NIH Global Health Research Meeting

January 6, 2010
5635 Fishers Lane
Rockville, MD

Executive Summary

Global health has taken on an urgency worldwide with changes in the burden of disease and new opportunities and support for intervening to improve the lives of entire populations. The United States has long been a leader and major donor in global health initiatives. Much of this effort in recent years has been targeted to support President Bush's Emergency Plan for AIDS Research (PEPFAR) and the Presidential Malaria Initiative and related programs. In May 2009, President Obama launched the U.S. Global Health Initiative and, with $63 billion in new funding for the next 5 years, the Administration is embracing a new framework for global health that emphasizes sustainability of efficient, integrated programs and substantive outcomes for the poorest people in the world.

Research is an essential part of this new framework for global health, and the National Institutes of Health (NIH) is a key partner in this government-wide effort as it brings research and research training to the fore. As set forth by the new NIH director, Dr. Francis Collins, global health is one of five major cross-cutting themes that the NIH will pursue over the next several years. To focus and stimulate NIH investments in global health, the director convened on January 6, 2010, the NIH Global Health Research Meeting, in Rockville, Maryland.

More than 60 leaders in global health research and development (R&D) attended the meeting. Their charge was to consider strategic needs and opportunities in global health R&D and to suggest areas in which the NIH could make additional investments to gain the greatest effects over the next 5–10 years. The NIH already makes a significant investment in global health R&D, which amounts to approximately $600 million a year across its 27 institutes and centers (ICs). The activities range in intensity across the ICs and employ various strategies to address many diseases and conditions that effect significant burdens globally.

Burden of Disease. The participants at the meeting defined global health as comprising infectious diseases; chronic, non-communicable diseases (e.g., cardiovascular disease and cancer); and emerging diseases (e.g., diabetes associated with obesity, environment-related conditions such as chronic obstructive pulmonary disease, and behavioral and mental health disorders such as depression and substance abuse and addiction). The emphasis on global health research to date has been on the "big three" infectious diseases, i.e., HIV/AIDS, malaria, and tuberculosis. Fortunately, recent advances in RNAi, small molecule screening, genomics of pathogens, and vaccine development, to name a few, have made an attack on infectious diseases more feasible than ever.

These research gains have provided an opportunity to broaden the global health research focus to include a long list of neglected tropical and noncommunicable diseases in low and middle income countries. Neglected tropical diseases (e.g., schistosomiasis, hookworm

infection, leishmaniasis, and filariasis) affect one billion people and result in approximately half-a-million deaths per year. Chronic noncommunicable diseases and injuries contribute to more than 50 percent of deaths in the developing world. Lessons learned from NIH research conducted with infectious diseases emphasize the importance of committing substantial financial and human resources, engaging the affected community, fostering cross-sector collaboration, and garnering the support of leaders and policymakers toward maximizing research and health gains.

Research Strategies. Among the possible research strategies that the NIH could pursue, the participants focused on and suggested four avenues of investment:

- Fundamental science
- Epidemiology and population-based approaches
- Diagnostics
- Therapeutics (drugs and vaccines)

The opportunities and challenges for global health R&D across this spectrum of research activity are many, and the NIH could gain the greatest return on investment by focusing on them. The participants' suggestions of specific opportunities for each strategy include the following.

Fundamental science—understanding the biology of pathogens and vectors, especially for tuberculosis; social and behavioral research (e.g., related to tobacco cessation) and biobehavioral studies that integrate health disparities research with delivery of care; gene–environment interactions and predisposition to disease; biomarkers of disease; role of nutrition and biofortification in health and disease; health effects of climate and other environmental changes; zoonotic diseases and vector biology; and regulatory frameworks and tools to ensure safe and effective therapeutics and other interventions.

Epidemiology and population-based approaches—creation of a genetic and epidemiological cohort of African populations and other large-scale, prospective cohort projects that include multi-morbidity and publicly available databases; community-based behavioral and biosocial interventions; nested case-control studies; implementation and improvement of health systems; implementation of new technologies, such as mobile health (mHealth) research applications; comparative cost-effectiveness research; use of national biobanks to relate treatments to conditions and predispositions to disease, and improved collection and applicability of surveillance data on morbidity and mortality.

Diagnostics—development of rapid, accurate, cost-effective, easy-to-use, point-of-care diagnostic tests for the "big four" and including influenza and diarrheal illness; design of an integrated, coordinated approach for the development and implementation of diagnostics; establishment of sites for comparative testing; involvement of end-users from countries with endemic disease; and improved regulation of diagnostics.

Therapeutics (drugs and vaccines)—prioritize the needs for therapeutics in developing countries, drawing on and refining methodologies used for previous assessments of priorities (e.g., by the Institute of Medicine, Wellcome Trust), and with consideration of downstream activities at the outset; basic science of vaccinology to underpin vaccine development; cutting-

edge approaches in engineered immunity and humanized antibodies; randomized trial of human papillomavirus and hepatitis B vaccine singly and in combination in infants; formulation of a polypill for cardiovascular disease; and research aligned with the NIH Therapeutics for Rare and Neglected Disease (TRND) program.

Sustaining Investments. Global health depends not only on R&D, but also, and importantly, on the building of research capacity in global health in the United States and in developing countries. The NIH cannot do this alone and must look to partner with other interested organizations and groups within and outside the United States. The sustainability of U.S. and NIH investments depends on partnerships with others. Underlying these partnerships is an emphasis on equity and mutual sharing of commitment and effort—among funders and with institutions and investigators in developing countries.

Capacity Building and Training. The building of capacity and the training of scientists are basic to any research strategy and are essential investments for the NIH. The participants called for a doubling of the current NIH investment in capacity building and training for global health R&D, and/or a commitment of 5 percent of the $63 billion allocated for the U.S. Global Health Initiative. These efforts should be targeted to the needs of particular countries and/or regions and include training for scientists from, and in, both the United States and developing countries. By undertaking a systematic research evaluation of past efforts, the NIH could derive best practices on which to model future efforts. Known successes such as the NIH-supported International Centers for Infectious Diseases Research and International Centers of Excellence in Research could be expanded profitably to other countries and regions. Some other suggestions made by the participants are as follows to:

- Provide pre- and postdoctoral NIH training grants for global health studies
- Offer all NIH trainees the opportunity to do part of their training internationally
- Emphasize broad, multidisciplinary research training, with substantive mentoring
- Support development of Centers of Excellence in developing countries, especially those that create regional research and research training consortia around them
- Incorporate training in informatics and information technologies
- Replicate NIH clinical research training programs, and incorporate research training into all clinical trials
- Expand use of NIH Clinical and Translational Science Awards (CTSAs) globally
- Support U.S. and international training in implementation science and in regulatory oversight
- Invest in leadership training for policymakers and ministers in developing countries, to create understanding of and demand for global health R&D
- Tap into the NIH alumni network around the world
- Address the NIH restriction on indirect costs for awards to foreign grantees.

Partnerships. The success of NIH investments in global health R&D depends on partnerships—among the ICs, with other U.S. agencies and industry, with investigators and institutions in other countries, and with non-governmental entities, foundations, and multilateral organizations. Global health is global—everyone must be involved to make a difference, public and private sectors alike. Within the NIH, the trans-NIH Global Health Working Group

identifies synergies and fosters data exchange across the ICs. As part of the Global Health Initiative, the NIH will be integrating its efforts with other agencies, organizations, and host countries. The participants encouraged the NIH to pursue the following as well:

- Establish effective partnerships with industry, particularly with pharmaceutical companies that have global health units, to achieve shared goals in global health

- Collaborate with non-governmental organizations such as the Wellcome Trust that have invested in capacity building and training programs

- Engage with foundations, such as the Bill & Melinda Gates Foundation, and other organizations to help integrate and align R&D resources in global health

- Pursue innovations in drug discovery and development through public–private Product Development Partnerships (PDPs).

Over the long term, such partnerships can be avenues to sustainability. As demonstrated by NIH-supported programs in China and India, long-term institutional partnerships yield long-term effects. The NIH now even has an opportunity to build on these longstanding relationships by engaging former partners and NIH alumni of training programs in the countries to participate in other global health R&D efforts.

Equity. Research and research training partnerships must be based on shared understanding and mutual commitment. For NIH investments in global health R&D to be sustainable, the science must drive partnerships between institutions and the partnerships must be led by scientists. Equality and empowerment are critical to assure that NIH partnerships involving developing countries are a "win-win" situation that yields a synergy of effort and mutual benefit. Two related elements that the NIH supports in this regard are:

- Open access to research data
- Development of informatics structures to enable scientists to access and use research data globally.

In sum, the NIH is pursuing global health research as part of its dual mission—to pursue fundamental knowledge about the nature and behavior of living systems and to apply this knowledge to extend healthy life and reduce the burdens of illness and disability. In the pursuit and application of knowledge, the NIH has an opportunity under its mandate to support research outside the United States when the research cannot be done within. The NIH has the research and research training potential to confront priority disease areas, by pursuing a variety of strategies in partnership with others and with equity for all, ameliorate the disease burdens felt by so many in the world today. Because of the public good it promises, global health R&D is a mighty instrument of diplomacy internationally and fulfills our sense of national responsibility.

NIH Global Health Research Meeting

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Meeting Summary

The National Institutes of Health (NIH) convened a meeting on global health research on January 6, 2010, in Rockville, Maryland. The purpose of the meeting was twofold:

- To gain the benefit of current thinking from academic, government, philanthropic, industrial, and international organizations on pressing strategic needs and opportunities in global health research and development (R&D)
- To identify a potential set of initiatives that might be supported by the NIH, independently or in partnership, and that would have the greatest multiplier effect on global health R&D in the next 5–10 years.

More than 60 leaders in global health R&D participated, sharing information and expertise and engaging in wide-ranging, open discussions. The meeting consisted of three panels, two presentations on the President's new Global Health Initiative, and a series of discussions of research opportunities. The panels of scientists presented perspectives on the challenges and directions of global health research supported by the U.S. Department of Health and Human Services (HHS), the building of research capacity in low- and middle-income countries, and philanthropic and private sector efforts to develop global health technologies. In the five discussion sessions, the participants identified research opportunities in fundamental science, epidemiology and population-based research, diagnostics, therapeutics (i.e., drugs and vaccines), and capacity building and training. This report summarizes all the presentations and discussions.

WELCOME AND INTRODUCTIONS

Francis S. Collins, M.D., Ph.D.

Dr. Collins welcomed everyone and described the context for the meeting. He noted that the NIH has a dual mission—to pursue fundamental knowledge about the nature and behavior of living systems and to apply this knowledge to extend healthy life and reduce the burdens of illness and disability. In the pursuit and application of knowledge, the NIH has an opportunity under its mandate to support research outside the United States when the research cannot be done within. This global health research amounts to approximately $600 million a year in the NIH budget.


Dr. Francis Collins (NIH)

On becoming director of the NIH in May 2009, Dr. Collins formulated five cross-cutting themes to guide the directions for NIH over the next few years, as follows:

Opportunity 1 – Applying unprecedented opportunities in genomics and other high throughput technologies to understand fundamental biology and to uncover the causes of specific diseases

Opportunity 2 – Translating basic science discoveries into new and better treatments

Opportunity 3 – Putting science to work for the benefit of health care reform

Opportunity 4 – Encouraging a greater focus on global health

Opportunity 5 – Reinvigorating and empowering the biomedical research community.

Dr. Collins elaborated on the opportunity to extend NIH's already significant investment in global health research. The rationale derives from the potential to advance against infectious diseases, confront neglected tropical diseases, and give attention to chronic, non-communicable diseases. In addition, the NIH can tap into a new generation of young researchers who are energized about the opportunities for global health research, pursue global health as an instrument of diplomacy and "soft power" internationally, and fulfill a sense of national responsibility.

Dr. Collins noted that the NIH would like to initiate a pilot project in global health research in Fiscal Year (FY) 2010. The funding for this project would come from the Common Fund, which the Congress authorized 3 years ago for use by the NIH director. This project would be in addition to the many programs already funded by many of NIH's 27 institutes and centers (ICs). Commenting on the complexity of the current landscape for global health research, Dr. Collins presented several templates depicting the intensity of research activity by organization, disease, and research strategy.

In closing, he urged the meeting participants to be bold, aim high, and engage in an active interchange of ideas. He asked them to focus, in particular, on explicit actions that the NIH could take to contribute more extensively to global health research.

I. PANEL – GLOBAL HEALTH RESEARCH AT HHS: CHALLENGES AND DIRECTIONS

Moderator: John T. Monahan, J.D., (OGHA).
Panel Members: Roger I. Glass, M.D., Ph.D.,(NIH-FIC); Anthony S. Fauci, M.D., (NIH-NIAID); Thomas R. Frieden, M.D., M.P.H., (CDC); and Margaret Hamburg, M.D. (FDA)

Mr. John Monahan (OGHA) and Drs. Roger Glass (NIH-FIC), Anthony Fauci (NIH-NIAID), Thomas Frieden (CDC), and Margaret Hamburg (FDA)

This panel consisted of brief presentations from five government officials within HHS.

Perspective from the Office of Global Health Affairs (OGHA). Mr. Monahan opened the panel by describing the functions of OGHA, which are to coordinate policy within HHS on global health issues and to represent HHS internationally with foreign governments, multilateral organizations, and other entities. From this perspective, he noted that research is vital to the Administration's agenda and that investing in research is part of a constant loop of acquiring knowledge, applying knowledge to interventions, and informing policy and programs. He further noted that research by its nature is about partnerships and, hence, is a tool of diplomacy as the United States engages in collaborative research initiatives.

Perspective of the Fogarty International Center (FIC). Dr. Glass commented that the Administration's commitment to science presents a unique opportunity in global health. He highlighted three "S's": science (what NIH does), synergy (partnerships), and sustainability (infrastructure and capacity building and training). Dr. Glass defined global health as embracing infectious diseases as well as chronic, non-communicable diseases and "diseases of the future" (e.g., obesity, environmental effects, addictions, and mental health). He noted that differences among developing countries (e.g., life expectancy) necessitate that science and interventions be tailored to each country and, as research priorities, he pointed to basic science and implementation science. Dr. Glass distinguished two areas for future investments and partnerships: middle-income countries (e.g., China) which, he noted, would benefit most from research collaborations and interaction, but would only need perhaps small, co-funded investments; and sub-Saharan Africa, which greatly needs capacity building and training programs to develop and expand centers of excellence and regional networks beyond a focus on infectious diseases. Partnerships and application of new information and communication technologies (ICT) would be essential for moving the global health agenda forward. Dr. Glass noted, in particular, that a commitment of 5 percent of the $63 billion allocated for the President's Global Health Initiative to training would make a major difference.

View from the National Institute of Allergy and Infectious Diseases (NIAID). Dr. Fauci noted that infectious diseases are the most obvious global health issue for research and implementation programs and that the imperative for research support goes well beyond the "big three" infectious diseases (HIV/AIDS, malaria, and tuberculosis) to include a fourth—neglected tropical diseases. Summarizing the experience with HIV/AIDS research, Dr. Fauci remarked that the NIH's extraordinary investment in this research (totaling approximately $42 billion since the early 1980s) has resulted in extraordinary advances across all areas of research, which are now being applied, for example, in the President's Emergency Program for AIDS Research (PEPFAR). He cited some of the lessons learned from this experience: commit substantial resources; recruit the best and brightest investigators; engage the affected community; foster cross-sectional collaboration, particularly with industry; and garner the support of leaders and policymakers. Dr. Fauci noted that, for malaria and tuberculosis, each of which exerts a high burden of disease globally, much more basic and implementation research is needed to develop diagnostics and effective intervention products, and these needs have been set forth in the NIAID research agendas for these diseases. The same situation applies to neglected tropical diseases (e.g., schistosomiasis, hookworm infection, leishmaniasis, and filariasis), for which diagnostic and intervention tools are deficient. Dr. Fauci emphasized that the enormous challenges in global health will require sustained, long-term commitments well after the world's attention to global health has faded.

Research Priorities at the Centers for Disease Control and Prevention (CDC). Dr. Frieden described CDC's international activities, which include a newly established CDC Center for Global Health. This center will work with ministries of health to plan, implement, and evaluate health programs; work toward goals to eradicate and eliminate diseases; expand programs targeting leading causes of illness, disability, and death; generate and apply new knowledge; and strengthen health systems. Dr. Frieden noted that the CDC supports sites and global disease detection centers around the world and partners with other agencies, organizations, and host-country institutions. It funds research to combat the "big four," as well as influenza, zoonotic diseases, other infectious and chronic diseases, and tobacco use. Through research, CDC aims to answer answerable and important questions; strengthen coordination between health ministries and in-country academic institutions; and improve tools to monitor, prevent, and control communicable and non-communicable diseases. Dr. Frieden outlined key challenges for combating each of the "big four" diseases. Overall, these include development of better diagnostic and treatment tools, development and evaluation of interventions, and scaling up of proven interventions. Additional challenges are to monitor drug resistance and to provide safe drinking water, sanitation, and hygiene to vulnerable populations. Dr. Frieden mentioned that, with the growing burden of chronic, non-communicable diseases in developing countries, the ability to combat these diseases will depend on the political will of governments.

Role of the Food and Drug Administration (FDA). Dr. Hamburg noted the unique position of the FDA as the gateway to ensuring that advances in science and technology and new discoveries actually translate into meaningful products for people who need them. As a science-based, science-driven regulatory agency with a public health mission, the FDA plays a critical role in helping to address the challenges for research in global and public health. Dr. Hamburg highlighted three main areas for increased activity:

Regulatory science research—More efficient and equally effective regulatory pathways are needed, for example, to gain more-predictive clinical trials relevant to global health, assess new technologies and emerging products, and develop accessible technologies to identify unsafe and poor-quality counterfeit products in developing countries that have the greatest burden of disease.

Harmonization of standards and approaches—Expansion of international collaborations and partnerships in global health will be stymied if research and practice standards (e.g., good manufacturing, laboratory, and clinical practices) are not harmonized and if common regulatory pathways are not established.

Capacity building—U.S. leadership in building capacity for regulatory oversight throughout the developing world is urgently needed. Technical assistance and support for building regulatory systems in resource-poor nations yield multiple benefits, by enhancing access to safe and effective products, creating jobs and economic development, and assuring the safety of foods and products entering the United States.

Discussion

The panelists specified the critical lessons they have learned in global health research, and, in discussion, the participants focused on several issues. Salient points and suggestions are summarized below under several topics.

SUSTAINABILITY OF GLOBAL HEALTH RESEARCH. Successful centers of excellence can be developed by investing in people, sustaining long-term investments, partnering with other funders, and twinning with U.S. institutions to empower in-country scientists and train U.S. scientists, both of whom will become advocates for global health. Full sustainability depends on full participation of in-country scientists and administrators and commitment of the host country. New ways, including perhaps longer cycles, of funding are needed to foster sustainability of research efforts. Documentation and publication of results to demonstrate that programs are effective and have made a difference could increase the likelihood of gaining sustainable support. Information systems and surveillance methodologies are needed to evaluate progress and defend programs. *(Drs. Glass, Fauci, Sewankambo, and Frieden)*

RESEARCH AND RESEARCH TRAINING. Global health research covers the spectrum from fundamental, basic science to clinical, operational, and implementation research. Training and capacity building (e.g., through field epidemiology training programs) should be an integral component of all global health research programs. *(Drs. Fauci, Laxminarayan, Glass, and Frieden)*

IMPLEMENTATION SCIENCE. The gap between what we know and what we do in global health research is enormous. This implementation science gap actually may be a responsibility gap—and who has responsibility for implementation science needs to be clarified. Implementation science is very important for preventing the loss of gains and developing new tactics to pursue. Substantial resources should be set aside for implementation research and training, and

behavioral scientists and experts in logistics should be involved. *(Drs. Godal, Fauci, Frieden, and Farmer)*

INTEGRATION OF NIH AND U.S. EFFORT. One challenge for the NIH is to identify the common elements and approaches in global health within the NIH and between the NIH and other U.S. Government agencies, in order to build partnerships across agencies. The NIH has established a trans-NIH Global Health Working Group to identify synergies (e.g., in data) among the ICs, and the Global Health Initiative emphasizes integration at three levels—with other organizations, among U.S. agencies, and with host countries. *(Drs. Evans, Glass, and Emanuel)*

II. PRESENTATION – PLANS FOR RESEARCH AND INNOVATION WITHIN THE U.S. GLOBAL HEALTH INITIATIVE--*Jacob J. Lew, J.D.*


Deputy Secretary Jacob Lew (DoS) and Dr. Francis Collins (NIH)

Mr. Jacob Lew addressed the role of research and innovation in the Global Health Initiative. Launched in May 2009, this 6-year $63 billion effort is a commitment to improve the welfare of the poorest people in the world by drawing on the gains made against specific diseases in recent years and the tremendous potential of programs that are well-designed, well-coordinated, and well-supported. Mr. Lew noted that it points to the central importance of health and development issues in the Administration's foreign policy as an avenue to a more secure, stable, and prosperous world.

The Global Health Initiative brings several new approaches to U.S. health assistance policies. It emphasizes integration and coordination of efforts, the strengthening of health services systems, and a women-centered focus. It will continue U.S. leadership in the fight against specific diseases (e.g., HIV/AIDS, tuberculosis) and build capacity of in-country partners to achieve broad and sustainable gains in the long term.

Mr. Lew noted that research and innovation are critical to achieving the goals of the initiative and will continue to involve public and private partners. The initiative will stimulate and incorporate advances in research, treatment, and delivery of health care services. In consultation with partners, priorities will be set for research, innovation, and evaluation with a focus on questions that are field-driven and will advance delivery of programs. It is expected that the generation of evidence and careful monitoring of programs, with clearly defined metrics, or benchmarks, will catalyze further innovation. The initiative will also support research on implementation and serve as a platform for innovative ways to improve delivery of service and interventions. In bringing treatments "from bench to bedside," an understanding of local infrastructure, health system capacity, cultural attitudes and social norms, and policies will be critical. Over the 6-year period, important steps will include:

- Accelerated support for research resulting in new or modified interventions and products
- Strengthening capacity among partner countries to conduct research, train scientists, and evaluate programs
- Development of a monitoring, evaluation, and research unit to track what works and to make advances and best practices available globally
- Development of indicators and involvement of researchers, implementers, and policymakers in the peer review of all practices in the initiative.

Deputy Secretary Jacob Lew (DOS)

Mr. Lew elaborated several areas in which successful new approaches and innovations will be key to meeting the objectives of the initiative and to making advances in global health. These are as follows.

Strengthening of health systems—with a clearer focus to create well-functioning public health systems that can meet basic health needs (e.g., immunizations) and respond to the expanding burden of chronic, non-communicable diseases. This effort will call for basic, clinical, applied operational, and health services research. It is crucial to achieving sustainable long-term improvements in global health.

A women-centered approach—that will address how the challenges in global health affect women in particular and how addressing women's health issues can have broader impact on families and communities. Some of the aims are to dramatically reduce preventable deaths surrounding childbirth with low-cost, high-impact interventions and to increase family planning and reproductive health activities.

Prevention and treatment of infectious diseases—building on past progress to create "game-changing" innovations such as better diagnostics for tuberculosis and malaria, improved therapies for drug-resistant tuberculosis, drugs and vaccines for neglected tropical diseases, and inexpensive and accurate point-of-care tests for HIV/AIDS.

Mr. Lew emphasized that success depends on public–private partnerships in the United States and around the world. Moving forward, the U.S. Government will foster the exchange of knowledge and understanding to ensure that the products developed are appropriately priced and fully functional in resource-poor settings.

Discussion

In response to comments and questions, Mr. Lew said that the Global Health Initiative includes opportunities for women's economic development and education, as integral to improving the health and lives of women, as well as the targeting of interventions to some countries in addition to global engagement. He noted that the initiative does not counter support for successful vertical programs (e.g., bednets for malaria), but provides the connective tissue between programs (vertical and/or horizontal) to gain a "win–win" situation. He agreed with the need for a holistic, global outlook that fosters development of generic approaches that can be tailored to

specific cultural and country contexts. Mr. Lew said that the Administration is sensitive to the fact that some false boundaries have impeded effectiveness in the past and that it is committed to presenting the role of the United States in a different way.

III. PANEL – REGIONAL PERSPECTIVES: BUILDING RESEARCH PARTNERSHIPS

Moderator: Timothy G. Evans, M.D., D. Phil., (WHO).
Panel Members: Prof. Depei Liu,(Chinese Academcy of Medical Sciences); Prof. Malegapuru (William) Makgoba, (University of KwaZulu-Natal), and Prof. Nelson K. Sewankambo (Makerere University).

Dr. Timothy Evans (WHO) and Prof. Depei Liu (Chinese Academy of Medical Sciences), Prof. Malegapuru (William) Makgoba (University of KwaZulu-Natal), and Prof. Nelson Sewankambo (Makerere University)

The panel members shared their perspectives on research partnerships between the United States and developing countries.

Global Vision and Mission. Prof. Liu emphasized the need to develop a global vision, mission, and policy; to create a platform for research and collaboration; and to promote understanding and support between and among countries. He highlighted China's participation in recent efforts to prevent and control the HIN1 influenza virus. Emphasizing the importance of capacity building and training, he noted that China and the United States are partnering to establish and organize a customized course using the NIH *Principles and Practice of Clinical Research* (PPCR) for physicians in China. He remarked that, for Chinese professionals, the NIH represents the highest international standard for biomedical research and science.

Framework for Effective Partnerships. Prof. Makgoba highlighted three aspects of effective partnerships:

- A shared understanding by the partners of the framework for the partnership
- A focus on capacity building, particularly the mentoring of future generations of scientists
- Upgrading of infrastructures to retain scientists in their own countries.

Prof. Makgoba noted that the essence of a good partnership is a framework in which science drives the partnership between institutions and the partnership is led by scientists and is sustainable. In addition, equality and empowerment should pertain to both partners and the overall intent should be to close the disparity between partner countries. For developing countries such as South Africa, research partnerships need to be established directly between scientific institutions to avoid the inefficiencies of bureaucracy. Prof. Makgoba encouraged the NIH to take the lead in (i) engaging NIH alumni and key scientists to collaborate on research

projects that can have a multiplier effect for global health (e.g., HIV/AIDS) and (ii) instilling the excitement of science for future generations of scientists.

Capacity Building and Sustainability. Prof. Sewankambo said that he has observed an increasing excitement for science among young researchers in Uganda, especially when they first publish in a journal, and he noted the importance of providing opportunities for students to participate in all phases of research, including research design. He, too, emphasized the need for capacity development and continued capacity building for both individuals and institutions and including the overall research environment, supportive units, and management functions. Particular issues to address include in-country capabilities for broadband usage, institutional review boards, storage of data specimens, and data analysis. With regard to sustainability, Prof. Sewankambo raised an issue that affects foreign institutions receiving NIH support—the 8 percent limit on indirect costs. He suggested that broader support for clusters of research projects may be helpful in retaining scientists in-country, and he noted the importance of networking among African countries, for example, through the recently organized Initiative for Strengthening Health Research Capacity in Africa (ISHReCA). Prof. Sewankambo cited three challenges for North–South partnerships: (i) to assure that partnerships are a "win–win" situation for all partners; (ii) to avoid the pitfalls of viewing the South as a "field" or playground for the North's research; and (iii) to attain synergy and a spirit of true partnership.

Discussion

The participants' comments and suggestions are summarized below, by topics.

