available have published a total of 228 journal articles, 95 abstracts, and 11 book chapters in the last 5 years (Appendix E). As would be expected, the grantees who began their work in 2000 and 2001 have published more prolifically than the more recent grantees.

Grantees published in a total of 113 different international, peer-reviewed journals. Among them are prestigious journals of broad scientific interest (*e.g.*, *Nature*), infectious disease and public health journals (*e.g.*, *The Lancet Infectious Diseases, Emerging Infectious Disease, Environmental Health Perspectives*), and top ecology journals (*e.g., Ecology, Ecological Applications, Behavioral Ecology*).

Although the EID program appears to be on track to produce research at the leading edge of discovery, it was deemed too early to look for evidence of new scientific principles emerging from the program. However, there were two projects that appear particularly promising in this regard. There are early indications that the first, focused on a parasitic disease of coral reefs, may be among the first studies to conclusively demonstrate that climate is a driver for infectious disease in marine ecosystems. The same project has also adapted an RNA-based biosensor for field diagnostics of the *Aspergillus* pathogen.

The second particularly promising project focuses on the microbial diversity and community ecology of the tick gut. The researchers have demonstrated that the community

composition of gut microflora varies in ticks taken from opposite sides of a valley. This suggests that environmental factors may influence the prevalence of tick-borne microbial parasites. As far as the Principal Investigator was aware, this project is one of the first to demonstrate both the microbial complexity of the tick gut and the possible importance of ecological factors external to the tick itself in determining the prevalence of pathogens.

Evidence for Capacity-Building Outcomes

Although EID is not a training program, it has considerable potential for impact with respect to capacity building, especially in the area of human capital. The interdisciplinary nature of the research increases the likelihood that participants will be exposed to a field of research in which they do not already have expertise. The EID program has also helped to train at least 208 students at the undergraduate, graduate, and post-doctoral levels (Table 2).

Agency	Post-Doctoral Researcher	Graduate Student	Undergraduate Student	Total Number
NIH	12	8	7	27
NSF	30	82	69	181
Total Number	42	90	76	208

Table 2: Total Number of Students Trained on EID Projects, 2000-2004*

*Note: These counts were derived exclusively from data available in annual progress reports, which are not complete for all years and all projects. Data on students were available for only 28 of 34 projects, and the degree of completeness for these 28 projects is unknown. Reporting requirements are also inconsistent between NIH and NSF. Accordingly, these counts likely underestimate the true number of students who have been involved with EID grants.

Qualitative accounts of training and capacity development impacts were received from interviewees. For instance, one EID Principal

Investigator stated that one of her minority PhD students had recently applied for and received a K08 Mentored Clinical Scientist Development Award from NIH-NIAID to develop mathematical models that explore how chronic infections are maintained in wildlife reservoirs.⁶ The project had no direct human disease component at all; instead, it was proposed as basic model that could be applied to human disease. The Principal Investigator was convinced that the parent EID grant played a large role in getting this funding.

"This program is starting to build research capacitybecause of EID, there will be some people who are prepared to deal with a hoof and mouth outbreak, or a new hantavirus...." -EID Principal Investigator

Another EID Principal Investigator stated that the program has allowed him to train his students in new disciplines and also draw entirely new talent into his group. Prior to the start of his EID award, the graduate students in his Environmental Sciences program had

⁶ The purpose of the Mentored Clinical Scientist Development Award (K08) is to support the development of outstanding clinician research scientists. This mechanism provides specialized study for individuals with a health professional doctoral degree committed to a career in laboratory or field-based research. For more information, please see the Program Announcement at <u>http://grants.nih.gov/grants/guide/pa-files/PA-00-003.html</u> (accessed 8/2/05).

primarily been interested in wildlife. Through EID, these students are now exposed to epidemiological training. Several biophysics and structural biologists have joined his group because of EID.

Evidence for Policy Impacts

There was preliminary evidence of policy impacts in two areas: adoption of novel interventions on a local scale and use of models by government agencies for the purpose of allocating scarce public health resources. Examples of new interventions that emerged from research conducted under the EID program and have already been implemented to a greater or lesser extent at the local level include the following:

- In Belize, researchers funded by the EID program have been working with public health officials to alter agricultural practices and local vegetation in order to limit the spread of malaria.
- In Malaysia, researchers funded by the EID programhave demonstrated that elimination of fruit trees from certain areas of land used for pig farming can limit exposure to Nipah virus.
- On Lake Malawi, Africa, researchers funded by the EID programhave been working with public health officials and directly with local fishermen to alter fishing practices in order to reduce exposure to schistosomes.

