National Institute of Allergy and Infectious Diseases
National Institutes of Health

March 17, 2005

Open Letter in *Science* Regarding NIH Biodefense Funding

Questions and Answers

On March 4, 2005, *Science* published an open letter criticizing the increased level of funding for biodefense research at NIH. The letter, which was signed by more than 750 microbiologists, maintains that biodefense research has diverted resources from non-biodefense research.

The National Institute of Allergy and Infectious Diseases (NIAID) disagrees with the conclusions of the letter. NIH would have received $1.5 billion less in FY 2003 and comparably fewer dollars in subsequent years had it not been for the addition of these biodefense funds. While we appreciate the concerns of our colleagues in the microbiology community, we take issue with the conclusions of the letter because they are based on the analysis of incomplete data as well as several unstated assumptions that are flawed.

The following information provides a more complete picture of the actual impact on our research programs of the additional funds given to the NIH for biodefense research. We describe in detail how the influx of funds for biodefense has benefited the microbiology and immunology research communities and has increased the capacity of the nation's public health community to respond to both naturally occurring and deliberately released pathogens.

1. Why was NIH given additional funds for biodefense research?

The terrorist attacks of September 11, 2001, and the dissemination of anthrax spores through the U.S. mail later that fall prompted the Administration, with bipartisan support from Congress, to dramatically increase spending on biodefense research, with the specific goal of developing medical countermeasures to protect the public against agents of bioterror. The Administration had determined that some entity—NIH, the Department of Defense or the Department of Homeland Security—was going to receive these new resources for biodefense research. In the end, approximately $1.5 billion in new money was added to the NIAID program in FY 2003 for biodefense research. This level of biodefense research funding has been maintained, with small to modest increases, in subsequent years. In sum, NIH would have received $1.5 billion less in FY 2003, and comparably fewer dollars in subsequent years, had it not been for the addition of the funds obligated for biodefense research.

If the Administration had given the $1.5 billion to an agency other than NIH, that other agency may not have embraced the academic microbiology and infectious diseases community. Furthermore, NIAID was fortunate to receive these resources because non-biodefense research areas—for example, research on naturally occurring emerging and re-emerging infections, immunology and certain basic research aspects of microbiology—have benefited directly and indirectly from this influx of new money.

2. How does NIAID decide what types of research to support with the new biodefense funds?

Beginning in February 2002, NIAID convened several panels of experts to develop a strategic plan and research agendas for biodefense research at NIH. These panels comprised distinguished researchers representing academia, private industry and government agencies. Based on the advice of the panels and extensive discussions with other Federal agencies, NIAID developed three key documents to guide its biodefense research program: the *NIAID Strategic Plan for Biodefense Research;* the *NIAID Research Agenda for Category A Agents* (agents that pose the gravest threat to human health, such as those that cause smallpox, anthrax, botulism and plague); and the *NIAID Research Agenda for Category B and C Priority Pathogens* (agents whose biological properties make them more difficult to deploy or less likely to cause widespread harm than Category A agents). In addition, NIAID also has convened other expert panels to help shape the NIAID biodefense research agenda in immunity and several other discrete biodefense-related areas. All these documents can be accessed at http://www2.niaid.nih.gov/biodefense/research/strat_plan.htm.

3. Has the NIAID budget for biodefense negatively affected the NIAID budget for non-biodefense?

No, it has not. At NIAID, funding for biodefense research has been additive to funding for non-biodefense research. In fact, non-biodefense NIAID resources increased by more than 50 percent from FY 2000 to FY 2005, in general, keeping pace with or exceeding the average annual increases received by NIH during this same period, as shown in Table 1 below.

Budget Comparisons

Dollars in Millions

	NIH		NIAID					
	Non-Biodefense (1)		Non-Biodefense (1)		Biodefense		Total (1)	
Fiscal Year	Amount	% Change	Amount	% Change	Amount	% Change	Amount	% Change
2000	17,771	—	1,744	—	33	—	1,777	—
2001	20,460	15.1%	1,999	14.6%	42	27.3%	2,041	14.9%
2002	22,802	11.4%	2,153	7.7%	187	345.2%	2,340	14.6%
2003 (2)	25,003	9.7%	2,445	13.6%	1,162	521.4%	3,607	54.1%
2004	26,243	5.0%	2,542	4.0%	1,600	37.7%	4,142	14.8%
2005 Appro.	26,728	1.8%	2,646	4.1%	1,658	3.6%	4,304	3.9%
2006 Est.	26,865	0.5%	2,695	1.9%	1,664	0.4%	4,359	1.3%

Note 1: This table excludes the below NIAID contributions to the Global Fund for AIDS, Malaria and TB to allow for better comparison of Non-Biodefense research.