FEATURES OF SUCCESS. The NIH should undertake a systematic research evaluation of past efforts in capacity building to derive best practices and strategies for research partnerships and infrastructure development. The features of success in building research centers at the University of KwaZulu-Natal and Makerere University and in the Rockefeller Foundation's longstanding relationship with China would be informative. *(Drs. Evans, Olopade, and Prof. Liu)*

RETENTION OF SCIENTISTS. The North needs to make a commitment in capacity building and training efforts to help ensure that scientists in the South who receive training return and stay in their host countries. *(Dr. Sebbag)*

CAPACITY DEVELOPMENT FOR UNIVERSITIES. In Africa, universities are increasingly being sidelined in favor of independent research organizations. Yet, the most effective way to develop capacity is with students in universities. University faculty are at a disadvantage because they have three responsibilities—service, teaching, and research. It may be possible to create "channels" whereby research faculty in universities can devote perhaps 70 percent of their time to research. *(Dr. Whitworth and Profs. Makgoba and Sewankambo)*

FLEXIBLE USE OF NIH FUNDING. While NIH should do what it does best, it also could allow investigators some flexibility to use research grant monies to help improve infrastructure within laboratories, for example, with the purchase of equipment. *(Dr. Rotimi)*

SUSTAINABILITY—GOVERNMENT INVOLVEMENT AND EXTERNAL SUPPORT. The NIH does not have the resources to assure long-term sustainability of research centers. National and local governments in developing countries need to be involved in funding research. On the other hand, past experience shows that institutions in low-income countries depend on continuous external support, and this support should be partly competitive and partly core. Perhaps U.S. medical schools could divert part of their students' tuition payments to the institutions in developing countries where the students are receiving training. *(Drs. Rotimi, Godal, and Yamada)*

EARLY SCIENCE EDUCATION. The importance of science needs to be conveyed globally to children at the earliest stages of education. *(Dr. Volkow)*

TRAINING IN NEW WAYS OF DOING SCIENCE. Increasingly, science is being done through the mining of data sets for information. Training in this area is less expensive than building laboratories and can decrease the gaps between countries. In addition, investigators need to be prepared to take advantage of the movement toward open innovation, whereby anyone anywhere can respond to requests for proposals. *(Dr. Volkow)*

CLINICAL RESEARCH TRAINING. A crucial issue in emerging-market countries is the lack of knowledge about clinical research, particularly guidelines pertaining to human subjects and ethics. Science education and information sharing are top priorities that are separate from training and need to be included in the Global Health Initiative. *(Dr. Shi)*

UPDATES OF EARLIER REPORTS. The NIH could take the lead to update two landmark reports: the *Commission on Health Research for Development* report and *Investing in Health Research and Development*. *(Dr. Frenk)*

INTERNATIONAL CONSORTIA. Building capacity through international collaborative consortia is more powerful and efficient than one-on-one relationships. *(Dr. Frenk)*

LEADERSHIP DEVELOPMENT. Creating the demand for science among policymakers and the public is a critical part of capacity building. This will require investments in leadership development at all levels in some developing countries. *(Dr. Frenk)*

IV. PANEL – GLOBAL HEALTH TECHNOLOGIES: PHILANTHROPIC AND PRIVATE SECTOR PERSPECTIVES

Moderator: Harvey V. Fineberg, M.D., Ph.D., (IOM/NAS)
Panel Members: Mark B. Feinberg, M.D., Ph.D., (Merck); Bernard Pécoul, M.D., M.P.H., (DNDi); Jimmy Whitworth, M.D., (Wellcome Trust); and Tadataka Yamada, M.D., (Bill & Melinda Gates Foundation)

Drs. Harvey Fineberg (IOM/NAS), Mark Feinberg (Merck), Bernard Pecoul (DNDi), Jimmy Whitworth (Wellcome Trust), and Tadataka Yamada (Bill & Melinda Gates Foundation)

The panel members provided perspectives on private-sector and philanthropic activities in R&D for global health.

Perspectives of the Pharmaceutical Industry. Dr. Feinberg focused on the role of the pharmaceutical industry in addressing R&D gaps in global health. He noted that the opportunities are promising and that the greatest benefits can be achieved through effective partnerships and collaboration. Specific contributions that the pharmaceutical industry can contribute include promising leads (e.g., candidate antigens); enabling technologies (e.g., high tech/high throughput screening); experience in product development, manufacture, and licensure; familiarity with the challenges and risks of new product development; and experience in the prioritization of options. The industry also offers a sincere interest in making a positive difference and an appreciation of the importance of incorporating end-users' needs into early development decisions. Yet, there are constraints, such as the current challenging financial circumstances, attendant opportunity costs, financial and other risks inherent in product development, and real or perceived barriers (e.g., intellectual property rights). Dr. Feinberg noted that the industry is partnering in R&D initiatives with the NIH, other private-sector organizations, foundations, and governments—to foster access to libraries, compounds, and technologies; transfer technology; conduct clinical trials and demonstration programs; and support treatment and prevention programs. He highlighted, in particular, Merck's partnership with the Wellcome Trust and Hilleman Laboratories to develop a world-focused research and development center. Dr. Feinberg emphasized the need to:

- Make the concept of public–private partnerships as broadly engaging and effective as possible and broaden the definition of partnerships to include, for example, private–private and multiple-partner arrangements
- Develop more proactive, strategic, predictable, and trusting models of partnership and collaboration that have an "end-to-end" view and that realistically prioritize opportunities, marshal contributions, and manage risks
- Develop a mechanism that supports the highly integrated approaches characteristic of successful R&D programs and the best leveraging of partners' skills and resources.

He suggested that the NIH can play a powerful, positive role via thoughtful planning, strategic engagement, and development of new models for collaboration with diverse external partners.

A Virtual Approach: Product Development Partnerships (PDPs). Dr. Pécoul addressed the need for new tools to combat diseases among the most disadvantaged populations. He noted that only 1 percent of new drugs developed over the past 30 years relate to neglected populations and neglected diseases, including malaria and tuberculosis. Dr. Pécoul focused on PDPs as part of the solution, in offering a creative way for large and small pharmaceutical companies and the public sector to bring innovation to neglected patients. As one example, he highlighted the Drugs for Neglected Diseases Initiative (DND*i*). Created in 2003 with several partners, DNDi has engaged public research institutions in developing countries (e.g., Brazil, India, Kenya, and Malaysia) to develop new drugs for targeted diseases (e.g., Chagas disease, leishmaniasis, malaria). The strategies include improving existing tools in the short- and mid-term and building a robust pipeline of new drugs over the long term. Proceeding from discovery to pre-clinical and clinical testing, DND*i* anticipates having 6 to 8 new treatments by 2014. Totally dependent on its ability to attract partners, DND*i* currently has more than 200 R&D partners from all sectors and from countries with endemic diseases, which have contributed $180 million to date (of an anticipated $330 million). Dr. Pécoul listed the challenges for these R&D efforts as follows:

- Attaining access to compounds and high-throughout screening
- Selecting and optimizing lead compounds for pre-clinical testing
- Developing clinical trial platforms in countries with endemic diseases
- Establishing high-quality clinical research programs
- Identifying biomarkers to support clinical research
- Ensuring availability, access, and rational use of treatments when implemented
- Strengthening regulatory capacities in countries with endemic diseases.

Non-governmental Efforts: The Wellcome Trust. Dr. Whitworth summarized the global health activities of the Wellcome Trust. He noted that the trust's strategy in global health is focused on low- and middle-income countries—to broaden the research base for scientific endeavor (i.e., capacity building), support areas of science that have potential to increase health benefits, and support networks and partnerships focused on the problems of these countries. The trust's major programs support core activities in centers, fellowships for researchers from developing countries, and strengthening of institutions and health education research. In the African Institutions Initiative, for example, the trust is funding consortia that involve 50 African institutions. To ensure that partnerships are equitable, the trust follows the 11 principles outlined by the Swiss Commission for Research Partnerships with Developing Countries. The Wellcome Trust also is involved in drug discovery and development through partnerships with industry and academia (e.g., to develop drugs for malaria and trypanosomiasis) and seed funding. Through other partnerships, the trust is supporting development of a platform for clinical trials in infectious diseases in Southeast Asia and, in India specifically, fellowships for Indian scientists, affordable health care products and devices, and affordable vaccines.

Foundations: The Bill & Melinda Gates Foundation. Dr. Yamada said that the large problem of global health is demonstrated by the fact that 9 million children under age 5 die each year unnecessarily. Given this, the commitment to global health is humanitarian at its core, even while it may be viewed as one of self-interest. Dr. Yamada emphasized that the world's investment in R&D for global health must be larger and must be supported by a broader base. Only about $3 billion of the $25 billion donated to global health each year is for R&D, and two donors—the U.S. Government, including the NIH, and the Gates Foundation—account for two-thirds of this amount. Investments in R&D are critical because technology-based health solutions (e.g., the measles vaccine) provide the best return of any investment in global health. Toward this end, the Gates Foundation tries to do what the NIH does not do in discovery, development, and delivery of therapeutics, including drugs and vaccines. The foundation can pursue a different strategy of starting with an endpoint (e.g., the Grand Challenges) and working toward the target through discussions and partnerships. The health needs that the foundation is currently grappling with, for example, include asphyxia in newborns, improved (e.g., pill-form) antidiarrheals, non-hormone-based contraception for pre-pubertal children, and nutrient assimilation in underweight children. In addition, the foundation works through PDPs and is currently supporting the development of 70 new chemical entities.

Dr. Yamada called for an "enterprise approach" to integrate and align R&D resources in global health so that organizations' activities are complementary and funding is not wasted. He particularly noted the need for increased investments to develop the pipeline of drugs and vaccines and to support clinical trials. He invited the NIH to focus its efforts in global health on the endpoints of research.

Discussion

Dr. Fineberg asked the panelists to clarify which activities the NIH should pursue. They identified the following:

- Establish effective partnerships with industry and other partners to achieve shared goals in global health *(Dr. Feinberg)*
- Continue strong support for basic research, as fundamental to the success of other initiatives in global health, and support drug discovery and development in broad PDPs *(Dr. Pécoul)*
- Increase support for clinical trials (e.g., through PDPs) on diseases unique to developing countries *(Dr. Yamada)*
- Strengthen research capacity in developing countries as a long-term solution *(Dr. Pécoul)*.

In discussion, the participants noted several additional points, as follows.

CONSORTIA TO EXPAND THE DONOR BASE. Global health researchers "need more to do more." For example, development of 60 new drug compounds will cost $1 billion per year for 10 years. Governments do not have the resources needed. The donor base needs to be expanded through consortia comprised of public and private entities. *(Dr. Freire)*

DEMONSTRATION OF SUCCESS. To elicit more resources, researchers must be able to demonstrate that they can deliver results. Emphasis should therefore be given to implementing existing technologies and interventions, to achieve results within 10 years. And, successes, such as the decreased mortality from measles in Africa, need to be published widely. *(Drs. Pécoul and Whitworth)*

NIH PARTNERSHIPS IN TRAINING AND PRODUCT DEVELOPMENT. The NIH needs to partner with other government agencies and industry to create innovative training programs in product development and to increase support for product development. *(Dr. Hotez)*

V. PRESENTATION – THE U.S. GLOBAL HEALTH INITIATIVE: FUNDING AND FRAMEWORK --*Ezekiel J. Emanuel, M.D., Ph.D.*


Dr. Ezekiel Emanuel (NIH and OMB)

Dr. Emanuel described the tremendous uptick in support for global health in recent years. Between 2000 and 2007, worldwide funding for global health doubled to almost $22 billion. He noted that the United States leads other nations in this funding and provided more than $6 billion in 2007, or nearly three times as much as any other country. These funds are allocated to both aid and research, and NIH support for global health research has increased accordingly.
Dr. Emanuel commented that the U.S. push in global health began with President Bush's initiatives, PEPFAR and the Presidential Malaria Initiative, and related programs. Between 2003 and 2008, the U.S. Government spent $27.5 billion on global health, of which $22 billion was devoted to PEPFAR and malaria. In the FY 2009 budget process, the Office of Management and Budget (OMB) acted on President Obama's commitment to enhance global health efforts, as a fundamental pillar of his Administration, in allocating $63 billion for the Global Health Initiative in FY 2009–2014. Of this total, $51 billion will be allocated to PEPFAR and malaria activities.

Dr. Emanuel emphasized that the Global Health Initiative is not simply more funding for global health, but, rather, includes enunciation of a new framework for global health. This framework has six pillars—to move (i) from emergency programs to sustainable programs; (ii) from a disease focus to an integrated approach involving funders at all levels and host countries; (iii) from process outcomes (e.g., number of people treated) to substantive outcomes (e.g., number of lives saved); (iv) toward efficiencies and more "bang for the buck"; (v) from reports to true accountability; and (vi) to integrate training as critical to the strengthening of health care systems. In this drive to improve global health, three key issues are:

- Shared responsibilities and partnerships with multilateral organizations
- Implementation of interventions that work (e.g., vaccination of children, prevention of malaria)
- Outcomes and sustainability.

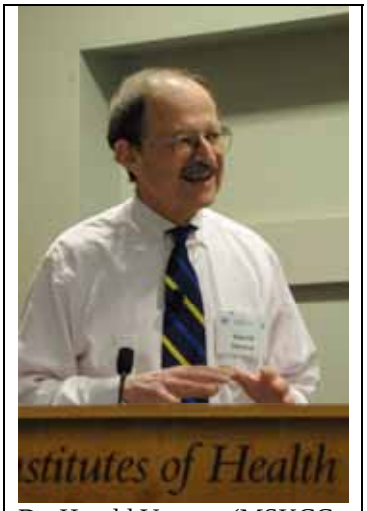
Dr. Emanuel said that research and innovation have been integral to the effort from the beginning. Illustrative areas of the research needed include (i) development of vaccines and inexpensive, efficient, and rapid diagnostics for malaria; (ii) development of vaccines for other endemic diseases; (iii) development and implementation of interventions for neglected tropical diseases; and (iv) interventions to achieve clean water and good sanitation and hygiene. Clearly, the needs cover the spectrum of research and include epidemiology, drug development, diagnostics, and interventions. Oversight and regulation of research will be important to ensure that the research adheres to international ethical standards.

Dr. Emanuel noted the need for integration of activities across U.S. agencies, and he commented that, given the priority the President places on the Global Health Initiative, fulfilling this initiative is an important priority for the NIH.

IV. RESEARCH OPPORTUNITIES

Dr. Collins introduced a series of discussions of R&D opportunities in global health. The discussions were led by moderators, and the participants posed specific opportunities in five areas: fundamental science, epidemiology and populations, diagnostics, therapeutics (drugs and vaccines), and capacity building and training.

FUNDAMENTAL SCIENCE--*Moderator: Harold E. Varmus, M.D., M.A.*



Dr. Harold Varmus (MSKCC and PCAST)

Dr. Varmus commented that the nation's attitude toward global health has reached a magical moment—as evident by the Global Health Initiative, dedicated financing by the OMB, commitments by the President, and interest of the President's Advisory Committee on Science and Technology in using science and technology in diplomacy. He noted the difficulty of delimiting the boundaries of fundamental science, and he suggested that fundamental science could be defined as trying to understand what is going on—be it a disease process or normal physiology, the functioning of health systems, or implementation and delivery of health methods.

Dr. Varmus emphasized the importance of capacity building to stimulate fundamental science globally. He highlighted two aspects not previously mentioned: (i) moving highly trained and experienced individuals from advanced economies to work in poor countries, and (ii) making better use of the Internet, for example, to create digital public libraries, publish in open-access mode, evaluate research findings post-publication, and create interactive scientific communities. He cited the Malaria Research and Training Center in Bamako, Mali, as an example of a very successful U.S. Government-supported effort with long-term benefits at many levels. Dr. Varmus cautioned that while the NIH can draw on many mechanisms of support to build capacity, its budget is limited and is unlikely to increase dramatically over the next 2 years.

In discussion, the participants suggested the following research opportunities in fundamental science.

SUPPORT PSYCHOLOGICAL, BEHAVIORAL, AND SOCIAL INTERVENTIONS. This research, addressing the range of conditions affecting people worldwide, would include, for example, evaluation of (i) health effects of social interventions such as microfinancing, which has been shown to empower women and reduce maternal and neonatal mortality, and (ii) in-country, traditional ways of addressing and treating psychological and behavioral conditions. *(Dr. Patel)*

INTEGRATE HEALTH DISPARITIES RESEARCH WITH DELIVERY OF CARE. This research, to integrate the science of health disparities with delivery of care in communities, would acknowledge that urban health is essential to global health. It would include biobehavioral research, from animal models to populations, and use of systems biology in the global context. *(Dr. Olopade)*

SEEK EQUITY IN NIH RESEARCH SUPPORT. Solutions are needed that are affordable and appropriate globally—that is, beyond the domestic context. In other words, "how will it play in Peoria, or Jakarta?" *(Dr. Whitworth)*

UNDERSTAND THE BIOLOGY OF PATHOGENS AND VECTORS. Understanding the biology of pathogens and vectors, particularly those for tuberculosis, should be a high priority. Development of effective treatments for tuberculosis depends on understanding the genetics and machinery of the bacterium. Large biobanks in China and the United Kingdom, which link samples to identification records, could be important resources for this research. *(Dr. Peto)*

BETTER UNDERSTAND GENE–ENVIRONMENT INTERACTIONS. These interactions need to be better understood in different diseases, such as asthma and cancer. *(Dr. Olopade)*

SUPPORT STUDIES OF NUTRITION, FOOD, AND HUNGER. Nutrition (and biofortification) are relevant to susceptibility to and reduction of chronic and other diseases. Climate change may relate to these factors and potentially affect disease vectors and the emergence of new risks in new locales. *(Dr. Tutwiler)*

ENHANCE TRAINING IN ZOONOTIC DISEASE AND VECTOR BIOLOGY. The NIH could reach out to the broader research community to enhance capacity and training in these two areas, which also link with climate change. *(Dr. Ewart)*

ASSESS THE EFFECTS OF CHANGING ENVIRONMENTS. The broadly changing environments in low- and middle-income countries have implications for global health. Changes relate not only to climate, but also, for example, to economic development, energy, transportation, and agriculture. *(Dr. Birx)*

STRENGTHEN HEALTH RESEARCH SYSTEMS. Interventions are needed to strengthen health research systems. The research would address regulatory frameworks, health research financing, production of knowledge through individual and institutional training, and globalization of research communities. *(Dr. Frenk)*

SUPPORT REGULATORY SCIENCE. Research is needed to develop knowledge and tools to enable effective and efficient evaluation of safety, efficacy, quality, performance, and potency. This knowledge base is important for implementation of interventions and drug development, and the research is not being funded currently. *(Dr. Hamburg)*

TARGET TRAINING. Training in the United States and developing countries is needed for both U.S. and developing-country scientists. This training would best be provided through mentorship programs that target specific expertise and needs in countries. The level of support needed is more than twice that available currently. *(Dr. Volkow)*

CREATE A CONSORTIUM FOR BUILDING CAPACITY GLOBALLY. A bold initiative for the NIH would be to create a consortium of research leaders in several countries to focus on the building of capacity in a research area (e.g., genomics) in these countries. *(Drs. Frenk and Varmus)*

CONTINUE AND EXPAND THE INTERNATIONAL CENTERS FOR INFECTIOUS DISEASES RESEARCH (ICIDRS). The NIH should continue and expand, by twofold, the very effective ICIDR initiative. *(Dr. Hotez)*

REPLICATE NIH CLINICAL RESEARCH TRAINING PROGRAMS. NIH could replicate its clinical research training programs (e.g., Principles of Clinical Research, Bioethics, Translational Oncology Research) in developing countries. China already has replicated programs in collaboration with the NIH Clinical Center, to train 1,500 physicians, and now has pilot programs offered via the Internet, for which 6,000 physicians have signed up. *(Dr. Shi)*

EPIDEMIOLOGY/POPULATIONS--*Moderator: Barry R. Bloom, Ph.D.*


Dr. Barry Bloom (HSPH)

Dr. Bloom proposed that the discussion of research opportunities related to epidemiology and populations focus on (i) new or emerging population-based problems or research areas that NIH could or should be addressing, (ii) new or emerging areas of knowledge where population-based research would be informative, and (iii) existing areas of research that should be extended to populations in developing countries. For perspective, he noted that approximately 0.3 percent of the $3.4 trillion Federal budget request for FY 2010 is directed to the Global Health Initiative and that most (64 percent) of the proposed funding for the initiative in FY 2010 is for HIV/AIDS activities. He also noted that, in FY 2004–2005, most (69 percent) of NIH's foreign research dollars went to scientists in OECD and high-income countries, while approximately 11.6 percent went to researchers in sub-Saharan Africa and only 1.6 percent went to investigators in Latin America.

Dr. Bloom stated the four-part paradigm for public health—define the problem, identify disease risks, design interventions, and evaluate outcomes. He defined the problem as four research opportunities for NIH:

- Acute and communicable diseases (the unfinished agenda)—specifically, emerging and persistent infections, maternal and infant mortality, and early childhood infections
- Chronic and non-communicable diseases (the coming epidemic)—for example, obesity, diabetes, cardiovascular diseases, neuropsychiatric diseases, and HIV/AIDS
- Surveillance and health information systems—to assess the burden of chronic and infectious diseases
- New technological advances—for example, rapid point-of-care diagnostics and treatment, biomarkers, and assessment of drugs and vaccines.

Dr. Bloom commented that the opportunities for identifying disease risks lie in linking intrinsic risks (e.g., genetic risks, causal mechanisms) with extrinsic risks (e.g., environmental, epidemiological associations). A variety of population-based strategies are available for this research and include observational and cohort studies, genome-wide association studies, randomized control trials, nested control studies, and modeling.

Dr. Bloom proposed two specific opportunities for the NIH:

- Creation of an African genetic/epidemiological cohort

  The rationale for this effort is twofold: Africa represents the greatest source of genetic polymorphisms in the world, and establishment and study of such a cohort would have a significant impact on global health. With regard to the latter, the NIH would have an opportunity to create an African scientific network around a coherent, long-term, multidisciplinary effort, and the sub-Saharan region has the greatest need for building research capacity and strengthening leadership. One limitation is that, traditionally, the NIH has had limited mechanisms for funding multi-disease, cross-IC projects. Support could be provided through the Common Fund.

- Development of expertise in global health systems research

  The NIH could be the best place for development of this expertise, for health systems are complicated structurally, consisting of many components, and NIH has the necessary analytical and research capability. The agenda would include development of capacity for implementation research (including the consolidation of platforms for multiple disease intervention programs), improving the process of health care delivery, translational and clinical research, and analysis and evaluation of complex interventions. Other activities would include engaging the private sector, building capacity in science administration, and leadership training for government officials.

In discussion, the participants suggested the following research opportunities related to epidemiology and populations.

SUPPORT BEHAVIORAL RESEARCH. Revisiting behavioral questions in interventions of behavioral change, to establish external validity and applicability to more one setting, is worthwhile. This

research is separate from implementation research on, for example, adoption and delivery of vaccines or drugs. *(Dr. Laxminarayan)*

INVEST IN COMMUNITY-BASED PARTICIPATORY RESEARCH. Involvement of communities fosters ownership of the research and capacity building. *(Dr. Olopade)*

EMPHASIZE MEDICAL ANTHROPOLOGY AND BIOSOCIAL ASPECTS. Medical anthropologists need to be involved in trans-disciplinary population research from the beginning to ensure that interventions are culturally appropriate and acceptable. Medical anthropology is increasingly important in global health insofar as all disease problems (e.g., drug resistance, nosocomial outbreaks) are biosocial problems. The NIH should require that population or global health research projects include biosocial methodologies. *(Drs. Olopade and Farmer)*

SUPPORT COMPARATIVE COST-EFFECTIVENESS RESEARCH. Support of this research in areas of significant concordance between domestic priorities and global health (e.g., hospital infections, drug resistance) might be helpful. *(Dr. Laxminarayan)*

PROMOTE MATHEMATICAL MODELING. Developing countries share in the demand for information on how to respond optimally to pandemic threats, for example, but have little capacity for the research needed. Modeling of these potentialities is a global public good and could be accomplished through networks involving partners in developing countries. *(Drs. Laxminarayan and. Bloom)*

EXPLORE NEW TECHNOLOGIES FOR IMPLEMENTATION. New technologies offer new possibilities for implementation that need to be explored. For example, use of cell phones could be integral in setting up population-based epidemiology and surveillance systems in developing countries. *(Drs. Insel and Bloom)*

PURSUE A UNIFIED APPROACH TO GLOBAL HEALTH. The NIH does not have a national institute of public, or global, health. Research that needs to be addressed in a unified way and is critical to the NIH research mission in the long term includes, for example, identification of inexpensive ways to obtain vital statistics, adaptation of leapfrog technology (e.g., "mobile" health), creation of population-based laboratories, and health services research. *(Dr. Glass)*

BETTER USE POPULATION COHORTS. The NIH invests significantly in research involving population cohorts, but data from this research could be better used internationally. The NIH could be more aggressive in creating a publicly available database of information from longitudinal cohorts that researchers could access for trans-disease analyses. *(Dr. Barker)*

IMPROVE ACCURACY OF MORTALITY DATA. Being able to "count the dead" accurately is essential. Better methods are needed to understand, determine, and document cause of death internationally. Monitoring a properly random sample carefully is more valid than trying to monitor an entire country inadequately. *(Drs. Evans and Peto)*

RELATE VITAL STATISTICS TO IMPACT. Vital statistics for pediatric and adult populations need to be collected in such a way that they are applicable to measuring the impact of health interventions. *(Dr. Birx)*

ADDRESS MULTI-MORBIDITY. Cohort studies of populations with multiple conditions are needed to improve understanding of multi-morbidity. To assure appropriate sample sizes, these studies could be pursued through multi-country research collaborations. Platforms are needed within health systems to attend to the multiplicity of chronic and acute diseases, particularly in elderly populations. *(Drs. Evans and Bloom)*

SUPPORT LONGITUDINAL STUDIES OF BIOSOCIAL TRENDS, RISK, AND OUTCOMES. Longitudinal cohorts yield enormous fundamental data for understanding trends. A number of centers could collaborate to study genetic, serological, and social indicators in a globally defined longitudinal cohort to understand differential risk across countries. *(Dr. Evans)*

DEVELOP REGIONAL INFRASTRUCTURES. Such infrastructures would allow for basic research and research training within large-scale population cohort studies to address multiple questions and to understand the epidemiology of complex diseases. The effort would facilitate establishment of consortia and attraction of additional infrastructure. *(Dr. Rotimi)*

IMPROVE LINKAGES AMONG PARTNERS. The gap in implementation science is largely one of a dislink among academic and public health institutions and ministries of health and between implementers and researchers in-country. Dramatic improvements could be gained by bringing together all HHS partners that are involved in global health "on the ground." *(Dr. Birx)*

ASSURE ACCESS TO AVAILABLE RESOURCES: BIOBANKS. Researchers now have an opportunity to use large, national biobanks in China and the United Kingdom to relate treatments to conditions and to clarify genetic predispositions. *(Dr. Peto)*

DIAGNOSTICS--*Moderator: Maria C. Freire, Ph.D.*

Dr. Maria Freire (Albert & Mary Lasker Foundation)

Dr. Freire approached the topic of diagnostics from a pragmatic perspective, viewing diagnostics as a tool. She characterized the field of diagnostics, saying that:

- Diagnostics for diseases of poverty have not been a priority for the private sector.
- Techniques for detecting most diseases in developing countries are inadequate or nonexistent (e.g., tuberculosis).
- Both traditional and new players are involved in the development of diagnostics.
- The needs span the spectrum from basic research to implementation.
- Diagnostics involve ethical, as well as technical, issues.