One outstanding example of direct policy impact emerged from an interview with a CDC employee listed as key personnel on three EID Awards. When asked about the impact of the research he had been involved with, he mentioned that a model of hantavirus ecology developed through an EID program project had been adopted directly by CDC to help in allocating scarce surveillance resources. This story suggests that the models developed under this program may be directly linked to increasing the efficiency of the public health infrastructure in the US.

VIII. Conclusion

Discovery of the principles governing relationships between ecological disturbances and transmission of infectious agents-- and utilization of the principles to develop predictive models of epidemics – can be seen a key component in our national biosecurity effort. The review panel concluded that in its first five years the NIH-NSF EID program has been highly successful in achieving program goals. The program has developed innovative approaches to some of the 21st century's most critical environmental and health challenges, while fostering a cadre of interdisciplinary scientists versed in multiple scientific disciplines. The EID program uniquely fills a critical gap in our national effort protect the health of the public – both in the USA and world-wide – against the threat of epidemic and emerging infectious diseases. The fourteen recommendations of the review panel discussed above offer strategies to further strengthen this important program.

Appendix A: Letter to Chair





National Institutes of Health

September 7, 2005

Donald S. Burke, M.D., Professor and Associate Chair Department of International Health Bloomberg School of Public Health Johns Hopkins University Room E5527 615 North Wolfe Street Baltimore, Maryland 21205-1901

Dear Dr. Burke:

We want to express our thanks for the comprehensive and thoughtful report of your panel entitled "Review of the Joint National Institutes of Health / National Science Foundation Ecology of Infectious Disease Program." This review, taken in conjunction with an excellent session on the same topic held under the auspices of the Heads of International Research Organizations, will provide the framework for future research in this cutting edge, interdisciplinary area.

It is our intention to use your report's recommendations to help guide us as we rewrite the program announcement for the Ecology of Infectious Disease competition. It was particularly gratifying that the panel recognized the extensive research accomplished thus far under this relatively young program. Both agencies are pleased that their sizable contributions to this endeavor have had substantive results. Equally satisfying was the panel's recognition of the key roles played by the NSF and FIC/NIH program officers in forging this unique partnership which has clearly paved the way for achievement in this field both nationally and internationally.

We are aware of the time commitment required by these reviews and greatly appreciate your lending both your expertise and time to assist us in the important area of evaluating our programs.

Again, thank your for all your work!

Sincerely,

Sharon Hrynkow, Rh.D. Acting Director Fogarty International Center National Institutes of Health

Mary Z. Ch

Mary E. Clutter, Ph.D. Assistant Director Directorate for **Biological Sciences**

Margaret Leinen, Ph.D. Assistant Director Directorate for Geosciences

Appendix B: Review Panelist Profiles

Joseph E. Bunnell, Ph.D. is a Research Biologist at the United States Geological Survey. At the USGS, Dr. Bunnell is involved with a number of public health science activities in the US and abroad He also serves as Adjunct Assistant Professor, Environmental and Occupational Health at the George Washington University School of Public Health. His research includes conducting GIS analysis of Lyme disease; contributing to Chinese residential coal combustion studies; leading research project of respiratory health effects of coal combustion-derived air pollution in the Navajo Nation; designing experiments to identify etiology of Balkan endemic nephropathy; acting as a liaison between USGS and NIH, NIEHS, CDC, WHO, NASA, DoD, state and local public health organizations, and university medical research and environmental science departments. He worked as a Lecturer of Chemistry at Texas A&M University, and completed a post-doctoral fellowship at the University of Texas Medical Branch, World Health Organization Collaborating Center for Tropical Medicine on an NIH training grant. He obtained his Ph.D. in Molecular Microbiology and Immunology from the Johns Hopkins University School of Public Health in 1999, his M.S. in Entomology from Montana State University in 1995, and his B.A. in Biology from the University of California at Santa Cruz in 1987.

Donald S. Burke, M.D. is Professor and Associate Chair at the Department of International Health, Bloomberg School of Public Health, Johns Hopkins University. He is also Director of the Center for Immunization Research and the Graduate Degree Program in Disease Prevention and Control at the Bloomberg School of Public Health. His current research includes ongoing work to conduct clinical trials of new vaccines against a wide range of infectious pathogens including HIV/AIDS and measles. He is Principal Investigator on a project to develop of mathematical models of associations between weather and climate and infectious diseases, especially dengue in Thailand.

