Expert Panel Review of the Division of Epidemiology and Population Studies (DIEPS) of the Fogarty International Center

Final Report

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Executive Summary

In 2001, the John E. Fogarty International Center (FIC) at the National Institutes of Health (NIH) established a Division of International Epidemiology and Population Studies (DIEPS) to conduct research in epidemiology and mathematical modeling of diseases. The guiding vision for DIEPS was to conduct research that would help to establish or enhance the scientific underpinnings of policies related to international health. Because available space and funding were limited, it was decided that the Division would focus primarily on epidemiology and specifically on application of novel and sophisticated computational approaches to existing data. Since 2001, the majority of DIEPS research has been concentrated in six focal areas: 1) vaccine-preventable diseases; 2) influenza and other rapidly-transmissible diseases; 3) malaria; 4) diarrheal diseases and nutrition; 5) disease modeling fundamentals; and 6) disease control priorities.

DIEPS is unusual at NIH in that its purpose is to conduct research in-house but it is not officially designated as an intramural program. Since FY 2002, the FIC contribution to the DIEPS budget has averaged around $1 million per year, including salaries for between four and five Federal full-time equivalent (FTE) staff members plus an administrative assistant. Particularly in recent years, however, the total DIEPS budget has been significantly larger due to contributions from other sources. In FY 2008, these included approximately $1.9 million from Department of Homeland Security (DHS) for a project focused on disease modeling fundamentals and approximately $740,000 from the Department of Health and Human Services (DHHS) for influenza work. In FY 2009, the Division expects or has already received similar contributions from DHS and DHHS plus an additional $700,000 as part of a grant from the Bill & Melinda Gates Foundation for a project focused on diarrheal diseases and malnutrition.

In late 2008, the FIC Director requested that a panel of extramural experts be convened in order to conduct an evaluation of DIEPS. The charge to the expert panel was to: 1) review and assess scientific and other impacts of the Division; 2) assess the Division's contribution to the mission, goals, and needs of the FIC; and 3) make recommendations for the future of DIEPS. During a series of four teleconferences and two in-person meetings held between December 2008 and April 2009, panel members reviewed evidence compiled from administrative sources and conducted interviews with stakeholders.

The evaluation found evidence that FIC derives a great deal of benefit from DIEPS. Briefly, scientific outputs and outcomes include:

- A total of 252 publications in peer-reviewed journals;
- For manuscripts published prior to 2008 (N=213), an average of 21.92 citations per publication as of February 2009;
- For DIEPS publications in journals for which a 2006 Journal Impact Factor was available (N=239), an average impact factor of 7.61;
- The 2006 report *Disease Control Priorities in Developing Countries (2nd Edition)*, commonly known as the DCP2 report, as well as two extended summaries and a website (URL: http://www.dcp2.org) for dissemination.

Policy impacts of DIEPS documented by the review include:

- The US Centers for Disease Control and Prevention (CDC) revised its guidelines for influenza vaccination in part based on findings of a DIEPS study published in 2008.

- US pandemic influenza plans were revised to include more flexible pandemic scenarios based in part on DIEPS studies of past pandemics.

- DIEPS has collaborated bilaterally and multilaterally with over 25 countries to develop policies relevant to the control of influenza.

- After the 2001 terrorist attacks against the US, DIEPS convened modelers and policy makers from across the US government as well as other experts in order to explore how modeling could help the US prepare for future terrorist attacks.

- The National Institute of General Medical Sciences (NIGMS) credits DIEPS with inspiring and providing support for its Models of Infectious Disease Agent Study (MIDAS) program, which funds extramural research on infectious disease modeling.

- At a symposium co-hosted by DIEPS and the National Institute of Allergy and Infectious Diseases (NIAID) in September 2007, concerns were raised about the current WHO strategy for global eradication of polio. Consistent with the symposium's recommendations, WHO has since softened its policy on not accepting inactivated poliomyelitis vaccine (IPV) and is reconsidering its policy of abandoning all polio vaccination after certification of the interruption of disease transmission.

- The DCP2 report has been widely used as a resource for evidence-based analysis and policymaking in developing countries. Traffic on the DCP2 website has ranged between a high of 101,414 users per month in April 2007 and a low of 26,020 users per month in July of 2006. The site has been accessed from over 170 countries.

- Estimates of malaria burden derived by DIEPS likely prompted WHO to revise its own estimates upwards and have stimulated new research on malaria burden at WHO, CDC, and elsewhere.

Based on these findings, the expert panel concluded that the scientific outputs and policy impacts alone justify the relatively small investment that FIC has made in DIEPS. However, FIC and NIH also derive additional benefit from the Division, especially with respect to training, strategic partnerships, and collaboration. These benefits have included:

- Experiential research training for 27 pre-doctoral students and/or junior staff members, 24 postdoctoral fellows, and seven researchers visiting from abroad.

- Collaboration with other FIC Divisions on projects and initiatives related to malaria, rotavirus, influenza, climate change, and disease control priorities.

- Strategic partnerships with:

- Other NIH Institutes and Centers including NIAID, NIGMS, National Institute for Child Health and Human Development (NICHD), the National Library of Medicine (NLM), National Institute of Environmental Health Sciences (NIEHS), the NIH Office of the Director, and the NIH Clinical Center.
- US Government agencies including CDC, DHHS, DHS, the Department of Defense, and the State Department.
- Global health NGOs including the World Health Organization, World Bank, Pan-American Health Organization, The Carter Center, and the Population Reference Bureau.
- The Bill & Melinda Gates Foundation.

- At least 583 collaborators on individual projects located at academic and government institutions in the US and abroad, including current collaborations with researchers in Bangladesh, Brazil, Canada, Denmark, France, India, Kenya, Nepal, Pakistan, Peru, Portugal, South Africa, South Korea, Tanzania, Thailand, and the United Kingdom.

The panel also found that the activities of the Division are consistent with all five current FIC strategic goals and contribute significantly to four of them (Goals I, II, III, and V). In particular, DIEPS is well-positioned to make unique contributions towards meeting strategic goals related to implementation research training and strategic partnerships.

The panel therefore recommends that FIC should commit to retaining and strengthening DIEPS (Recommendation 1). Assuming that resource levels remain relatively constant, the panel considered three possible future scenarios for the Division. As a default position, the panel recommends that DIEPS should retain its current status but that efforts should be made to improve administrative processes, strategic planning, and communication. However, the panel also favors exploring the option of transitioning DIEPS to full intramural status in order to realize potential benefits including access to intramural funds and administrative resources (Recommendation 2). A third option considered by the panel, to "spin off" key staff members to another institution, is not recommended because FIC would lose most of the benefits currently provided by DIEPS as well as the opportunity to put staff resources to other uses (Recommendation 3).

Recommendation 1: FIC should commit to retaining DIEPS as a Division and strengthening it if possible.

Recommendation 2: The Division should continue as an internal research group while FIC explores the option of transitioning DIEPS to full intramural status.

Recommendation 3: DIEPS staff should not be "spun off" to another institution.

The expert panel found that FIC and DIEPS currently face a variety of challenges. Three of these challenges—reliance on "soft" money, limited space, and problems with staff recruiting/retention-- are directly tied to resource constraints. However, problems related to lack

of strategic planning (Recommendation 4), administrative processes (Recommendations 5), and administrative management and support (Recommendation 6), and oversight by FIC leadership (Recommendation 7) can and should be addressed at relatively little cost to FIC.

Recommendation 4: In collaboration with the FIC Office of the Director, DIEPS should develop a set of Division-level strategic goals.

Recommendation 5: Standard procedures should be established for DIEPS administrative processes.

Recommendation 6: Administrative management and support at a more senior level should be provided to DIEPS.

Recommendation 7: Oversight of the Division by FIC senior leadership should be improved.

Looking towards the future, the panel also recommended that DIEPS and FIC leadership work together to clarify the role played by DIEPS and its staff in relation to the rest of the Center (Recommendations 8 and 9). Finally, if additional resources were to become available in the future, the panel believes it would be desirable and consistent with FIC strategic priorities to expand the focus of DIEPS to include non-communicable as well as infectious diseases (Recommendation 10).

Recommendation 8: FIC should clarify the role of Associate Director for Science.

Recommendation 9: FIC leadership should work with the Division to explore additional opportunities for DIEPS to become more integrated with FIC extramural research and training programs.

Recommendation 10: If new funds and/or additional FTEs become available, FIC should consider expanding the DIEPS focal areas to include non-communicable conditions that adversely impact global health.

I. Introduction

The John E. Fogarty International Center (FIC) at the National Institutes of Health (NIH) supports international collaborative research and training programs that advance the NIH mission through international partnership. In 2001, FIC established a Division of International Epidemiology and Population Studies (DIEPS or the Division) to conduct research in epidemiology and mathematical modeling of diseases. In FY 2008, five full-time staff members were assigned to the Division from FIC and FIC contributed $1.29 million towards the Division's operating expenses. However, the FIC contribution represented only a small portion of the Division's staff and operating expenses in that year; the total DIEPS budget for FY2008 was $6.75 million and there were approximately 40 full and part-time staff members supported through a variety of mechanisms.

DIEPS is unusual at NIH in that its purpose is to conduct research in-house but it is not officially designated as an intramural program. It is therefore not subject to the annual review procedures administered by the Office of Intramural Research (OIR), and in its eight-year history the Division has never undergone a formal review of any kind. In late 2008, the FIC Director requested that a panel of extramural experts be convened in order to conduct a review of the DIEPS. The charge to the expert panel was to do the following:

1. Review and assess scientific and other impacts of the Division

2. Assess the Division's contribution to the mission, goals, and needs of the FIC

3. Make recommendations for the future of DIEPS.

This report describes the results of the DIEPS review. It begins with a brief description of review methodology (section II), followed by a description of the Division in terms of history, structure, and funding sources (section III). The next three sections present the expert panel's findings with respect to the following questions:

- Does DIEPS contribute value to FIC, NIH, and the international health community? (section IV)

- Is the Division's work consistent with the mission of FIC? (section V)

- What challenges does DIEPS currently face? (section VI)

The panel's recommendations are summarized at the end of the report (section VII). Appendices include biographical information on the review panelists and a logic model for the Division.

II. Methods

FIC routinely conducts reviews of its extramural programs using the FIC Framework for Program Assessment.[1] Initiated around the five-year mark, these reviews are typically conducted by a panel of extramural experts with support from a contractor with expertise in research program evaluation. Although DIEPS is not an extramural program, it was decided that a similar process would be appropriate for this review.

The expert panel convened for the DIEPS review included:

1. Enriqueta Bond, PhD, Former President, Burroughs Wellcome Fund (1994-2008, recently retired)

2. W. Paul Glezen, MD, Professor, Department of Molecular Virology and Microbiology, Baylor College of Medicine

3. Arthur Reingold, MD, Professor and Division Head, School of Public Health, University of California, Berkeley

4. Eleanor Riley, PhD, Head of the Immunology Unit and Professor of Immunology, Department of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine

Please see Appendix A for biographical information on the review panel members. The contractor selected by FIC to support the review was the Science and Technology Policy Institute (STPI).

Expert panel members participated in a preliminary teleconference on December 22, 2008 in order to approve the proposed logic model (Appendix B) and data collection strategy. Most of the evaluation data were collected and summarized for the panel by STPI, although three of the four panel members visited FIC during the data collection phase in order to conduct certain key interviews in person. The panel discussed its findings and recommendations during additional conference calls held on February 24, March 24, and April 10, 2009. The panel members also corresponded with each other and with STPI via email throughout the process.

Data collection for the review of DIEPS included the following:

- *Roster of Current and Former DIEPS Staff Members.* The roster included information on the role played by each staff member, the mechanism and duration of their financial support, and the current position and affiliation for former staff members. Where possible, the primary mentor for staff members receiving training was identified.

- *DIEPS Funding Sources.* Information on funding streams and operating expenditures was provided by the FIC Office of Administrative Management and International

[1] Available online at http://www fic nih.gov/about/plan/eval_framework htm; accessed April 30, 2009.

Services (OAMIS). Information on funding accepted by the Foundation for NIH on behalf of the Division was obtained from Division records.

- *DIEPS Publications.* The Division maintains a comprehensive list of publications by DIEPS staff members. For the purpose of the review, the publications were coded by topic/thematic area and supplemented with bibliometric information such as number of citations for each publication and 2006 Journal Impact Factors. Network diagrams based on co-authorship were also created to show linkages among DIEPS publications.

- *Qualifications of Core Staff Members.* The panel reviewed curriculum vitae for each of the four senior research staff members who are current full-time DIEPS employees. Supplemental information on indicators of esteem (e.g. honors and awards, appointment to external committees, invitations to international meetings) during the last five years was also provided by staff members.

- *Interviews with DIEPS Core Staff Members.* Each of the four senior research staff members participated in a preliminary phone interview with the evaluation contractor and at least one in-person follow-up interview directly with panel members.

- *Interviews with FIC Senior Leadership.* Panel members spoke in person on two separate occasions with the current FIC Director and the Deputy Director. Former Director Dr. Gerald Keusch was consulted via telephone. The FIC Executive Officer was interviewed in order to discuss the administrative burden associated with DIEPS.

- *Other Interviews.* Several additional telephone interviews were conducted with individuals who have collaborated with the Division in various capacities. A former staff member from the Office of Intramural Research was also consulted to clarify rules associated with intramural programs.

III. Description of the Division

Division History and Focal Areas

With the approval of the NIH Director, DIEPS was established as an in-house research unit by former FIC Director Dr. Gerald Keusch in FY 2000. At the time, Dr. Mark Miller had recently been recruited to FIC as Associate Director for Science. As part of what he anticipated would be a broader role for scientific coordination across the entire Center, Dr. Miller agreed to take on leadership of the new Division. Following Dr. Keusch's departure in 2003, directing DIEPS became Dr. Miller's primary role, but Dr. Miller retains the title of Associate Director for Science.

The original budget proposed for DIEPS with the support of Dr. Keusch was $17.5 million for the first five years, which would have put it at roughly ten percent of the FIC budget by year five. However, the actual FIC contribution to the Division budget during the first five years was much smaller than initially anticipated (less than $800,000 in the first year and about $5 million total during the first five years). The decision not to pursue formal intramural status for DIEPS appears to have been made largely because of the small approved budget combined with the belief that FIC would have been required to pay fees to the Office of Intramural Research (OIR) that would have further depleted the Division's financial resources.[2]

It does not appear that a formal mission or set of strategic priorities was ever developed for DIEPS, but the initial guiding vision was to conduct research that would help to establish or enhance the scientific underpinnings of policies related to international health. A conscious effort was made to carve out a niche for the Division that would take advantage of the long-term scientific perspective available at NIH. Because both space and funding were severely limited, it was decided that the Division would focus primarily on epidemiology and specifically on application of novel and sophisticated computational approaches to existing data.