2002	*$25M*
2003	*$99M*
2004	*$149M*
2005 Appro.	*$99M*
2006 Est.	*$100M*

Note 2: The FY 2003 biodefense funding for NIAID does not reflect the $371M for biodefense in the FY 2003 NIH Buildings and Facilities (B&F) Appropriation. The biodefense B&F funds were realigned to support biodefense research as of FY 2004.

Table 1. The annual percentage change in NIAID biodefense and non-biodefense research budgets between FY 2000 and FY 2006 compared with the annual percentage change in the NIH non-biodefense budget during the same time period.

In addition, biodefense funding has indirectly benefited non-biodefense research areas. Before the designation of "biodefense funding" in FY 2003, many pathogens with bioterror potential (e.g., the agents of anthrax and plague) were supported by general microbiology funds. With the establishment of designated biodefense funding, studies on many pathogens previously supported by microbiology funds were then supported by biodefense money, allowing additional grants for non-biodefense pathogens to be funded.

4. Did the number of NIAID non-biodefense research grants decrease from FY 1996 to FY 2005?

The numbers of grants cited in the letter are based on incomplete data and do not accurately reflect the growth in non-biodefense research that has occurred since FY 1996. The actual data for NIAID-supported research project grants (RPGs) are presented in Table 2 below. The funding for both biodefense and non-biodefense research has increased annually. The number of non-biodefense RPGs also increased until FY 2004. Since then, the number of non-biodefense RPGs has dropped slightly, not because of cuts in non-biodefense spending but rather because of annual inflationary costs over the lifecycle of each grant during a time of a flattening of the NIAID budget.

Breakout of NIAID-supported Research Project Grants (RPGs), FY 1996 to FY 2005
(Dollars in millions)

	Actual 1996		Actual 1997		Actual 1998		Actual 1999		Actual 2000	
TOTAL RPGs	#	$	#	$	#	$	#	$	#	$
Non-Biodefense	2,448	$ 727	2,669	$ 798	2,829	$ 879	3,029	$ 1,000	3,168	$ 1,162
Biodefense	-	$ -	36	$ 8	47	$ 10	63	$ 15	82	$ 21
Total RPGs	2,448	$ 727	2,705	$ 807	2,876	$ 888	3,092	$ 1,015	3,250	$ 1,182

	Actual 2001		Actual (1) 2002		Actual 2003		Actual 2004		Estimated 2005	
TOTAL RPGs	#	$	#	$	#	$	#	$	#	$
Non-Biodefense	3,242	$ 1,324	3,398	$ 1,422	3,478	$ 1,483	3,376	$ 1,565	3,280	$ 1,622
Biodefense	95	$ 27	190	$ 46	491	$ 205	741	$ 477	887	$ 484
Total RPGs	3,337	$ 1,351	3,588	$ 1,468	3,969	$ 1,688	4,117	$ 2,042	4,167	$ 2,106

Note 1: 2002 data includes biodefense research supported by supplemental funding from Congress.

Table 2. History of NIAID non-biodefense and biodefense research project grants from FY 1996 to FY 2005. Non-biodefense grant data are highlighted in yellow.

5. In Fiscal Year 2004, how did the success rates for NIAID biodefense and non-biodefense research project grant applications compare?

In FY 2004, the success rates for NIAID biodefense and non-biodefense research project grant applications, including R01, R21, R03, R37, R15, P01, U01 and UC1 mechanisms, were comparable at 25.9 percent and 23.5 percent, respectively.

6. The open letter implies that biodefense research has diverted money away from non-biodefense research at NIH. Is this true?