James P. Collins, Ph.D. is currently Virginia M. Ullman Professor of Natural History and Environment in the newly created School of Life Sciences at Arizona State University. From 1989 to 2002 he was Chairman of the Zoology, then Biology Department. In 1983 Dr. Collins was Visiting Professor at Duke University, and served as Director of the Population Biology and Physiological Ecology program at the National Science Foundation (NSF) in 1985-86. Dr. Collins's research centers on understanding the origin, maintenance, and reorganization of morphological variation within species. Amphibians, especially salamanders, are used as model organisms for field and laboratory studies of the ecological and evolutionary forces shaping intraspecific variation and how this variation affects population dynamics. A special focus of the research is host-pathogen biology and its relationship to the global decline of amphibians; Collins heads an international team of 26 investigators studying this issue under two grants from NSF's Integrated Research Challenges in Environmental Biology program. The intellectual and institutional factors that have shaped Ecology's development as a science are also a focus of Dr. Collins's research. Stephen S. Morse, Ph.D. is Director of the Center for Public Health Preparedness at the Mailman School of Public Health of Columbia University and a faculty member in the Epidemiology Department. Dr. Morse recently returned to Columbia from 4 years in government service as Program Manager at the Defense Advanced Research Projects Agency (DARPA), Department of Defense, where he co-directed the Pathogen Countermeasures program and subsequently directed the Advanced Diagnostics program. Before coming to Columbia, he was Assistant Professor (Virology) at The Rockefeller University in New York, where he remains an adjunct faculty member. Dr. Morse is the editor of two books, Emerging Viruses (Oxford University Press, 1993; paperback, 1996) and The Evolutionary Biology of Viruses (Raven Press, 1994). He currently serves as a Section Editor of the CDC journal "Emerging Infectious Diseases" and was formerly an Editor-in-Chief of the Pasteur Institute's journal "Research in Virology". Dr. Morse was Chair and principal organizer of the 1989 NIAID/NIH Conference on Emerging Viruses (for which he originated the term and concept of emerging viruses/infections); served as a member of the Institute of Medicine-National Academy of Sciences' Committee on Emerging Microbial Threats to Health (and chaired its Task Force on Viruses), and was a contributor to its report, Emerging Infections (1992); was a member of the IOM's Committee on Xenograft Transplantation; currently serves on the Steering Committee of the Institute of Medicine's Forum on Emerging Infections, and has served as an adviser to WHO (World Health Organization), PAHO (Pan-American Health Organization), FDA, and other agencies. He is a Fellow of the New York Academy of Sciences and a past Chair of its Microbiology Section. He was the founding Chair of ProMED (the nonprofit international Program to Monitor Emerging Diseases) and was one of the originators of ProMED-mail, an international network inaugurated by ProMED in 1994 for outbreak reporting and disease monitoring using the Internet.

Lee Riley, M.D. is Professor of Epidemiology and Infectious Diseases at the University of California Berkeley School of Public Health. His main research interests are bacterial pathogenesis and molecular epidemiology of infectious diseases of international importance. The main theme of his laboratory program is the identification of molecular basis for disease transmission. His laboratory currently studies Mycobacterium tuberculosis, which causes tuberculosis; Salmonella enteritidis, which causes foodborne disease associated with egg products; Leptospira, which causes leptospirosis in urban centers of many developing countries; and Escherichia coli associated with urinary tract infection. In addition to his laboratory research, he conducts field research abroad, including Brazil, India, and Czech Republic. He is a director of the FIC Program in International Training and Research in Global Infectious Diseases, which trains scholars from Brazil.

Estelle Russek-Cohen, Ph.D. is a Team Leader in the Diagnostics Branch, Division of Biostatistics, FDA Center for Devices and Radiological Health. She retired from the University of Maryland, College Park in 2004 where she was a Professor of Animal and Avian Sciences and Director of the UM Biometrics Program. Her methodological interests within Biometrics include linear and nonlinear mixed models and high dimensional classifiers. She worked on collaborative research projects with

entomologists, ecologists and microbiologists as well as scientists in many other disciplines. She was part of an EPA funded project on climate and disease and part of an NIH funded project related to Cholera in Bangladesh. She was a member of the editorial board of Environmental Monitoring and Assessment for 10 years. She participated in the original workshop in 1999 to develop recommendations for the initial EID RFA and served on the first three review panels as a reviewer.

Juli Trtanj, M.E.M. is Director of the Oceans and Human Health Initiative at the National Oceanic and Atmospheric Administration. She has a longstanding interest in issues of environmental conservation and development and the use of earth science information for public health policy and decision-makers. Ms. Trtanj was the Manager of NOAA's Climate Variability and Health Program and has also worked on Capitol Hill. Her research interests include climate change, common resource management, international relations, ocean and coastal issues, and the policy sciences. She earned her Masters in Environmental Management from Yale University School of Forestry and Environmental Studies, and her Bachelors in Environmental Science from the University of California, Santa Barbara.