The Division started out with three broad areas of interest. The first was vaccine-preventable diseases, which had been Dr. Miller's primary research focus prior to joining FIC. Work in this area has included studies focused on unsafe injection practices, haemophilus influenzae type B, rotavirus, pneumococcus, hepatitis, measles, pertussis, polio, and meningitis. In parallel, Dr. Miller has also continued to work closely with the vaccine development lab of Dr. John Robbins at the National Institute of Child Health and Human Development (NICHD).

[2] Please note, however, that information provided by a former employee of the Office of Intramural Research (OIR) who was contacted as part of this review indicated that OIR is sometimes willing to negotiate exceptions to these requirements.

The second area of interest identified was influenza and other rapidly transmissible agents, which the Division considered to be area of inquiry that was underdeveloped at the time. The importance of modeling for rapidly-transmissible diseases such as smallpox became more widely recognized following the terrorist attacks against the US in 2001. Modeling for pandemic influenza in particular became more urgent as the avian influenza epizootic that began in Hong Kong in 1997 re-emerged in 2003 and began spreading throughout Asia, Africa, and Eastern Europe. In 2006, DIEPS launched the large-scale Multinational Influenza Seasonal Mortality Study (MISMS) project (please see text box for more information). The Department of Health and Human Services (DHHS) began providing support to DIEPS for influenza modeling work in FY 2008.

The third original focal area was malaria, which was selected for its importance to global health and complex ecological dynamics. Malaria modeling was the primary research interest of Dr. Ellis McKenzie when he was recruited as the Division's first staff scientist in 2001. Malaria epidemiology and control are of interest to Dr. Joel Breman, who joined DIEPS from the FIC Division of International Training and Research (DITR) at around the same time.

Two additional focal areas were added later as the Division's portfolio evolved. Diarrheal diseases and malnutrition became a fourth area of interest largely due to encouragement from the Bill and Melinda Gates Foundation. Around 2003-4, Dr. Miller served as an external reviewer for a Gates project focused on vaccines for diarrheal diseases. That relationship expanded to a series of three Gates grants to support DIEPS work focused on nutrition and enteric diseases. The most recent of these grants—and the largest by far at about $30 million—will support collaborative, multi-site studies of malnutrition and enteric infections involving sites in Bangladesh, Brazil, India, Nepal, Pakistan, Peru, South Africa, and Tanzania.

DIEPS Project: Multinational Influenza Seasonal Mortality Study (MISMS)

MISMS is an international collaborative effort to analyze national and global mortality patterns associated with influenza virus circulation.

Funding sources: FIC, DHHS

Duration: 2006-present

Specific aims:

1. Describe synchrony in seasonal variations of causes of influenza mortality;
2. Describe long-term temporal trends and inter-annual variations in influenza mortality;
3. Explore seasonal patterns and burden of influenza mortality in tropical countries;
4. Develop a world map of influenza mortality burden and seasonal patterns.

Accomplishments:

- Developed and distributed detailed protocol for data collection and analysis
- Received data from 25 countries on six continents
- Held four regional meetings and planning for one more: Buenos Aires (February 2007); Hanoi (August 2007); Portugal (September 2008); Dhaka, Senegal (April 2009); and Bethesda, MD (June 2009)
- Trained visiting investigators from eight countries: Brazil, Denmark, Italy, Japan, Portugal, South Africa, South Korea, and Taiwan
- Published more than 50 manuscripts

For more information see:
http://origem.info/misms/index.php

The fifth focal area, which might be called "modeling fundamentals," evolved gradually in parallel with DIEPS efforts to raise awareness of the relevance of modeling to biosecurity and biodefense starting in 2001-02. This focal area includes exploration of the underlying theory and methods for disease modeling as well as its uses and limitations as a tool for policy. Starting in 2003, DHHS provided about $1.1 million to support work on modeling for anthrax and smallpox. In 2008 DIEPS received funding from the Department of Homeland Security's Science and Technology Directorate (via a subcommittee of the National Science and Technology Council) to address fundamental questions and challenges involved in modeling more systematically. The Research and Policy for Infectious Disease Dynamics (RAPIDD) project will include a series of conferences, seminars, working groups, and postdoctoral fellowships (please see text box for more information).

One additional DIEPS activity does not fit neatly into any of the five focal areas described above, but, during the peak of DIEPS involvement, it was sufficiently large and sufficiently important to constitute a sixth focal area in its own right. The Disease Control Priorities Project (DCPP) is an ongoing effort to assess disease control priorities and produce evidence-based analysis and resource materials to inform health policymaking in developing countries. The project is funded by the Bill & Melinda Gates Foundation. Partners include the World Health Organization (WHO), World Bank, and Population Reference Bureau. DCPP was housed and managed at FIC from 2001 to 2006.

Finally, it should be noted that the focal areas are fairly broad and partially overlapping; for example, influenza and many diarrheal diseases are vaccine-preventable, and many DIEPS research efforts have been relevant to exploration of modeling fundamentals and biosecurity. Furthermore, the focal areas have always been regarded as guidelines rather than rigid boundaries for the types of projects DIEPS would be willing to take on. The Division has intentionally remained open to any opportunity where staff members believed their analytic skills could be put to good use. Projects can and do take place outside of the focal areas, including but not limited to topics such as antibiotic resistance, dengue and other vector-borne diseases, hemorrhagic fever, HIV/AIDS, and cholera.

DIEPS Project: Research and Policy for Infectious Disease Dynamics (RAPIDD)

The premise of RAPIDD is that the development of scientifically sound modeling for forecasting and analysis, aligned with the needs of U.S. Government decision makers, will require the resolution of a number of important cross-cutting scientific questions in a more than ad hoc manner. For instance, it is not yet understood which models and modeling approaches will be needed for adequate operational capacity, how the necessary models can be related to each other and to data of various quality and scale, or how actual needs of decision-makers can be characterized and addressed.

Funding sources: FIC, Department of Homeland Security

Duration: 2008-present

Focal areas in year 1:

1) Characteristics that make zoonoses "good" or "bad" for modeling their dynamics and control

2) Hierarchies of models and their validation against epidemiological data

Accomplishments:

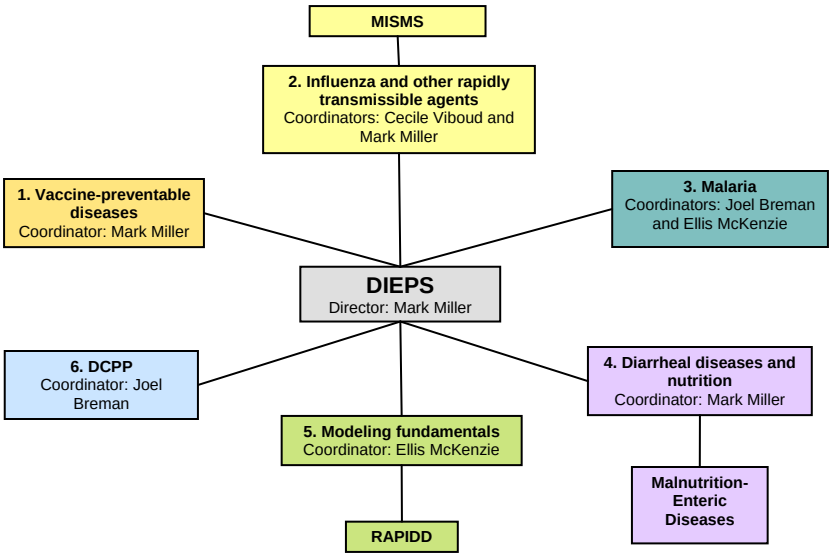
- Fourteen senior collaborators and seven postdoctoral fellows currently receiving support; several more expected to be brought on staff in the next few months

Organization and Staffing

Historically, DIEPS has been loosely organized around the six focal areas described in the previous section (Figure 1); however, intensity of activity within the focal areas has shifted over time. DIEPS no longer participates in DCPP. Vaccine preventable diseases remains an active area of research, but much of the current work in this area overlaps with the influenza and diarrheal disease focal areas (although there are also ongoing projects in the areas of measles and pertussis and meningococcal meningitis). Meanwhile, the diarrheal diseases and modeling fundamentals focal areas have expanded significantly with the influx of funding from the Gates Foundation and DHS, respectively.

As Division Director, Dr. Miller has overall administrative responsibility for the Division, including all of the focal areas. In addition, each focal area also has at least one senior, full-time Federal employee who functions as leader and coordinator for projects in the area. However, the "coordinator" designation is unofficial and leadership responsibilities below the level of the Division Director are not well-defined except in the context of individual research projects.

Figure 1: DIEPS focal areas (current and historical) with unofficial coordinators.



For the purposes of the review, an individual was considered to be a DIEPS staff member if he or she met any of the following criteria:

1. Federal employee assigned to the Division;

2. Received compensation for services rendered to the Division via contract or interagency personnel agreement (IPA);

3. Volunteer working onsite.

Using this definition, there have been at least 102 DIEPS staff members, of whom 49 were active on April 1, 2009 (Table 1).

Table 1: Composition of DIEPS staff by functional role and funding mechanism.

	Number on Staff, April 2009	Percent of Staff, April 2009	Number on Staff, 2000-2009
Senior Research Staff: Core (FIC/DIEPS employees)*	4	8%	4
Senior Research Staff: Non-core (Contract/IPA)	24	49%	52
Postdocs/Fellows (Contract/IPA or Volunteer)	13	27%	21
Predocs/Research Assistants (Contract/IPA or Volunteer)	6	12%	23
Admin (FIC/DIEPS employees)	2	4%	2
Total	49		102

*Excludes Dr. David Smith, who was formerly a Federal employee but now receives support via an IPA with the University of Florida. Dr. Smith has been counted as an active staff researcher.

Of the 49 current staff members, 28 (57%) are senior researchers (faculty level or equivalent). Dr. Miller and the three other area coordinators are the "core" research staff. All four are permanent Federal employees and work full-time and on-site at FIC.

There are 24 other senior research staff members, of whom 23 are supported via contract or IPA. The exception is a former AAAS fellow who was recently hired by FIC as a non-permanent (three-year limited) Federal employee; she will split her time with another division. Most (79%) of the senior staff researchers work only part-time for the Division, and the vast majority (92%) work offsite. Most have academic faculty appointments, and it is particularly notable that five are full Professors at Penn State. Four are located in countries other than the US (India, France, Kenya, and the United Kingdom).

Another 13 current staff members (27%) are postdoctoral fellows, and all but one are supported via contract or IPA. The exception is a volunteer who receives support via the Department of Defense (DoD) Science, Mathematics & Research for Transformation (SMART) program. More than half (56%) of postdocs work on DIEPS projects part-time, and most (63%) work offsite. Two postdoctoral fellows are located in other countries (Canada and Brazil).

The remaining current staff members are six Master's level research assistants and two administrative assistants. All of the research assistants are contractors; three are full-time/onsite, two are part-time/offsite, and one is a short-term visitor from Denmark. Both administrative assistants are full-time, onsite Federal employees. It should be noted that the administrative staff was recently doubled from one to two employees and still accounts for only four percent of Division staff.

Figure 2 shows the organization of the current staff by focal area and role.

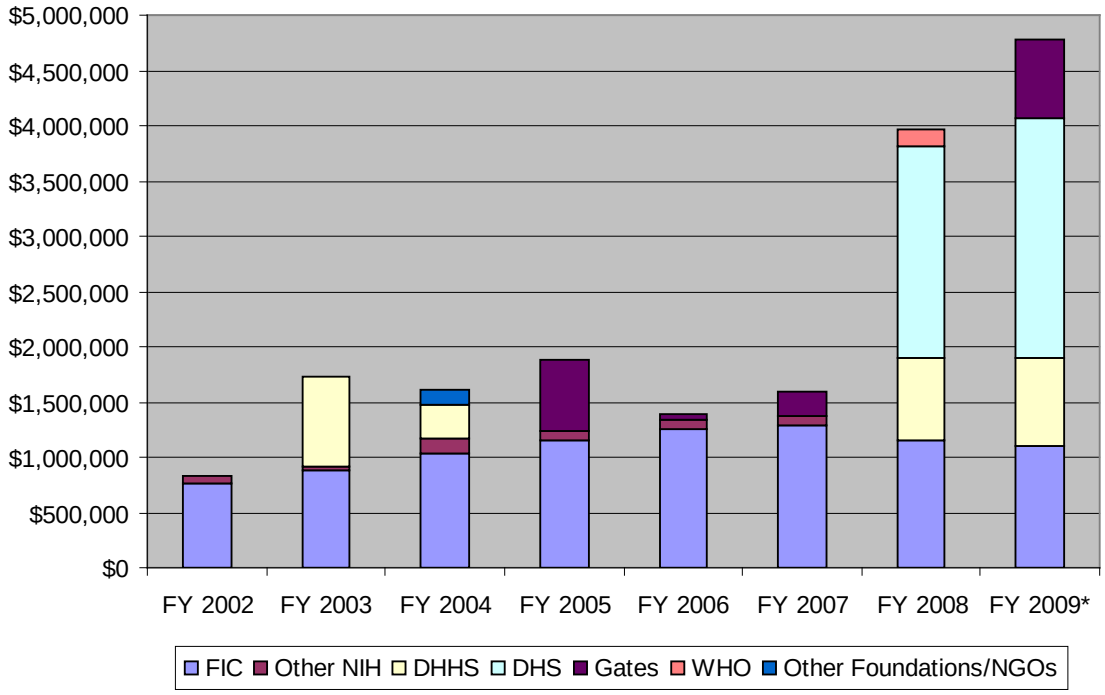
Figure 2: DIEPS organization and personnel as of April 1, 2009. Includes current staff plus active collaborators who do not currently receive compensation through the Division.

The RAPIDD project currently involves the largest number of staff members, and that number is expected to grow during the next few months. It should also be noted that there are several staff members who are involved in more than one focal area. Figure 2 also includes active collaborators who do not meet the "staff" criteria outlined above; these individuals are not currently receiving compensation through the Division and are not located onsite, but they were identified by the area coordinators as actively involved in current DIEPS research projects.

Funding Sources and Operating Budget

For the purpose of this review, the DIEPS budget was defined to include all sources of support for DIEPS projects except the DCPP.[3] Between FY 2003 and 2007, the total DIEPS budget ranged between approximately $1.3 million and $1.8 million before almost tripling to $3.96 million in FY 2008 (Table 2, Figure 3). In FY 2009, the budget is projected to be in the $5 million range.

Figure 3: DIEPS Funding by FY and Source, FY2002-08, with projection for FY 2009.