Dr. Freire noted that the goal is to have accurate, robust, and rapid diagnostics as near as possible to where patients seek care. The purpose is to avoid complications from treatable conditions, help determine appropriate levels of care and effective/efficient treatments, and protect patients and their communities. An ideal diagnostic would have exquisite sensitivity, be inexpensive to produce and portable, not require additional accessories, be energy efficient or independent and intuitive, and not require extensive training or technical knowledge.

What is needed? Dr. Freire cited the need to implement existing technologies; develop sustainable, improved diagnostics; and introduce innovative technologies with new business models, to take advantage of the most sophisticated and easily adopted technologies and implement them in the field. She highlighted three areas of research opportunity:

- Biomarkers and surrogate markers
- Multidisciplinary research, including biomedical engineering and bioimaging
- Regulatory hurdles for diagnostics.

Dr. Freire noted that research on diagnostics could have a direct impact on global health in the short term. She encouraged the partners in the field, including the FDA and CDC, to shorten the timeline for moving new diagnostics into the field to 2–3 years.

In discussion, the participants suggested the following opportunities for research on diagnostics.

IMPROVE REGULATION OF DIAGNOSTICS. This topic is highly visible, challenging, and difficult to address. The role of the FDA is essential for assuring the quality and value of a product. Regulation will become increasingly important and issues will become more focused as global health moves toward personalized medicine in the era of genomics. *(Dr. Hamburg)*

COLLABORATE WITH INDUSTRY. Better ways are needed to encourage industry to collaborate with academe and government to identify critical gaps in the needs for diagnostics and the best ways to leverage advancing science and technology to improve the quality of diagnostics. The NIH Small Business Innovation Research (SBIR) program could support partnerships with small companies in the United States and other countries to develop diagnostics. Small businesses would respond if they perceive a market and an interested consortium. Many of the principles of engagement with the for-profit sector are similar for drugs, vaccines, or diagnostics. Successful partnerships have brought forward lower-cost, near-point-of-care diagnostics for other diseases (e.g., human papilloma virus). *(Drs. Hamburg, Alving, and Feinberg)*

ADOPT A STRATEGIC APPROACH. The development and implementation of diagnostics has a life cycle that warrants a strategic approach with continual evaluations. Integration and coordination of many different components is at the core of the strategy, not unlike a defense research project. The Bill & Melinda Gates Foundation will soon announce a Grand Challenges program to establish platforms that could be used for diagnostics in multiple diseases. Other efforts are under way to gain industry and academic agreement on best standards for products that could be applied at point of care. Significant investments are being made in a wide range of technologies, but the problem is larger and more difficult than many might think. Technology is not

necessarily the issue; one issue is to define the purpose of a diagnostic—that is, is it to monitor or diagnose a disease, or recurrence of a disease? *(Drs. Alving, Collins, Yamada, and Barker).*

CHANGE THE DYNAMIC. The NIH has an opportunity to define what it can do to change the dynamic in the development of diagnostics and to make a difference. The NIH should stimulate collaborations and partnerships among biologists, epidemiologists, clinical scientists, and biophysicists and other scientists pursuing relevant technologies. As with the Human Genome Project, getting the right disciplines to learn to talk with each other may be one of the biggest barriers. *(Drs. Feinberg and Collins)*

INVOLVE END USERS. Engaging the broad community, including partners from countries with endemic disease, will be important. End users must be engaged early in developing the business models, thinking about anthropological issues, designing and developing diagnostics, and even investing in the technology. *(Drs. Barker, Freire, and Daar)*

ESTABLISH SITES FOR COMPARATIVE TESTING. Given the need to know which diagnostics are most effective and sensitive and the rapidly changing science, sites with well-characterized patients need to be established to comparatively test diagnostics for a variety of diseases in developing countries. For example, there are approximately 120 different point-of-care diagnostics for malaria, and this is a success story, but analysis of the predictive values of these diagnostics indicates that only about a dozen are in the range of acceptability. *(Drs. Bloom and Yamada)*

DEVELOP TECHNOLOGIES FOR ONGOING MONITORING. The NIH could address the gap in research on technologies for ongoing monitoring of point-of-care diagnostics. This would include includes technologies for monitoring and managing individual and population resistance to drugs for chronic and non-communicable diseases. *(Dr. Plumley)*

DEVELOP DIAGNOSTICS FOR TUBERCULOSIS. Development of point-of-care diagnostics for tuberculosis is a priority and is doable within perhaps 3–5 years. As with other diseases of importance in global health, the HIV/AIDS experience provides a model. The Bill & Melinda Gates Foundation has invested in a product-development partnership (FIND) that is largely focused on diagnostics for tuberculosis. A multipronged approach is focused on the technology and the measure (e.g., biomarkers). Related to this, the FDA is looking at qualifying biomarkers in an aim to distinguish between biomarkers and diagnostics. *(Drs. Fauci, Yamada, and Barker)*

DEVELOP DIAGNOSTICS FOR PARASITIC INFECTIONS. Because of the unavailability of diagnostics, not much is known about parasitic infections, which are prevalent in the United States among Hispanic Americans and African Americans. More efforts are needed to develop diagnostics for these infections, which are truly a global health problem and a significant health disparity in the United States. *(Dr. Hotez)*

THERAPEUTICS—DRUGS AND VACCINES--*Moderator: B. Tore Godal, M.D., Ph.D.*


Dr. Tore Godal (Ministry of Foreign Affairs, Norway)

Dr. Godal drew on his experiences in downstream implementation of research to consider upstream research activities. He emphasized six points for research on therapeutics:

- Know the disease burden—that is, assure that the burden of disease has been measured appropriately, and prepare for advocacy and decision-making.
- Establish that a therapeutic works—randomized, controlled trials in the countries or regions where a therapeutic will be introduced are preferable to extrapolating from evidence gained in other countries.
- Ensure affordable pricing of a therapeutic—less than $1 per vaccination is reasonable for low-income countries. Securing production and product at the lowest possible price is very important in developing countries, as are donations of therapeutics.
- Assess "downstream" effects vis-à-vis implementation and coverage of therapeutics. For example, combination vaccines may yield higher coverage than single vaccines.
- Consider why oral attenuated vaccines are not effective in socioeconomically deprived populations. This problem is significant, for example, in vaccines for rotovirus.
- Better understand the role of adjuvants in the effectiveness of vaccines.

Dr. Godal noted that 100,000 deaths serves as a cutoff point for mobilizing broad-based introduction of a vaccine. He suggested that the NIH should therefore focus on the "big 3" priorities in therapeutics—that is, therapeutics for HIV/AIDS, malaria, and tuberculosis and, possibly, diarrheal diseases.

In discussion, the participants suggested the following research opportunities in therapeutics.

PRIORITIZE NEEDS. The needs for development of drugs and vaccines should be prioritized in a rational way. Reasonable parameters would include the following: (i) Is a therapeutic available that works well and is inexpensive and for which research would address distribution and delivery? (ii) How many individuals are affected and how severe is the disease? (iii) Is there a special scientific opportunity to pursue (e.g., new understanding about a particular pathogen)? *(Dr. Collins)*

ADAPT AND REFINE METHODOLOGIES FOR PRIORITIZATION. The prioritization of new vaccine targets, which is published periodically by the Institute of Medicine (IOM) and in *The Jordan Report*, could be refined to focus more on diseases relevant to global health. Other possibilities include revisiting and updating (a) the methodology used for two reports on vaccine priorities in the developed and developing world that were published in the late 1990s; (b) a matrix used by

The Wellcome Trust approximately 5 years to prioritize interventions for neglected diseases; and (c) the "best buys" reported by the Disease Control Priorities Project approximately 3 years ago. Caution is needed as existing methodologies for defining priorities (e.g., that used by the World Health Organization) and available data on incidence and prevalence of disease may have limitations. *(Drs. Feinberg, Fineberg, Whitworth, Glass, and Pécoul)*

ADDRESS OVERALL PRIORITIES FOR DRUG AND VACCINE DEVELOPMENT. A broad understanding is needed of disease priorities (based on both disease burden and potential public health impact of a vaccine or drug), scientific opportunities that would guide the NIH investment, and scientific and practical barriers to drug and vaccine development (e.g., need for epidemiology and expertise in clinical studies). Additional aspects that need to be addressed include the role of regulatory authorities and barriers in facilitating development effectively and how the NIH investment would be integrated into the global health priorities of the U.S. Government. *(Dr. Feinberg)*

INVEST IN BASIC SCIENCE TO UNDERPIN VACCINE DEVELOPMENT. The challenge in vaccine development is the science. The NIH can best invest in (i) understanding the basic biological machinery of organisms and finding ways to attack them, and (ii) the science of vaccinology. The latter would include pursuing opportunities in reverse vaccinology, correlates of protection, assay development, and potency testing. In addition, the NIH could pursue (iii) cutting-edge approaches in engineered immunity, and (iv) humanized animal models for testing vaccines. *(Drs. Mahmoud, Hotez, and Daar)*

LAUNCH A RANDOMIZED TRIAL OF HPV AND HBV VACCINES. Two interventions that are available and could be tested now in a randomized controlled trial are HPV and HBV vaccines, singly and in combination during infancy. *(Dr. Peto)*

FORMULATE A POLYPILL FOR VASCULAR DISEASE. Generic drugs are available for primary and secondary prevention of risk factors for cardiovascular diseases. They need to be formulated into a single pill that could be provided at low cost and used routinely for secondary prevention in individuals seeking treatment. This intervention could reduce their risk of recurrent diseases over the next 10 years from one-half to one-sixth and would have an appreciable impact on morbidity in middle age. (A trial using a polypill for primary prevention is under way in India.) *(Drs. Peto and Daar)*

CAPACITY BUILDING AND TRAINING--*Moderator: Ambassador Eric Goosby, M.D.*

Ambassador Eric Goosby (Office of Global AIDS Coordinator, U. S. Department of State and PEPFAR)

Ambassador Goosby commented on the opportunities afforded by PEPFAR and the Global Health Initiative. He said that the PEPFAR programs yield an opportunity to benefit from the knowledge and data gained and the machinery of discovery set in place, and he suggested that proceeding forward with implementation will depend on better crystallizing the ability to use PEPFAR findings, shortening the timeframe from discovery to application, and better ensuring the application of discoveries. He noted that the Global Health Initiative offers an opportunity to aggregate or converge commitments of vertical funding so that providers at different levels are not confounded, limited, or precluded from applying these resources to the diagnosis, treatment, and care of patients.

Ambassador Goosby suggested that the NIH could collaborate with others to pursue the following areas of opportunity:

- Better define the strengthening of health systems—for example, to identify, enroll, and retain patients in care; to prevent and treat disease; to translate basic findings into interventions.
- Identify and integrate efficiencies in potential synergies and partnerships within existing portfolios and expenditures.
- Move expectations in the global community to include shared responsibility among partner countries.
- Foster country ownership of programs through long-term mentoring relationships.
- Address the deficit of health care workers and identify outcomes that would yield a complete system for delivering medical care.
- Incorporate anthropological methodologies into the collective research effort to ensure that programs are relevant and continue to identify, enroll, and retain patients in care.
- Better define the need and place for translational and operational research within NIH research support.
- Develop and employ metrics to measure and act on progress in the above areas.

In discussion, the participants suggested the following opportunities for NIH-supported capacity building and training.

PROVIDE NIH TRAINING GRANTS FOR GLOBAL HEALTH STUDIES. NIH research training support is needed for the large and increasing number of medical and university students seeking global health careers or an international experience in health. At Brigham and Women's Hospital, for example, the training of residents in global health is solely funded by philanthropy. *(Dr. Hiatt)*

SEEK RECIPROCAL SUPPORT FROM INTERNATIONAL PARTNERS. The potential for engaging partner countries to support training of students and faculty in global health research needs to be explored. Reciprocity between partners would foster equity. PEPFAR has generated brisk, formal, and reciprocal bilateral exchanges between medical schools in developing countries and the United States which the NIH could help support. The presidents of universities participating in the recently formed Consortium of Universities for Global Health have agreed to commit university resources to enable students and faculty members to pursue interests in global health. The concerns are about who pays for U.S. participants to train abroad, and who pays for foreign participants to train in the United States? *(Drs. Olopade, Farmer, and Quinn)*

ENSURE THAT CAPACITY BUILDING AND TRAINING ARE EQUITABLE. As U.S. and European students come to developing countries for training, a difficult question often emerges concerning the benefit of these efforts to partners and institutions in these countries. The possibility of students paying a fee to the institutions in developing countries should be considered in this regard. In addition, it must be recognized that (a) students and institutions in developing countries are generally unable to pay for training in the United States and (b) the training they receive is limited to observation, rather than hands-on training, in contrast with the training that is offered to U.S. students in developing countries. *(Dr. Sewankambo)*

USE CENTER GRANTS TO SUPPORT INFRASTRUCTURE DEVELOPMENT. One of the best investments NIH could make in global health is to offer center grants along with training grants to support the development of infrastructure (e.g., laboratories, information technology, and research administration) for partnerships between the best scientists in the United States and those in developing countries. Existing NIAID networks could be expanded to help build these research capacities. Two models of successful long-term support for capacity building are FIC's AIDS International Training and Research Program (AITRP) and the United Kingdom's MRC program. *(Dr. Quinn)*

INTEGRATE NIH EFFORTS WITH PEPFAR AND CDC ACTIVITIES. The NIH should partner with PEPFAR and the CDC to achieve more meaningful outcomes on the ground to improve global health. *(Dr. Quinn)*

VII. WHERE DO WE GO FROM HERE?--*Francis S. Collins, M.D., Ph.D.*


NIH Global Health Research Meeting

Dr. Collins summarized the points made during the discussions and asked the participants to reflect on the highest priorities for NIH investments in global health research (i.e., "if you were the NIH director, what single global health program would be a top priority?"). He posed three criteria: the program must not be illegal, must fit within the NIH mission, and must be specific and able to be evaluated in terms of success or failure.

Dr. Collins' summary points of possible areas for

additional NIH investment are listed in Appendix 1. The participants' reflections on the highest priorities are grouped below into six priority areas for the NIH:

- Define and communicate the NIH role in global health research
- Foster capacity building and training
- Stimulate partnerships and collaborations
- Support establishment of centers of excellence and regional networks
- Focus on priority research areas
- Assure open access to data.

The participants' specific suggestions are detailed below for each priority area.

DEFINE AND COMMUNICATE THE NIH ROLE IN GLOBAL HEALTH RESEARCH

- Pursue more deliberate discussions over a longer timeframe (similar to that embraced in developing the Grant Challenges) to define the NIH role in global health research and to delineate how and where NIH can best put its efforts to help resolve diseases and burdens of disease in developing countries. Engage all ICs in these deliberations, and begin with first principles by defining and communicating within and outside NIH how NIH will engage and have a special role in global health and interface and work effectively with other groups. The definition of a philosophy will help to facilitate prioritization across the NIH research portfolio to achieve the greatest impact and meet the greatest need in global health. *(Drs. Varmus, Makgoba, and Feinberg)*

- Tag NIH leadership and research to the Global Health Initiative. NIH has a specific, enormous opportunity to lead global health action and gain momentum and support from different countries for global health R&D by defining the relationship of this research to the Global Health Initiative and then promoting this relationship together or in tandem through advocacy, engagement, and commitment from other countries. Three principles define the "different way of doing business" in this initiative: multilateralism, coordination within the U.S. Government, and true partnerships with countries. It should be noted that President Obama and the Prime Minister of Norway recently agreed to efforts related to (i) maternal and child health and (ii) the health system. *(Drs. Godal, Phillips, and Monahan)*

- Communicate health as diplomacy. As NIH director, Dr. Collins can have an important role in communicating to the Congress that health is global and is a very important diplomatic tool for the United States and developing countries. *(Dr. Sebbag)*

- Publicize NIH's contributions to biomedical research in global health. The NIH has made much progress, but the message has not gotten out. Use the platform of the NIH director to make this possible. For example, summarize NIH's contributions in an article for *Science* and, even, the *New York Times* or *Wall Street Journal*. *(Dr. Bloom)*

- Galvanize others into action and raise awareness about global health. The NIH has not only a convening power, but also a galvanizing power with which to elicit action from its partners that also bear appropriate roles in global health. Enlist a recognized spokesperson to relay the importance of global health to the American public. *(Drs. Freire and Agre)*

- *Secure funding*. Now is the time to issue a "call to arms" to secure sufficient, long-term funding to meet the needs for global health research. *(Dr. Freire)*

FOSTER CAPACITY BUILDING AND TRAINING

- Identify the needs for capacity building and training in partnership with others and address them specifically in different contexts. *(Dr. Varmus)*

- Expand funding and capacity building for translational medicine and development of therapeutics (drugs and vaccines) in developing countries. Being readily able to test new drugs and interventions (e.g., for malaria, tuberculosis) depends on in-country capacity in translational medicine. *(Drs. Pécoul and Cammack)*

- Establish pre- and postdoctoral training programs in appropriate technologies for global health—development of drugs, vaccines, and diagnostics, and design of low-cost, maximally efficient, broadly accessible interventions. *(Dr. Hotez)*

- Support U.S. and international training in implementation science and regulatory science as part of the continuum of global health R&D. *(Dr. Jones)*

- Link health and disease to poverty reduction and nation building. Disease control and disease technologies have a broader impact than health and need to be linked with critical poverty-reduction and nation-building measures. New programs in training and policy development focused on this end need to be developed in partnership with other agencies, such as the Department of State and intelligence agencies. *(Dr. Hotez)*

- Build capacity for understanding the needs and impact of global health R&D among leaders and policymakers in developing countries. The socioeconomic impact of health and the value of research need to be communicated to in-country administrators to garner support for public and private sector involvement in global health research. *(Dr. Shurin)*

STIMULATE PARTNERSHIPS AND COLLABORATIONS

- Pursue effective partnerships. To design, finance, and implement global health programs, NIH should explore partnerships with U.S. universities and centers of excellence in combination with counterparts in the developing world. *(Dr. Phillips)*

- Catalyze broad scientific partnerships. By virtue of its size and scientific weight, the NIH can serve as an intentional catalyst to bring together broad scientific partnerships, rather than just ad hoc collaborations. For example, broad partnerships that transcend the NIH

to include other U.S. Government agencies, non-governmental organizations, industry, academia, and institutions in developing countries are needed to progress in the development of diagnostics, therapeutics, and vaccines. The recently completed HIV vaccine trial conducted in Thailand by NIAID is an example of such a successful partnership. *(Dr. Kester)*

- Seek partnerships with industry. The NIH research capability is essential, but development of products cannot be done without industry. The NIH should seek collaborations with industry, particularly with companies that have already formed institutes for global health, to develop diagnostics, therapeutics, and vaccines for the "big four"—HIV/AIDS, malaria, tuberculosis, and neglected tropical diseases. *(Dr. Fauci)*

- Marry translational research and global health through public partnerships. Invest in products, but not only with the private sector. The public partnership model adopted by the CDC has been extraordinarily effective in development of medications. *(Dr. Volkow)*

- Emphasize partnerships for sustainability. Long-term institutional partnerships are essential for gaining long-term effects. For example, the 20-year U.S. Department of Agriculture partnership in India engendered an entire system of agricultural research in India. *(Dr. Jones)*

- Support portfolio projects in research partnerships. In order for the NIH to pursue PDPs, mechanisms will be needed to support portfolio projects, rather than individual scientific projects. *(Dr. Pécoul)*

- Directly fund institutions in developing countries. Partnerships in the 21st century must give control to institutions in developing countries. NIH funds should be given directly to these institutions, which would then find partners in industrialized countries, rather than to U.S. or other industrialized institutions, to find partners in developing countries. *(Dr. Fineberg)*

- Organize a consultative group on global health research. With its convening power, NIH could organize a consultative group on global health research (similar to the effective Consultative Group on International Agricultural Research) to foster research collaborations. *(Dr. Laxminarayan)*

- Find ways to support engagement of ministries of health in global health research, training, and implementation. Supporting the public health sector in poor countries lays the foundation for global health programs. *(Dr. Farmer)*

SUPPORT ESTABLISHMENT OF CENTERS OF EXCELLENCE AND REGIONAL NETWORKS

- Invest in research centers of excellence. NIH should support establishment of centers of excellence to bring together a critical mass of scientists to drive research on specific questions. By building up research infrastructures and personnel in multidisciplinary centers of excellence in developing countries, NIH can achieve a multiplier effect such

that well-trained, young investigators could focus on multiple, specific diseases endemic in their countries and pursue NIH-supported research grant applications. The International Centers of Excellence in Research (ICERs) in Mali and Uganda are two model sites. Centers such as these would facilitate long-term research on large population cohorts. Consideration should be given to directly funding these institutions as a measure of true reciprocity. *(Drs. Rotimi, Quinn, and Cammack)*

- Incorporate capacity building and training in centers of excellence. Few U.S. investigators work in global health fields other than infectious diseases. Training needs to be provided through centers of excellence in developing countries. For example, the ICIDRs could be expanded to include research and training in other fields. *(Dr. Glass)*

- Establish a center of excellence in Africa for the Human Genome Consortium project. This center would link cross-cutting issues in global health, from fundamental science to public health. *(Dr. Makgoba)*

- Support a network of demographic surveillance sites. The NIH might consider supporting INDEPTH, a South-driven network of 20-some demographic surveillance sites throughout Africa and Asia. These sites are collecting longitudinal information and are highly committed to capacity building. The sites and data could serve as platforms for genetic studies, clinical trials, and sharing of data (which is especially needed in epidemiology and population sciences) among developing countries in the regions. The potential of this network has not been fully realized because of the lack of long-term, committed funding. (*Dr. Whitworth)*

- Establish biobanks. Capacity building to facilitate personalized medicine must take place in developing countries in parallel with efforts in Western countries. The NIH could support establishment of a series of biobanks connected across developing regions and countries (e.g., in Asia and Latin America, India) to enable difficult and extensive patient studies. *(Dr. Barker)*

FOCUS ON PRIORITY AREAS

- Build on successes. The NIH has achieved much success in global health R&D over the years and it should not be afraid to build on (i.e., expand, amplify) its successful efforts. *(Drs. Fineberg and Feinberg)*

- Fill research gaps. The NIH needs to be open-minded about the types of research it pursues and to engage in whatever research is needed to fill gaps between the need for and delivery of global health care. For example, the NIH might support research to obtain basic knowledge, develop products, improve delivery, and/or inform policymakers. *(Dr. Fineberg)*

- Integrate global health needs with translational medicine. The NIH should take the lead to institutionalize the movement of basic research findings into implementation and

delivery. By doing so, the NIH can ensure that significant findings are automatically rolled into the health care delivery system. *(Prof. Liu and Ambassador Goosby)*

- Do what can already be done. To have effect within the next decade, NIH needs to focus on translating existing knowledge into delivery of care. Two examples are:

  - Maternal and child survival. Improving these outcomes can be done now.
  - Randomized trial using antiretroviral drugs for hepatitis B and C. NIH could undertake a low-level randomized control trial (perhaps in China) to test whether antiretroviral drugs can cure individuals chronically infected with hepatitis B or C virus. Even if for only a small proportion of a population, these drugs could be a very cost-effective treatment for young adults. *(Dr. Peto)*

- Continue funding for genome studies. NIH needs to continue support for basic and applied genome studies (e.g., genome-wide association assays) to answer global health research questions pertinent to developing countries. *(Dr. Rotimi)*

- Globalize the Human Microbiome Project. As the NIH did when sequencing the human genome, it needs to issue a rallying call to engage researchers worldwide in the Human Microbiome Project. This would involve raising a scientific and research agenda for the International Human Microbiome Consortium. *(Dr. Mahmoud)*

- Target hepatitis C, tuberculosis, and treatment of cardiovascular diseases. In these special problem areas, NIH could be very productive. (*Dr. Varmus)*

- Reduce the burden of depression. According to the World Health Organization, depression will be the number-one source of the global burden of disease by 2020. A grand challenge for NIH would be to reduce the burden of depression—which is an eminently treatable disease—to number two or three within 10 years. Treatments are available, but research is needed on ways to implement interventions on a large scale. *(Dr. Insel)*

- Increase investments in research on mental health, substance abuse, and neurological disorders. These diseases have historically received a disproportionate amount of NIH support compared to their burden of disease. Suggested research topics include drug discovery and delivery to improve the quality of care at affordable levels, mapping of phenotypes and genomes in diverse populations, and mapping of traditional remedies for these conditions. Global health research on these conditions is cross-cutting, in that solutions found outside the United States could be applied within the United States. *(Dr. Patel)*

- Increase research support for treatment of nicotine addiction and alcoholism. Treatment of these conditions has been under-investigated and under-invested in, yet the conditions incur a tremendous burden among the world's population. Medications could be developed. *(Dr. Volkow)*

- Clarify early-life influences on health. Detailed explorations are needed in multiple settings to better understand intrauterine and early-life influences on risk for cardiovascular and metabolic syndromes later in life. Specific studies could address whether there is an epigenetic component to these effects, how risk may be manifested, and whether and what nutritional interventions could reduce later risks. *(Dr. Daar)*

- Reduce health disparities. A unifying theme for NIH would be to focus on using science and deploying technology to reduce health disparities in the United States and globally. There are solutions based on science that could reduce the burden of diseases that disproportionately affect U.S. minorities (e.g., hepatitis B among Asian Americans, breast cancer and asthma among African Americans). *(Dr. Olopade)*

- Raise the profile of nutrition and nutrition research at NIH. Nutrition and diet are important aspects of many diseases, particularly those affecting maternal and child health. Increased attention is needed on nutrition, both in terms of research and delivery. *(Dr. Tutwiler)*

- Focus on non-communicable diseases and capacity building related to these diseases. A focus on these diseases should include opportunity for the participation of many different players, including different NIH components. Broadened participation could be achieved, for example, through capacity building, networking and consortia, and research and training on issues of health systems and implications of implementation science. *(Dr. Sewankambo)*

- Explore economic behavioral research. NIH could explore this research area in collaboration with other institutions. *(Dr. Laxminarayan)*

- Establish a clear framework for evaluation. This needs to be done at the outset, to establish the metrics of success. The NIH could consider adopting, for some initiatives (e.g., partnerships with industry, PDPs), a milestone-based approach whereby administrators would have a more active involvement in projects than otherwise. *(Dr. Ewart)*

- Take leadership in global comparative effectiveness and systems research. The NIH could provide guidance to leaders in other countries who are struggling with this type of research. *(Dr. Bloom)*

- Expand the use of NIH Clinical and Translational Science Awards (CTSAs) globally. The NIH has a significant investment in supporting CTSAs at 46 U.S. academic health centers. In this effort to speed basic science discoveries into preclinical and clinical research and dissemination, almost all of the centers have robust global efforts. The NIH could foster a link between the CTSAs and institutions in developing countries, to engage a global perspective and trainees from other countries in interdisciplinary clinical and translational research, which would include working with the FDA and industry. *(Dr. Alving)*

- Study the clinical science of drug development. Studies of the discipline of clinical science are needed to better understand and improve the efficiency of drug development and the affordability and accessibility of these products to consumers. This extension of regulatory science would complement past emphases on improving the quality and speed of drug development. *(Dr. Chin)*

- Support research on health care systems and delivery. Research on health care systems and delivery in the United States and globally could facilitate translation of existing knowledge to patient care. *(Dr. Hiatt)*

- Take a rigorous biosocial look at the challenges of delivery of implementation. This effort would strengthen NIH's traditional role in basic science discovery. *(Dr. Farmer)*

- Address the ethical and sociopolitical impact of the new understandings surrounding global health and global health research. Finding ways to institutionally consider these issues and to publicly address them is important. *(Ambassador Goosby)*

- *Invest in regulatory science*. Research that would yield efficiencies in regulatory science in the United States and elsewhere is very important for improving the discovery, development, and delivery of drugs and other products. *(Drs. Lynch and Hamburg)*

- Democratize scientific knowledge. The NIH could help foster in developing countries the organization of patient advocacy groups and the development of regulatory structures for new drugs and products. *(Dr. Simon)*

ASSURE OPEN ACCESS TO DATA

- Extend open access to data. The NIH might consider extending open access to research data—for example, when licensing out a product, the NIH could require that the information technology be developed for global health and available to developing countries. *(Dr. Chin)*

- Support development of informatics structures with free access to data. The NIH support of structures (e.g., those resulting from the Malaria Genome Project) could enable investigators in developing countries (e.g., in Africa) to "mine" the data for research and participate fully in global health R&D. *(Dr. Rotimi)*

ADJOURNMENT

Dr. Francis Collins (NIH)

Dr. Collins invited the participants to continue the dialogue and to forward additional thoughts and suggestions to Dr. Vesna Kutlesic at kutlesicv@mail.nih.gov. He thanked all for graciously sacrificing their time and sharing their wisdom openly with the NIH.