Appendix C: List of All Recommendations

Recommendation 1: NIH and NSF should continue and expand the EID program.

Recommendation 2: The EID program should add a special emphasis on those infectious diseases that are serious pandemic threats

Recommendation 3: The EID program should foster translational research in order to develop public health interventions based on research findings.

Recommendation 4: Key programmatic elements that should be continued include: ecology, epidemiology, field studies, dynamics in reservoir species, modeling, and public health. A new emphasis should be put on evolutionary ecology and microbial genomics. The program should encourage but not require an emphasis on anthropogenic change.

Recommendation 5: Proposal application and review should be streamlined into a single process for interagency submissions.

Recommendation 6: The EID program should require standardized, annual progress reports that include scientific progress and metrics of success.

Recommendation 7: The EID program should develop procedures that promote data and sample sharing. At a minimum, proposals should provide plans for how data and samples will be shared and stored.

Recommendation 8: Planning Grant opportunities should be available.

Recommendation 9: **Giv**en its inherently interdisciplinary nature, the EID program should continue to evolve as a model for interagency cooperation. Consistent with the NIH Roadmap, the EID program should pursue opportunities for substantive participation of other institutional partners across the NIH (NIAID, NIGMS, and NIEHS) and the NSF (Geosciences and Social, Behavioral, and Economic Sciences).

Recommendation 10: The EID program should facilitate opportunities for coordination and collaboration with federal agencies with capacity for prediction and prevention of epidemic diseases including: Centers for Disease Control and Prevention (CDC), Department of Defense (DoD), Department of Agriculture (USDA), National Oceanic and Atmospheric Administration (NOAA), United States Geological Survey (USGS), National Atmospheric and Space Administration (NASA), United States Environmental Protection Agency (EPA), and Department of Homeland Security (DHS). Recommendation 11: As an especially creative new program, the visibility of the EID program and the discipline of infectious disease ecology should be raised in relevant scientific communities.

Recommendation 12: The EID program should nurture the development of a community of scientists interested in the ecology of infectious diseases. Interactions between EID investigators – at all levels of training and experience – should be facilitated.

Recommendation 13: Because interdisciplinary and international studies often require a substantial start up time and long-term follow up, a longer funding period is essential to maximize productivity and return on investment.

Recommendation 14: Where possible, projects should be developed in cooperation with local health agencies.

Appendix D: Supplementary Program Data

Start Year	Agency	Principal Investigator Full Name	Grant Title	Disease Focus
		Unnasch, Thomas R.	Ecology Of Encephalitis Virus In The Southeastern USA	Encephalomyelitis virus
		Weaver, Scott	Effect Of Neotropical Deforestation On Arbovirus Ecology	Alphavirus
	NIH	Rejmankova, Eliska	Environmental Determinants Of Malaria In Belize	Malaria
	NIT	King, Charles H.	Human Population Growth Impact On S. Haematobium	Urinary schistosomiasis
		Craig, Philip S.	Parasitic Zoonosis (Echinococcosis) Transmission In China	Human alveolar echinococcosis
2000		McGarvey, Stephen T.	Ecology And Transmission Of S. Japonicum: Philippines	Schistosoma japonicum
		Getz, Wayne	Metapopulation Models and Control of TB in African Buffalo	Bovine Tuberculosis
	NCE	Hobbs, N. Thompson	Spatial & Temporal Dynamics of Prion Disease in Wildlife: Responses to Changing Land Use	Chronic Wasting Disease
	NSF Dhondt, Andre		Dynamics of an Emerging Pathogen in an Introduced Host	Mycoplasma
		Lowenstine, Linda	Ecology of Herpesvirus Infection and Cancer in Sea Lions	Herpesvirus/ Cancer
		Bowen, Richard	Ecology of Virus Transmission in Commensal Bat Colonies	Rabies
	Briggs, Cheryl J. Amphibian Disease Dynamics in a Fragmented Landscape Kitron Uriel Ecoepidemiology of Chagas disease in northwest Argentina		Chytridiomycosis	
			Ecoepidemiology of Chagas disease in northwest Argentina	Chagas disease
	NIH	Vinetz, Joseph	Leptospirosis Transmission in the Peruvian Amazon	Leptospirosis
		Daszak, Peter	Anthropogenic change & emerging zoonotic paramyxoviruses	Hendra virus and Nipah virus
2002		Collinge, Sharon	Landscape Effects on Disease Dynamics in Prairie Dogs	Plague
2002		Kuris, Armand Michel	Anthropogenic effects on host-trematode dynamics	Trematodes
	NCE	Brown, Mary	URTD & Environmentally-Threatened Gopher Tortoises	Mycoplasma
NSE		Stauffer, Jay R	Schistosomiasis: Ecological Interactions Among Schistomes, Snail Hosts, Human Hosts & Fish Predators	Schistosomiasis
		Packer, Craig	Viral Transmission Dynamics in the Serengeti	Rabies, CPV, CDV
2003	NSF	Harvell, (Catherine) Drew	Collaborative Research: Origins and Spread of the	