Description: Bar graph showing DIEPS funding by fiscal year for FY2002 through FY2008, and projected funding for FY2009: FY2002 ~ $800,000 | FY2003 ~ $1,700,000 | FY2004 ~ $1,600,000 | FY2005 ~ $1,900,000 | FFY2006 ~ $1,400,000 | FY2007 ~ $1,600,000 | FY2008 ~ $4,000,000 | FY2009 projected ~ $4,750,000. The source for the funding is indicated by color, including: FIC, Other NIH, DHHS, DHS, Gates, WHO, Other Foundations/NGO's.

[3] DCPP funding has been excluded from the DIEPS budget because it was shared by other FIC Divisions. However, Dr. Breman's salary is included for the relevant years.

Table 2: DIEPS Funding By Source, Purpose, and Mechanism, FY2002-09.

Source	Purpose	Mechanism	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009*
FIC	Core Operating Budget	RMS budget	$766,286	$879,437	$1,037,692	$1,156,217	$1,246,127	$1,291,397	$1,160,302	$1,096,446*
FIC	*AJHTM* malaria suppl	Transfer to RMS			$10,000		$10,000			
Other NIH										
NIAID	Reichert contract	Reimburseable (IAA)	$40,000	$40,000						
NIAID	*AJHTM* malaria suppl	To journal via FNIH (2004); Direct transfer (2006)			$10,000		$10,000			
NICHD	Meningitis vaccine studies	Reimburseable (IAA)			$100,000	$82,500	$55,260			
NICHD	*AJHTM* malaria suppl	Direct transfer					$10,000			
NIEHS	*AJHTM* malaria suppl	To journal via FNIH (2004); Direct transfer (2006)			$25,000		$7,500			
OD/ORD	Rare diseases conference	Reimburseable (IAA)	$20,000							
OD/OSPA	AAAS fellow	Direct transfer						$79,767		
Other USG										
DHHS	Smallpox and anthrax modeling	Reimburseable (IAA)		$810,000	$300,000					
DHHS	Avian influenza	Supplemental							$742,675	$800,000*
DHS	RAPIDD	Reimburseable (IAA)							$1,915,000	$2,175,000
Foundations/NGOs										
Gates Foundation	Zinc project	Conditional gift via FNIH					$51,030			
Gates Foundation	DD burden project	Conditional gift via FNIH				$641,232		$217,125		
Gates Foundation	Mal-Ed project	Conditional gift via FNIH								$716,527
Burroughs-Wellcome	*AJHTM* malaria suppl	To journal via FNIH			$1,000					
Malaria Vaccine Initiative	*AJHTM* malaria suppl	To journal via FNIH			$20,000					
The Rockerfeller Foundation	*AJHTM* malaria suppl	To journal via FNIH			$25,000					
Swiss Development Corporation	*AJHTM* malaria suppl	To journal via FNIH			$30,000					
UN Foundation	*AJHTM* malaria suppl	To journal via FNIH			$40,000					
The Wellcome Trust	*AJHTM* malaria suppl	To journal via FNIH			$8,240					
WHO-Afro	*AJHTM* malaria suppl	To journal via FNIH			$10,000					
WHO	Pertussis and measles	Conditional gift via FNIH							$143,350	
		Grand Total	**$826,286**	**$1,729,437**	**$1,616,932**	**$1,879,949**	**$1,389,917**	**$1,588,289**	**$3,961,327**	**$4,787,973***

*FY 2009 allocations from FIC and DHHS are only projections at this time.

Major sources of support for DIEPS besides FIC include DHS ($4.09M through FY2009), DHHS ($2.65M), and The Bill and Melinda Gates Foundation ($1.63M). Three other NIH Institutes and Centers (NIAID, NICHD, NIEHS) plus the Office of the Director (OD) have contributed approximately $480,000 combined, while WHO has contributed $153,000. Six other Foundations and NGOs have made smaller contributions (Table 2). In general, funds from other US Government agencies have been transferred via inter-agency agreements. Funds from outside organizations have been solicited, secured, and administered by the Foundation for NIH (FNIH). In some cases, this complicates the budget picture for DIEPS; for instance, the most recent Gates Foundation grant will total approximately $30 million over five years, but much of that funding will be dispersed by the Foundation on behalf of DIEPS. Only the portion that will support DIEPS activities directly has been included in Table 2.

The FIC contribution to the DIEPS core operating budget averaged about $1 million per year between FY 2002 and 2008, increasing slowly until FY 2007 and then dropping slightly in FY 2008. As a percentage of the Division's total budget, the FIC share has fluctuated; it was particularly low in FY 2003, FY 2005, and FY 2008 and higher in other years (Table 3). Since the Division is not extramural and FIC does not have an intramural program, the FIC contribution is drawn from the Center's Research Management and Support (RMS) budget.

Table 3: Core Operating Budget from FIC as a Percentage of DIEPS Budget, FY 2002-09.

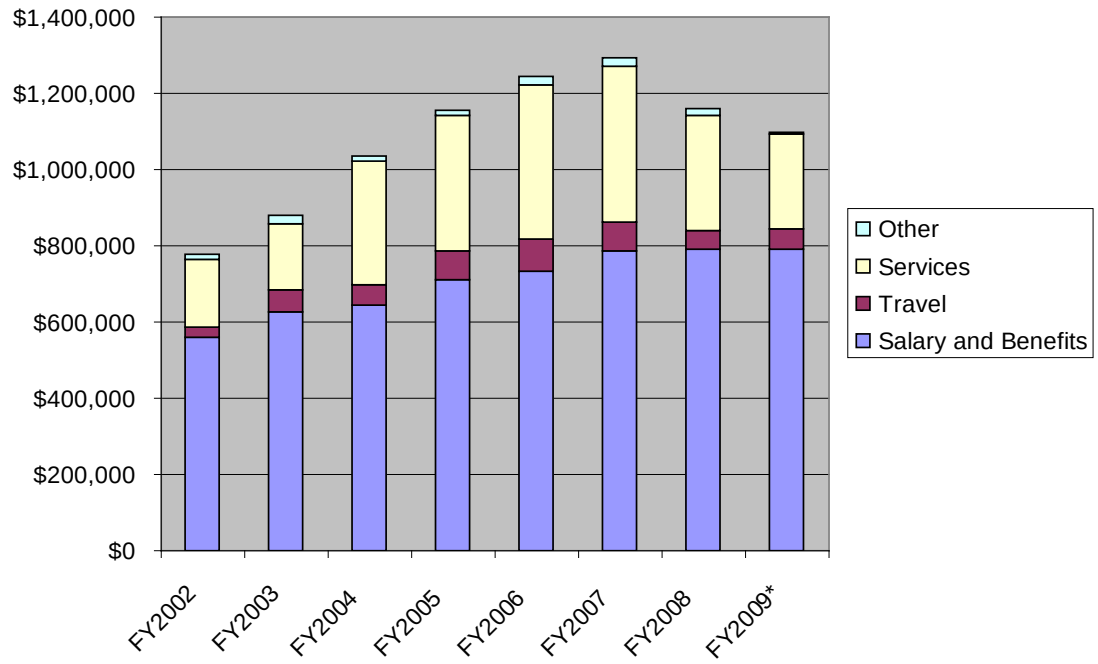
	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009 (estimated)
Core funds from FIC	$766,286	$879,437	$1,037,692	$1,156,217	$1,246,127	$1,291,397	$1,160,302	$1,096,446*
Total DIEPS budget	$826,286	$1,729,437	$1,616,932	$1,879,949	$1,389,917	$1,588,289	$3,961,327	$4,787,973*
FIC share of Total	93%	51%	64%	62%	90%	81%	29%	23%

* FY 2009 allocations from FIC and DHHS are only projections at this time.

The vast majority of the Division's core operating funds have been used to support salary and benefits for the Federal staff members and to procure the services of other staff members through contracts and IPAs (Figure 4). A relatively small portion of the FIC funds (between four and seven percent per year) were used for travel.

*FY 2009 allocations from FIC and DHHS are only projections at this time.

Figure 4: Expenditures from DIEPS Core Operating Budget by Category, FY 2002-08, with projection for FY 2009.



*FY 2009 allocations from FIC and DHHS are only projections at this time.

Description: Bar graph showing expenditures from DIEPS core operating budget for FY2002 through FY2008, and projected expenditures for FY2009: FY2002 ~$800,000 | FY2003 ~$900,000 | FY2004 ~$1,000,000 | FY2005 ~ $1,100,000 | FFY2006 ~ $1,200,000 | FY2007 ~$1,300,000 | FY2008 ~$1,100,000 | FY2009 projected ~$1,100,000. The category of the funding is indicated by color, including: salary and benefits; travel; services; other.

Similar US Government Programs

As far as the panel could determine, the Division's focus on epidemiology and infectious disease modeling makes it unique among in-house research efforts at NIH. Interviewees reported that there are a few other modelers scattered across the NIH intramural programs, but they tend to focus on modeling at the cellular and molecular levels. One notable exception is the Laboratory of Biological Modeling at the National Institute for Diabetes and Digestive and Kidney Diseases (NIDDK), which uses modeling approaches to explore the dynamics of human body weight change and its consequences for conditions such as obesity, diabetes, cardiovascular disease, starvation, and wasting syndromes such as anorexia nervosa and cancer cachexia. Reports from several sources suggested that NIAID, the most logical home for an overlapping intramural research program, has chosen not to engage in epidemiology and disease modeling research.

Intramural research groups focused on disease modeling exist at other US government agencies including DHHS, DoD, DHS, and CDC. An in-depth comparison of DIEPS with each of these groups was beyond the scope of this review, but reports from interviewees suggest that DIEPS is among the most mature and sophisticated of US government disease modeling laboratories. DIEPS has also collaborated with several of these groups, particularly on biodefense-related

projects.

When asked whether there is sufficient support for disease modeling in the extramural community, interviewees reported that the funding situation is not perfect but has been improving in recent years. At least three NIH extramural programs currently provide support for disease modeling:

1. Modeling of Infectious Disease Agents Study (MIDAS), a National Institute of General Medical Sciences (NIGMS) U01/U24 program focused on "providing the U.S. scientific and public health communities better resources, knowledge, and tools to improve their ability to identify and prevent the spread of diseases resulting from the emergence or intentional release of pathogens and their products."[4] As described in Section IV, NIGMS credits DIEPS with helping to inspire the MIDAS program, and DIEPS staff members have participated on the MIDAS Steering Committee from the beginning.

2. Evolution of Infectious Diseases, a NIGMS R01 program soliciting proposals to "study the evolutionary principles that underlie the emergence, spread, and containment of infectious disease."[5]

3. Ecology of Infectious Disease (EID), a program jointly administered by FIC and the National Science Foundation (NSF) to support "the development of predictive models and the discovery of principles governing the transmission dynamics of infectious disease agents."[6] As reported in Section IV, DIEPS corresponds frequently with the EID Program Director and has collaborated with EID awardees on projects related to influenza and climate change.

[4] See RFA-GM-09-001 and RFA-GM-09-002.
[5] See PA-07-130.
[6] See NSF solicitation 08-601.

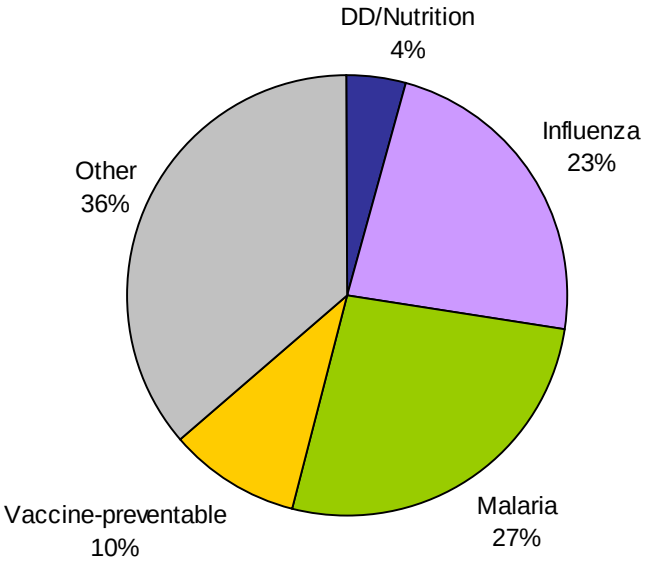
IV. Outputs, Outcomes, and Impacts

Publications

As of March 2009, the list of publications maintained by DIEPS included 252 peer-reviewed publications.[7] A DIEPS staff member (defined for the review as described in section III) was first author on half of these publications (125 or 50%).

As coded based on titles and abstracts, about half of all DIEPS publications have focused on malaria and influenza combined (27% and 23% respectively, Figure 5). Vaccine-preventable diseases account for an additional 10%, while diarrheal diseases account for 4%.

Figure 5: DIEPS Publications by Thematic Area (N=252).



The remaining 36% of DIEPS publications focus on a variety of diseases and other topics (Table 4). The two categories most relevant to the RAPIDD project (zoonoses/animal diseases/foodborne pathogens and ecological theory/modeling) account for 11% of DIEPS publications. Interestingly, however, most of these publications pre-date the RAPIDD program itself, suggesting that the modeling fundamentals focal area was productive even before the large influx of funding from the Department of Homeland Security in 2008.

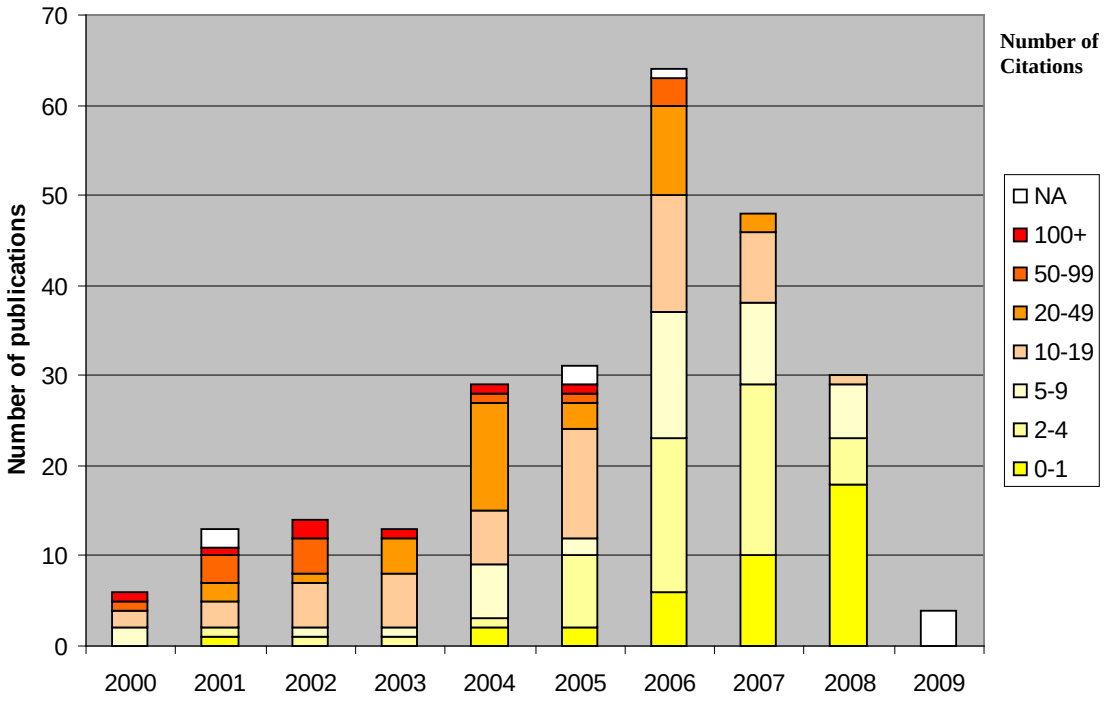
[7] The bibliography plus full text for all DIEPS publications is available online at http://origem.info/FIC/Bibliography.html.