The meeting was adjourned at 5:10 p.m. on January 6, 2010.

APPENDICES

1 Research Opportunities: Summary of Possible Areas for Additional NIH Investment (prepared by Dr. Francis Collins during the course of the meeting on January 6, 2010.

2 List of Participants

3 Meeting Agenda

APPENDIX 1

RESEARCH OPPORTUNITIES: SUMMARY OF POSSIBLE AREAS FOR ADDITIONAL NIH INVESTMENT

Fundamental Science

- Pathogen and vector biology – especially for tuberculosis
- Behavioral research, especially tobacco cessation – what works in the developing world?
- Genomic variation and predisposition to disease
- Nutrition research – biofortification (with the U.S. Department of Agriculture)
- Climate change and health consequences
- Environmental factors, such as cook stoves
- Biomarkers
- Regulatory science

Epidemiology/Populations

- An African Genetic/Epidemiologic Cohort – genotypes and phenotypes on a large scale
- Other large-scale prospective cohort projects
- Nested case-control studies
- Global health systems research – implementation, quality improvement
- mHealth research applications
- Comparative effectiveness research
- Explore use of Biobanks (China)
- Huge problem of lack of surveillance data about morbidity and mortality in many countries

Diagnostics

- Rapid, accurate, cost-effective, easy-to-use, point-of-care diagnostic tests for:
  - Tuberculosis
  - Malaria?
  - CD4 counts
  - Drug resistance
  - Influenza
  - Diarrheal illness
  - Neglected tropical diseases
- Challenge of recruiting the right disciplines and setting explicit goals – needs exquisite project management
- Regulatory science
- Need to engage end-user at the beginning, not the end
  - Includes need for samples for method validation

Therapeutics – Drugs and Vaccines

- Take advantage of NIH Therapeutics for Rare and Neglected Disease (TRND) program
- Prioritization of therapeutic needs for the developing world? Revisit the Institute of Medicine recommendations on vaccines (10 years ago), the Wellcome Trust report on vaccines/drugs (5 years ago), TDR? Must depend on scientific opportunity as well as public health need.
- Engineered immunity/humanized antibodies
- HBV alone vs. HBV + HPV trial in infants
- Non-communicable diseases: polypill for cardiovascular disease?
- Must include consideration of downstream activities at the outset

Capacity building/training

- Training grants in global health research
- Offer all NIH trainees the chance to do some component of training internationally?
- Expand U.S. training opportunities for scientists from low-income countries, but strongly encourage return to home country; tap into NIH alumni network
- Strengthen academic institutions by investing in Centers of Excellence in the developing world, especially those that build consortia around them
- Explore indirect cost rate restrictions
- Expand ICIDR?
- Leadership training for institutional managers

Science Policy

- Continue to emphasize open data access
- Allow more facile support of in-country infrastructure with R01s
- Better communication/public relations – emphasizing equity

APPENDIX 2

NIH GLOBAL HEALTH RESEARCH MEETING JANUARY 5 & 6, 2010 List of Meeting Participants			
Participant	**Institution**	**Title**	**Email**
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NIH GLOBAL HEALTH RESEARCH MEETING JANUARY 5 & 6, 2010 List of Meeting Participants			
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NIH GLOBAL HEALTH RESEARCH MEETING JANUARY 5 & 6, 2010 List of Meeting Participants			
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NIH GLOBAL HEALTH RESEARCH MEETING JANUARY 5 & 6, 2010 List of Meeting Participants			
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APPENDIX 3

NIH Global Health Research Meeting
January 5 & 6, 2010
Meeting Agenda

Objective: To identify actions that would have the greatest multiplier effect on global health R&D in the next five-ten years based on several criteria, including an assessment of current gaps, scientific and translational potential, public health impact, and feasibility.

8:00 - 8:20 **Welcome and Introductions**
Francis S. Collins, M. D., Ph. D., Director, U. S. National Institutes of Health

8:20 - 8:50 **Panel: Global Health Research at HHS: Challenges and Directions**
Moderator:
John T. Monahan, J. D., Counselor to the Secretary and Interim Director, Office of Global Health Affairs, U. S. Department of Health and Human Services
Panel Members:
Roger I. Glass, M. D., Ph. D., Associate Director for International Research and Director, Fogarty International Center, U. S. National Institutes of Health
Anthony S. Fauci, M. D., Director, National Institute of Allergy and Infectious Diseases, U. S. National Institutes of Health
Thomas R. Frieden, M. D., MPH, Director, Centers for Disease Control and Prevention
Margaret Hamburg, M. D., Commissioner of Food and Drugs, Food and Drug Administration (FDA)

8:50 - 9:20 Discussion

9:20 - 9:50 Break

9:50 - 10:05 **Plans for Research and Innovation within the U. S. Global Health Initiative**
Jacob J. Lew, J.D., Deputy Secretary of State for Management and Resources, U. S. Department of State

10:05 - 10:15 Discussion

10:15 - 10:45 **Panel: Regional Perspectives: Building Research Partnerships**
Moderator:
Timothy G. Evans, **M. D., D. Phil.**, World Health Organization, Assistant Director General
Panel Members:
Prof. Depei Liu, President, Chinese Academy of Medical Sciences
Prof. Malegapuru (William) Makgoba, Vice Chancellor & Principal, University of KwaZulu-Natal, South Africa

Prof. Nelson K. Sewankambo, Principal, Makerere University, College of Health Sciences, Uganda

10:45 - 11:15 Discussion

11:15 - 11:45 **Panel: Global Health Technologies: Philanthropic and Private Sector Perspectives**
Moderator:
Harvey V. Fineberg, M. D., Ph. D., President, Institute of Medicine, U. S. National Academy of Sciences
Panel Members:
Mark B. Feinberg, M. D., Ph. D., Vice President, Medical Affairs and Policy, Merck
Bernard Pecoul, **M. D., M. P. H.,** Executive Director, Drugs for Neglected Diseases International (DNDi)
Jimmy Whitworth, M. D., Head of International Activities, Wellcome Trust
Tadataka Yamada, M. D., President, Global Health Program, Bill & Melinda Gates Foundation

11:45 - 12:15 Discussion

12:15 - 1:00 **Lunch Presentation**
Ezekiel J. Emanuel, M.D., Ph.D., Department of Bioethics, Clinical Center National Institutes of Health and Special Advisor for Health Policy, Office of Management and Budget

1:00 - 1:30 **Research Opportunities: Fundamental Science**
Moderator: **Harold E. Varmus, M. D., M. A.,** President & CEO, Memorial Sloan Kettering Cancer Center and Co-Chair, Council of Advisors on Science and Technology

1:30 - 2:00 **Research Opportunities: Epidemiology/Populations**
Moderator: **Barry R. Bloom, Ph. D.,** Harvard University Distinguished Service Professor, Harvard School of Public Health

2:00 - 2:30 **Research Opportunities: Diagnostics**
Moderator: **Maria C. Freire, Ph.D.,** President, Albert and Mary Lasker Foundation

2:30 - 3:00 Break

3:00 - 3:30 **Research Opportunities: Therapeutics—Drugs and Vaccines**
Moderator: **B. Tore Godal, M. D., Ph. D.,** Special Adviser to the Prime Minister on Global Health, Ministry of Foreign Affairs, Norway

3:30 - 4:00 **Research Opportunities: Capacity Building & Training**

Moderator: **Ambassador Eric Goosby, M. D.,** U. S. Global AIDS Coordinator, Office of the U. S. Global AIDS Coordinator, U. S. Department of State, *The U.S. President's Emergency Plan for AIDS Relief (PEPFAR)*

4:00 - 5:00 **Where do we go from here?**
Francis S. Collins, M. D., Ph. D., Director, U. S. National Institutes of Health

5:00 **Adjourn**

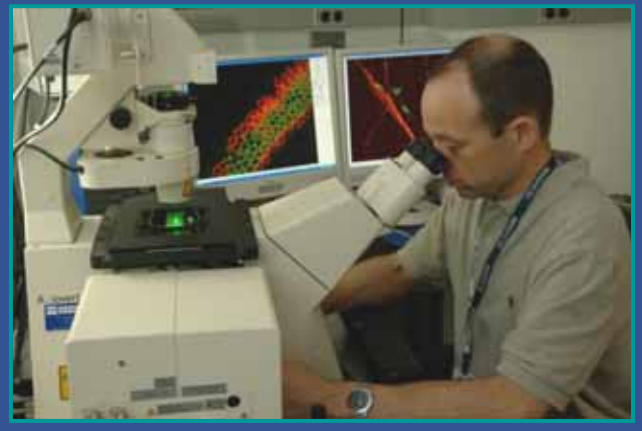
Future Opportunities in Global Health Research

Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health

January 6, 2010

NIH: Steward of Medical and Behavioral Research for the Nation

"Science in pursuit of fundamental knowledge about the nature and behavior of living systems... and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability."



RESEARCH AGENDA

Opportunities for Research and NIH

The promise of fundamental advances in diagnosis, prevention, and treatment of disease has never been greater.

Francis S. Collins

The mission of the National Institutes of Health (NIH) is science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and to reduce the burdens of illness and disability. The power of the molecular approach to health and disease has steadily gained momentum over the past several decades and is now poised to catalyze a revolution in medicine. The foundation of success in biomedical research has always been, and no doubt will continue to be, the creative insights of individual investigators. But increasingly those investigators are working in teams, accelerated by interdisciplinary approaches and empowered by open access to tools, databases, and technologies, so a careful balance is needed between investigator-initiated projects and large-scale community resource programs. For both individual and large-scale efforts, it is appropriate to identify areas of particular promise. Here are five such areas that are ripe for major advances that could reap substantial downstream benefits.

High-Throughput Technologies

In the past, most biomedical basic science projects required investigators to limit their scope to a single aspect of cell biology or physiology. The revolution now sweeping the field is the ability to be comprehensive—for example, to define all of the genes of the human or a model organism, all of the human proteins and their structures, all of the common variations in the genome, all of the major pathways for signal transduction in the cell, all of the patterns of gene expression in the brain, all of the steps involved in early development, or all of the components of the immune system. Further development of technologies in areas such as DNA sequencing, imaging, nanotechnology, proteomics, metabolomics, small-molecule screening, and RNA interference are ripe for aggressive investment. Furthermore, these technologies will spur the production of massive and complex data sets and will require major investments in computational biology.

As one example, the Cancer Genome Atlas (*1*) is now poised to derive comprehensive information about the genetic underpinnings of 20 major tumor types. This information will likely force a complete revision of diagnostic categories in cancer and will usher in an era where abnormal pathways in specific tumors will be matched with the known targets of existing therapeutics. Another example is the opportunity to understand how interactions between ourselves and the microbes that live on us and in us (the "microbiome") can influence health and disease (*2*).

Translational Medicine

Critics have complained in the past that NIH is too slow to translate basic discoveries into new diagnostic and treatment advances in the clinic. Some of that criticism may have been deserved, but often the pathway from molecular insight to therapeutic benefit was just not discernible. For many disorders, that is now changing. Three major factors have contributed to this: (i) the discovery of the fundamental basis of hundreds of diseases has advanced dramatically; (ii) with support from the NIH Roadmap, academic investigators supported by NIH now have access to resources to enable them to convert fundamental observations into assays that can be used to screen hundreds of thousands of candidates for drug development; (iii) public-private partnerships are being more widely embraced in the drug-development pipeline to enable biotech and pharmaceutical companies to pick up promising compounds that have been effectively "de-risked" by academic investigators and to bring them to clinical trials and U.S. Food and Drug Administration (FDA) approval.

As one example, the NIH Therapeutics for Rare and Neglected Diseases (TRND) (*3*) program will allow certain promising compounds to be taken through the preclinical phase by NIH, in an open environment where the world's experts on the disease can be involved. Furthermore, as information about common diseases increases, many are being resolved into distinct molecular subsets, and so the TRND model will be even more widely applicable.

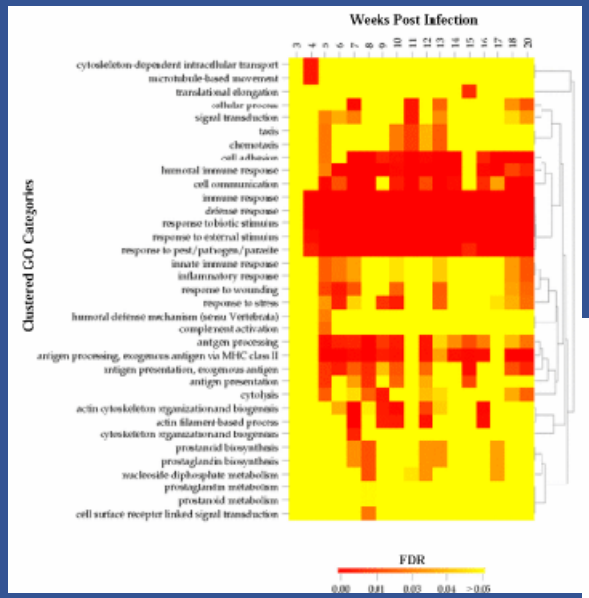
The first human protocol (for spinal cord injury) involving human embryonic stem cells (hESCs) was approved by the FDA in 2009, and the opening up of federal support for hESC research will bring many investigators into this field. The capability of transforming human skin fibroblasts and other cells into induced pluripotent stem cells (iPSCs) opens up a powerful strategy for therapeutic replacement of damaged or abnormal tissues without the risk of transplant rejection (*4*–*6*). Although much work remains to be done to investigate possible risks, the iPSC approach stands as one of the most breathtaking advances of the last several years, and every effort should be made to pursue the basic and therapeutic implications with maximum speed.

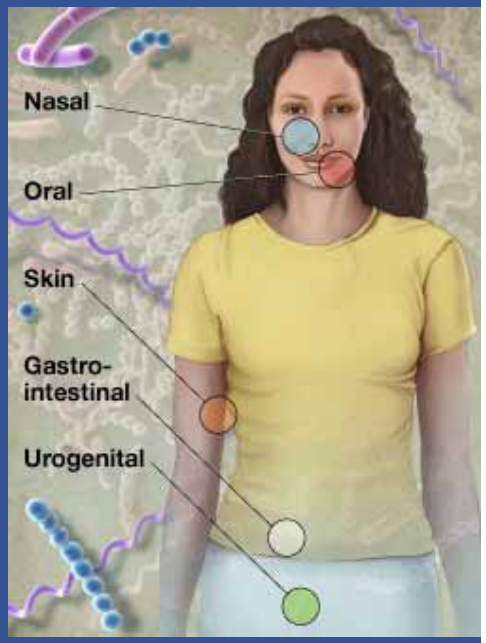
Benefiting Health Care Reform

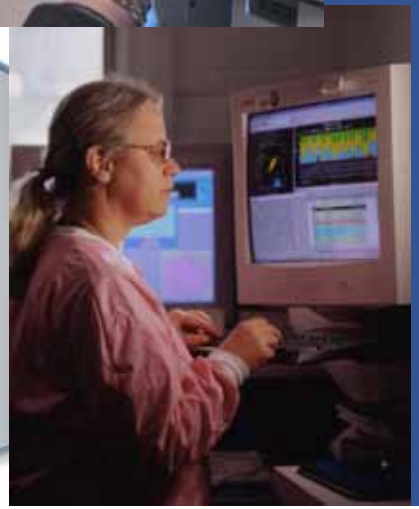
U.S. expenditures on health care now represent 17% of our Gross Domestic Product, are continuing to grow, and are excessive as a percentage of per capita gross income com-

National Institutes of Health, Bethesda, MD 20892, USA. E-mail: collinsf@mail.nih.gov

Opportunity 1: Applying unprecedented opportunities in genomics and other high throughput technologies to understand fundamental biology, and to uncover the causes of specific diseases







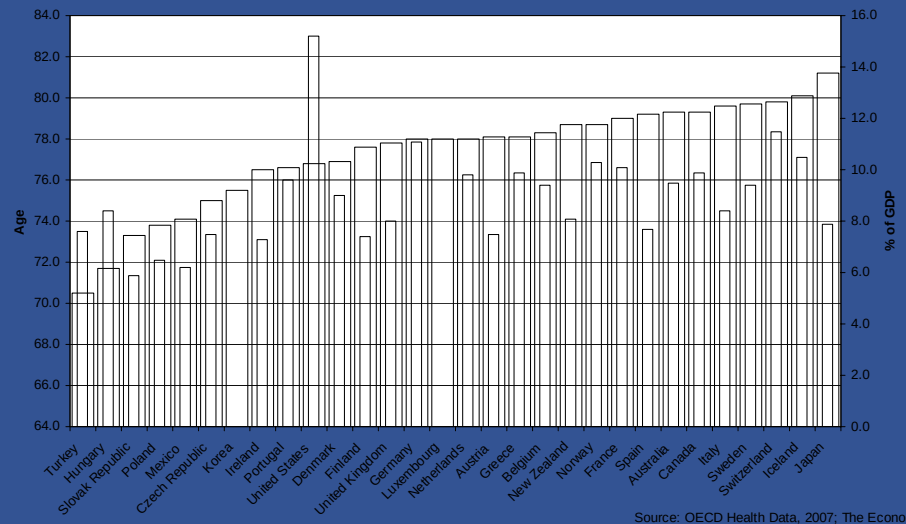
HUMAN MICROBIOME PROJECT

DACC

HMP

Opportunity #2: Translating basic science discoveries into new and better treatments

Opportunity #3: Putting science to work for the benefit of health care reform



Source: OECD Health Data, 2007; The Economis

small steps
big rewards
Prevent type 2 Diabetes

The NEW ENGLAND JOURNAL of MEDICINE

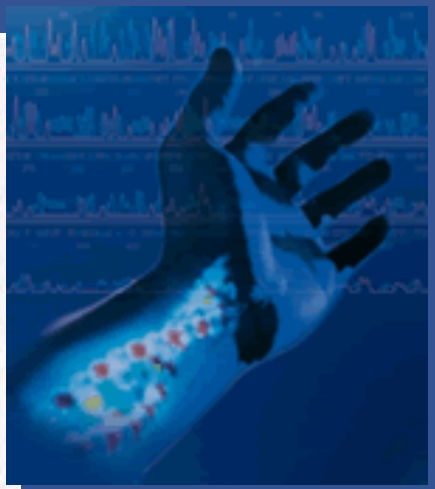
ESTABLISHED IN 1812 SEPTEMBER 22, 2005 VOL. 353 NO. 12

Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia

Jeffrey A. Lieberman, M.D., T. Scott Stroup, M.D., M.P.H., Joseph P. McEvoy, M.D., Marvin S. Swartz, M.D., Robert A. Rosenheck, M.D., Diana O. Perkins, M.D., M.P.H., Richard S.E. Keefe, Ph.D., Sonia M. Davis, Dr.P.H., Clarence E. Davis, Ph.D., Barry D. Lebowitz, Ph.D., Joanne Severe, M.S., and John K. Hsiao, M.D., for the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators*

HEALTHY PEOPLE 2010

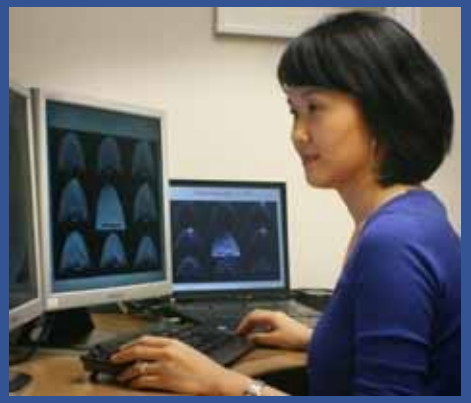
Understanding and Improving Health



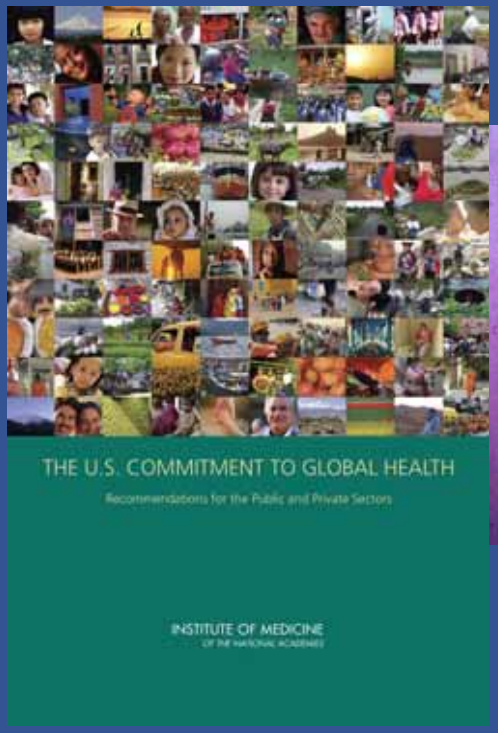
Opportunity #5: Reinvigorating and empowering the biomedical research community

NIH Roadmap for Medical Research

NIH DIRECTOR'S PIONEER A·W·A·R·D



Opportunity #4: Encouraging a greater focus on global health



Why Global Health Research?

- Scientific advances make an attack on infectious diseases more feasible than ever
  - RNAi
  - Small molecule screening
  - Genomics of pathogens, vectors, host
  - Vaccine development
- Opportunity to push beyond AIDS, malaria, TB to a long list of neglected tropical diseases (NTDs)
- Need for increased emphasis on chronic noncommunicable diseases and injuries, responsible for more 50% of deaths in developing world
- Tapping into the passion of young medical researchers
- Emphasis on global health fits with U.S. emphasis on “soft power” as an effective diplomatic tool
- Growing sense of national responsibility

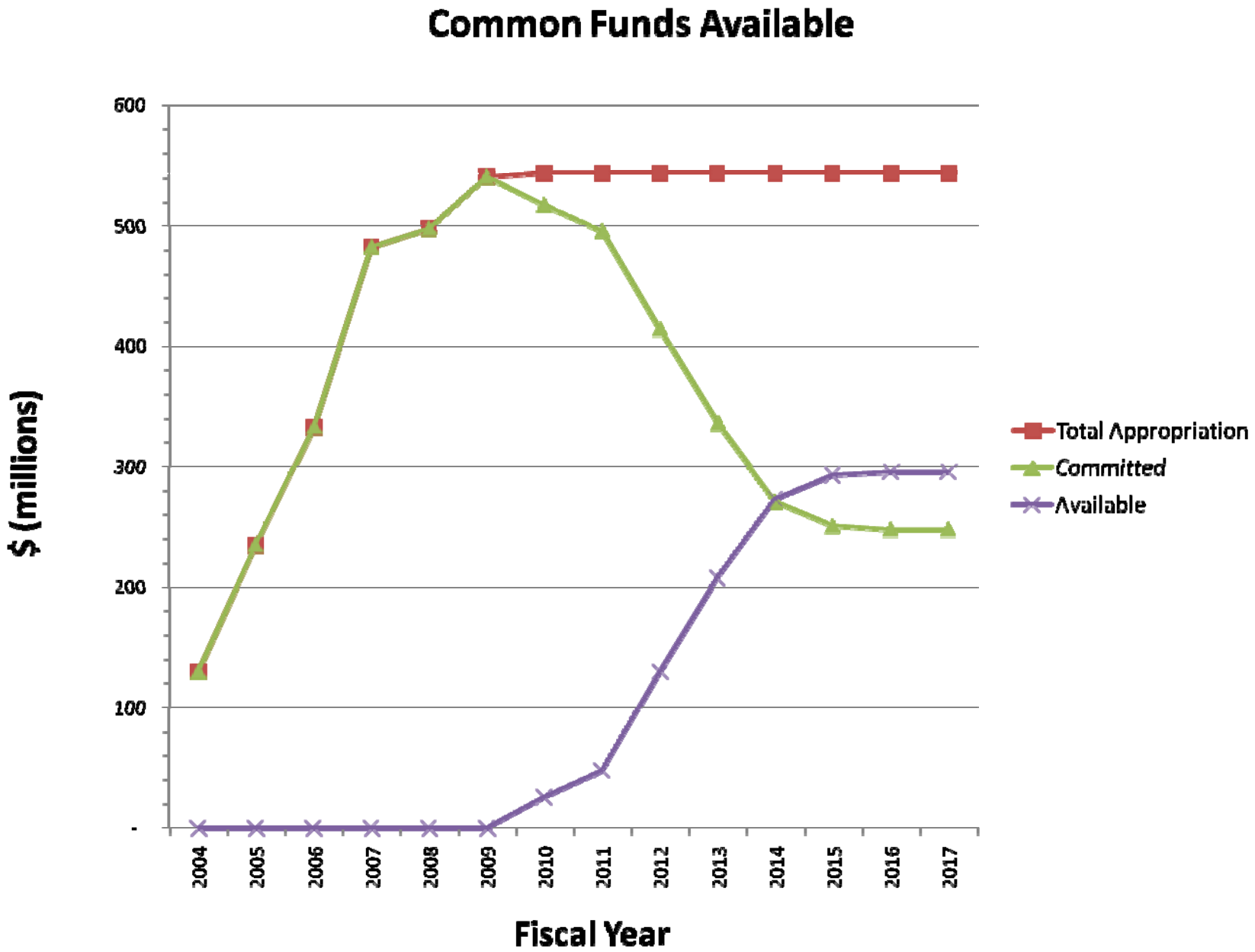
Presidential Visit to NIH – September 30, 2009

Main Objectives of Today's Meeting

- To gain the benefit of current thinking from academic, government, philanthropic, industrial, and international organizations on some of the most pressing strategic needs and opportunities in global health R&D.

- To identify a potential set of initiatives that would fit NIH's mission as a research organization, that might be supported independently or in partnership, and that would have the greatest multiplier effect on global health R&D in the next five to ten years.