No, it is not true. NIAID's commitment to research on important non-biodefense pathogens has not decreased. In fact, support for research on many non-biodefense pathogens has increased with the influx of biodefense funds. In addition, research that can be considered as both biodefense and non-biodefense, i.e., research on multidrug-resistant tuberculosis and staphylococci, also has increased in concert with the influx of biodefense funds. For example, between FY 2000 and FY 2004, the funding increases listed below were seen in NIAID extramural research. These increases occurred as a result of both the doubling of the NIH budget as well as the additional new monies provided by the increase in biodefense funds in FY 2003 and FY 2004. In fact, a portion of the research on the microbes listed below was supported by biodefense funds

- Basic medical bacteriology research associated with sepsis and hospital infections increased 49 percent
- Sexually transmitted infection research (non-HIV pathogens) increased by 65 percent
- Staphylococci and enterococci research increased 63 percent
- Malaria research increased by 40 percent
- Tuberculosis research increased by 105 percent
- Hepatitis B and C research increased by 88 percent
- *Helicobacter pylori* research increased by 49 percent

7. What pathogens are currently being studied by researchers receiving NIAID biodefense funds?

NIAID biodefense funding supports research on NIAID Category A, B and C Priority Pathogens, including more than 50 organisms. The complete list can be viewed at http://www.niaid.nih.gov/Biodefense/bandc_priority.htm. This list includes "traditional" biodefense pathogens such as those that cause anthrax and smallpox; newly emerging infectious agents such as the SARS coronavirus; and pathogens that cause long-standing serious global health problems, such as multidrug-resistant tuberculosis; influenza; and enteric diseases due to *Escherichia coli*, *Vibrio cholerae*, *Salmonella* and *Listeria*. These diseases have public health significance because of their dual potential, i.e., they can occur naturally or result from the deliberate release of an infectious agent.

Of note, three diseases specifically listed in Appendix 1 of the open letter as having high public health importance —tuberculosis, salmonellosis and shigellosis—are among those supported in part by biodefense funding.

8. How have biodefense funds been used to further research on microbes that represent a significant public health concern?

As discussed in the response to Question 7, NIAID biodefense funds support research on several pathogens that cause diseases cited in Appendix 1 of the open letter as being of high public health importance. Biodefense funds also support research on several other common food- and water-borne pathogens. Between FY 2000 and 2004, the following increases in NIAID extramural research funding occurred, much of which were attributable to biodefense funding that began in FY 2003

- *Salmonella* research increased by 270 percent
- Diarrheagenic *E. coli* research increased by 122 percent
- *Shigella* research increased by 560 percent
- *Campylobacter* research increased by 617 percent
- *Vibrio* research increased by 206 percent
- *Listeria monocytogenes* research increased by 203 percent
- Calicivirus research (including norovirus) increased by 307 percent
- Hepatitis A research increased by 140 percent

9. Can you explain how all infectious diseases research benefits from NIAID biodefense research?

Basic research supported by NIAID often has interdisciplinary applicability. For example, an examination of basic research on bacterial systems that NIAID currently supports with biodefense funds shows that work is being done on physiologic and pathogenic features common to many bacteria, whether they are categorized as biodefense or non-biodefense. Pathways and processes being studied in biodefense organisms common to non-biodefense organisms include: cellular transport mechanisms, signal transduction pathways, secretion systems, metabolic pathways, chemical communication pathways, cellular structures and virulence factors.

In addition, because NIAID has emphasized the importance of product development, researchers in the biodefense community are focusing their basic science findings on the discovery of new products. Product development-oriented biodefense research is expected to lead to knowledge and products that can be applied to traditional and emerging non-biodefense pathogens.

For example, a study supported with biodefense funds and that focuses on the discovery and development of anti-infectives for specific Gram negative bacteria may yield broadly applicable knowledge and products targeting common pathways in many other Gram negative bacteria, including those that are not biodefense-related.

Another study that focuses on the discovery and development of antiviral drugs for smallpox that inhibit cellular signal transduction may yield a new class of antiviral drugs that may be active against multiple families of viruses. (See news release at http://www2.niaid.nih.gov/Newsroom/Releases/poxblock.htm.)

10. The authors of the letter published in *Science* recommend the "…consolidation of study sections for research on prioritized bioweapons-agents with study sections for research on basic microbial science." Do you agree with this recommendation?

Investigator-initiated basic research grant applications are peer-reviewed in the NIH Center for Scientific Review (CSR). CSR does not have biodefense study sections; biodefense and non-biodefense research applications are reviewed together. Each application is first reviewed for scientific merit, and then a priority score is determined and used to rank the applications to obtain a percentile. The more meritorious applications (as evidenced by the percentile and priority score) receive funding priority.