Table 4: Topics of DIEPS publications classified as "Other"

Topic/Disease Area	Number of Publications	Percent of Total (N=252)
Zoonoses, animal diseases, and foodborne illness	18	7%
Virology/viral evolution	16	6%
Mosquito-borne other than malaria (dengue and WNV)	13	5%
Antibiotic resistance	11	4%
Ecological theory/modeling	11	4%
Disease priorities and LMIC research capacity	6	2%
HIV/AIDS	5	2%
Cholera	3	1%
Other (includes: AGEP, biofilms, guinea worm, heart disease, hemorrhagic fever, polymocrobial blood infections, SARS, Sjogren's syndrome)	9	4%
Total	92	36%

In general, DIEPS publications appear to have been frequently cited, especially given that most of these publications have been available for citation for fewer than five years (Figure 6).

Figure 6:Number of DIEPS Publications by Year and Citation Frequency. Citation counts for DIEPS publications based on Web of Science searches performed in February 2009.



Description: Bar graph showing the number of DIEPS publications for the years 2000 through 2009: 2000 ~6 | 2001 ~12 | 2002 ~13 | 2003 ~12 | 2004 ~29 | 2005 ~21 | 2006 ~65 | 2007 ~48 | 2008 ~30 | 2009 ~4. The number of citations is indicated by color, including: 0-1; 2-4; 5-9; 10-19; 50-99; 100+; NA.

For DIEPS publications prior to 2008 (N=213), the average number of citations per publication was at least 21.92.[8] Of the 252 DIEPS publications, 54 (21%) had been cited at least 20 times in February of 2009, 20 (8%) had been cited at least 50 times, and seven (3%) had been cited at least 100 times (Table 5).

Table 5: DIEPS publications with 100+citations as of February 2009.

Citation Count*	DIEPS Publication
497	Parashar UD, Hummelman EG, Bresee JS, Miller MA, Glass RI. 2003. The global illness and deaths caused by rotavirus disease in children. *Emerging Infectious Disease*; 9:565-72.
363	Breman JG. 2001. The ears of the hippopotamus: manifestations, determinants and estimates of the malaria burden. *American Journal of Tropical Medicine and Hygiene*; 64 (Suppl 1-2):1-11.
183	Breman JG, Alilio MS, Mills A. 2004. Conquering the intolerable burden of malaria: II. What's new, what's needed: A summary. *American Journal of Tropical Medicine and Hygiene*; 71(2 Suppl):1-15.
180	Borio L, Inglesby T, Peters CJ, Schmaljohn AK, Hughes JM, Jahrling PB, Ksiazek T, Johnson KM, Meyerhoff A, O'Toole T, Ascher MS, Bartlett J, Breman JG, Eitzen EM Jr, Hamburg M, Hauer J, Henderson DA, Johnson RT, Kwik G, Layton M, Lillibridge S, Nabel GJ, Osterholm MT, Perl TM, Russell P, Tonat K. 2002. Hemorrhagic fever viruses as biological weapons: medical and public health management. *Journal of the American Medical Association*; 287:2391-405.
177	Lieu TA, Ray GT, Black SB, Butler JC, Klein JO, Breiman RF, Miller MA, Shinefield HR. 2000. Projected cost-effectiveness of pneumococcal conjugate vaccination of healthy infants and young children. *Journal of the American Medical Association*; 283:1460-8.
164	Breman JG, Henderson DA. 2002. Diagnosis and management of smallpox. *New England Journal of Medicine*; 346:7300-08.
125	Simonsen L, Reichert TA, Viboud C, Blackwelder WC, Taylor RJ, Miller MA. 2005. Impact of Influenza Vaccination on Seasonal Mortality in the US Elderly Population. *Archives of Internal Medicine*; 165(3):265-72.

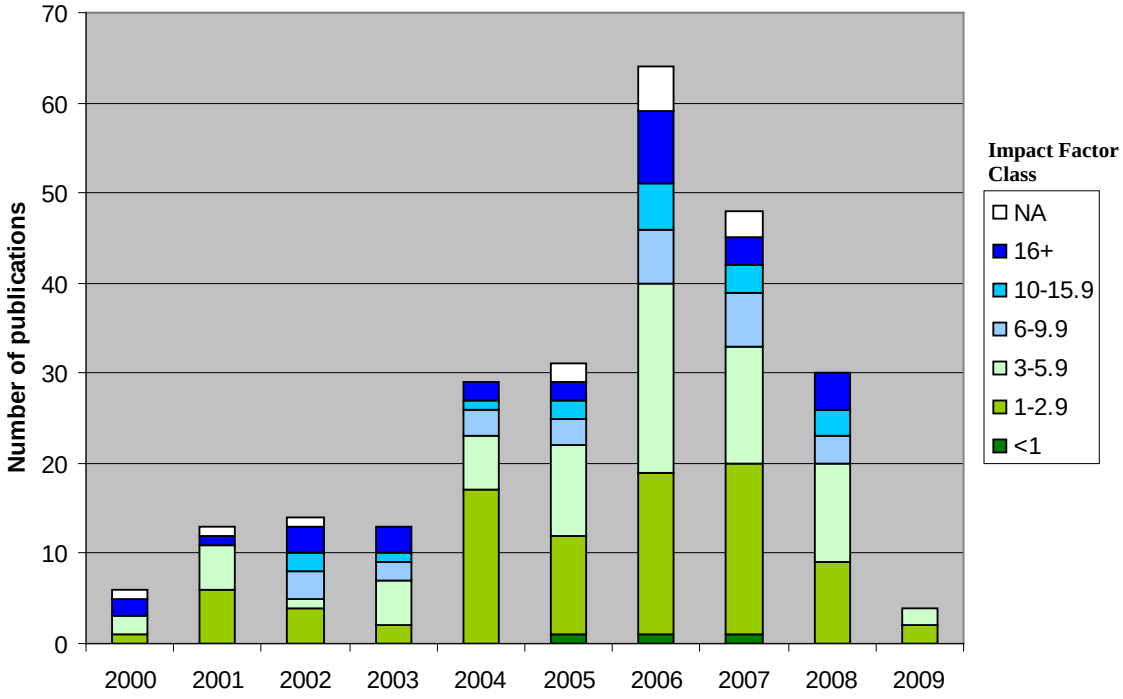
*Citation counts for DIEPS publications based on Web of Science searches performed in February 2009.

DIEPS publications also appeared frequently in journals with high Journal Impact Factors (Figure 7). Of the 239 DIEPS manuscripts published in journals for which a 2006 Journal Impact Factor was available from Thomson/Reuters, the average Journal Impact Factor was 7.61. There were 45 DIEPS publications in journals with an impact factor of at least 10 (19%) and 28 publications in journals with an impact factor of at least 16 (12%). Highest impact journals publishing DIEPS manuscripts include: *New England Journal of Medicine* (4 publications), *Science* (5 publications), *Nature* (5 publications), *Lancet* (7 publications), *Nature Genetics* (1

[8] Citation counts for DIEPS publications based on Web of Science searches performed in February 2009.

publication), *JAMA* (4 publications), and *Nature Reviews Genetics* (2 publications).

Figure 7: Number of DIEPS Publications by Year and 2006 Journal Impact Factor Class.



Description: Bar graph showing the number of DIEPS publications for the years 2000 through 2009: 2000 ~6 | 2001 ~12 | 2002 ~13 | 2003 ~12 | 2004 ~29 | 2005 ~21 | 2006 ~65 | 2007 ~48 | 2008 ~30 | 2009 ~4. The journal impact factor class is indicated by color, including: <1; 1-2.9; 3-5.9; 6-9.9; 10-15.9; 16+; NA.

In addition to the DIEPS publications in peer-reviewed journals, it should also be noted that DIEPS played a critical role in the 2006 publication of *Disease Control Priorities in Developing Countries (2nd Edition)*,[9] commonly known as the DCP2 report, as well as extended summaries titled *Global Burden of Disease and Risk Factors*[10] and *Priorities in Health*.[11] DCPP chapters were peer-reviewed via an Advisory Group panel organized by the US Institute of Medicine and Inter-Academies Medical Panel as well as each of the participating partner organizations (NIH, WHO, World Bank).

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[9] Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, Jha P, Mills A, Musgrove P, eds. 2006. *Disease Control Priorities in Developing Countries (2nd Edition),* New York: Oxford University Press. Full text available online at http://www.dcp2.org/pubs/DCP, accessed April 2009.

[10] Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJL,eds. 2006. *Global Burden of Disease and Risk Factors*. New York: Oxford University Press. Available online at http://www.dcp2.org/pubs/GBD, accessed April 2009.

[11] Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, Jha P, Mills A, Musgrove P, eds. 2006. *Priorities in Health*. New York: Oxford University Press. Available online at http://www.dcp2.org/pubs/PIH, Accessed April 2009.

Patents

A Provisional Patent Application for an M2e peptide vaccine against influenza was filed with the US Patent and Trademark Office on behalf of DIEPS and NICHD in August 2008.[12] Dr. Miller is listed as an inventor on the application. A patent application for a second recombinant influenza haemaglutinin vaccine is currently being prepared.

Policy and Public Health

DIEPS staff members and others described a wide variety of policy impacts from DIEPS research and other activities. Those considered by the panel to be most significant are described briefly below.

Revision of CDC guidelines for influenza vaccination. An influential DIEPS study published in 2008 (see text box, #1) demonstrated that the current vaccination strategy in the US was not working to reduce mortality in seniors and that vaccination recommendations should be extended to cover other age groups. DIEPS staff reported that they were contacted by CDC following publication of the study to discuss the findings. CDC later released statements and revised its recommendations based on the findings.

Key DIEPS Publications: Influenza

1. Miller MA, Viboud C, Olson DR, Grais RF, Rabaa MA, Simonsen L. Prioritization of influenza pandemic vaccination to minimize years of life lost. *J Infect Dis* 2008;198:305-11.

Found that mortality burden by age group has varied for past pandemics, suggesting that pandemic vaccination strategies should not ignore younger populations, that scenarios should be flexible and not limited to the groups at high risk for complications during interpandemic periods.

2. Barry JM, Viboud C, Simonsen L. Cross-protection between successive waves of the 1918-1919 influenza pandemic: epidemiological evidence from US Army camps and from Britain. *J Infect Dis* 2008;198:1427-34.

Found that exposure to influenza in the spring and summer of 1918 provided mortality and morbidity protection during the fall pandemic wave, suggesting that pandemic preparedness plans should account for naturally acquired immune protection during a first wave of mild influenza illnesses. The immunity from the 1918 springtime outbreaks were overlooked by groups assessing "social distancing" programs. They may have incorrectly attributed milder autumn epidemics to these programs.

3. Reichert TA, Simonsen L, Sharma, Pardo SA, Fedson, Miller M. Influenza and the winter increase in mortality in the United States, 1959-1999. *Am J Epidemiology* 2004;160:492-502.

Identified influenza as the most likely determinant of the winter increase in US mortality.

4. Simonsen L, Reichert, TA, Viboud C, Balckwelder WC, Taylor RJ, Miller MA. Impact of influenza vaccination on seasonal mortality in the US elderly population. *Arch Intern Med* 2005;165:265-72.

Attributed the decline in influenza-related mortality among elderly people in the decade after the 1968 pandemic to the acquisition of immunity to the emerging A(H3N2) virus, but could not correlate increasing vaccination coverage after 1980 with declining mortality rates in any age group.

5. Nelson MI, Edelman L, Spiro DJ, Boyne AR, Bera J, Halpin R, Ghedin E, Miller MA, Simonsen L, Viboud C, Holmes EC. Molecular epidemiology of A/H3N2 and A/H1N1 influenza virus during a single epidemic season in the United States. *PLoS Pathology* 2008 Aug 22;4(8):e1000133.

Initial paper resulting from complete genomic analysis of influenza viruses prevalent in the US. In addition to conducting the analysis, DIEPS spearheaded the collection of the viruses for sequencing.

[12] U.S. Provisional Application No. 61/089,384 (HHS Reference No. E-304-2008/0-US-01). For more information, see http://ott.od.nih.gov/db/abstxt.asp?refno=1899; accessed May 2009.

Revision of US pandemic influenza plans. The same study and other work by DIEPS suggested that the first US pandemic response plan, which focused on vaccination of seniors, may have been flawed. DIEPS studies of past pandemics demonstrated that seniors aren't as affected during pandemics and don't typically respond well to the vaccine. DIEPS research also showed that past pandemics had very different mortality burden and there is no single optimal strategy that fits all situations. The US plan has gone through several revisions since publication of the DIEPS study, and it now includes flexible pandemic scenarios.

Influence on influenza control policies worldwide. DIEPS has worked bilaterally and multilaterally with over 25 countries to develop policies relevant to the control of influenza. This includes work with six of the eight G8 country planners involved in pandemic influenza plans.

Early work on computational biology/mathematical modeling for biodefense. In the wake of the 2001 terrorist attacks against the US, DIEPS staff took the initiative to organize a number of meetings to explore what modeling could and couldn't do to help the US prepare for a bioterrorist attack. At that time, there were only about a few experienced infectious disease modelers in government. The first meeting brought together modelers and policy makers from across the US government (DOD, DHHS, DHS, NSF, the State Department, the Central Intelligence Agency, and the Executive Office of the President) as well as others in order to develop a research agenda. A case study for smallpox was suggested, and several studies were eventually commissioned and overseen by this group and a parallel group focused on anthrax. The conclusion of the extensive smallpox modeling exercise was that "surveillance-containment" and selective vaccination of priority groups would be more advantageous then mass vaccination of the entire U.S population.