NATIONAL CANCER INSTITUTE
NATIONAL INSTITUTES OF HEALTH
NIMH
NIDA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Fiscal Year
Total Appropriation
Committed
Available

Current landscape of global health research is complex

- Many organizations
- Many countries
- Many programs
- Many target diseases
- Many scientific approaches


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SABIN
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FOUNDATION FOR THE National Institutes of Health
ExxonMobil
MERCK
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MEMORIAL SLOAN-KETTERING CANCER CENTER
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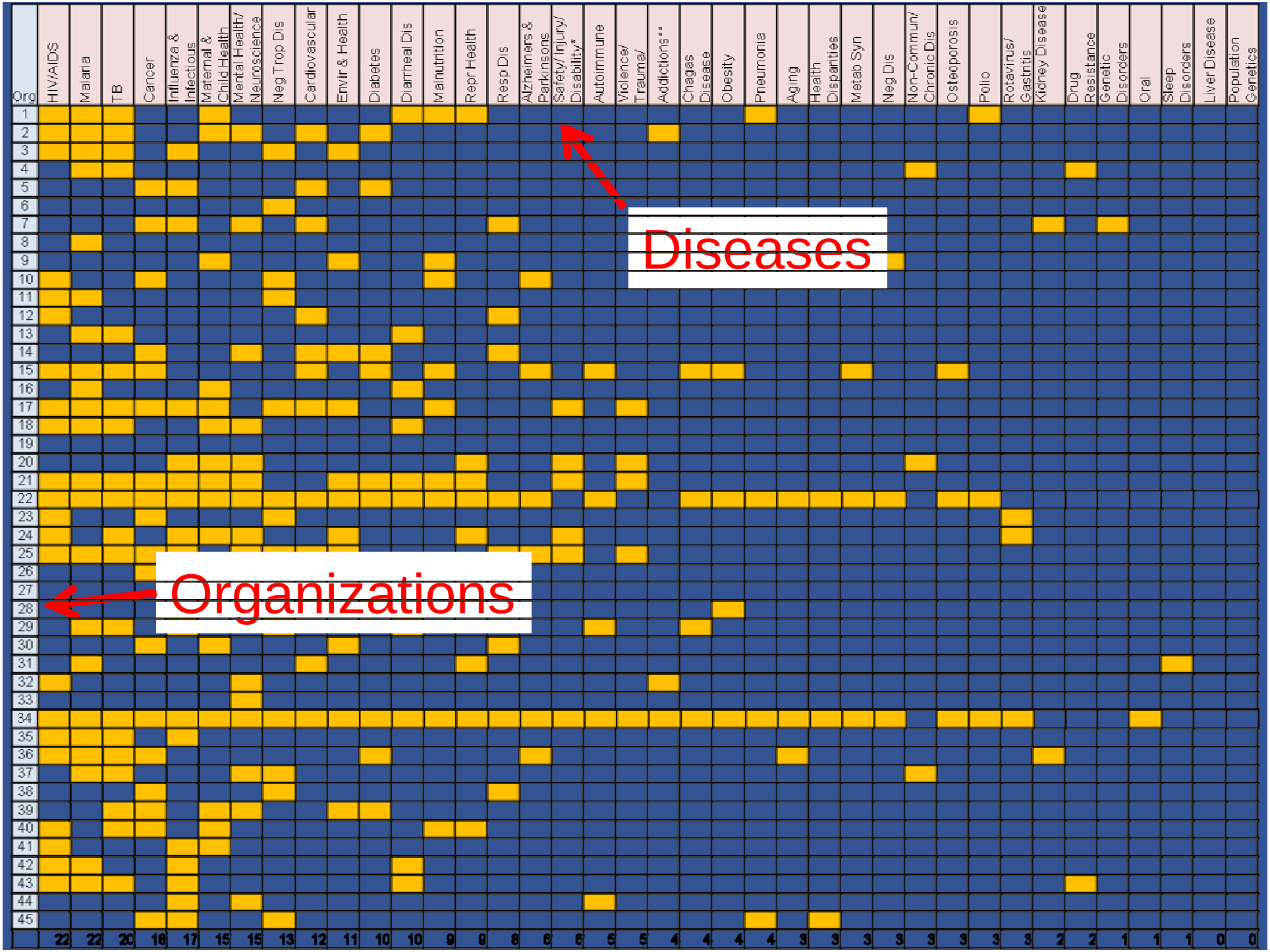
FDA
THE UNIVERSITY OF CHICAGO MEDICAL CENTER
DNDi
wellcome trust
JHMRI
JOHNS HOPKINS MALARIA RESEARCH INSTITUTE
Johnson & Johnson
iWH
Institute for OneWorld Health
UNIVERSITY OF TORONTO
DALLA LANA SCHOOL OF PUBLIC HEALTH
GLOBAL ALLIANCE FOR CHRONIC DISEASE
PROTECT · SUSTAIN
Pfizer
DEPARTMENT OF STATE · UNITED STATES OF AMERICA
MRC Medical Research Council
BILL & MELINDA GATES foundation
HARVARD School of Public Health
LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE
USDA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Mental Health/ Neuroscience
Neg Trop Dis
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Diarrheal Dis
Malnutrition
Repr Health
Resp Dis
Alzheimers & Parkinsons
Safety/ Injury/ Disability*
Autoimmune
Violence/ Trauma/
Addictions**
Chagas Disease
Obesity
Pneumonia
Aging
Health Disparities
Metab Syn
Neg Dis
Non-Commun/ Chronic Dis
Osteoporosis
Polio
Rotavirus/ Gastritis
Kidney Disease
Drug Resistance
Genetic Disorders
Oral
Sleep Disorders
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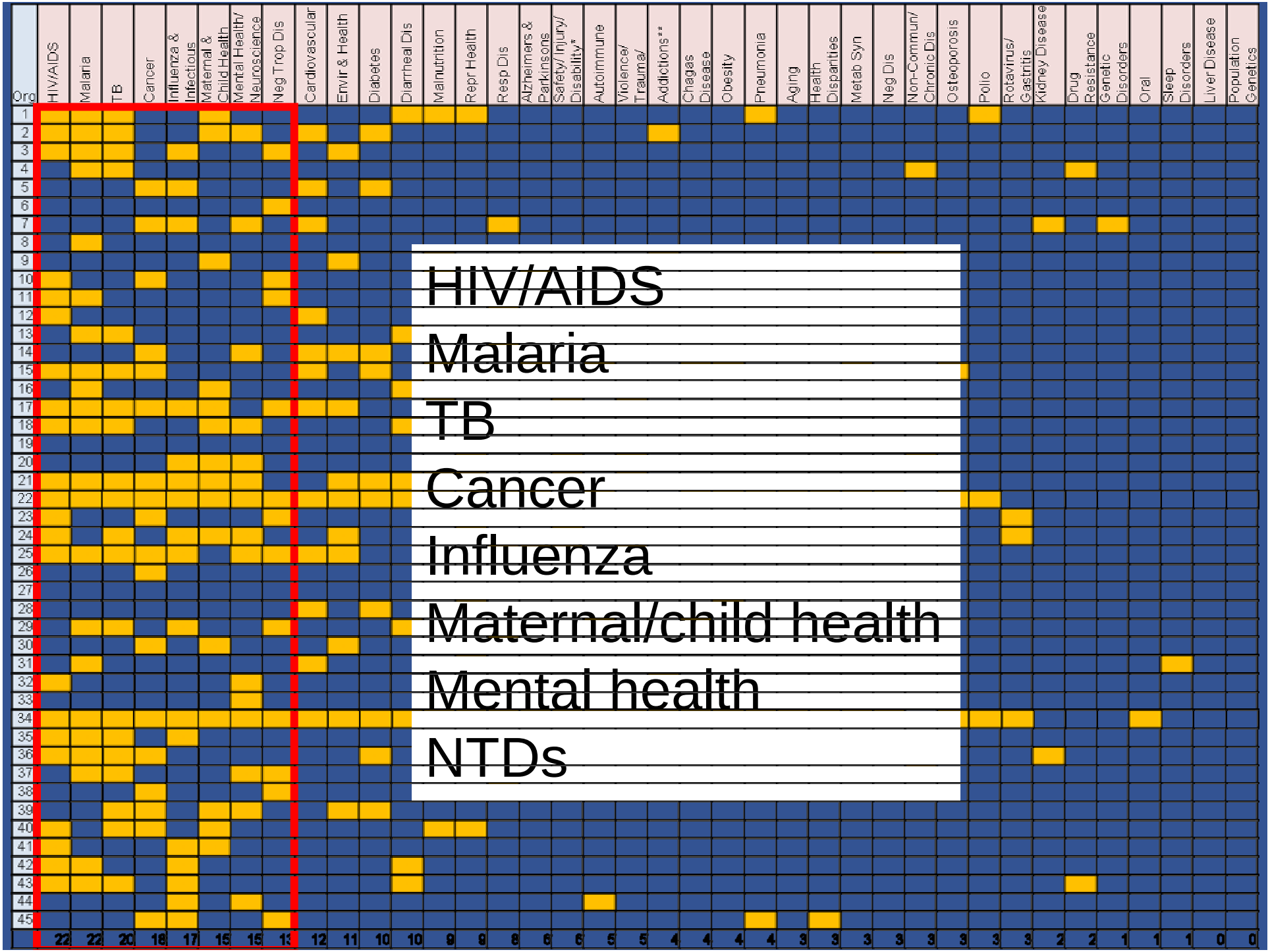
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Osteoporosis
Polio
Rotavirus/ Gastritis
Kidney Disease
Drug Resistance
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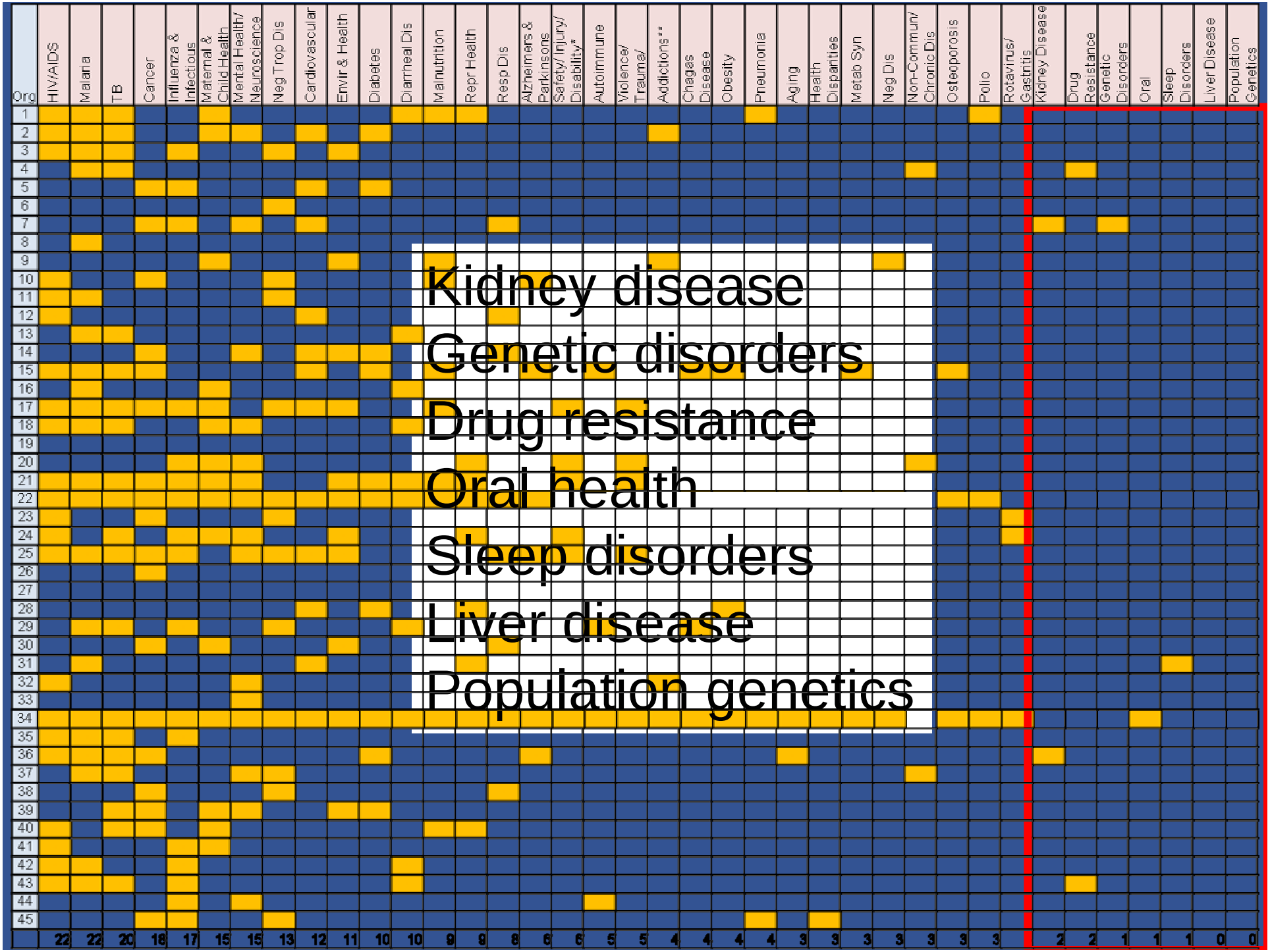
Mental health
NTDs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Polio
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Kidney Disease
Drug Resistance
Genetic Disorders
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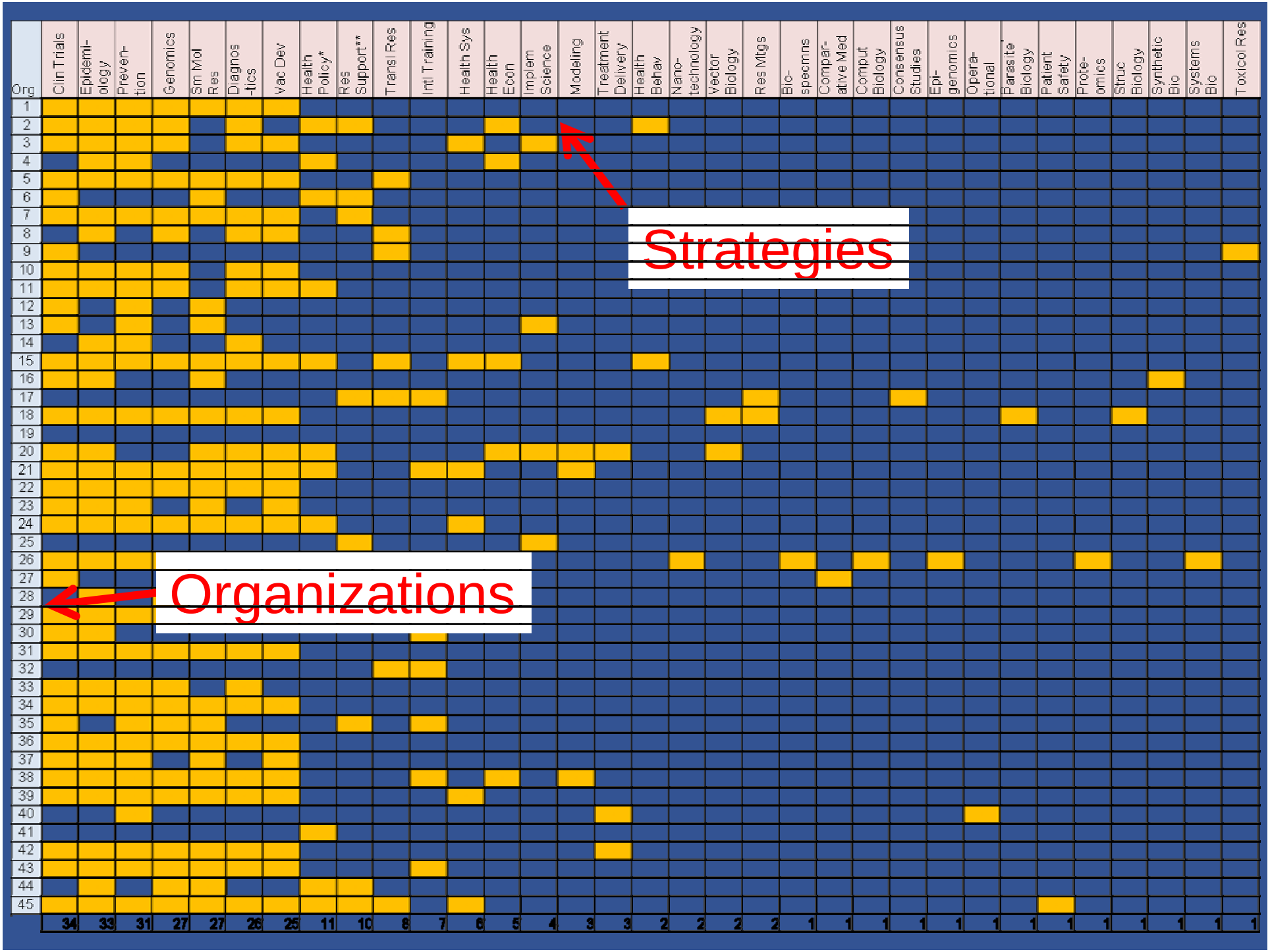
Sleep Disorders
Liver Disease
Population Genetics
Kidney disease
Genetic disorders
Drug resistance
Oral health
Sleep disorders
Liver disease
Population genetics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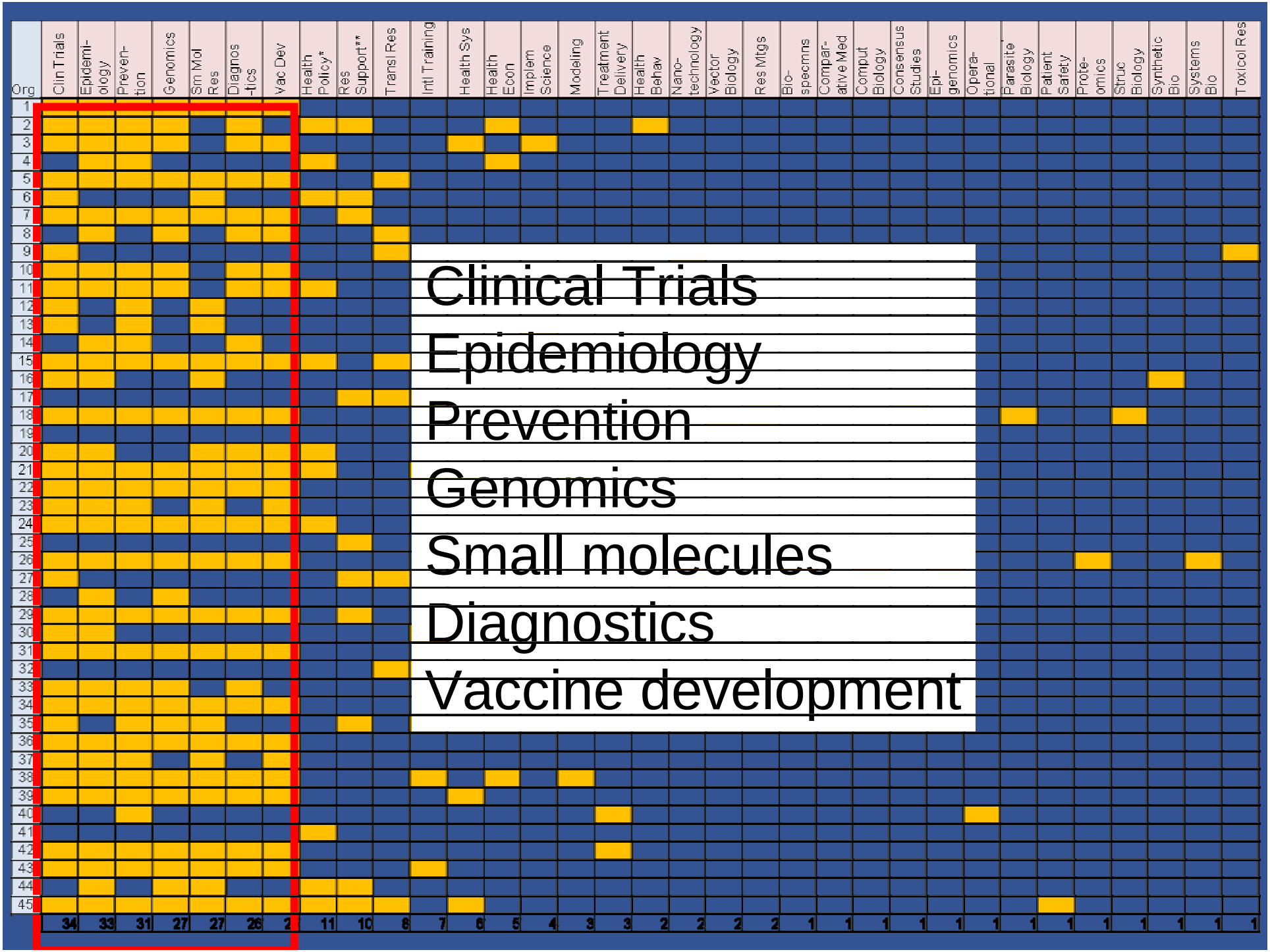
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Parasite Biology
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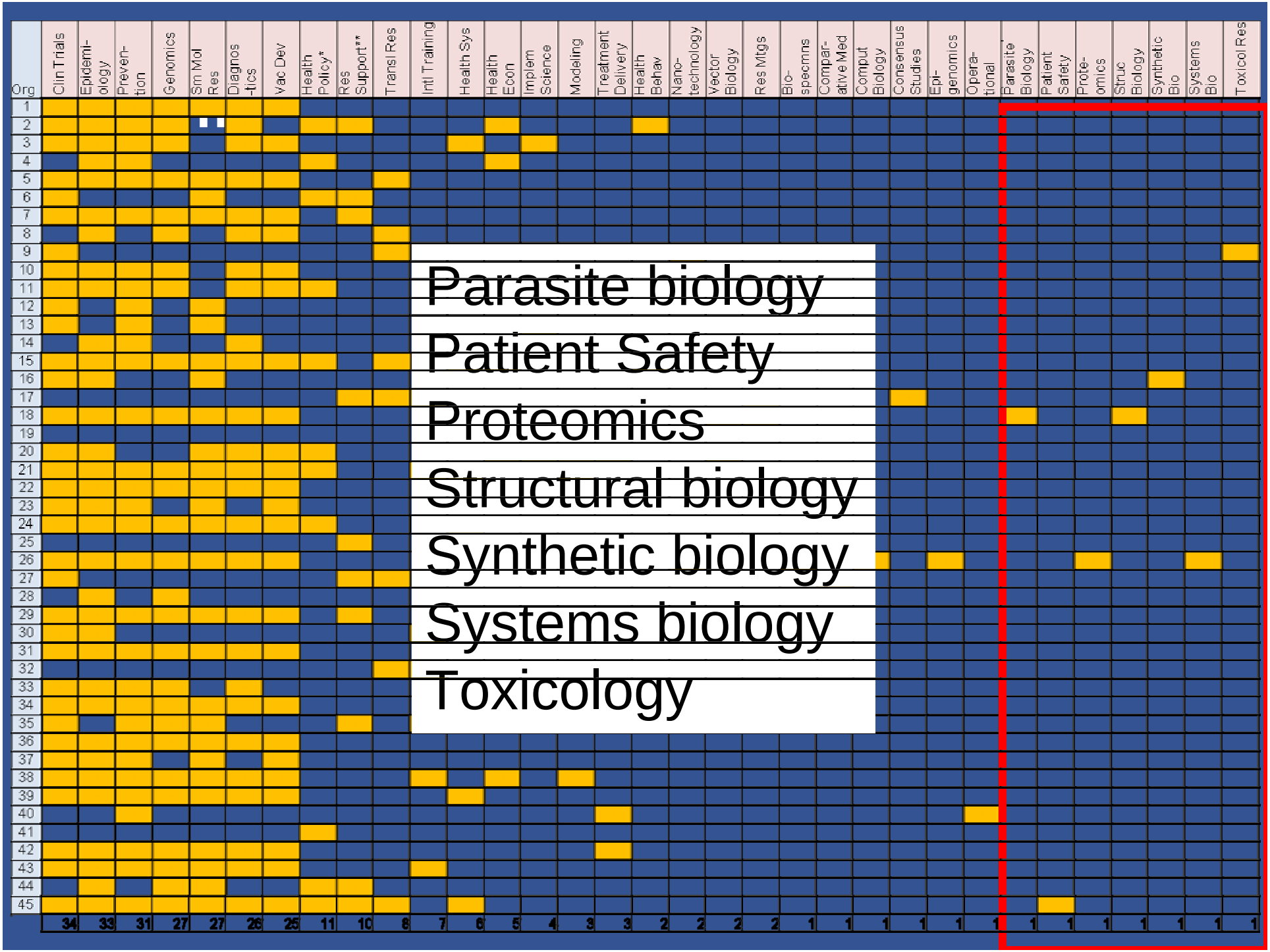
Genomics
Small molecules
Diagnostics
Vaccine development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Nano-technology
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Compar-ative Med
Comput Biology
Consensus Studies
Epi-genomics
Opera-tional
Parasite Biology
Patient Safety
Prote-omics
Struc Biology
Synthetic Bio
Systems Bio
Toxicol Res
Parasite biology
Patient Safety
Proteomics
Structural biology
Synthetic biology
Systems biology
Toxicology

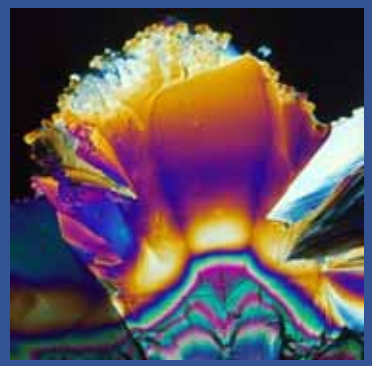
Some Ground Rules For Today's Meeting

- Cell phones don't really work in this room, but maybe that's just as well?
- Please identify yourself when you first speak
- Apologies that introductions, even of very distinguished speakers, will be brief
- Try to keep the focus on explicit actions that NIH can take to contribute more extensively to global health research
- Be prepared that I will ask each of you in the final session to identify one or two specific projects that NIH should consider
- Schedule is very tight – so timekeeper will be ruthless!

Not failure, but low aim, is a crime.

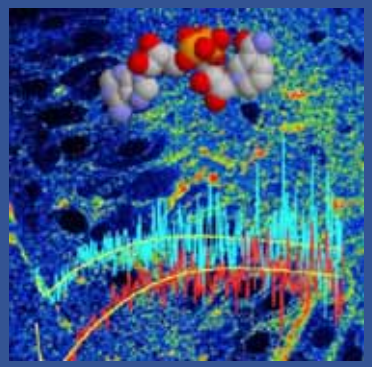
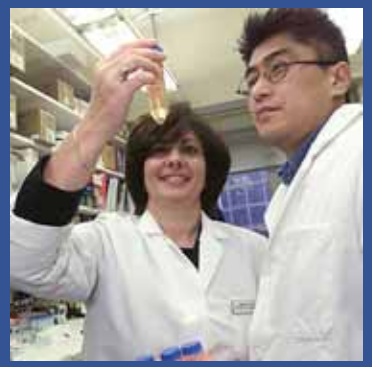
— James Russell Lowell






NIH

Transforming medicine and health through discovery


Global Health Research at NIH:
Challenges & Directions

Roger I. Glass, M.D., Ph.D.