Table D1: Complete List of EID Awards, 2000-2004

Start Year	Agency	Principal Investigator Full Name	Grant Title	Disease Focus
		Naug, Dhruba	How Social Organization Influences An Infectious Process: The Honey Bee Colony As A Model	N/A
		Yates, Terry L	Ecological Drivers of Rodent-borne Disease Outbreaks: Trophic Cascades and Dispersal Waves.	Hantavirus, Plague and Bartonella
		Clay, Keith	Microbial Community Ecology of Tick-Borne Human Pathogens	Lyme Disease, others
		Antolin, Michael	Plague as a model for low prevalence/epizootic disease dynamics	Plague
		Crawford-Brown, Douglas	Impacts of anthropogenic change on the ecology of human pathogens in a eutrophying estuary: the Neuse River estuary, NC	Various bacteria
	NIH	Jonsson, Colleen	Impact Of Land Cover Change On Hantavirus Ecology	Hantaviruses
	Dearing, M. Denise Hungerford, Laura		The Effect of Anthropogenic Disturbance on the Dynamics of Sin Nombre	Sin Nombre Hantavirus
			Modeling Ecology, Dynamics and Spatial Spread of Raccoon Rabies	Rabies
2004		Ward, J. Evan	Linking Marine Pathogens to Molluscan Shellfish: The Ecological Role of Marine Aggregates	Shellfish Pathogens
2004	NSF	Kitron, Uriel	West Nile virus: Eco-epidemiology of disease emergence in urban areas	West Nile Virus
		Pascual, Mercedes	The interplay of extrinsic and intrinsic factors in epidemiological dynamics: cholera as a case study	Cholera
	Smith, Thomas		Effects of Deforestation on the Prevalence of Blood-Borne Pathogens in African Rainforest Birds	Malaria, Trypanosomiasis, Filiariasis, and Tuberculosis
		McCracken, Gary	Ecological Influences on Rabies Infections in Bats	Rabies

Tuble D2: Multiper of Elip Multip by Elocation of Study Site, 2000 2004				
Location	NIH	NSF	Total Number of Grants	
United States	2	17	19	
International	9	6	15	
Total Number of Grants	11	23	34	

Table D2: Number of EID Awards by Location of Study Site, 2000-2004

Table D3: Number of EID Awards by Focal Pathogen Type, 2000-2004

Pathogen Type	NIH	NSF	Total Number of Grants
Viral (including prions)	4	8	12
Bacterial	1	8	9
Parasitic (Protists and Multicellular)	6	3	9
Not Specified	0	2	2
Bacterial and Viral	0	1	1
Parasitic and Bacterial	0	1	1
Total Number of Grants	11	23	34

Table D4: Number of EID Awards by Ecosystem Type, 2000-2004

Ecosystem Type	NIH	NSF	Total Number of Grants	
Terrestrial	10	17	27	
Wetland, Coastal or Freshwater	1	4	5	
Marine	0	2	2	
Total Number of Grants	11	23	34	

Table D5: Number of EID Awards by Use of Human Subjects, 2000-2004

Involves Human Subjects?	NIH	NSF	Total Number of Grants
Yes	7	2	9
No	4	21	25
Total Number of Grants	11	23	34

Appendix E: List of Program Publications

Note: Initial publication information from 2000-2003 was provided by the program officers at NIH and NSF. This database was supplemented with information from the grantee's progress reports (self-reported information). Because complete information was not available for all grantees, the publication data should be viewed as an underestimate. As the publication data was self-reported by the individual PIs, it is possible that they included some citations that are not entirely attributable to their EID grant. Alternatively, PIs may not have included all publications that should be attributed to EID. It should also be mentioned that some of the publications presented are submitted, or in press, but have been included to illustrate the full range of journals represented.

Journal Articles

Abbasi I, Branzburg A, Campos-Ponce M, Abdel Hafez SK, Raoul F, Craig PS, Hamburger J. Copro-diagnosis of *Echinococcus granulosus* infection in dogs by amplification of a newly identified repeated DNA sequence. *Am J Trop Med Hyg.* 2003;69(3):324-30.

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Appendix F: List of Interviewees

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Other Experts

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