MIDAS program. An interviewee from NIGMS confirmed that DIEPS deserves credit for helping to inspire and motivate the development of that Institute's Models of Infectious Disease Agent Study (MIDAS) program, which funds extramural research on infectious disease modeling. Prior to the biodefense-related meetings organized by DIEPS in 2002, NIGMS had not been planning any initiatives in the area of infectious disease modeling, and the efforts by DIEPS to convene the community and develop a research agenda were instrumental in demonstrating to NIGMS that there was an unmet need for funding in this area. DIEPS staff members have participated on the MIDAS Steering Committee ever since the program was founded, and the MIDAS Program Director participates on the Steering Committee for RAPIDD.

Key DIEPS Publications: Vaccine-Preventable Diseases

1. Ehrenfeld E, Glass RI, Agol VI, Chumakov K, Dowdle W, John TJ, Katz SL, Miller MA, Breman JG, Modlin J, Wright P. Immunization against poliomyelitis: moving forward. *Lancet* 2008; 371:1385-7.

Raised concerns about WHO plans to cease vaccination against poliomyelitis and urged exploration of strategies involving use of inactivated poliomyelitis vaccine (IPV).

2. Parashar UD, Hummelman EG, Bresee JS, Miller MA, Glass RI. The global illness and deaths caused by rotavirus disease in children. *Emerging Infectious Diseases* 2003; 9:565-72.

Estimated global burden of illness and death due to rotavirus. Found a yearly average of 352,000–592,000 deaths in children, of which 82% occur in the poorest countries.

3. Lieu TA, Ray GT, Black SB, Butler JC, Klein JO, Breiman RF, Miller MA, Shinefield HR. Projected cost-effectiveness of pneumococcal conjugate vaccination of healthy infants and young children. *Journal of the American Medical Association* 2000; 283:1460-8.

Evaluated projected cost and economic impact of pneumococcal conjugate vaccination of healthy infants and young children in the US. Found that vaccination has the potential to be cost-effective in addition to reducing morbidity and mortality from pneumococcal disease.

Polio eradication efforts. In September 2007, DIEPS and NIAID co-hosted a symposium entitled "Polio Immunization: Moving Forward." The purpose of the meeting was to discuss impediments facing the WHO Global Polio Eradication Initiative (GPEI) and define a research agenda to improve polio eradication strategies. The resulting report raised concerns about WHO plans to cease vaccination against poliomyelitis post-eradication and urged exploration of strategies involving use of inactivated poliomyelitis vaccine (IPV). [13]

Since the meeting, WHO has softened its policy on not accepting IPV as part of the global eradication campaign. WHO is also reconsidering its policy of abandoning all polio vaccination after certification of the interruption of disease transmission.

DCPP. The DCP2 report has been widely used as a resource for evidence-based analysis and policymaking in developing countries. Traffic on the DCPP website (URL: http://www.dcp2.org), which was launched in April 2006 to disseminate the report and related information, has ranged between a high of 101,414 users per month in April 2007 and a low of 26,020 users per month in July of 2006. In the most recent month for which data are available, February 2009, there were 34,554 visitors to the website. The site has been accessed from over 170 countries, with most traffic coming from the US and the United Kingdom. Among low and middle income countries, the site has been most frequently accessed from the Philippines, India, and South Africa.[14]

[13] Ehrenfeld E, Glass RI, Agol VI, Chumakov K, Dowdle W, John TJ, Katz SL, Miller MA, Breman JG, Modlin J, Wright P.. 2008. Immunization against poliomyelitis: moving forward. Lancet; 371:1385-7.

[14] Information on website traffic provided by Dr. Fariyal Fikree of the Population Reference Bureau on behalf of DCPP.

Key DIEPS Publications: Malaria

1. Smith DL, Dushoff J, McKenzie FE. The risk of a mosquito-borne infection in a heterogeneous environment. *PLoS Biology* 2004; 2(11): e368.

Predicted that peaks in human biting rate and proportion of mosquitoes that are infectious are not necessarily positively correlated, and estimates for the average risk of infection that are based on the average entomological inoculation rate may be strongly biased in heterogeneous environments.

2. Smith DL, McKenzie FE. Statics and dynamics of malaria infection in Anopheles mosquitoes. *Malaria Journal* 2004; 3(1):13.

Reviewed and re-derived classic formulae for malaria transmission and related them to cyclical feeding models.

3. Smith DL, Dushoff J, R. W. Snow, and S. I. Hay. The entomological inoculation rate and Plasmodium falciparum infection in African children. *Nature* 2005; 438:492-95.

Developed a mathematical framework to estimate the heterogeneity of infection rates from the relationship between rates of infectious bites and community prevalence. Found that 20% of the exposed population receives 80% of infections.

4. O'Meara WP, Smith DL, and McKenzie FE. Potential impact of intermittent preventive treatment (IPT) on spread of drug-resistant malaria. *PLoS Med.* 2006; May;3(5):e141.

Predicted that effectiveness of WHO-recommended intermittent preventive treatment of malaria in infants is likely to be lower in areas with low or unstable transmission rates due to its contribution to the development of anti-malarial drug resistance.

5. Smith DL, McKenzie FE, Snow RW, Hay SI. Revisiting the basic reproductive number for malaria and its implications for malaria control. *PLoS Biology* 2007; 5: 531-542.

Estimated the basic reproductive number for malaria (R_0) in a novel way for 121 African populations. Found a very wide range (between 1 and 3000), supporting the long-held notion that malaria control presents variable challenges across its transmission spectrum.

Malaria burden estimates. For five decades, the WHO estimate of morbidity and mortality from malaria of "one million deaths" was based on a 1952 report by Leonard Bruce-Chwatt that looked at autopsies in Lagos, Nigeria, and extended those findings to all of Africa. A series of three supplements to the *American Journal of Tropical Medicine and Hygiene* (2001, 2004, 2007) on the "intolerable burden of malaria" coordinated and edited by DIEPS estimated malaria burden at up to 2 to 3 million deaths as well as several billion febrile episodes resembling malaria in patients in malaria-endemic zones. These controversial findings helped to stimulate new research on the burden of malaria at CDC, WHO, and elsewhere. WHO also briefly raised its estimate of malaria burden to 1-2 million deaths, although the 2008 World Malaria Report scaled the estimate back to less than 1 million deaths and several hundred million "cases due to malaria." This may be based, in part, on recent success with the control programs

Training

Although DIEPS has not established any stand-alone research training programs or formal links to FIC extramural training programs, research training and mentoring is a significant component of the Division's activities. All four DIEPS "core" staff members described taking their mentorship responsibilities very seriously, and several went as far as to say that they consider helping to bring promising young researchers into the field of modeling as one of the Division's most important accomplishments. They emphasized that it can be difficult for disease modelers to acquire the right mix of math skills and the biology or public health background required to develop and interpret such models. The panel agrees that DIEPS provides an excellent and rare opportunity for this essential multidisciplinary and interdisciplinary training to occur.

For the purpose of quantifying DIEPS training impact, the panel focused on three categories of individuals:

1. Pre-doctoral students and research assistants (any duration);

2. Postdoctoral fellows (six months or more);

3. Visiting fellows and scientists (less than six months, generally from abroad).

Although estimates are uncertain because the Division does not have an established process for tracking trainees, the panel identified at least 27 pre-doctoral students/research assistants, 24 postdocs, and seven short-term visitors (Table 6). Countries of origin for the seven visiting scientists were Australia, Cameroon, Denmark, Italy, Portugal, South Africa, and South Korea.

Table 6: Number of DIEPS "trainees" by category.

	Number, April 2009	**Historical Total, 2000-2009**
Pre-doctoral students/junior staff	6	27
Postdoctoral fellows	13	24
Visiting scientists	1	7

Of the 11 postdoctoral fellows who have completed training with DIEPS, at least four (Chowell, Dushoff, Prudhomme O'Meara, Tozan) currently have academic faculty appointments, and two others (Viboud, Sturm-Ramirez) have transitioned to staff positions with FIC (Table 7).

Table 7: Current positions of former DIEPS postdocs.

Last	Degree	Current Position	Current Country	Focal area	DIEPS Mentor(s)
Chowell	PhD	Assistant Professor, Arizona State University	US	influenza, malaria	McKenzie, Miller, Viboud
Depinay	MD	unknown	France	malaria	McKenzie
Dushoff	PhD	Assistant Professor, McMaster University	Canada	influenza	Miller, Viboud, McKenzie
Freeman-Grais	PhD	Sr. Epidemiologist, Epicentre	France	DD/nutrition	Miller, Viboud
Gager	PhD	unknown	New Zealand	malaria	McKenzie
Kelly-Hope	PhD	Senior Research Assistant, Liverpool School of Tropical Medicine	UK	malaria	Miller, McKenzie
LeMenach	DVM	Postdoctoral Fellow, INSERM RFF	France	malaria	McKenzie, Smith
Prudhomme O'Meara	PhD	Assistant Professor, George Washington University School of Public Health	Kenya	malaria	McKenzie, Breman
Sturm-Ramirez	PhD	Research Fellow, DIEPS and DITR	US	influenza	Miller, Viboud
Tozan	PhD	Assistant Professor, Boston University	US	malaria	Breman
Viboud	PhD	Staff Scientist, DIEPS	US	influenza	Miller

Training "success stories" described anecdotally by DIEPS staff members include the following:

- Dr. Viggo Andreasen is a Danish mathematical modeler who had not focused on epidemiological data analysis before working with DIEPS. He collaborated with the Division on historical analysis of the 1918 pandemic in Denmark.[15] The collaboration helped to shift his interest towards applied research, and one of his graduate students (Nesli Saglanmak) is currently spending six months with DIEPS.

- Dr. Wendy Prudhomme O'Meara was a DIEPS postdoc whose research focused on malaria. Now employed by George Washington University and based at the Kenya Medical Research Institute, she continues to collaborate with DIEPS. Dr. Prudhomme O'Meara has published several important papers on malaria and implementation research, including one that predicts regional variability in the effectiveness of WHO-recommended intermittent preventive treatment of malaria in infants.[16]

[15] Andreasen V, Viboud C, Simonsen L. Epidemiologic characterization of the 1918 influenza pandemic summer wave in Copenhagen: implications for pandemic control strategies. *J Infect Dis* 2008 Jan 15;197(2):270-8.

[16] O'Meara WP, Smith DL, and McKenzie FE. Potential impact of intermittent preventive treatment (IPT) on spread of drug-resistant malaria. *PLoS Med*. 2006 May;3(5):e141.

- Dr. Caterina Rizzo came from the University of Bari to spend three months with DIEPS for the purpose of gaining statistical expertise and co-authoring two papers on Italian influenza mortality.[17][18] In part because of this work, she was recruited by the Istituto Superiore di Sanità, CNESPS (the Italian equivalent of NIH), where she now works as a senior scientist.

- Dr. Jennifer Rosen was a Howard Hughes Research Scholar who chose to do her research in epidemiology rather than in a lab. She trained with DIEPS for a year as a pre-doctoral student, publishing a paper in *Malaria Journal*[19] and another in the *Lancet*.[20] After completing a residency at NYU Medical Center in 2007, she joined the Epidemic Intelligence Service at CDC.

- Dr. Yesim Tozan spent just under one year with DIEPS as a postdoctoral Research Associate, during which time she collaborated with pre-doctoral student Shobha Sadasivaiah on insecticides for malaria control[21] . Dr. Tozan now has a faculty position at Boston University where she is working on cost-effectiveness of rectal artesunate for severe malaria in a rural setting. Dr. Tozan recently received an award of $50,000 per year for the next three years as one of their most promising new faculty members. Ms. Sadasiviah is expected to graduate from Weill Medical College at Cornell University in 2009.

- Dr. Cecile Viboud came to DIEPS in 2003 as a postdoctoral fellow visiting from France. In 2006, she was offered permanent position with the Division as a Staff Scientist, and she received a Distinguished Service Award from the US Department of Health and Human Services for work on rotavirus in the same year. In 2008, she received both the Fogarty International Center Director's Merit Award and a Young Scientist Award from the European Scientific Working Group on Influenza. Since 2003, Dr. Viboud has published more than 50 papers on influenza and other infectious diseases.

Integration with Other FIC Divisions

In general, there are few formal links between DIEPS and other FIC Divisions. Perhaps the most extensive interaction takes place through the three FIC working groups on which DIEPS is represented: communications and information technology, implementation science, and malaria. Of these, interviewees indicated that the malaria working group has been the most active. An intern from NIAID spent three months helping this group to put together a summary of FIC

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[17] Rizzo C, Viboud C, Montomoli E, Simonsen L, Miller MA. Influenza-related mortality in the Italian elderly: no decline associated with increasing vaccination coverage. Vaccine 2006 Oct 30;24(42-43):6468-75.

[18] Rizzo C, Bella A, Viboud C, Simonsen L, Miller MA, Rota MC, Salmaso S, Ciofi degli Atti ML. Trends for influenza-related deaths during pandemic and epidemic seasons, Italy, 1969-2001. *Emerg Infect Dis.* 2007 May;13(5):694-9.

[19] Rosen J, Breman JG, Manclark CR, Meade BD, Collins WE, Lobel HO, Saliou P, Roberts JM, Campaore P, Miller MA. Malaria chemoprophylaxis and the serologic response to measles and diphtheria-tetanus-whole-cell pertussis vaccines. *Malar J.* 2005 Nov 6;4:53.

[20] Rosen J and Breman JG. Malaria intermittent preventive treatment in infants, chemoprophylaxis, and childhood vaccinations. *Lancet*. 2004 Apr 24;363(9418):1386-8.

[21] Sadasivaiah S, Tozan Y, Breman JG. Dichlorodiphenyltrichloroethane (DDT) for indoor residual spraying in Africa: how can it be used for malaria control? *Am J Trop Med Hyg.* 2007 Dec;77(6 Suppl):249-63.

activities and successes in malaria. Interviewees reported that attending these meetings and getting administrative support has helped participants to keep on top of what everyone else is doing. Most recently, in March 2009, DIEPS and the Division of International Relations (DIR) organized an interagency meeting with the President's Malaria Initiative, CDC, and several NIH Institutes and Centers (FIC, NIAID, NICHD, NLM) to promote closer collaboration on malaria.

Other notable interactions between DIEPS and the rest of FIC include the following:

- Extramural staff members attend research seminars given by DIEPS on a semi-regular basis.

- DIEPS has worked closely with grantees of the joint NIH-NSF Ecology of Infectious Disease (EID) Program, collaborating on projects related to influenza and climate change. Staff members reported frequent interaction with EID Program Officer Dr. Joshua Rosenthal.

- DIEPS also works closely with DITR on issues related to climate change and influenza.

- The DCPP involved extensive interaction with the Division of International Science Policy, Planning, and Evaluation (DISPPE), OAMIS, and the FIC Office of the Director.