NIH Associate Director for International Research

Director, Fogarty International Center




DEPARTMENT OF HEALTH & HUMAN SERVICES USA

NATIONAL INSTITUTES OF HEALTH

FOGARTY INTERNATIONAL CENTER

Global Health Research: Where would we like to be in 5 to 10 years ….

- Increase exchange of scientists, collaborations
- Expand focus -- IDs, chronic diseases, new global threats
- Improve standards of research, clinical trials, ethics
- Broaden use of new technologies, -omics, ICT
- Strengthen Centers of Excellence in LMICs
- Enhance research workforce – domestic & foreign
- Extend **partnerships** for collaboration, funding
- Reduce administrative hurdles to research
- Accelerate discovery and implementation of results
- **Demonstrate impact to improve human health**

"***Take science where the problems are*** "

GLOBAL BURDEN OF DISEASE (DALYS)

1990		2020
Lower Respiratory Infection	1	**Ischaemic heart disease**
Diarrhoeal Disease	2	**Depression**
Perinatal	3	**Road Traffic Accidents**
Depression	4	Cerebrovascular
Ischaemic Heart Disease	5	COPD
Cerebrovascular	6	Lower Respiratory Infection
Tuberculosis	7	Tuberculosis
Measles	8	War
Road Traffic Accidents	9	Diarrhoeal Disease
Congenital Diseases	10	HIV
Malaria	11	Perinatal Disease
COPD	12	Violence
Falls	13	Congenital
Iron-deficiency anemia	14	Self-inflicted injury
Protein calorie malnutrition	15	Bronchial and Lung Cancer

Makerere University, Uganda

- 1960's Center of Excellence for E. Africa - major past discoveries - Burkitt's lymphoma, chemotherapy
- 1980's – Training grants to fellows, twinning grants with US institutions
- Major growth as center of excellence
- Other partnerships = Center of Excellence in HIV, infectious diseases
- Links to 8 other schools of public health
- Key discoveries – PMTCT, circumcision

Good science encourages strong collaborations

Benefits accrue from many partnerships!


中美肿瘤研究合作30年高层论坛
迈向肿瘤个体化医学
Personalized Cancer Medicine
Building on 30 Years of China-U.S. Scientific Progress
2009年11月9 -10日 北京
Nov. 9 -10, 2009 Beijing

China-NCI: 30 years of training & collaboration

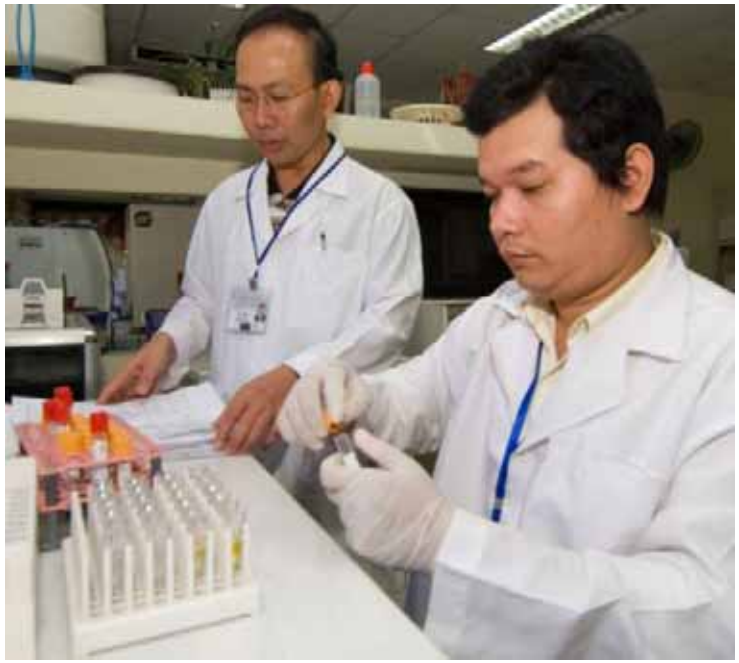
FOGARTY

- Many senior cancer researchers trained thru NCI
- Participated in human genome studies/Ca atlas
- Extraordinary cohorts for follow-up – smoking, folate
- Unusual cancer types: liver, esophagus..
- Novel science – imaging, nanotechnology
- Willingness to partner and co-fund research
- Strong institutions, good human chemistry

Need contacts, collaborations, improvements in research methods, trials, interactions- not funding!

Lessons learned

- Investments in Centers of Excellence for research, training & service can yield extraordinary returns that increase over time!
- Sustainability--good leaders can build long-term partnerships- with academic institutions, donors, PPPs, other branches of USG……& become independent !
- Countries at different levels of development require different strategies for collaboration in science
- We need to engage our own investigators as well!
- Must take a long-term view



Cambodian researchers receive training through Fogarty's AIDS International Training and Research Program.

Partnerships in global health will be essential to accelerate knowledge & discovery

- Access to:
  - Patients with rare diseases…
  - Exposures…
  - Gene pools…
  - Creative scientists….
  - New technologies…..
- To work through new treatments and solutions & support clinical trials where diseases are prevalent

Cellphones are ideal for research projects such as this one in the Kenya/Sudan border region.

Global health can be a new frontier of biomedical research!

Some initial steps

- Established the GH Working Group at NIH
- Many ICs are developing GH strategic plans, eg. NHLBI, NCI, NEI, NIBIB, NIDDK…
- Extend training programs for US investigators to work in LMICs
- Expand opportunities for partnerships:
  - With foreign countries – eg. India, China….
  - With other USG agencies – GHI, PEPFAR, CDC
  - With donors – Wellcome, Gates,
  - With G8
- Encourage GH activities at US universities

Initial meeting of the Trans-NIH Global Health Research Working Group in August, 2009.

Take home messages

- Surge in GH interest presents a unique opportunity to advance biomedical research
- Build upon the synergy between GH program implementation and GH research; produce scientific advancement and increase in-country implementation capacity
- Research opportunities extend to non-communicable diseases and to new & emerging common global health problems

Take home messages

- Partnerships: Establish partnerships that reflect levels of scientific development and local capacity
  - In some middle-income countries, stimulate bilateral collaborations with co-funding
  - For low-income countries, seek broader partnerships with G8, PPPs, donors, development agencies to build research capacity, strengthen institutions, and address local needs
- Training for leadership and research competence will be essential

A technology partnership is increasing the effectiveness of a research project in Indonesia.

How can we take advantage of current interest in global health to:

- Increase opportunities for US researchers to work in LMICs ?
- Increase researcher pool and strengthen institutions in LMICs ?
- Build productive and catalytic partnerships ?
  - Centers of Excellence in SSA
  - Special funds to stimulate collaboration in key countries (India, China, Brazil, S. Africa, Russia….)
  - USG activities: GHI, PEPFAR, Fulbright
  - PPPs, donors, G8 and beyond…..
- Remove hurdles to population-based research ?
- Provide leadership training for foreign scientists?
- Encourage research to implement innovations ?

A research trainee learns how to examine specimens at the National Institute for Respiratory Disease in Mexico City.

Global Health Research: A View from NIAID

Anthony S. Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
January 5, 2010

Selected Established Infectious Diseases of Global Public Health Importance

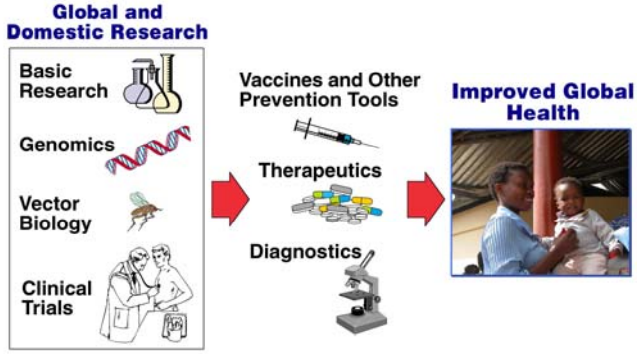
	Estimated Annual Deaths
Respiratory Infections	4.0 million
HIV/AIDS	2.0 million
Diarrheal Diseases	1.8 million
Tuberculosis	1.8 million
Vaccine Preventable Childhood Diseases (measles, pertussis, tetanus, etc.)	1.1 million
Malaria	863,000
"Neglected" Tropical Diseases (schistosomiasis, hookworm infection, leishmaniasis, trypanosomiasis, etc.)	534,000

Sources: WHO; Hotez, 2009

Infectious Diseases Research

Implementation of Infectious Diseases Programs

The Research Path

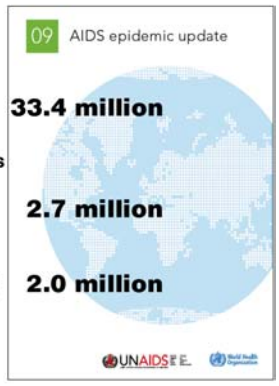


The "Big Three"

- HIV/AIDS
- Malaria
- Tuberculosis

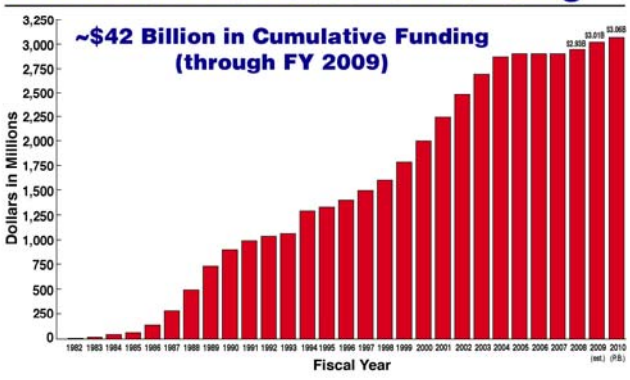
UNAIDS 2008 Global HIV/AIDS Estimates

- People living with HIV — **33.4 million**
  - ~50% are female
  - incl. 2.1 million children <15 years
- New HIV infections in 2008 — **2.7 million**
  - incl. 430,000 children <15 years
- Deaths due to AIDS in 2008 — **2.0 million**
  - incl. 280,000 children <15 years



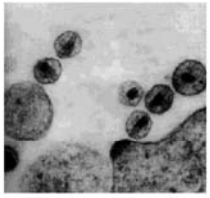
Source: UNAIDS, 11/24/2009

NIH HIV/AIDS Research Funding



Advances in AIDS Research, 1981-2009

- Etiology
- Diagnosis
- Molecular Virology and Epidemiology
- Pathogenesis
- Natural History
- Treatment
- Prevention
- Vaccine Development



Antiretroviral Therapy Dramatically Increases Life Expectancy for HIV-Infected Individuals


THE LANCET
Volume 372 Number 9635 Founded 1823 Published weekly July 26, 2008

Life Expectancy of Individuals on Combination Antiretroviral Therapy in High-Income Countries: a Collaborative Analysis of 14 Cohort Studies

Antiretroviral Therapy Cohort Collaboration

- An HIV-infected 20-year-old appropriately treated with ART can expect to live to >69 years in high-income countries

Lessons Learned from HIV/AIDS

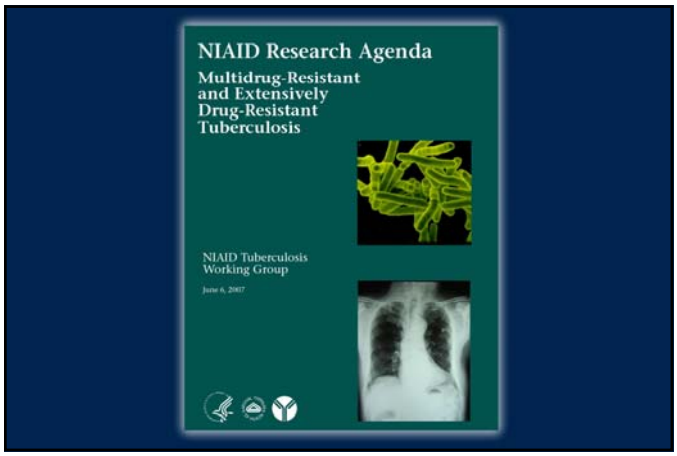
- Commit substantial financial and human resources
- Enlist the "best and the brightest" investigators in basic and clinical research, domestically and internationally
- Engage the affected community
- Foster cross-sector collaboration with industry, academia, global organizations, philanthropies, NGOs
- Garner support of leaders and policymakers

The Global Burden of Tuberculosis, 2008

- One-third of the world's population is infected with *Mycobacterium tuberculosis* (Mtb)
- In 2008
  - 9.4 million new TB cases, incl. 1.4 million among HIV-infected people
  - 1.8 million deaths, incl. 500,000 among HIV-infected people
  - ~500,000 new cases of MDR TB
  - 57 countries have reported XDR TB cases

Source: WHO, 12/2009

Image: CDC



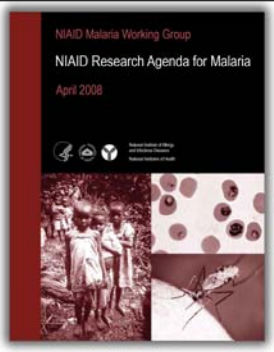
The Global Burden of Malaria, 2008

- ~863,000 malaria deaths, 89% in Africa
- ~243 million malaria cases
- Malaria present in 108 countries and territories
  - Half the world's population is at risk
- Every 30 seconds a child dies from malaria

Credit: S. Hollyman

Source: WHO, 12/2009

NIAID Malaria Strategic Plan and Research Agenda



The "Big Four"

- HIV/AIDS
- Malaria
- Tuberculosis
- **Neglected Tropical Diseases**

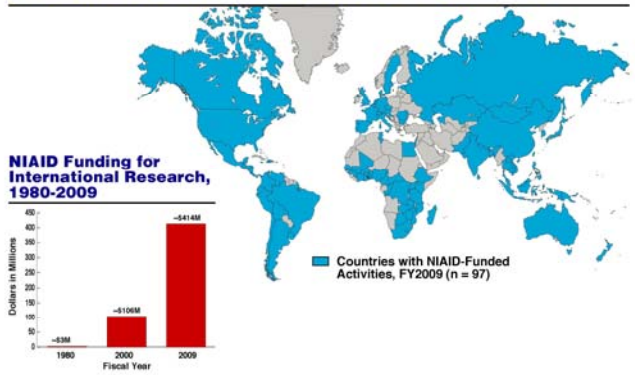
Neglected Tropical Diseases (NTDs)

- Examples: schistosomiasis, hookworm infections, leishmaniasis, filariasis, etc.
- One billion people – 1/6 of the world's population – suffer from one or more NTDs
- ~534,000 deaths, 56 million DALYs/yr.

Photo: WHO/P. Virot

Source: WHO; Hotez et al., 2009

Global Health Research at NIAID



"It is imperative that we use our current momentum to move forward, recognizing that the enormous challenges of global health...will require a long-term commitment that is sustained even when global health and those fighting to improve it are no longer in the headlines."

Global Public Health Progress

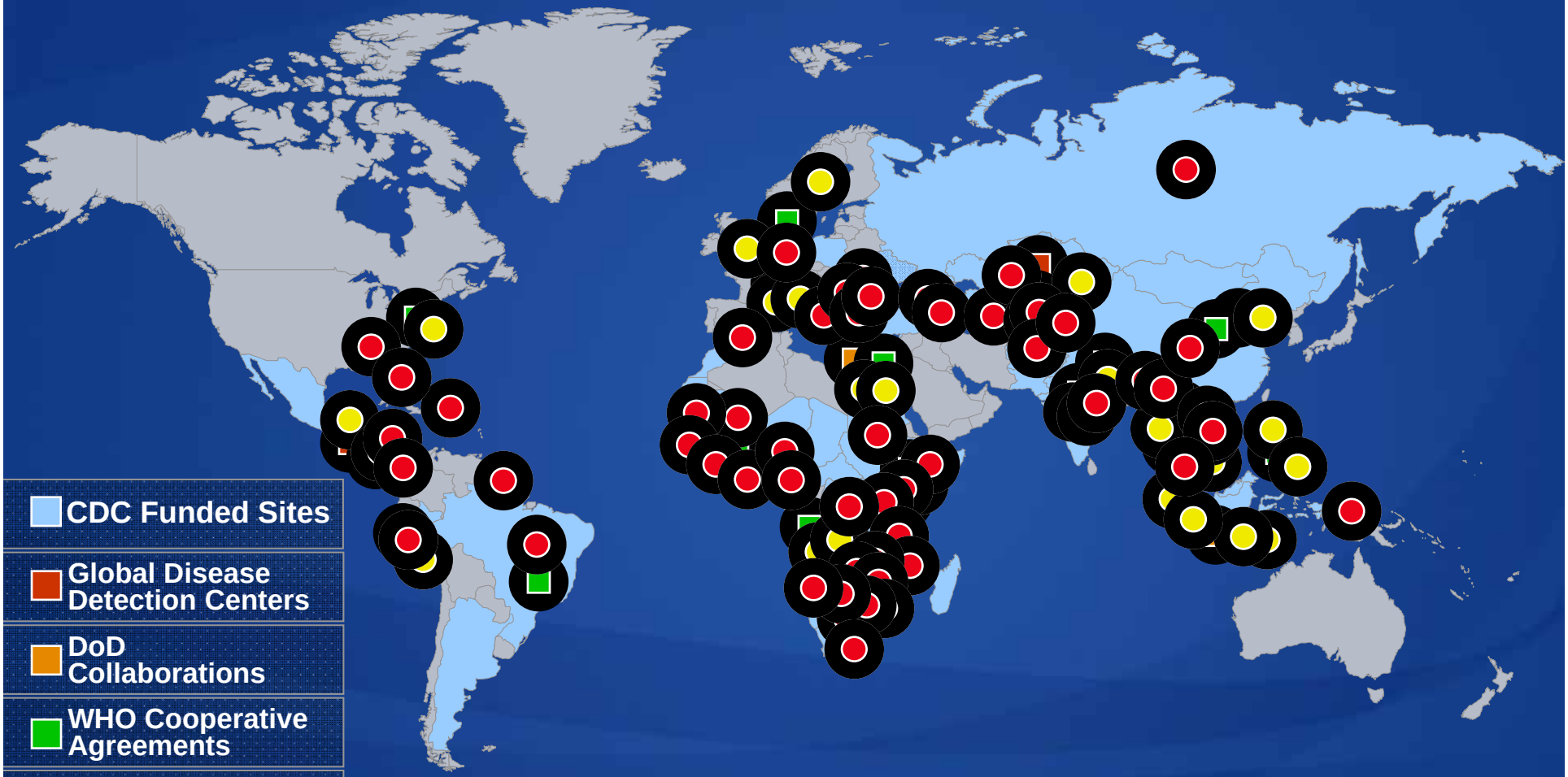
Research Priorities at CDC

Thomas R. Frieden, MD, MPH
Director, CDC; Administrator, ATSDR

Global Public Health Progress Requires…

- Political will and sufficient funding
- Surveillance, epidemiology, and laboratory capacity
- Effective, country-appropriate implementation
- Environmental protection and safety
- Infectious and chronic disease control
- Emergency preparedness
- Immunization
- Clinical oversight
- Health education

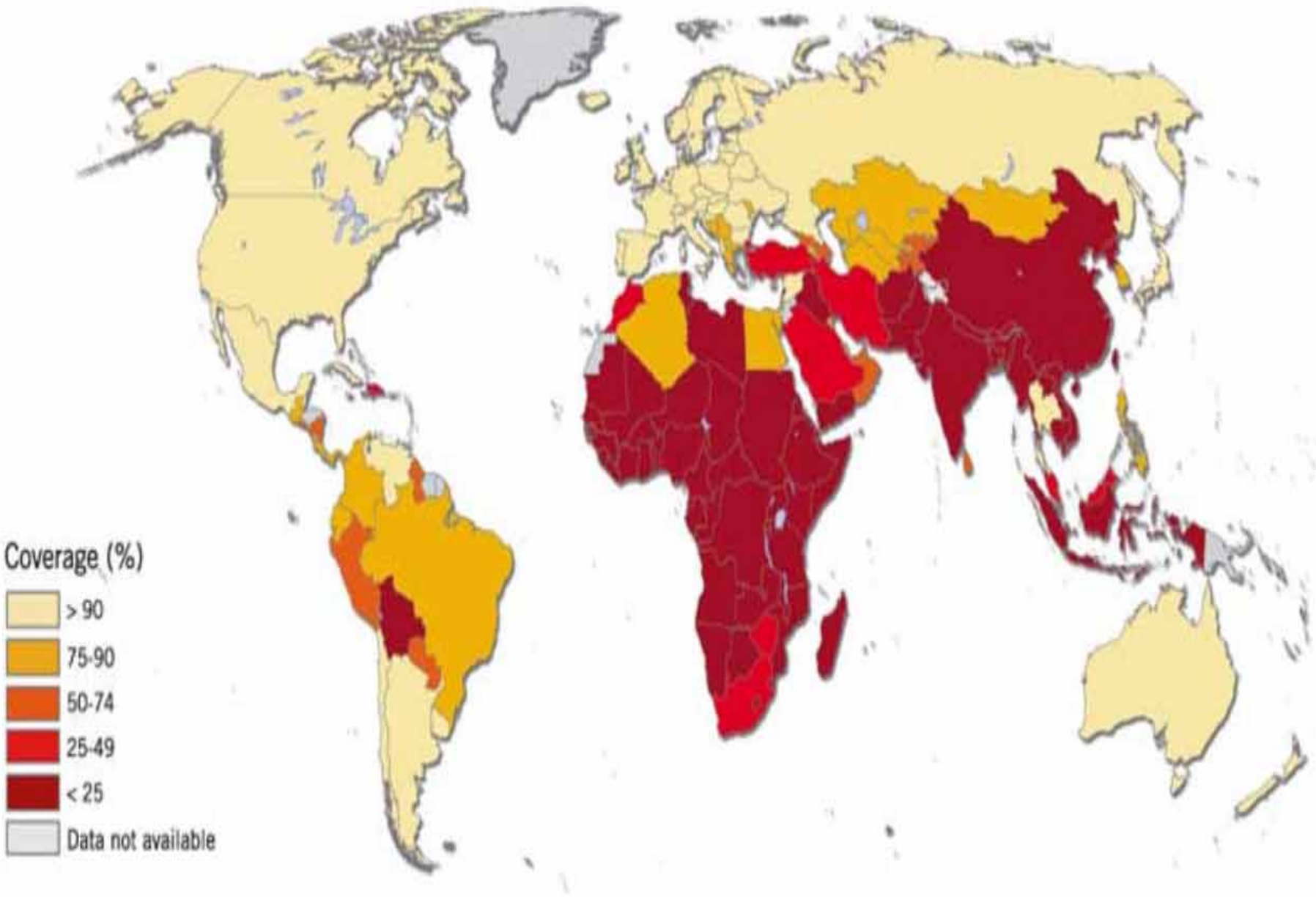
CDC International Activities and Support

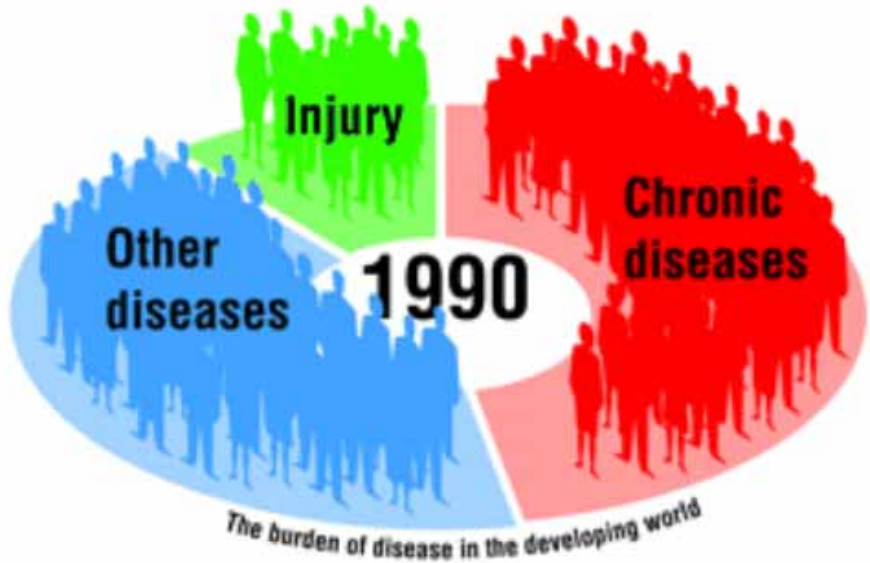


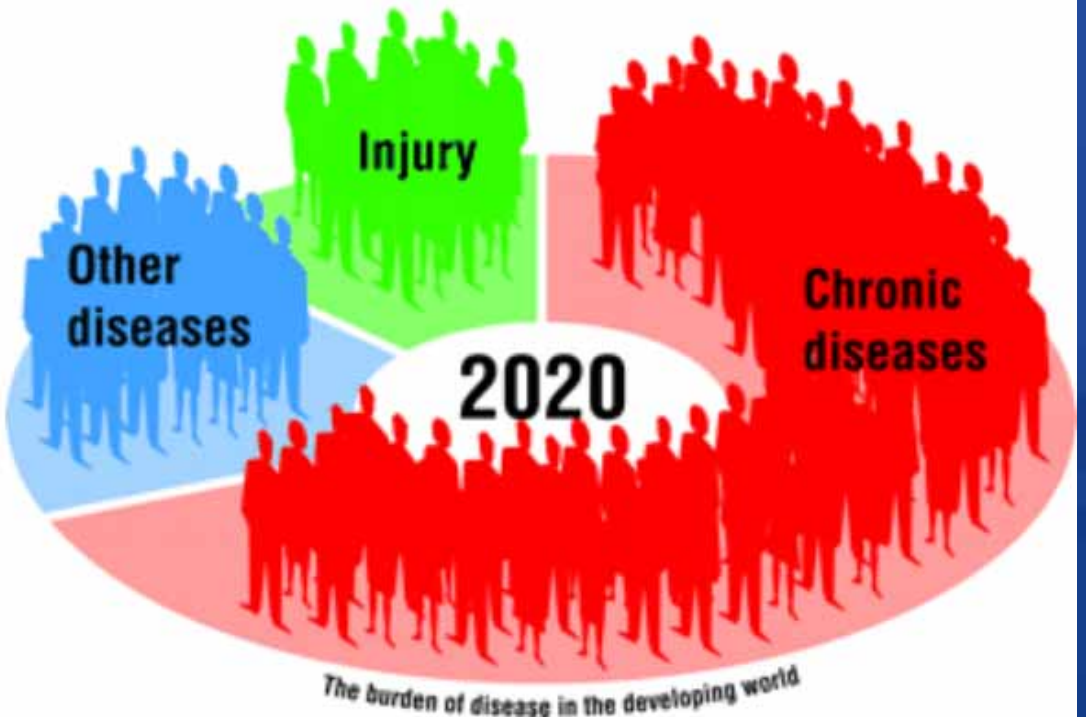
CDC Center for Global Health

- Help ministries of health plan, implement, and evaluate effective health programs
- Achieve U.S. and international health goals, including disease eradication and elimination
- Expand global health programs targeting leading causes of illness, disability, and death
- Generate and apply new knowledge to achieve health goals
- Strengthen health systems and their impact