NIAID does issue initiatives to stimulate research in specific areas, or to encourage more extensive collaboration among scientists than a typical investigator-initiated single project grant would. Grant applications or contract proposals submitted in response to the announcement of such initiatives are reviewed by special review panels located at NIAID. While it is true that funds for such biodefense initiatives are set aside, the reserved funds are biodefense funds and do not in any way compete with non-biodefense funds. A complete list of current initiatives from NIAID can be found at http://www.niaid.nih.gov/ncn/budget/opps.htm.

11. Are you concerned that many researchers may be leaving the non-biodefense field to pursue biodefense research?

Whether researchers are working with microbes for biodefense or non-biodefense, they are still contributing to the broad base of knowledge in infectious diseases and immunology. As science evolves, new opportunities emerge and fields change. The relatively new biodefense field shares many aspects with the non-biodefense and emerging infectious disease fields. Biodefense has provided additional opportunities for experienced non-biodefense researchers to apply their knowledge to scientific questions in biodefense. In addition, biodefense has created new training and research opportunities for early career scientists. As we have seen in the past, whenever a new field of science emerges with many unanswered questions, scientists move forward to fill the gaps using the foundation of their knowledge from other scientific fields. For example, when SARS emerged, talented and established influenza researchers were well positioned to help solve this new problem without compromising the status of influenza research. It is expected that as knowledge in the biodefense field increases, scientific exchange and crossover among the biodefense, non-biodefense and emerging infectious disease fields will also increase.

12. NIAID has stated that the numbers cited in the open letter are incomplete or based on inaccurate assumptions. Please explain further.

There are several significant problems associated with the analysis done and conclusions stated in the open letter. The analysis was based on several major unstated and incorrect assumptions that are described below.

Major Unstated Assumptions Used in the Analysis by the Authors of the Open Letter

a. *Assumption*: The four study sections used in the analysis***** reviewed most of the basic bacterial physiology research grants awarded during the nine-year period analyzed (FY 1996–January 2005).

Fact: The four study sections used in the analysis reviewed only a portion of the bacterial physiology grant applications awarded by NIAID during the period analyzed. As seen in Figure 1, between FY 2000 and FY 2004, an additional nine study sections began reviewing bacterial physiology grant applications awarded by NIAID, thus increasing the number of study sections from 21 to 30. During this same time, additional CSR study sections reviewed bacterial physiology grant applications for other NIH Institutes and Centers (ICs).

****** *The four study sections were from the Bacterial and Mycology (BM) and Microbial Physiology and Genetics (MBC) Initial Review Groups (IRGs).*

Increase in the Number of Study Sections Reviewing Bacterial Physiology Grants Awarded by NIAID

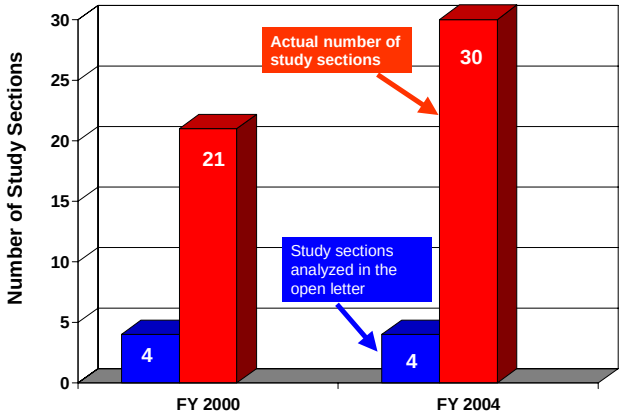

Figure 1. Blue bars represent the number of study sections analyzed by the authors of the open letter; red bars represent the actual number of study sections that reviewed bacterial physiology grant applications awarded by NIAID.

Figure 2 shows how the analysis in the open letter, which was based on data from only four study sections, vastly underestimates the actual number of NIAID bacterial physiology grant awards reviewed by all study sections between FY 2000 and FY 2004. In addition, the graph shows the significant rise in the total number of bacterial physiology grant awards that occurred when the dramatic increase in biodefense funding began in FY 2003.