- Dr. Cecile Viboud of DIEPS collaborates with FIC Director Dr. Roger Glass on a research project looking at impact of new rotavirus vaccination program in the US. The pair has co-authored two published papers and another has been submitted for publication.

Collaboration and Strategic Partnerships

Within NIH, DIEPS has collaborative relationships with at least six other NIH Institutes and Centers, including several of strategic importance to FIC (Table 8). DIEPS partnerships with NICHD on vaccine work and NIGMS on MIDAS have been described elsewhere in this report. DIEPS has also collaborated with the Office of the Director, NIEHS, National Library of Medicine (NLM), the NIH Clinical Center, Center for Information Technology (CIT), and several different intramural and extramural groups at NIAID. DIEPS staff members participate on several NIH-wide committees, including the NIH DIR Scientific Directors, the systems science working group and the influenza working group.

Beyond NIH, DIEPS has close working relationships with US Government agencies including the Centers for Disease Control and Prevention, Department of Health and Human Service's Office of Global Health, the Department of Homeland Security, DoD, and Department of State. DHHS and DHS have each contributed substantial amounts of funding to DIEPS projects. Dr. Ellis McKenzie spent substantial amounts of time with DHS and DoD, and DoD is also sponsoring one of the current RAPIDD postdoctoral fellows.

Relationships with major global health NGOs include the World Health Organization, World Bank, Pan-American Health Organization, The Carter Center, and the Population Reference Bureau. Collaborative projects have included the DCPP and work on pandemic influenza, and

DIEPS staff members also participate on various boards and committees for these organizations. DIEPS has also demonstrated success in forming partnerships with the Gates Foundation. In addition to the three Gates grants the Division has received, DIEPS staff members frequently serve as reviewers and consultants for Gates.

Table 8: Examples of DIEPS Partnerships with Other NIH Institutes and Centers.

Partner	Examples of collaboration
NICHD	DIEPS collaborated with the Robbins lab on meningitis vaccine work, including transfer of funds FY 2004-06. NICHD contributed funds for *AJHTM* malaria supplements in FY2006
NIGMS	DIEPS and NIGMS have collaborated on the MIDAS program, including DIEPS staff members serving as Steering Committee members. MIDAS Program Director Dr. Irene Eckstrand also participates on the RAPIDD Steering Committee.
NIAID	DIEPS and NIAID co-hosted polio meeting in 2007 NIAID contributed funds to support contract work by DIEPS collaborator Dr. Thomas A. Reichert of the Entropy Research Institute in FY2002-03 NIAID contributed funds for AJHTM malaria supplements in FY2004 and 2006 DIEPS staff members have relationships with NIAID's extramural Influenza Genome Sequencing Project ; the DMID Parasitology and International Programs Branch (malaria); Virology Branch (monkeypox, smallpox) DIEPS staff have research exchanges and collaborations with various intramural researchers, including: Drs. Mike Bray, Barney Graham, Bob Gwadz, Lee Hall, Al Kapikian, Rebecca Prevots, Lone Simonsen, Jeffrey Taubenberger, Tom Wellems, Jon Yewdell
NIEHS	Contributed funds for *AJHTM* malaria supplements in FY2004 and 2006
OD	Office of Research and Development contributed funds for rare diseases conference in FY2002 Office of Science Policy Analysis contributed funds to support AAAS Fellow Christine Jessup in FY2007
NIH Clinical Center	DIEPS staff members have clinical privileges for support of vaccine development studies
NLM	Worked with NCBI to establish influenza resource center and genomic analysis; malaria supplement dissemination via the NLM e-bookshelf and MIM activities.
CIT	Dr. McKenzie co-authored three papers with CIT staff member Dr. Phillip McQueen

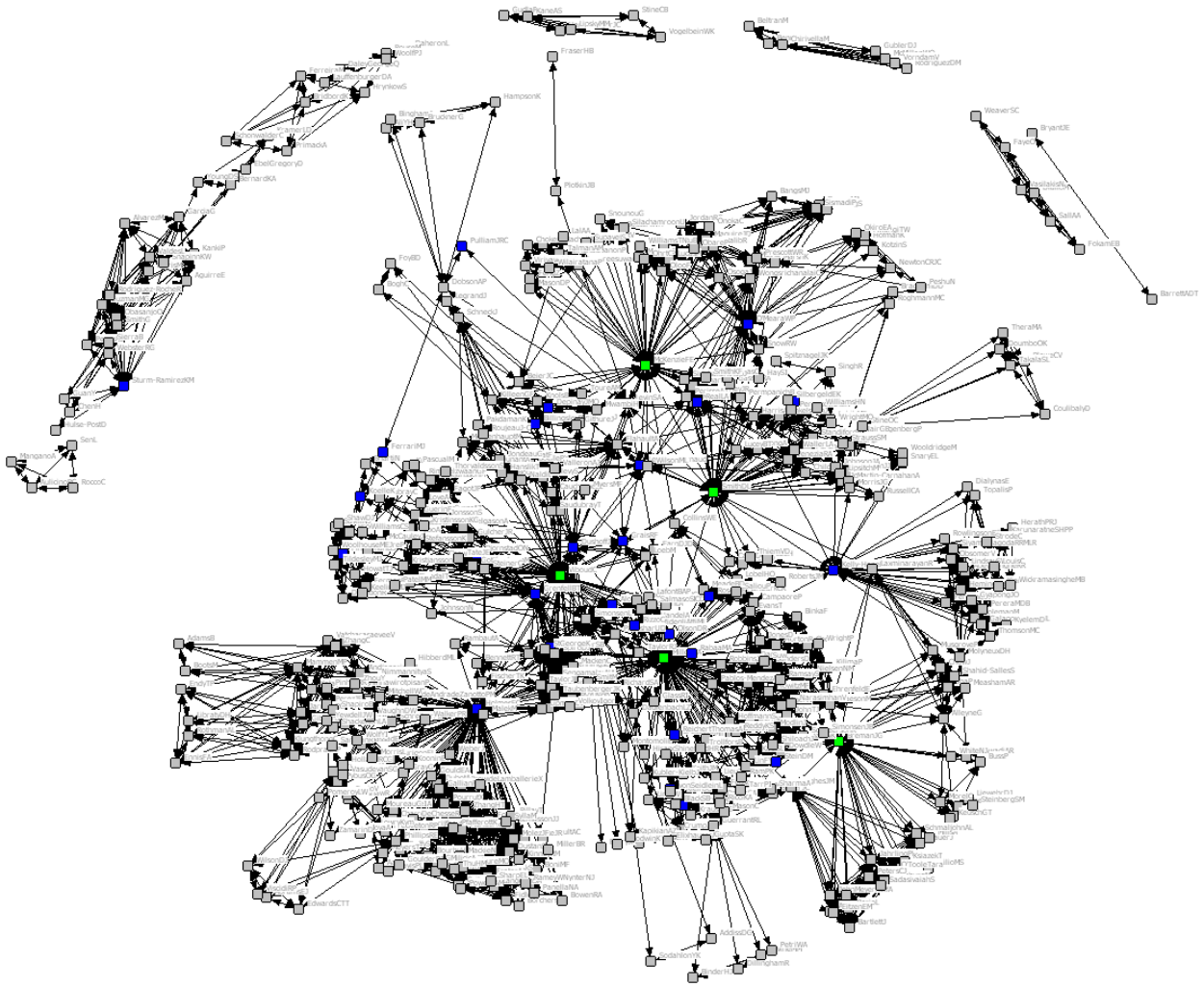
DIEPS also has a very large number of collaborators on individual projects located at academic and government institutions in the US and abroad. An exhaustive list of collaborators was not compiled as part of this review. However, as a ballpark estimate, the panel noted that there were 583 unique authors on DIEPS publications. Co-authorship patterns reveal that the four core research staff members (Breman, McKenzie, Miller, Viboud) plus former staff member Dr.

David Smith appear to be "hubs" connecting multiple author groups, as do certain other senior research staff members (Figure 8). One set of collaborations that is particularly notable is with the Center for Infectious Disease Dynamics at the Pennsylvania State University; this collaboration involves at least five professors and four postdoctoral fellows. Internationally, current collaborations are known to be ongoing with researchers in at least 16 other countries (Bangladesh, Brazil, Canada, Denmark, France, India, Kenya, Nepal, Pakistan, Peru, Portugal, South Africa, South Korea, Tanzania, Thailand, and the United Kingdom).

Summary of Findings

The panel found evidence that FIC derives a great deal of benefit from DIEPS. The scientific outputs and policy impacts alone would justify the small investment of funds, space and personnel. However, FIC and NIH also derive additional benefit from the Division, especially with respect to training and strategic partnerships.

Figure 8: Co-authorship network diagram for DIEPS publications. Nodes represent individual authors and are color-coded as follows: green=core research members, blue=other staff (paid or onsite volunteers), grey=other collaborators.



Description: An intricate, detailed diagram of approximately hundreds of points connected to each other by lines. The text by the items too small to read. The lines indicate co-authorship for publications. The points are of various colors, and represent different categories of authors, including: core research members; other staff (paid or onsite volunteers); and other collaborators. There are approximately 5 smaller groups of points not connected to a main, larger group of interconnected points in the center.

V. Fit with FIC Strategic Priorities

When considering how DIEPS fits with FIC strategic priorities, it is important to note at the outset that FIC leadership has shifted several times since DIEPS was founded in 2000. Former FIC Director Dr. Gerald Keusch left shortly after the Division was up and running, and then Dr. Sharon Hrynkow served as Acting Director for several years before the current Director, Dr. Roger Glass, took over in 2006. In the same period, there have been two different FIC strategic plans. In the interest of looking towards the future, the review focused on the Division's fit with current goals and strategic priorities as reflected in the FIC Strategic Plan for 2008-2012.[22] A summary of the panel's findings with respect to each of the five strategic goals is provided below.

FIC Strategic Goals

Goal I: Mobilize the scientific community to address the shifting global burden of disease and disability

Strategic priorities associated with this goal in the FIC strategic plan include expanding FIC investment in non-communicable disease research and training as well as continuing to invest in infectious disease research and training. The vast majority of DIEPS research and training activities have focused exclusively on infectious diseases, including conditions like malaria and diarrheal diseases that disproportionately impact low and middle income countries as well as rapidly-transmissible pathogens such as influenza that pose a significant threat globally. The few notable exceptions have generally focused on interactions between communicable and non-communicable conditions; these include the recent Gates-supported work on interactions between nutrition and enteric diseases and at least one study of interactions between influenza and heart disease.

In general, the panel found the Division's focus on infectious disease to be valuable, productive, and appropriate to the expertise of the current staff. In particular, the panel noted that the Division's depth and versatility make it well-placed to respond quickly to new infectious disease threats as they emerge. This is a strength that should be maintained. If the Division were to be expanded in the future, however, the panel believes that similar approaches could usefully be applied to non-communicable disease as well.

It is also worth noting that the DCPP, a project to which DIEPS staff members made significant contributions, helped to raise awareness of the importance of non-communicable diseases and disorders as contributors to the disease burden in low and middle income countries.

Goal II: Bridge the training gap in implementation research

The vast majority of DIEPS research can meaningfully be described as implementation research. The Division's core function is to use modeling and other approaches in order to fully exploit

[22] Full version available online at: http://www fic.nih.gov/about/plan/stratplan_fullversion.pdf; Executive summary available online at: http://www fic nih.gov/about/plan/exec_stratplan.pdf.

epidemiological and population data as an evidence base to inform public health policy. Examples of implementation research offered by interviewees include:

- Modeling the potential impact of novel vaccines and drugs for the purpose of formulating biodefense strategies;

- A study demonstrating geographic variability in the effectiveness of malaria prophylaxis for infants in Africa currently recommended by WHO;

- A study demonstrating that school children are the spreaders of influenza in the community and introducers into the household, suggesting that this age group should be a priority for pandemic vaccination strategies;

- Exploration of use of routing-analysis systems to optimize anti-malarial supply chains;

- Assessment of local and regional disease burdens in order to set disease control priorities.

This list is by no means exhaustive; many more examples could be added, and several have already been described in Section IV of this report. The DCPP is also focused on implementation. As already noted, experiential research training is a significant component of DIEPS, so in a real sense DIEPS is already contributing to this strategic goal.

The FIC strategic plan explicitly acknowledges the importance of "in-house expertise" in developing a Center-wide approach to filling this training gap:

> Fogarty will identify the tools, methods, and training needed to build a research workforce able to advance implementation research. Fogarty will encourage the use of complex systems analysis and predictive modeling as research tools, using its in-house expertise to advance this approach.[23]

DIEPS is by far the largest reservoir of such expertise at FIC and could be an invaluable resource as the Center seeks to expand its extramural training programs to include implementation research. To the extent that it is feasible to do so, the panel encourages FIC to draw on that expertise in developing new training programs.

Goal III: Develop human capital to meet global health challenges

The strategic priorities associated with this goal in the plan include providing training opportunities and support for aspiring international health researchers from the US and abroad. As already discussed at length, DIEPS provides experiential training opportunities for pre-doctoral students, postdoctoral fellows, and visiting researchers from both the US and abroad. Given the mission and budget constraints of the Division, the DIEPS contribution to development of human capital is adequate and appropriate.

[23] FIC Strategic Plan 2008-2012, page 21.

Goal IV: Foster a sustainable research environment in low- and middle-income countries

Under this goal, the strategic plan refers specifically to development of research hubs, expertise, and alumni networks at foreign institutions. Although this is not an area where the panel believes DIEPS can reasonably be expected to have much impact, as noted previously, DIEPS does have ongoing collaborations with researchers at institutions in low- and middle-income countries including Bangladesh, Brazil, India, Kenya, Nepal, Pakistan, Peru, South Africa, Tanzania, and Thailand. The Division has also hosted visiting scientists from Cameroon and South Africa. The panel wonders whether short-term exchanges of personnel between DIEPS and collaborating institutions might be useful in strengthening these collaborations.

Goal V: Build strategic alliances and partnerships in global health research and training

In the area of building partnerships and strategic alliances with other organizations, the panel found that DIEPS does make a substantial and unique contribution. Despite being bound by the rules prohibiting fundraising by Federal employees, DIEPS has attracted partnerships in the form of financial support for its projects from three other NIH Institutes and Centers (NICHD, NIAID, NIEHS), other US government agencies (DHHS, DHS), the World Health Organization, and the Gates Foundation. Division collaborators include intramural staff members from other NIH Institutes and Centers, US government agencies, NGOs, and well-respected academic research centers. DIEPS has also worked successfully with policy-makers and ministries of health in other countries, most notably on pandemic influenza plans.