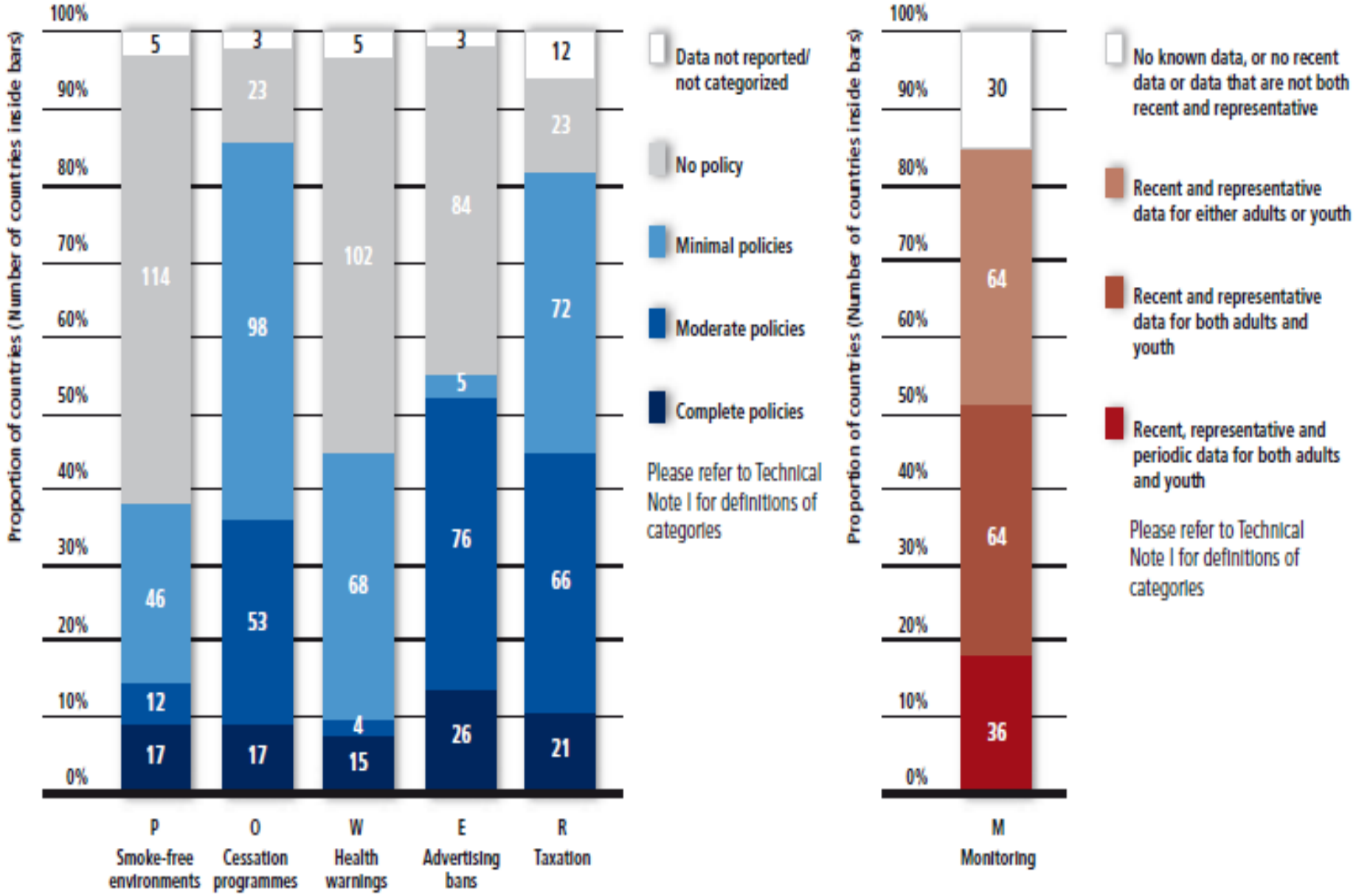
Coverage of vital registration of deaths, 1995-2003




Injury
Other diseases
1990
Chronic diseases
The burden of disease in the developing world


Injury
Other diseases
2020
Chronic diseases
The burden of disease in the developing world

THE STATE OF SELECTED TOBACCO CONTROL POLICIES IN THE WORLD, 2008



CDC Supports Research to Combat…

- HIV/AIDS
- Malaria
- Tuberculosis
- Influenza
- Zoonotic and other emerging infectious diseases
- Neglected tropical diseases and other diseases that can be eliminated
- Tobacco use
- Other infectious and chronic diseases

Key Research Areas

- Unanswered, answerable, and important questions
- Research process that strengthens coordination between health ministries and in-country academic institutions
- Improve tools for to monitor, prevent, and control communicable and non-communicable diseases

Some Key Knowledge Gaps…HIV/AIDS

- How to scale up proven preventive interventions (condoms, circumcision, etc.)
- How to develop new effective, scalable preventive interventions
- How to develop effective strategies to reduce risky behaviors
- How to increase empowerment and protection for girls and young women

Some Key Knowledge Gaps…

Tuberculosis

- Accurate diagnosis in areas without electricity or expertise
- How to hasten entry into treatment

Malaria

- Development and use of low-cost, rapid diagnostic tests
- Monitoring drug and insecticide resistance
- Evaluate new bed net, indoor spraying, and other preventive interventions

Some Key Knowledge Gaps…

Neglected tropical diseases

- When has transmission stopped?
- Better diagnostic and treatment tools

Water, sanitation, and hygiene

- How to provide safe drinking water, sanitation, and hygiene to vulnerable populations quickly and cost-effectively
- How to scale up successful, sustainable interventions

Some Key Knowledge Gaps… Chronic Diseases

- Surveillance for disease burden and risk factors
- Potential impact of individual and synergistic effects on tobacco use prevalence of implementation of WHO MPOWER strategy
- Identify epidemiologic and food patterns of salt intake
- Identify and implement strategies to reduce salt intake

CDC Maintains Strong Research Partnerships

- Department of Health and Human Services
- Department of Defense
- USAID
- WHO
- UNAIDS
- Host country institutions
- Gates Foundation
- Roll Back Malaria
- National Climate Data Center

Thank You

The Role of the Pharmaceutical Industry in Addressing Global Health R&D Gaps

Mark Feinberg, MD, PhD
Merck Vaccines and Infectious Diseases

NIH Global Health Research Meeting
January 6, 2010

MERCK

Promising opportunities, but a need to do more and better

- Current interest in Global Health is very encouraging--including significant contributions of governments and philanthropies to R&D, and substantially increased funding for implementation efforts
- The advent of new partners (eg, PDPs) provides valuable new contributors to the development of new live-saving products
- Available and emerging technologies can enable tremendous progress in overcoming Global Health challenges
- However, we need to maximize the effectiveness of models for partnership and collaboration to achieve the greatest public health benefit

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What does Pharma have to contribute?

- *A sincere interest in making a positive difference in Global Health*
- Promising leads (eg, compound libraries, lead molecules, candidate antigens)
- Enabling technologies (eg, high tech/high throughput screening, protective antigen discovery, novel adjuvants)
- *Experience in product development, manufacture and licensure*
- *Familiarity with the challenges and risks of new product development (and with critical decision points)*
- *Experience in prioritization of promising options (and killing less promising ones), and in the importance of portfolio management*
- *An appreciation of the critical importance of incorporating the end-user needs/optimal target product profiles into early development decisions (a "line of sight" or "end to end view")*

MERCK

What constrains Pharma's ability to contribute?

- Challenging financial circumstances and the need to improve the productivity of new product development efforts
- Attendant opportunity costs associated with activities that are not directly linked to increased R&D productivity
- Need to share financial and other risks inherent in product development where return on investment is not feasible
- Lack of independent expertise in Global Health needs, realities, opportunities and priorities
- Skepticism of some external parties about sincerity of positive intent and concerns about potential conflicts of interest
- Real or perceived (eg, Intellectual Property) barriers that compromise ability to bring together the most effective partnerships (including those that may require consortia of industrial, government, PDP and academic partners)

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Decreasing Barriers to Pharma's active engagement

- ***Strategic collaborations with external partners (eg, academic and government researchers, PDPs, and philanthropic donors) can help decrease or eliminate factors that limit the extent to which pharmaceutical companies can contribute their discovery and development capacity to advance global health research***

- A number of positive partnership models have been already been developed, but significant opportunities for innovation and impact via creative new partnership solutions between public and private sector entities are now before us

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How is Pharma now engaging in Global Health R & D Initiatives*?

- Access to Libraries, Lead Compounds and Enabling Technologies (eg, DNDi, MMV, IPM and NIH)
- Technology Transfer (eg, Merck-China Hepatitis B Vaccine Partnership)
- Internal Discovery Programs (eg, HIV vaccines and therapeutics)
- Clinical Trial Collaborations (eg, NIH [HIV Vaccines: STEP and Phambili], PATH/GAVI [Rotavirus Vaccine], PATH and IARC [HPV Vaccine])
- Feasibility/Effectiveness Demonstration Projects (eg, Nicaragua MOH [Rotavirus Vaccine], PATH [HPV Vaccine])
- Comprehensive Disease Prevention Programs (eg, Merck-Qiagen Partnership for Comprehensive Cervical Cancer Prevention)
- Pioneering National Treatment and Prevention Programs (eg, the ACHAP collaboration with the Gates Foundation and the Government of Botswana)
- Developing World-Focused R&D Center (eg, the MSD-Wellcome Trust Hilleman Laboratories)

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* Merck examples (and that do not include pricing policies and other access or training initiatives in support of Global Health goals)

What limits Pharma's impact in Global Health Research?

- Current partnerships are often pursued in isolation and can be opportunistic (rather than optimal) in nature (with respect to both available products and partners)
- Partnerships are often developed *de novo* ("reinventing the wheel") around each new R&D project rather than following a common, clearly defined, and well accepted path
- Uncertainties about how complex and expensive development processes will be funded (especially late stage clinical development) and how regulatory pathways for developing world-focused products can best be navigated
- Need for greater comfort between partners with respect to sharing of risk and mutual trust in intent and commitment
- Need for an encouraging environment to innovate and implement new models of collaboration

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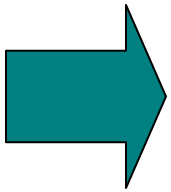
MSD-Wellcome Trust Hilleman Laboratories: Working to Facilitate New Collaborative Models in Global Health R&D

- Many promising research concepts do not reach those who need them the most
- New models of public and private engagement are needed to meet the opportunities and challenges of product development for developing world populations
- Merck and the Wellcome Trust, working together and with other partners, can help meet these needs



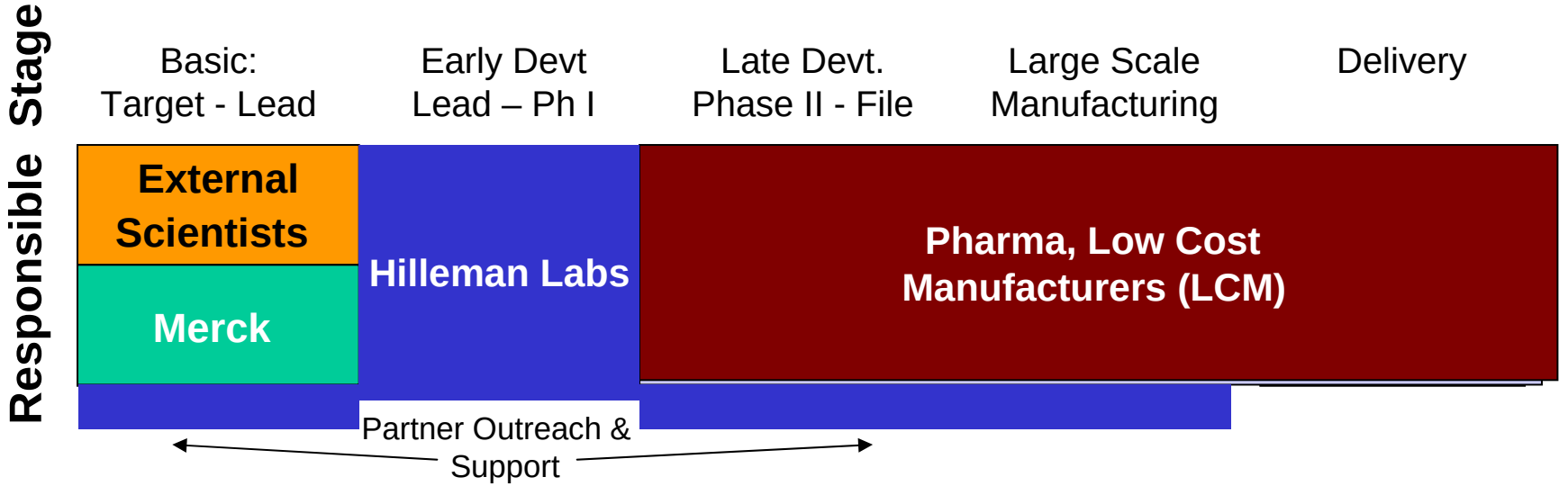
- Leverage Merck's strengths in vaccine discovery and product development
- Leverage the Wellcome Trust's strengths in understanding the needs of the developing world and supporting research of relevance to the DW
- Attract a broad range of potential partners
- Encourage innovation, transparency and sustainability for a long term impact

MERCK

wellcome trust

Filling A Key Gap While Leveraging the Expertise of Diverse Additional Partners

- Complete focus on developing most appropriate and affordable vaccines to meet developing country needs
- Leverages basic research innovations in academia, government, NGOs and industry
- Resident expertise in vaccine bioprocess, formulation and analytics to facilitate transitioning "concepts to proof of concept"—a major obstacle in vaccine development
- Establishes and manages linkages and partnerships among discovery, development, manufacturing and delivery experts



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MSD · Wellcome Trust
Hilleman Laboratories
Developing vaccines for global health

wellcome trust

Enabling fuller realization of Pharma's potential

- Broaden the definition of partnership models (eg, public:private, private:private and those involving multiple relevant partners with the greatest potential skills/assets to contribute)

- More fully engage product development experts resident in industry as advisors for public sector Global Health R&D efforts

- Development of a mechanism, when diverse partners are involved, to recapitulate the highly integrated approaches that characterize successful industry R&D programs and that best leverage each partner's skills/resources at successive stages

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Some concluding thoughts

- We can (and need to) do much better in making the concept of “public-private partnerships” as broadly engaging and effective as possible

- We need to develop more proactive, strategic, predictable and trusting models of partnership and collaboration that have an “end to end” view and that realistically prioritize opportunities, marshal contributions and manage risks

- ***The NIH can play a powerful positive role via thoughtful planning, strategic engagement and the development of new models for collaboration with diverse external partners***

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NIH Global Health Research Meeting

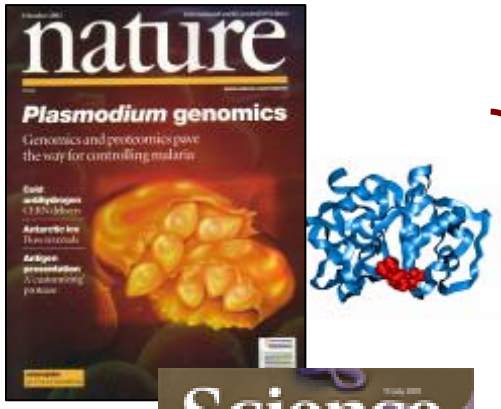
Needs, Opportunities, Challenges and Partnerships

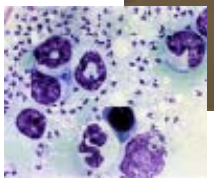
Bernard Pécoul,
Executive Director

DNDi
Drugs for Neglected Diseases *initiative*

Best Science for the Most Neglected

Product Development Partnerships (PDPs): Filling the Gaps in Translational Research and Product Development





malaria vaccine initiative

FIND FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS

INTERNATIONAL PARTNERSHIP for MICROBICIDES

Medicines for Malaria Venture

PATH

AERAS GLOBAL TB VACCINE FOUNDATION

iOWH Institute for OneWorld Health

DNDi Drugs for Neglected Diseases *initiative*

avi International AIDS Vaccine Initiative

IVI International Vaccine Institute Dedicated to preventing infectious diseases through science

SABIN VACCINE INSTITUTE

TB ALLIANCE GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

PDVI Pediatric DENGUE VACCINE INITIATIVE

DNDI Project Portfolio (January 2010)

Discovery (S / LS / LO)	Pre-clinical	Clinical	Available

Best Science for the Most Neglected

Discovery Activities
- Compound mining
- Chemical classes
- Target-based
- Screening

HAT LO Consortium
- *Scynexis*
- *Pace Univ.*

VL LO Consortium
- *Advinus*
- *CDRI*

Chagas LO Consortium
- *CDCO*
- *Epichem*
- *Murdoch Univ*
- *FUOP*

Nitroimidazole backup (HAT)

Oxaborole (HAT)

Alternative formulations Amphotericin B (VL)

Drug combination (Chagas)

Exploratory

Fexinidazole (HAT) (sanofi-aventis)

Combination therapy (VL in Asia)

Combination therapy (VL in Africa)
- **Paromomycin** (Gland Pharma)
- **AmBisome®** (Gilead)
- **Miltefosine** (Paladin)

Combination therapy (VL in Latin America) – in preparation

Paediatric benznidazole (Lafepe) (Chagas)

Azoles Eisai1224 (Chagas)

Exploratory

NECT
Nifurtimox - Eflornithine Co-Administration Stage 2 HAT

ASMQ
(Malaria) Fixed-Dose Artesunate/ Mefloquine Farmanguinhos ; Cipla

ASAQ
(Malaria) Fixed-Dose Artesunate/ Amodiaquine Sanofi-aventis

a robust pipeline

6 to 8 new treatments by 2014

Major Collaborators
- **Sources for hit and lead compounds:** *GSK, Anacor, Merck, Pfizer, Novartis (GNF, NITD), GATB,…*
- **Screening Resources:** *Eskitis, Institut Pasteur Korea, Univ. Dundee,…*
- **Reference screening centres:** *LSHTM, Swiss Tropical Institute, University of Antwerp*

Best Science for the Most Neglected

Well-balanced public/private partnerships

Donors

$180 M of $33O M Secured

(2004-2014)

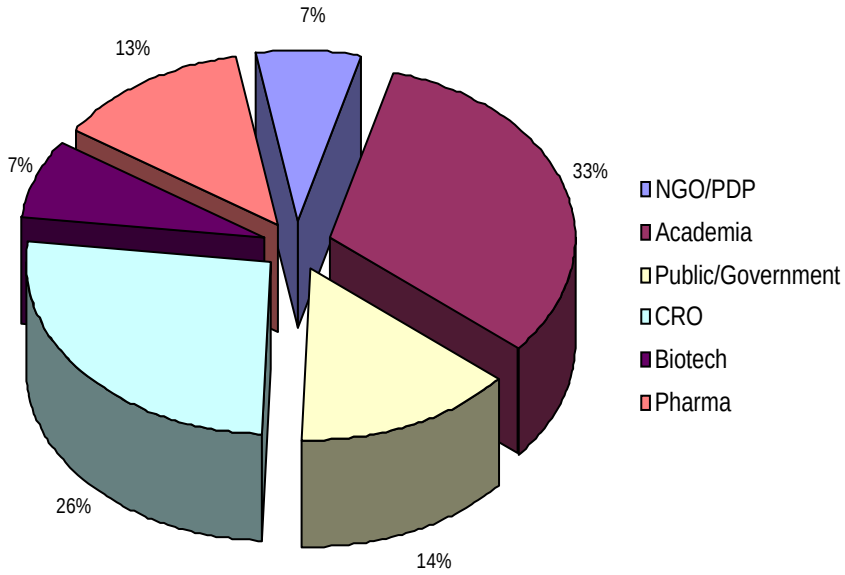
Private Donors

- Médecins Sans Frontières ($ 61M)
- Bill & Melinda Gates Foundation ($ 41M)
- Other Private Foundations

Public Donors

- United Kingdom - DFID ($ 40M)
- France – AFD & MAEE ($ 11,5 M)
- Spain – AECID ($ 11M)
- Netherlands – DGIS (€4,5M)
- Germany – GTZ ($ 1,5 M)
- USA-NIH/NIAID ($ 1,4 M)
- Other governments, EU

204 R&D Partners



Best Science for the Most Neglected

Discovery & Preclinical

Needs/Opportunities	Challenges	Potential Partnerships
• **Screening and access to compounds** • **Pipeline of New Chemical Entities to meet Target Project Profile**	• **Access to compound libraries** • **Investment in High Throughput Screening** • **Lead optimization / disease consortia** • **Pre-clinical package**	• **Pharmas, Biotechs** • **Research institutes (public & private) & universities** • **New donors supporting discovery portfolio vs individual projects** (ie. NIH/NIAD, EU…)

Best Science for the Most Neglected

DNDi

Clinical

Needs/Opportunities	Challenges	Potential Partnerships
• **New Chemical Entities in clinical development** (ie DNDI: 6 NCEs for HAT, VL & Chagas) • **Biomarkers to support clinical development**	• **Develop clinical research capacities in endemic countries** (ie clinical trial platforms) • **High quality clinical research programs** • **Support partners / develop biomarkers** (ie FIND)	• **Public research institutes & nat. control programs in endemic countries** • **CROs** • **New funding partners like USAID, NIAID, endemic countries public funders or new mechanisms**

Best Science for the Most Neglected

Access

Needs/Opportunities	Challenges	Potential Partnerships
• **Introduction of new treatments** (ie. DNDi: 3 available now & 3 potentially available in 2010)	• **Implementation of treatments in endemic countries to ensure availability, access, rational use** • **Strengthening regulatory capacities in endemic countries**	• **National programs, NGOs, pharmas** • **WHO & regulatory agencies** (FDA, EMEA, NRA in endemic countries) • **Multilateral or bilateral funding organizations** (ie. USAID, endemic countries public funders)

By working together in a creative way, PDPs, large and small pharma, and the public sector can bring innovation to neglected patients!

www.dndi.org

DNDi

Drugs for Neglected Diseases *initiative*

Global Health Research - Strategy

- Broaden the research base for scientific endeavour in under-resourced environments
- Support areas of science that have potential for increasing health benefits for people and livestock
- Support international networks and partnerships focused on problems of resource-poor countries

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Major Overseas Programmes

Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam

Director: Jeremy Farrar

Chairman: Nick White

Mahidol University, Bangkok.
Sites across Thailand and Lao

Director: Nick Day

GLOBAL HEALTH FUNDING

Wellcome Trust total charitable expenditure 2007:
£520m (US$1020m)

Wellcome Trust total international charitable expenditure 2007:
£75m (US$147m)

- Developing and restructuring countries: the focus of our global health research funding
- UK: £33m was awarded to researchers at institutions in the UK and Republic of Ireland in 2007 for research to be carried out overseas
- Major Overseas Programmes

KEMRI, Nairobi, Kilifi
Director: Kevin Marsh

Africa Centre, KwaZulu-Natal
Director: Marie-Louise Newell

College of Medicine, Blantyre
Director: Rob Heyderman

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Fellowship schemes for Developing Country researchers*

*which aim to stimulate and foster research on tropical medicine and public health

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African Institutions Initiative

Strengthening African Higher Education and Research Institutes

- To create equitable and sustainable networks and partnerships between institutions through South-South and North-South linkages
- To build a critical mass of local research capacity geared to national priorities
- To support human resources and infrastructure necessary for the development of the administrative, governance, financial and management
- To develop and build leadership at individual, institutional and national levels so countries can better initiate and lead research activities
- To support research leaders to act as beacons and role models to enthuse young scientists to develop research careers

www.wellcome.ac.uk/globalhealth

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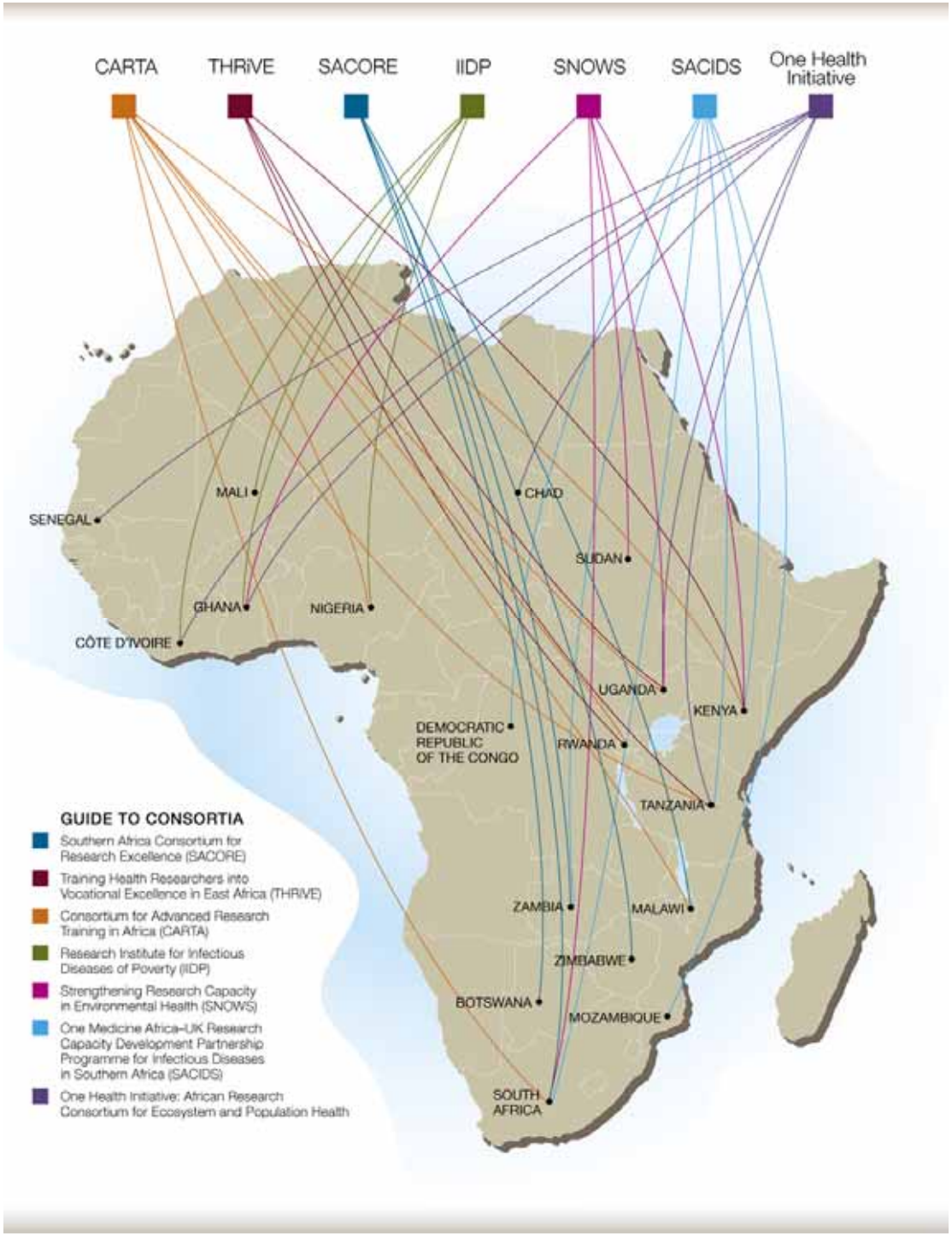

African Institutions Initiative

- 7 awards made to consortia involving 70 institutions (50 in Africa)
- 5 year period, starting August 2009
- £28m in total

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Swiss Commission for research partnerships with Developing Countries