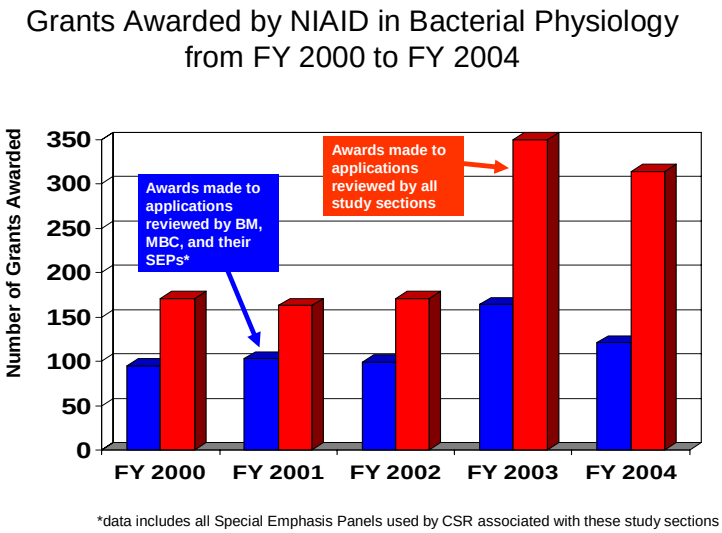

Figure 2. Blue bars represent the number of grants awarded that were reviewed by the four study sections analyzed by the authors of the open letter; red bars represent the total number of grants awarded that were reviewed by all study sections.

b. *Assumption*: CRISP (Computer Retrieval of Information on Scientific Projects) can be used to accurately analyze the relative funding being awarded to different biomedical research areas.

Fact: CRISP is a simple searchable database of information about biomedical research projects funded by NIH and other agencies within the Department of Health and Human Services. CRISP was not intended to be used to conduct complex comparative statistical analyses of the relative funding for different biomedical research areas. CRISP was designed to be used to find limited information about funded research projects: e.g., the title of the grant or contract; the name of the principal investigator and the Institution with which the investigator is affiliated; the research award period; and the research project abstract.

CRISP provides neither financial information about funded grants nor information about grant applications that were not funded. In addition, while CRISP does contain the abstracts of funded grants, any analysis based on searching the text of the abstracts has significant limitations: i.e., the number of grants that include the name of a specific disease in the abstract is not the same as the number of grants actually studying the organism causing that disease. The term “plague,” for example, appears in more abstracts than grants funded to actually study *Yersinia pestis*, the microbe that causes plague.

c. *Assumption*: An analytical approach that compares the total number of grants awarded in a baseline 5-year period (FY 1996 to FY 2000) with the total number of grants awarded during a 4 1/3-year period (FY 2001 to Jan 2005) is fair and valid.

Fact: It is impossible to draw fair and valid conclusions by comparing grant data from two time periods that differ in length by eight months. The total number of grants awarded during the shorter time period (FY 2001 to Jan 2005) will significantly understate the total number of grants awarded during the full five-year period (FY 2001 to FY 2005).

Conclusion

In conclusion, we appreciate the concerns raised about NIH biodefense funding in the open letter published in *Science.* While the letter may have been well-intentioned, the methods and data used in the analysis to support the letter have significant limitations that resulted in flawed conclusions.

As we have stated, the biodefense resources given to the NIAID biodefense program starting in FY 2003 are new and additive to NIAID's non-biodefense resources. These new biodefense funds did not and will not divert resources from other important infectious diseases research. Finally, biodefense funding has enabled us to increase our research capacity in microbiology, immunology and infectious diseases and thereby build a broader base of researchers who can develop diagnostics, treatments and vaccines to protect the public against many naturally occurring or deliberately released microbes.

Finally, we at NIAID would be happy to discuss these issues with our scientific colleagues in order to provide further clarification. We are always willing and available to engage in a productive dialogue concerning these important matters.

Media inquiries can be directed to the NIAID OCPL media group at 301-402-1663.

NIAID is a component of the National Institutes of Health (NIH), an agency of the U.S. Department of Health and Human Services. NIAID supports basic and applied research to prevent, diagnose and treat infectious diseases such as HIV/AIDS and other sexually transmitted infections, influenza, tuberculosis, malaria and illness from potential agents of bioterrorism. NIAID also supports research on transplantation and immune-related illnesses, including autoimmune disorders, asthma and allergies.

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U.S. Department of Health and Human Services