The panel believes that the Division's success in cultivating these relationships is largely due to the respect afforded to the DIEPS staff members by the global health research and policy community because of the quality of their work. As originally envisioned by Dr. Keusch when he supported its creation, DIEPS has succeeded in enhancing FIC's prestige as a research organization. FIC should seek to capitalize on that success by further developing and expanding these relationships as appropriate to advance the goals of the Center.

Summary of Findings

Activities of the Division are consistent with all five FIC strategic goals and contribute significantly to four of them (Goals I, II, III, and V). In particular, DIEPS is well-positioned to make unique contributions towards meeting goals II (implementation research training) and V (strategic alliances).

VI. Challenges

When asked to identify challenges facing the Division, interviewees raised a variety of concerns. The most serious of these are described below.

Funding and Growth Potential

The first set of challenges described by DIEPS staff members concerns funding and growth potential for the Division. The overall FIC contribution to the Division is quite small in both relative and absolute terms, and it is arguably too small to maintain a synergistic and productive "critical mass" of researchers and projects on its own. However, the staff's perception is that the FIC contribution to the Division budget is highly unlikely to increase beyond current levels in the foreseeable future. This is partially because DIEPS funds are drawn from the FIC RMS budget, which remains relatively constant even when the Center's overall budget is increasing. Any potential for growth or expansion is therefore dependent on DIEPS bringing in funds from outside sources.

While DIEPS has been successful in doing that, this approach to growth has serious limitations. First, as government scientists, Division staff members are prohibited from soliciting funding from outside sources. Rather than proactively seeking to expand its portfolio in a strategic manner, therefore, the Division is limited to accepting or refusing funds for specific projects as they are offered by other agencies or foundations. They are also unable to compete for funds, making them ineligible to receive extramural funding from NIH or other government agencies. Second, the availability of long-term, guaranteed ("hard") funding typically enables government researchers to set their own priorities and engage in longer-term research projects. In contrast, funding from outside sources ("soft money") is usually limited in duration (1-5 years is typical), shortening time horizons for research and making the long-term funding situation less predictable. DIEPS therefore finds itself in the unenviable position of receiving inadequate support from FIC to function and plan effectively as a government research lab while also being highly constrained in the options it can pursue to bring in additional funding from other sources.

Finally, several staff members expressed concern that, in an era of flat or declining budgets, it may be tempting for FIC to cut the Division's core budget because of its success in obtaining "soft" money. The panel found no evidence to suggest that this is seriously being contemplated, but such fears are understandable in the absence of a clear statement of intent from FIC leadership regarding the future of the Division.

Space

DIEPS currently occupies some of the second and most the third floor of the Lawton Chiles International House. Even though most of the research staff works offsite, the available space is more than fully occupied, with some staff members forced to coordinate their hours in order to facilitate sharing of desks. The space situation makes it difficult to bring in new people, whether they are short-term visitors or fully-funded contract staff members.

The panel is concerned that this lack of flexibility with respect to space has the potential to severely limit the Division's ability to develop new collaborations and contribute to FIC's

training goals. For example, one interviewee reported that the Division had recently been forced to delay the start date of a new postdoctoral fellow so that there would be a desk available for a mathematician from Cameroon who was visiting for a month in order to lay the groundwork for future collaboration with DIEPS on a malaria modeling project. The panel believes that both training of postdoctoral fellows and accommodation of foreign visitors are critical to the mission of DIEPS, and every effort should be made to ensure that neither activity is unduly constrained by availability of desk space.

Staff Recruiting and Retention

A third set of concerns centers around staff recruiting and retention. FIC has a limited number of full-time equivalent (FTE) slots for Federal employees, almost all of which are currently filled. Six permanent Federal staff members are currently assigned to DIEPS full time (Drs. Breman, McKenzie, Miller, Viboud, and two administrative staff members). A seventh Federal staff member (Dr. Katherine Sturm-Ramirez) was recently hired by FIC following a DIEPS postdoctoral fellowship; her position is a limited (three-year) FTE, and she is assigned to split her time between DIEPS and DITR. Dr. David Smith was also a permanent member of the DIEPS research staff at one time, but the FTE he occupied was re-assigned to another Division when he left FIC in 2007. Although the panel understands that FTE assignments are necessarily somewhat fluid within the Center, it is clear that the loss of Dr. Smith's FTE has diminished the Division's research capacity. It also appears to be the case that the manner in which this decision was communicated to remaining staff had a negative impact on morale.

Because new FTE slots are rarely available to the Division,[24] additional research staff members can only be recruited as contractors, and there is little chance that even the most talented of them will be able to advance in their careers while remaining with DIEPS. Staff members reported that this lack of opportunity, coupled with the fact that demand for skilled disease modelers is increasing, has made it difficult to recruit and retain staff members in recent years. Also contributing to recruiting and retention problems are the perceived uncertainty concerning FIC's commitment to the long-term future of the Division and long administrative delays between the time the Division reaches agreement with a new staff member and final authorization for that individual to begin work.

Division Level Strategic Planning and Portfolio Management

As described in Section III, DIEPS has historically been loosely organized around six focal areas, each of which has an unofficial coordinator or co-coordinators with no formal management responsibilities except in the context of individual projects. New projects have been added opportunistically based on consensus among the core staff members regarding their individual merits as projects, timeliness, potential policy impact, and the Division's ability to make an appropriate contribution. Strategic importance relative to an overarching plan or vision for the future of the Division does not appear to have been a factor.

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[24] The panel understands that an FTE slot will soon be available because the Division's administrative assistant has given notice, but she will likely be replaced with another administrative staff member. The level of seniority for her replacement has not yet been determined.

In fact, as far as the panel is aware, there has never been a formal strategic planning process of any kind at the Division level, nor is there an established procedure through which Division-level plans are communicated to FIC senior management for input and approval. Resource constraints, uncertainty over the Division's long term future, and shifting research priorities for the Center as a whole may have posed significant barriers to long term planning in the past. Looking towards the future, however, the panel would like to see planning processes established to ensure that DIEPS activities remain consistent with FIC strategic priorities and that opportunities for synergy are fully realized.

Administrative Burden

The FIC Office of Administrative Management and International Services (OAMIS) provides general administrative services to all FIC Divisions. These services include review, approval, and processing of travel requests; purchasing; budget administration; and processing of paperwork for HR and hiring. Interviews with staff members on both sides indicated that the relationship between DIEPS and OAMIS is generally collegial and respectful but that the administrative burden associated with DIEPS is large relative to other FIC divisions. The large number of staff members supported through contracts and IPAs, the high volume of travel requests, and the need to process funds brought in from outside sources are all contributing factors. OAMIS acknowledged that these factors are probably unavoidable given the current structure and goals of DIEPS and can be accommodated within the existing administrative structure. However, OAMIS reported that several additional factors make the workload especially difficult to manage:

1. Lack of planning and approval processes that might allow OAMIS to anticipate periods with heavy volume of administrative requests in advance;

2. A relatively high frequency of non-trivial mistakes on administrative paperwork submitted by DIEPS, including the same errors being made repeatedly;

3. Frequent miscommunication with new hires regarding processing requirements, sometimes including allowing new staff to begin work before contracts are in place.

The panel believes that these concerns should be addressed with better administrative leadership and adoption of formal processes at the Division level.

Communication

A final challenge that was apparent to the panel was a general lack of effective two-way communication between the Division and FIC senior leadership. It was clear that each side was frustrated with and somewhat wary of the other. Several interviewees in the FIC Office of the Director appeared to feel that they were not adequately informed about DIEPS plans and activities, while Division staff expressed varying degrees of uneasiness about FIC's commitment to the future of DIEPS. Since the panel is aware that the DIEPS Director meets with senior FIC leadership on a regular basis, frequency of communication does not appear to be the problem. The panel suspects that conflicting personalities, lack of formal administrative and planning processes, FIC's history of frequent leadership changes, and actual uncertainty on all sides about

the Division's role within FIC have contributed to the problem. Encouragingly, however, all interviewees were able to communicate their concerns candidly and articulately to the panel, suggesting that communication might be significantly improved under the right circumstances.

Summary Findings

FIC and DIEPS currently face a variety of challenges. The challenges related most directly to resource constraints (budget, space, and FTEs) probably cannot be resolved without substantial increases in the FIC budget and other resources, which the panel understands to be unlikely in the near future. However, the challenges related to administrative processes, strategic planning, and communication can and should be addressed at relatively little cost to the Center.

VII. Options for the Future and Recommendations

Having concluded that DIEPS provides a great deal of value to FIC relative to its costs and that the Division makes a unique contribution to advancing FIC strategic goals, the panel concluded that FIC should commit to retaining and strengthening DIEPS. Assuming that there will not be any large increase in available funding, the panel considered three possible future scenarios. These options are described below, as are the panel's findings with respect to possible advantages and disadvantages of each. *The panel recommends that Option 1 and 2 should be considered by FIC leadership. Option 3 is not recommended by the panel.* The panel's recommendations for the future of DIEPS are included at the end of this Section.

Possible Future Scenarios for DIEPS

Option 1: Retain current status but improve administrative processes, strategic planning, and communication

Under this scenario, FIC would commit to continuing the Division in its current form as neither an extramural nor an intramural program. The Division would continue to be supported through a combination of FIC RMS funds and money brought in from outside. However, the panel feels that substantial improvements could be made within the existing framework. In particular, the panel would like to see the adoption of administrative and planning practices similar to processes in place for true NIH intramural programs. Additional recommended improvements are described at the end of this Section.

Advantages

- This is likely the most feasible option in the short-term and would minimize upheaval.
- The panel believes that it would be possible to address many process and management concerns within the existing framework.

Disadvantages

- DIEPS would continue to depend on the FIC RMS budget plus soft money, which limits future expansion potential and ability to conduct long-term research.
- Space and staff recruiting/retention problems would likely continue or escalate.

Option 2: Transition DIEPS to full intramural status

This option would involve working to establish DIEPS as an official NIH intramural program. A former employee of the Office of Intramural Research (OIR) has confirmed that there is no minimum acceptable size for an intramural program and that OIR would likely be willing to work with FIC.

Advantages

- Under this scenario, DIEPS would become eligible to compete for OIR resources, including the centralized pool called the "Common Fund" created by the NIH Reform Act of 2006. In FY2008, the Common Fund totaled $498 million, of which 70% was competitively awarded and open to intramural researchers.

- OIR has well-established processes for oversight, reporting, and review that could improve Division management without the need to establish new procedures. OIR could also serve as an advocate and guide to facilitate expansion of the Division.

- Under this scenario, FIC would have an intramural budget line, so funds for DIEPS would no longer be included with the RMS budget. This would not automatically mean that the funding available to DIEPS would increase; it would simply move to a different part of the FIC budget. From a political standpoint, however, this might make it easier for FIC to increase its contribution to DIEPS in the future, because it would be clear to outside observers that the additional funds were intended to support research as opposed to administrative activities.

- Although all available evidence suggests that the Division is already very well-known and respected in its field, it is possible that intramural status might enhance perceptions of legitimacy/prestige among certain stakeholder groups within NIH and beyond.

Disadvantages

- Intramural programs are typically required to pay fees in order to support the NIH Clinical Center or for other purposes, which would cut into the Division's already small budget. However, a retired OIR staff member indicated to the panel that these requirements may be negotiable.

- Space assigned to intramural programs is typically controlled by OIR, which might be undesirable to FIC in the case of the third floor of Lawton Chiles International House. However, the same former OIR staff member suggested that, this, too, may be negotiable.

- In the past, other Institutes and Centers have raised objections to the idea of FIC developing an intramural research program of its own. Because DIEPS fills a specific and fairly narrow gap in the NIH intramural research portfolio that has not historically been of interest to the other Institutes and Centers, the panel believes that such issues can be overcome. However, should FIC decide to pursue this option, it should be approached in a manner that is sensitive to possible political ramifications.

<u>Option 3: "Spin off" DIEPS staff members to another institution or institutions</u>

Under this option, one or more core DIEPS staff members would continue as FIC employees but would be allowed to continue their work at another institution in a manner similar to CDC's practice of detailing researchers to other institutions throughout the world. Collaborators and contractors would presumably follow the project leaders to other institutions, although it is possible that work could be sent back to staff members remaining at FIC via subcontracts. Logical choices for host institutions include the Foundation for NIH, various academic research

centers, other government labs, or NGOs. There are two known precedents for this kind of arrangement between NIH Institutes and Centers and intramural researchers.[25]

Advantages

- This type of arrangement would likely strengthen the relationship between FIC and the host institution(s) and could enhance opportunities for partnerships. It should be noted, however, that the prohibitions against fundraising would remain in effect for the Federal employee(s) "spun off."

- The space currently occupied by DIEPS would be freed up for other uses by the Center, as would the non-salary portion of the current FIC contribution to the DIEPS budget.

Disadvantages

- Under this scenario, the benefit FIC derives from DIEPS activities would be greatly reduced, as would opportunities for synergy. Being away from the NIH campus would likely decrease interaction between DIEPS staff members and others at NIH, including FIC staff and leadership.

- FIC would also lose control over and use of the staff members "spun off" to another institution and would not have the opportunity to absorb them into other Divisions.

Recommendations of the Panel

1) FIC should commit to retaining DIEPS as a Division and strengthening it if possible.

It is clear to the panel that DIEPS contributes significant value to FIC, NIH, and the international health research and policy communities relative to the size of the investment made by FIC. The Division's activities are also consistent with and in some cases critical to achieving FIC strategic priorities. DIEPS is an asset to FIC and should be recognized as such. To underscore this commitment, the FIC Director should consider making a public statement expressing support for the Division and confidence in its long-term viability**.**

2) The Division should continue as an internal research group while FIC explores the option of transitioning DIEPS to full intramural status.

Based on very preliminary conversations, the panel believes that it would be possible for FIC to negotiate a mutually beneficial arrangement with OIR with respect to DIEPS. Some of the perceived barriers mentioned by interviewees (e.g. that there is a minimum acceptable size for intramural programs, that the Division would be required to cede space or pay fees for services they wouldn't use) appear to be misconceptions. However, this is an opportunity the Center will have to investigate more fully on its own, likely with involvement by the new NIH Director and

[25] Dr. Thomas Quinn transitioned from NIAID to the Bloomberg School of Public Health at Johns Hopkins and Dr. John Clemens went from NICHD to the International Vaccine Institute.

other NIH Institutes and Centers that might potentially be impacted.

3) DIEPS staff should not be "spun off" to another institution.

Under an arrangement such as the third option considered by the panel, FIC would lose the benefits currently provided by DIEPS as well as the opportunity to put most resources currently invested in DIEPS to other uses. Such an arrangement would not be in the interest of the Center or of NIH. Furthermore, it is not clear that this arrangement would be sustainable in the long term, because the employees "spun off" would have little incentive to remain Federal employees after fulfilling their contractual obligations. If FIC were to decide to dissolve DIEPS entirely, this scenario might have some merit as an "exit strategy" for current employees who could not easily be re-assigned to other Divisions, but the panel does not favor that option.