11 principles

- Decide on objectives together
- Share information
- Create transparency
- Disseminate results
- Share profits equitably
- Build on achievements
- Build upon mutual trust
- Share responsibility
- Monitor and evaluate collaboration
- Apply results
- Increase research capacity

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Initiative to Strengthen Health Research Capacity in Africa (ISHReCA)

Aim: promote self-sustaining pools of researchers capable of initiating and carrying out high quality health research in Africa

Mission: facilitating translation of research products into policy and practice through integrated approaches to capacity building at individual, institutional and system levels

ISHReCA Steering Committee members:
Uganda, Kenya, Ethiopia, Tunisia, Ghana, South Africa, Cameroon, Congo Brazzaville, Guinea Bissau, Burkina Faso, Mozambique

Secretariat: Tropical Disease Research (TDR) WHO

See: http://ishreca.tropika.net/

ISHReCA
Initiative to Strengthen Health Research Capacity in Africa

Sida

TDR For research on diseases of poverty
UNICEF • UNDP • World Bank • WHO

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Complementary approaches to drug discovery

Industry Joint Venture

NOVARTIS INSTITUTE FOR TROPICAL DISEASES

- Novartis Institute (since 2005)
- Syndicate Funding ($20M, 5 yrs)
- Disease Specific: P. vivax & falciparum
- Portfolio Based
- Multiple Collaborations
- Linkage with MMV clinical programs

University Infrastructure

UNIVERSITY OF DUNDEE

- University of Dundee (since 2006)
- Syndicate Funding (£13M, 5 yrs)
- Disease focus: African trypanosomiasis
- Portfolio Based
- Industry Recruitment
- Independent SAC

Seeding Drug Discovery

- Academia / SME / Pharma (since 2006)
- £91M, 5 Year Fund
- Any Therapeutic Area
- Projects Complementary to Industry
- Project-based
- Outsourcing Model

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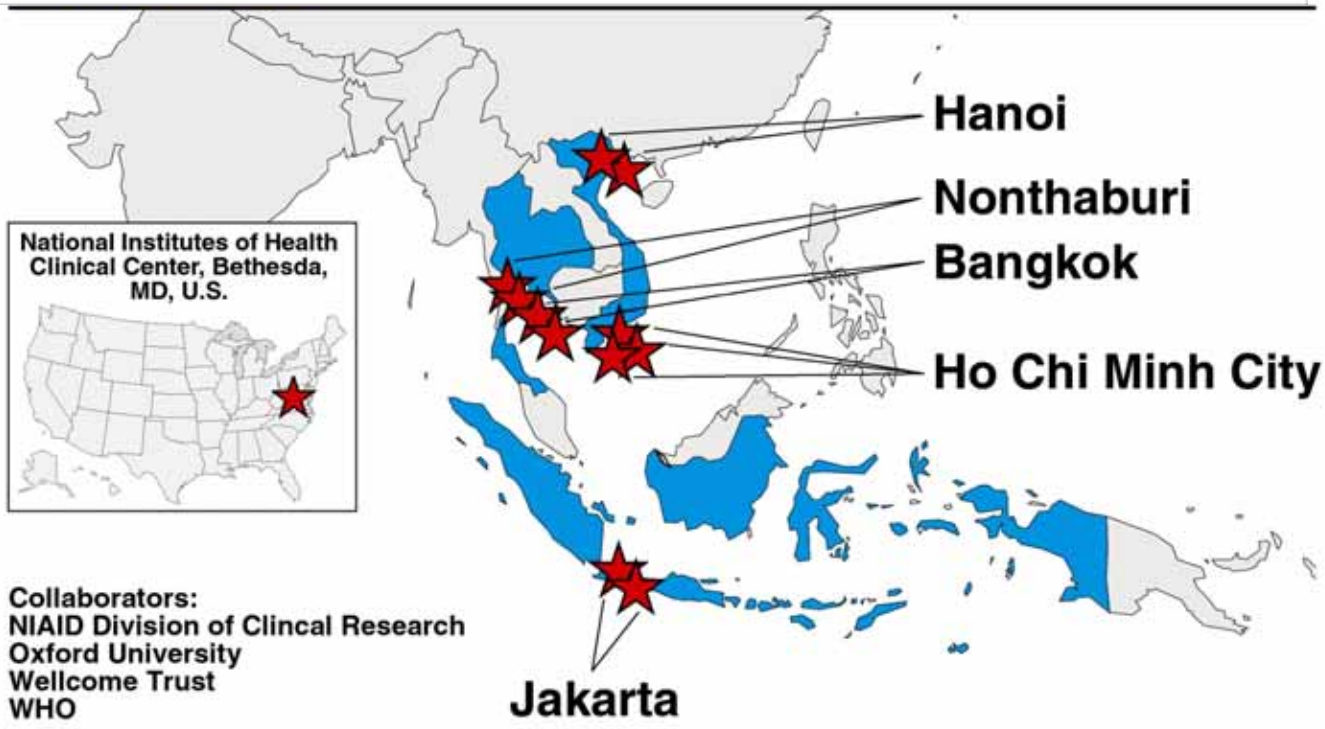
SEA

Infectious Disease Clinical Research Network



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Wellcome Trust/Department for Biotechnology India Alliance

- Launched in September 2008
- £8m WT and £8m DBT per year (5 years)
- Headquarters in India
- CEO and grants team in place
- Funding committees meet and make awards in Hyderabad every 3 months
- Awards at key stages:
  - early career fellowships
  - intermediate fellowships
  - senior fellowships
- **www.wellcomedbt.org**

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Department of Biotechnology
Ministry of Science and Technology

Indian Affordable Healthcare

New, £30M scheme, launched October 2008
Local sourcing of projects
Funding by dedicated Indian R&D committee

Focus on:

- **the poor**
- **the marginalised (eg rural communities)**
- **those set to escape the poverty trap**

Looking for:

- **Affordability**
- **Dissemination potential**
- **Health impact**

First award:

Cardiovascular polypill for primary prevention of CVD

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MSD-Wellcome Trust Hilleman Laboratories

Vision

A sustainable, not-for-profit operating model to turn innovative science into practical solutions for those in greatest need

➢Mission

➢To develop high impact, affordable vaccines for people in developing countries in an innovative and sustainable manner

•Focus

- Novel vaccines for diseases of developing countries

» Vaccines optimized for developing country needs

Overall, achieve formulations that meet the needs of large procurement agencies (e.g. WHO, UNICEF, GAVI)

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- Free standing, not-for profit company
- Founding partners, Merck & Co Inc and the Wellcome Trust
- Core funding of $140M over 7 years from founders
- Planned location in India
- Joint Merck & Wellcome Board
- Executive team (CEO, CSO, COO) & staff of 60 people
- Advisory board of external experts to input on strategy
- Focus on R&D, outsourcing as required
- Transfer of process to external parties for manufacture/sale
- Development of a portfolio of projects (4-6) balanced for time to delivery/novelty/risk

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NIH MEETING ON FUTURE OPPORTUNITIES IN GLOBAL HEALTH RESEARCH

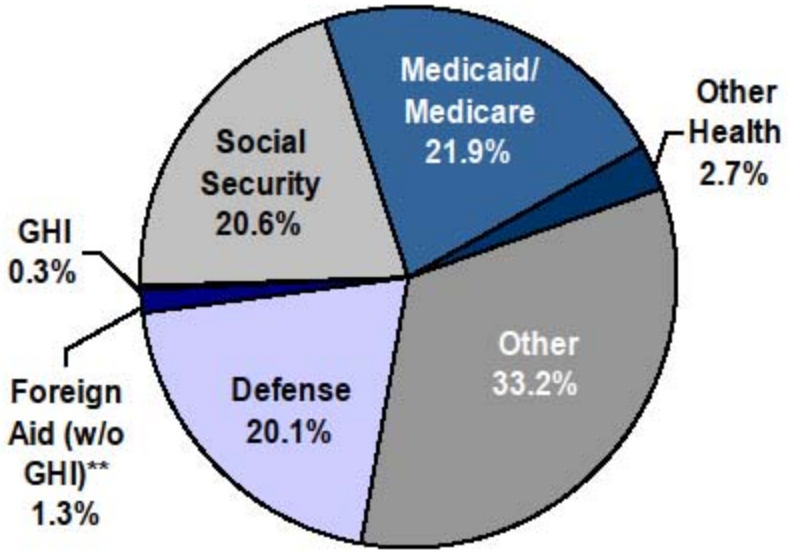
Epidemiological and Population Research

Barry R. Bloom
Harvard School of Public Health
January 6, 2010

Focus Discussion on Epidemiology and Population Science

- New or Emerging Population-Based Problems or Research Areas that NIH Could or Should be Addressing
- New or Emerging Areas of Knowledge where Population based Research would be Informative
- Existing Areas of Research that Should be Extended to Populations in Developing Countries.

Figure 16: Funding for the U.S. Global Health Initiative as Share of Federal Budget Request, FY 2010*

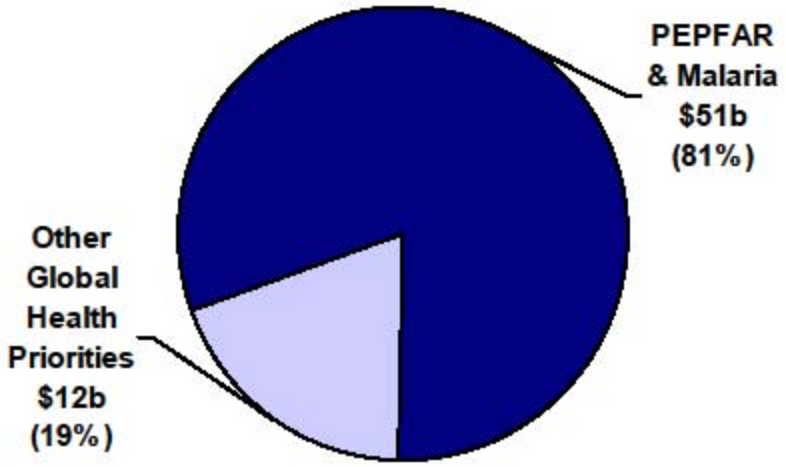


Federal Budget Request $3.4 trillion

US GDP = $14.24 trillion

*FY 2010 represents the President's budget request only. **International Affairs "150 Account" excluding the portion of the GHI that is funded through the 150 Account. Also excludes international financial programs (SF155).
Source: Kaiser Family Foundation analysis of data from the Office of Management and Budget, Agency Congressional Budget Justifications, Congressional Appropriations Bills, and White House Statement by the President on Global Health Initiative, May 5, 2009. Federal budget data by major category were obtained from Historical Tables of the Federal Budget, Table 5.1, "Budget Authority by Function and Subfunction: 1976-2014".

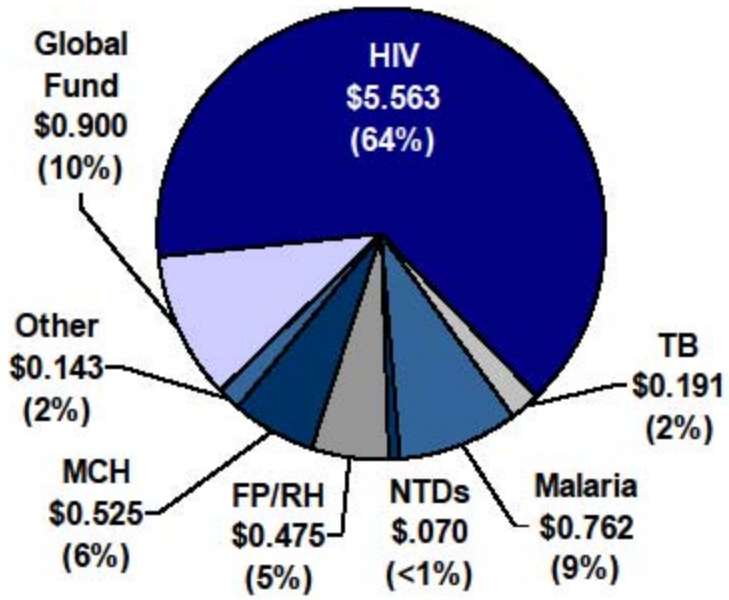
Figure 2: U.S. Global Health Initiative, Proposed Funding for PEPFAR, Malaria, & Other Global Health Priorities, FY 2009-2014 (in billions)



Total = $63 billion

*FY 2010 represents the President's budget request only and FY 2011-FY 2014 would need to be part of future budget requests and approved by Congress.
Source: Kaiser Family Foundation analysis of data from the Office of Management and Budget, Agency Congressional Budget Justifications, Congressional Appropriations Bills, and White House Statement by the President on Global Health Initiative, May 5, 2009.

Figure 1: U.S. Global Health Initiative, The FY 2010 Budget Request (in billions)

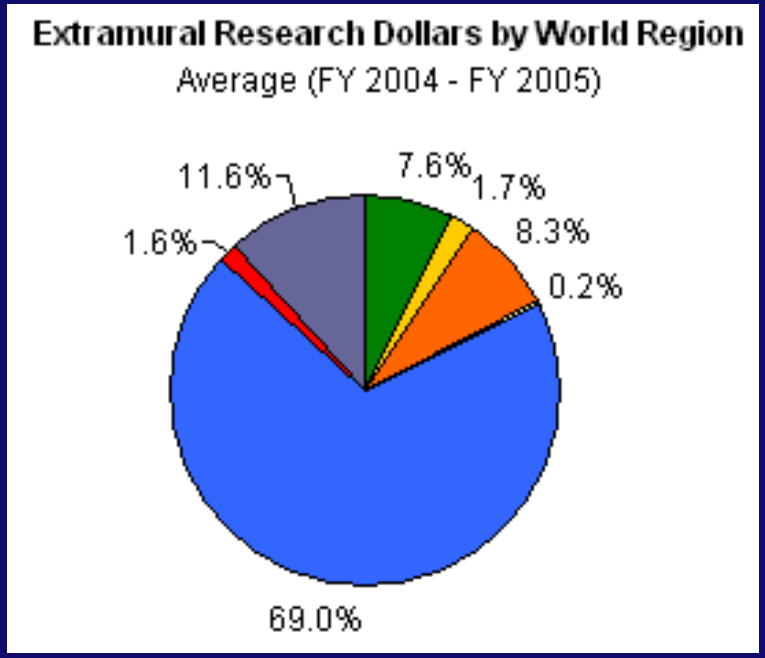


Total = $8.6 billion

*FY 2010 represents the President's budget request only.
Source: Kaiser Family Foundation analysis of data from the Office of Management and Budget, Agency Congressional Budget Justifications, Congressional Appropriations Bills, and White House Statement by the President on Global Health Initiative, May 5, 2009.

NIH Foreign Research Support by World Region

N = $597,916,000



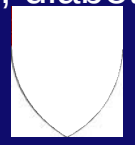
Health of Populations
The Public Health Paradigm

- Define the Problem, including the Burden of Disease
- Identify the Risk Factors
- Design Interventions to Prevent or treat the Disease or Problem

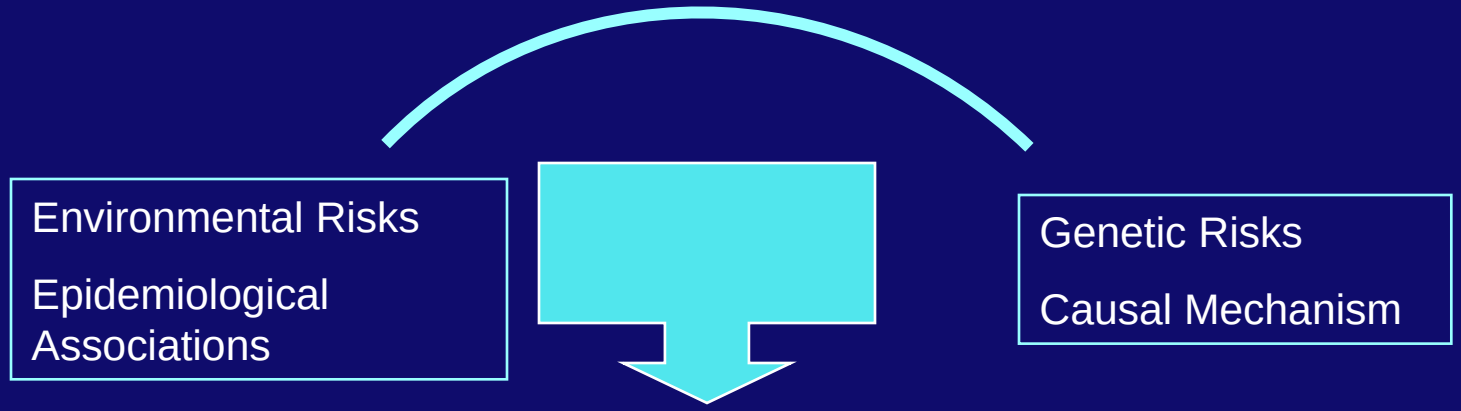
Evaluate the Outcome of Interventions

Defining the Problem

- The Unfinished Agenda of Acute and Communicable Disease
  - Emerging and Persisting Infections –
    - HIV,/AIDS, Malaria, TB, parasites,
    - Emerging Drug Resistance
  - Maternal and Infant Mortality
  - Early childhood infections
- The Coming Epidemic of Chronic and Non-Communicable Disease
  - Obesity, Diabetes, CVD, Neuropsychiatric diseases
  - HIV/AIDS
- Surveillance
  - Need for better Surveillance and Health Information Systems, incl. labs,
  - Need to assess Burden of Chronic as well as Infectious Diseases
  - Use DHS, Hospital, Household surveys, symptomatic surveillance, satellite
- New Technological Advances
  - Rapid Point of Care/Treatment Diagnostics, e.g. TB, HIV, malaria, CVD, diabetes
  - Biomarkers, eg for vaccine protection, CVD risk
  - Assessing Drugs and Vaccines



Identifying Disease Risks
Linking Extrinsic Risks to Intrinsic Risks



INTERVENTIONS

Population-based Strategies

- For Extrinsic Risks
  - Observational Studies
    - Case Control Studies – Prospective or Retrospective
    - Time Series,
  - Cohort Studies, continuous, multifactorial information
- For Intrinsic Risks
  - Genetic Studies
    - Family, case control or cohorts
    - GWAS
- For Interventions
  - Randomized Controlled Trials
    - Individuals, Hospitals, Countries, districts, towns, villages
  - Nested Case Control studies
  - Modeling

Proposal for Creating an African Genetic/Epidemiologic Cohort

- Africa represents the Greatest Source of Genetic Polymorphisms
  - human genetic potential,
  - Infer selection pressures on the human genome
  - Shortest linkage disequilibrium intervals to map genes
  - Opportunity to learn epidemiological as well as intrinsic risks for disease in in countries and societies in transition.
  - Enhance phenotyping for human genome project
- Global Health Impact
  - Opportunity to create an African scientific network around a coherent long-term, multidisciplinary project
  - Sub-Saharan Region in Greatest Need for Research Capacity and Leadership Strengthening
  - Necessary to create critical capacity for development of biotech and pharmaceutical sectors
- Problem: Traditionally NIH has had Limited Mechanisms and Incentives to fund Multi-Disease, Cross-Institute projects.

Needs for Global Health Systems Research

Health systems are the institutional arrangements by which societies provide for health needs of their people. They includes all the activities whose *primary purpose* is to promote, restore or maintain health.

Components of health systems include:

- Agenda setting
- Health workforce and human capacity
- Financing and resource allocation
- Leadership and Management
- Governance
- Sustainable drug acquisition
- Access to health services
- Platforms for delivery of health services
- Scale up and equity of health services
- Role of public and private sectors
- Metrics and evaluation

Proposed Agendas for Global Health Systems Research

- Implementation Research
  - How to get what we know to the populations that could benefit
  - Consolidating platforms, e.g. acute and childhood, chronic, injuries.
- Quality Improvement Research
  - How to improve the process of health delivery, e.g. medical errors, incentives
- Developing capacity for translational and clinical research
  - Networks and Centers of Excellence
- Engaging the Private Sector
  - PPPs, PDPs,
- Capacity building, strengthening, and Leadership Training.
- Complex Intervention Research: Analysis and Evaluation
  - Methods for real time vs retrospective analysis
  - Comparative effectiveness and value for money

Focus Discussion on Epidemiology and Population Science

- New or Emerging Population-Based Problems or Research Areas that NIH Could or Should be Addressing
- New or Emerging Areas of Knowledge where Population based Research would be Informative
- Existing Areas of Research that Should be Extended to Developing Countries.

Potential Specific Investments in Global Health Research

Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health

January 6, 2010

Main Objectives of Today's Meeting

- To gain the benefit of current thinking from academic, government, philanthropic, industrial, and international organizations on some of the most pressing strategic needs and opportunities in global health R&D.

- To identify a potential set of initiatives that would fit NIH's mission as a research organization, that might be supported independently or in partnership, and that would have the greatest multiplier effect on global health R&D in the next five to ten years.

Possible areas for additional NIH investment – fundamental science

- Pathogen and vector biology – especially TB
- Behavioral research, especially tobacco cessation – what works in the developing world?
- Genomic variation and predisposition to disease
- Nutrition research – biofortification (with USDA)
- Climate change and health consequences
- Environmental factors, such as cookstoves
- Biomarkers
- Regulatory science

Possible areas for additional NIH investment – epidemiology/populations

- An African Genetic/Epidemiologic Cohort – genotypes and phenotypes on a large scale
- Other large scale prospective cohort projects
- Nested case-control studies
- Global health systems research – implementation, quality improvement
- mHealth research applications
- Comparative effectiveness research
- Explore use of Biobanks (China)
- Huge problem of lack of surveillance data about morbidity and mortality in many countries

Possible areas for additional NIH investment – diagnostics

- Rapid, accurate, cost-effective easy to use point-of-care diagnostic tests for:
  - TB
  - Malaria?
  - CD4 counts
  - Drug resistance
  - Influenza
  - Diarrheal illness
  - NTDs
- Challenge of recruiting the right disciplines and setting explicit goals – needs exquisite project management
- Regulatory science
- Need to engage end-user at the beginning, not the end
  - Includes need for samples for method validation

Possible areas for additional NIH investment – drugs and vaccines

- Take advantage of NIH TRND program (Therapeutics for Rare and Neglected Disease)
- Prioritization of therapeutic needs for the developing world? Revisit the IOM recommendations on vaccines (10 years ago), WT on vaccines/drugs (5 years ago), TDR? Must depend on scientific opportunity as well as public health need.
- Engineered immunity/humanized antibodies
- HBV alone vs. HBV + HPV trial in infants
- Noncommunicable diseases: polypill for cardiovascular disease?
- Must include consideration of downstream activities at the outset

Possible areas for additional NIH investment – capacity building/training

- Training grants in global health research
- Offer all NIH trainees the chance to do some component of training internationally?
- Expand US training opportunities for scientists from low income countries but strongly encourage return to home country; tap into NIH alumni network
- Strengthen academic institutions by investing in Centers of Excellence in the developing world, especially those that build consortia around them
- Explore indirect cost rate restrictions
- Expand ICIDR?
- Leadership training for institutional managers

Possible areas for additional NIH investment – science policy

- Continue to emphasize open data access
- Allow more facile support of in-country infrastructure with R01s
- Better communication/PR – emphasizing equity

What I'd like to hear now from each of you

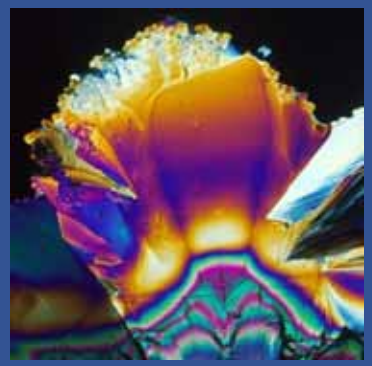
- If you were the NIH Director, what single global health program would you put at the top of your priority list
- Caveats:
  - Must not be illegal
  - Must fit within NIH's mission
  - Must be specific, with the ability to judge success or failure
  - Must be possible to describe in 30 seconds or less
- Hoping particularly to hear from those who have not had a chance to speak today
- But it's OK to pass if your idea has already been articulated

Send additional observations to

Vesna Kutlesic:

kutlesicv@mail.nih.gov

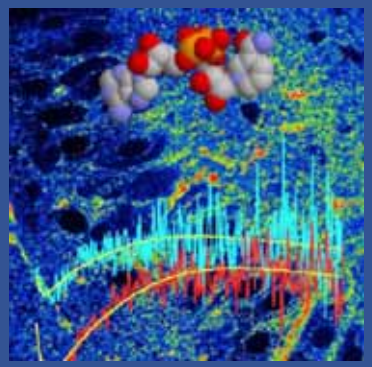
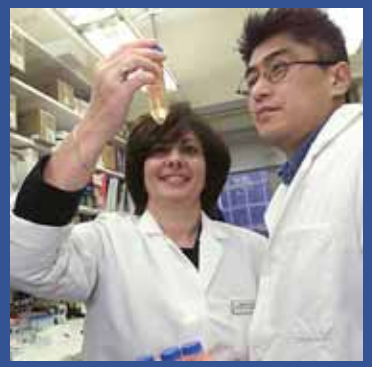





NIH

Many thanks to all,

and safe travels home!


Global Health Research Meeting, January 5–6, 2010
Reception Photos

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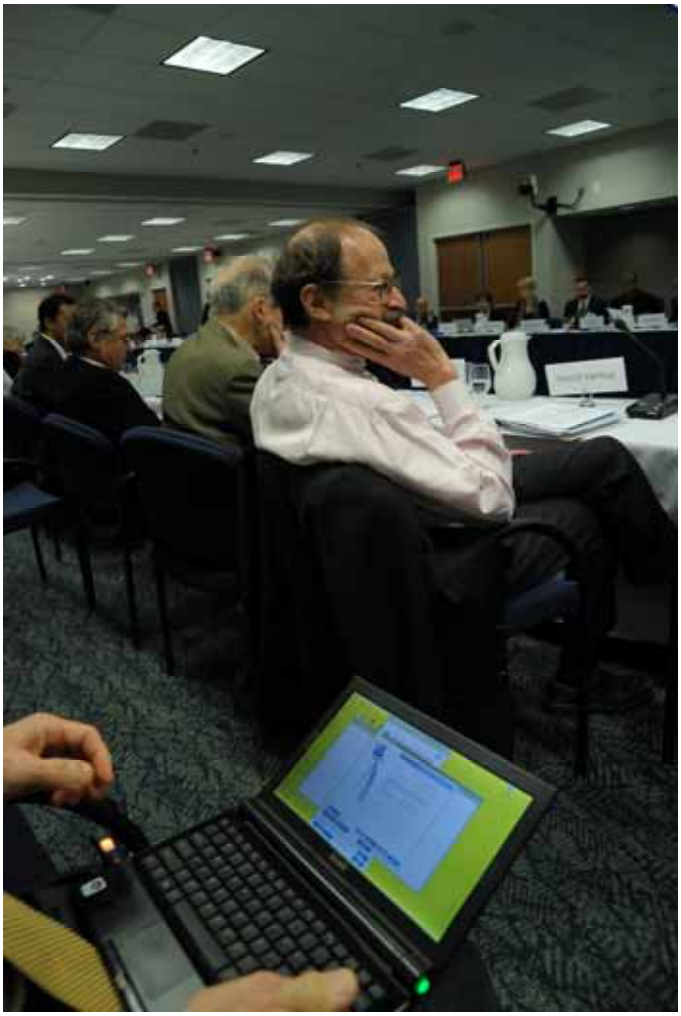

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