4) In collaboration with the FIC Office of the Director, DIEPS should develop a set of Division-level strategic goals.

The Office of the Director should lead a collaborative effort to develop a set of division-level strategic goals with links to the FIC strategic plan. These strategic goals should be used to guide future decisions with respect to Division staffing and research portfolio. Progress relative to the strategic goals should be reported regularly to the FIC Director, perhaps in the form of a periodic report. The goals should also be adjusted as needed to reflect shifting priorities of the Center as well as changes in the global disease burden.

5) Standard procedures should be established for DIEPS administrative processes.

Processes that should be considered for standardization include, but are not limited to, review of project aims and budgets prior to submission to funding agencies, administrative and financial profiling of new projects, employee oversight and review, tracking of Division outputs and alumni, updates to the Division website, preparation and verification of travel and personnel requests, and communication with potential new hires. Even if FIC ultimately decides not to convert DIEPS into an intramural program, the Center should request help from OIR in developing administrative and management practices similar to those in effect for intramural programs.

6) Administrative management and support at a more senior level should be provided to DIEPS.

The vacancy created by the imminent departure of the Division's administrative assistant represents an opportunity to improve Division administrative management. Ideally, the Division should seek to hire a professional with management experience as well as some scientific background to coordinate with the scientific staff, act as a liaison to OAMIS and the Office of the Director, oversee planning and management processes for the Division, and supervise the existing administrative staff. The right individual could greatly improve Division management while freeing up the scientific staff to focus on their research.

7) Oversight of the Division by FIC senior leadership should be improved.

Although the DIEPS Director and FIC senior leadership do meet regularly, communication in

both directions appears to be problematic. The panel believes that imposing additional structure might help to improve the situation. The Director and the Division should agree on a list of management decisions for which review and approval by the Office of the Director will be required to ensure that activities are consistent with strategic goals and that they would not place undue strain on existing Division and Center resources. FIC should also consider keeping a written record of important meetings and requiring that notifications and decisions be communicated in writing.

8) FIC should clarify the role of Associate Director for Science.

Dr. Miller currently holds two titles: Director of DIEPS and Associate Director for Science of FIC. The role and responsibilities associated with the former title are clear, while the role for the latter does not appear to be well-defined. Dr. Miller's current workload is already very heavy. The panel believes it is time to clarify whether an Associate Director for Science is necessary for the Center and, if so, how those needs can best be met.

9) FIC leadership should work with the Division to explore additional opportunities for DIEPS to become more integrated with FIC extramural research and training programs.

The panel found that integration between DIEPS and FIC extramural programs does not appear to have been a priority. While formal links to the extramural research and training programs are probably unnecessary, it is likely that there are opportunities for synergy that could be realized with additional coordination. The malaria working group has been a particularly effective mechanism for enhancing communication and integration across the Center that should be encouraged and replicated as appropriate. FIC might also explore opportunities to integrate DIEPS training activities more closely with the extramural training programs. For example, principal investigators on FIC research training awards should be made aware of training opportunities available through DIEPS.

10) If new funds and/or additional FTEs become available, FIC should consider expanding the DIEPS focal areas to include non-communicable conditions that adversely impact global health.

The panel believes that the Division's current focus on infectious diseases is appropriate given current staff expertise and budget constraints, and the panel also recognizes that it is important for DIEPS to retain its current flexibility to respond quickly to changes in the infectious disease research agenda. However, with additional resources, the Division's approaches could productively be expanded into non-communicable disease areas in order to complement the Center's extramural programs and strategic priorities. Examples of current FIC research interest that might be addressed using modeling approaches include tobacco use, trauma, brain disorders, cerebrovascular disease, lung disease, environmental/occupational health, genetic disorders, and obesity.

Appendix A: Panel Bios

Enriqueta (Queta) Bond, PhD

Dr. Queta Bond became the first full-time President of the Burroughs Wellcome Fund (BWF) in July 1994, and she served in that capacity for 14 years before retiring in 2008. Dr. Bond received her undergraduate degree from Wellesley College, her M.A. from the University of Virginia, and her Ph.D. in molecular biology and biochemical genetics from Georgetown University. Early in her career, she was an Assistant Professor at Chatham College in Pittsburgh and Southern Illinois University School of Medicine. She later moved to the Institute of Medicine, starting as a Staff Officer and eventually becoming Director of the Division of Health Promotion and Disease Prevention and the Division of Health Sciences Policy before her appointment as Executive Officer. Dr. Bond chairs the Academies' Board on Capacity Development of African Academies of Science and serves on the Report Review Committee for the Academies and the IOM Forum on Microbial Threats. She served on the board of a number of organizations including, the Research Triangle Park Foundation, the National Institute for Statistical Sciences, the Northeast Biodefense Center, and the New England Center of Excellence in Biodefense and Emerging Infectious Diseases. She is a member of the council of the National Institute of Child Health and Human Development.

W. Paul Glezen, MD

Dr. Glezen is Professor, Department of Molecular Virology and Microbiology and Professor and Head, Preventive Medicine Section, Department of Pediatrics at Baylor College of Medicine. He is also Adjunct Professor of Epidemiology, School of Public Health, University of Texas Health Science Center, Houston. He was recruited to join the Influenza Research Center at Baylor College of Medicine in 1975 as the epidemiologist. He was a member of the Epidemiology and Disease Control study section, NIH, 1985-1989. He served as a member of the Advisory Committee on Immunization Practices (ACIP) from 1987-1990 and was the liaison representative of the Infectious Diseases Society of America to the ACIP from 1993-1998. He was a member of the Influenza Technical Advisory Group for the Medicare Demonstration Project, HCFA, from 1990-1993 and the Consultative Group for Vaccine Development, National Vaccine Program Office, from 1991-1993. He has been appointed to the Task Force on Adult and Maternal Immunization for the American College of Obstetricians and Gynecologists for 2005-08. He has been the study chair for an NIAID research grant entitled, Control of Epidemic Influenza, located in Central Texas. Dr. Glezen is chair of the Vaccine subgroup of the BCPA Biodefense Working Group sponsored by the National Institute of Child Health and Human Development, NIH. Dr. Glezen received the 2004 Distinguished Physician Award from the Pediatric Infectious Diseases Society and the 2006 Distinguished Alumnus Award from the College of Science, Purdue University.

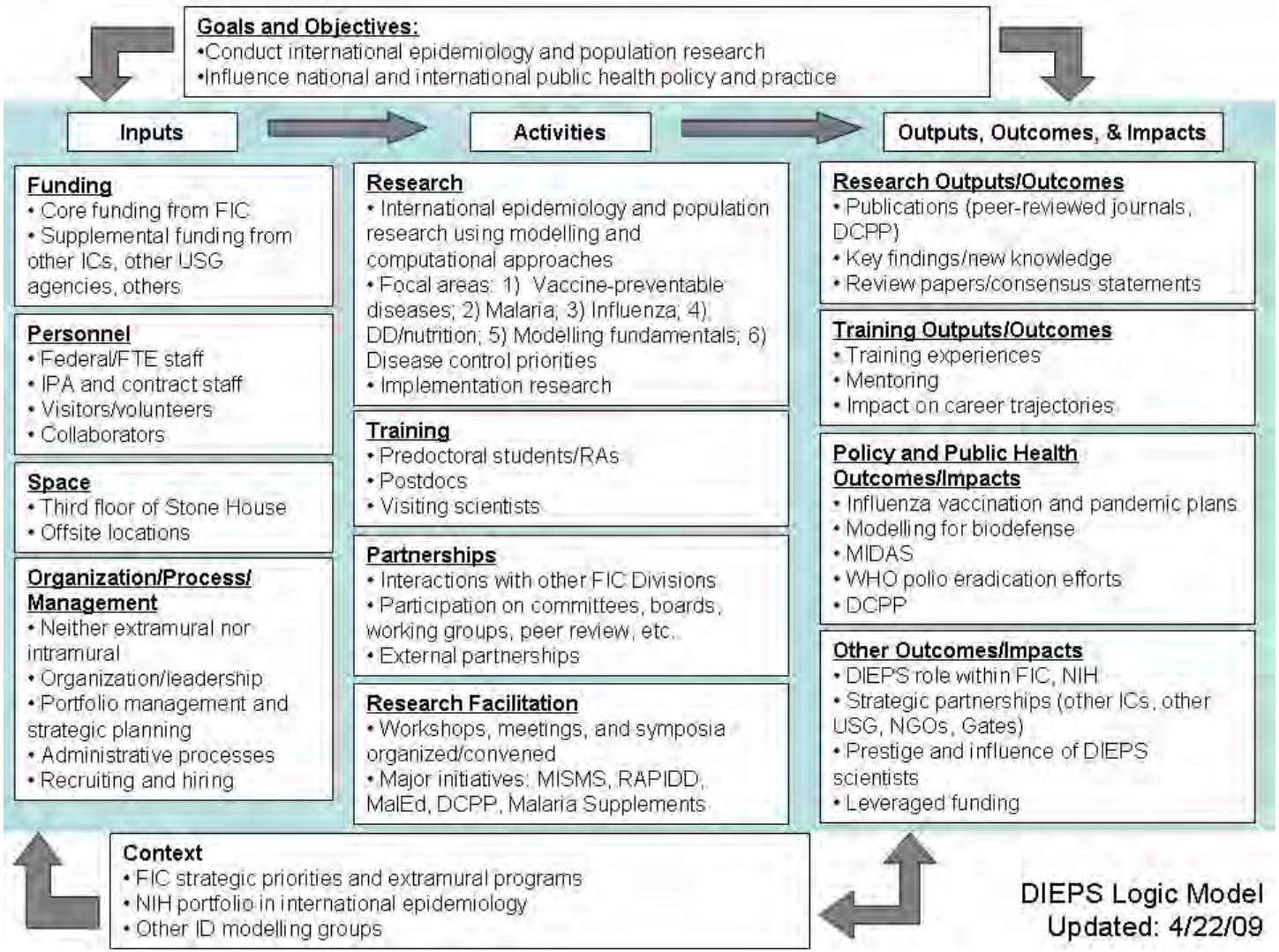
Arthur Reingold, MD

Arthur Reingold, MD, is Professor of Epidemiology, Head of the Division of Epidemiology, Associate Dean for Research, and Edward Penhoet Distinguished Professor of Infectious Diseases and Global Health at the School of Public Health, University of California, Berkeley. He holds concurrent appointments as Professor of Medicine and of Epidemiology and Biostatistics at UCSF. After spending eight years working for the US Centers for Disease Control and Prevention in Atlanta, Dr Reingold joined the faculty at Berkeley in 1987. His research interests include the prevention and control of infectious diseases in the US and in developing countries, including meningitis, respiratory tract infections, vaccine preventable diseases, and tuberculosis, among others. Since its inception in 1988, he has been the Director of the NIH Fogarty AIDS International Training and Research Program at UC Berkeley/UCSF. He has also been the Director of the CDC-funded California Emerging Infections Program since its inception in 1994. He currently serves on the Strategic Advisory Group of Experts (SAGE) of the World Health Organization and on the IOM Committee for Review of the US National Vaccine Plan. He has authored or co-authored over 200 original research publications and was elected to the Institute of Medicine in 2003. Dr. Reingold is also a member of the External Advisory Board of the John E. Fogarty International Center.

Eleanor Riley, BSc, BVSc, PhD

Dr. Eleanor Riley is Professor of Immunology and Head of the Immunology Unit, Department of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine. She graduated from Bristol University (UK) with degrees in Cellular Pathology and Veterinary Science, Cornell University (internship in Veterinary Pathology) and the University of Liverpool (PhD in immunology and parasitology). Dr. Riley has studied the immunology of malaria since 1985, at the Medical Research Council Laboratories in The Gambia, at the University of Edinburgh and, since 1998, at the London School of Hygiene and Tropical Medicine where she is Professor of Infectious Disease Immunology and Head of the Immunology Unit. Dr. Riley's work concentrates on the immunological consequences of malaria infection in endemic and non-endemic populations; immunoepidemiological and immunogenetic studies of the relationship between defined immune responses and acquisition of clinically protective immunity; immune responses to prototype malaria vaccines. Dr Riley is a member of the UK special advisory committee on transfusion transmitted infections; Chair of the Biotechnology and Biological Sciences Research Council (BBSRC) "Animal systems, health and wellbeing" research funding committee; Chair of the BBSRC/Department for International Development "Combating Infectious Diseases of Livestock for International Development" initiative, and a Member of the Lister Institute.

Appendix B: DIEPS Logic Model



DIEPS Logic Model

Goals and Objectives:

- Conduct international epidemiology and population research
- Influence national and international public health policy and practice

Inputs

Funding

- Core funding from FIC.
- Supplemental funding from other ICs, other USG agencies, others.

Personnel

- Federal/FTE staff.
- IPA and contract staff.
- Visitors/volunteers.
- Collaborators.

Space

- Third floor of Stone House.
- Offsite locations.

Organization/Process/ Management

- Neither extramural nor intramural.
- Organization/leadership.
- Portfolio management and strategic planning.
- Administrative processes.
- Recruiting and hiring.

Activities

Research

- International epidemiology and population research using modelling and computational approaches.
- Focal areas: 1) Vaccine-preventable diseases; 2) Malaria; 3) Influenza; 4) DD/nutrition; 5) Modelling fundamentals; 6) Disease control priorities.
- Implementation research.

Training

- Predoctoral students/RAs.
- Postdocs.
- Visiting scientists.

Partnerships

- Interactions with other FIC Divisions.
- Participation on committees, boards, working groups, peer review, etc.
- External partnerships.

Research Facilitation

- Workshops, meetings, and symposia organized/convened.
- Major initiatives: MISMS, RAPIDD, MalEd, DCPP, Malaria Supplements.

Outputs, Outcomes, & Impacts

Research Outputs/Outcomes

- Publications (peer-reviewed journals, DCPP)
- Key findings/new knowledge.
- Review papers/consensus statements.

Training Outputs/Outcomes

- Training experiences.
- Mentoring.
- Impact on career trajectories.

Policy and Public Health Outcomes/Impacts

- Influenza vaccination and pandemic plans.
- Modelling for biodefense.
- MIDAS.
- WHO polio eradication efforts.
- DCPP.

Other Outcomes/Impacts

- DIEPS role within FIC, NIH.
- Strategic partnerships (other ICs, other USG, NGOs, Gates)
- Prestige and influence of DIEPS scientists.
- Leveraged funding.

Context

- FIC strategic priorities and extramural programs.
- NIH portfolio in international epidemiology.
- Other ID modeling groups.