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Item

Antibiotic Resistance – The agreement reflects concern about growing antibiotic resistance. The agreement encourages NIAID, BARDA, CDC, and other appropriate partners, within 180 days, to conduct a workshop and develop a coordinated action plan to address research, public health and preparedness issues in this field. It is anticipated that NIAID will work with partners to develop a comprehensive plan with a timeline and measurable objectives for each partner to address the issues over the next five years. The agreement also urges NIAID to increase its efforts to accelerate the development of new antibiotics.

Action taken or to be taken

Research to address the growing concern of antimicrobial-resistant pathogens is a longstanding priority of the National Institute of Allergy and Infectious Diseases (NIAID), lead component of the National Institutes of Health (NIH) for research on antimicrobial resistance. As outlined in the 2014 report, "[NIAID's Antibacterial Research Program: Current Status and Future Directions](#)," NIAID supports a robust research portfolio that includes basic research on how microbes develop resistance; development of novel antibiotics and rapid diagnostics; and clinical trials designed to find new treatments and vaccines effective against drug-resistant microbes. To complement these efforts, in 2013, NIAID established an Antibacterial Resistance Leadership Group to design, implement, and manage a new clinical research agenda for antibacterial resistance. The President's fiscal year 2016 budget proposes to expand NIH antimicrobial resistance research with \$100 million in additional funding, including clinical trials to facilitate rapid testing of new drugs.

In September 2014, the White House announced comprehensive Federal actions to combat antibiotic-resistant bacteria and protect public health, including an Executive Order and National Strategy on Combating Antibiotic-Resistant Bacteria (CARB). As part of these Federal actions, NIH and the Biomedical Advanced Research and Development Authority (BARDA) will fund a \$20 million prize to incentivize the development of a rapid diagnostic for antibiotic-resistant bacteria. The Executive Order on CARB establishes a Federal Task Force on CARB, and NIH is collaborating in this effort with other Federal agencies, including the Centers for Disease Control and Prevention (CDC), BARDA, the Food and Drug Administration (FDA), and the Department of Defense (DOD), among others. The Task Force will develop a five-year National Action Plan outlining specific milestones, timelines, and metrics for measuring progress in implementing the National Strategy on CARB. In light of its role in the Task Force efforts, the Department of Health and Human Services does not plan to launch a duplicative effort.

NIAID works closely with partners in academia and industry to advance the development of diagnostics, therapeutics, and vaccines for antimicrobial-resistant infections. In collaboration with FDA, NIAID held a series of workshops in 2014 that focused on advancing the development of antimicrobial therapeutics and diagnostics, including: 1) *The Development of New Antibacterial Products: Charting a Course for the Future*; 2) *Overcoming Bottlenecks in Antibacterial Product Development*; and 3) *Coordinated Development of Diagnostics and Therapeutics*. NIAID, FDA, and other Federal agencies are working together to respond to the recommendations of these workshops.

With NIAID support, scientists recently identified the novel antibiotic teixobactin from bacteria that live in dirt. This antibiotic has shown promise against drug-resistant microbes in a mouse

model, and will be investigated further. Currently, NIAID is supporting the advanced development of several novel broad-spectrum therapeutic candidates, including a protein synthesis inhibitor, next-generation aminoglycoside and tetracycline drugs, and bacterial DNA replication inhibitors with broad activity against Gram-negative pathogens. NIAID-supported clinical trials began in 2014 for a new formulation of a drug to treat urinary tract infections as well as a novel bicyclolide antibiotic for methicillin-resistant *Staphylococcus aureus* (MRSA) infections. In addition, NIAID intramural researchers discovered an essential *S. aureus* toxin export system with key roles in pathogenesis. The researchers plan to target this export system to develop novel drugs that could be effective against drug-resistant *S. aureus*, including MRSA.

NIAID will continue to participate in trans-Federal efforts and collaborate with colleagues from CDC, BARDA, FDA, DOD, and the White House, among others, to address preparedness, public health, and research on antimicrobial resistance. In partnership with academic and industry scientists, NIAID will continue to conduct and support promising research to develop new antimicrobial drugs.

Item

Big Data – The agreement continues to expect NIH to protect the privacy of individuals who are the subject of research. As the Big Data to Knowledge Initiative (or any similar initiative) creates new methods of collecting data from research, attention must be paid to new ways of protecting the data of individuals involved. NIH is directed to include requirement related to privacy protections in every grant that involves human research, such as the issuance of certificates of confidentiality.

Action taken or to be taken

The National Institutes of Health (NIH) agrees that as expectations and processes for collecting and sharing research data grow, it is vitally important to be attentive to any new vulnerabilities that might be created in terms of our ability to protect the privacy of individual research participants from whom the data are obtained. Protecting personal privacy and the confidentiality of information obtained from research participants, whether in small primary research studies or through the secondary analysis of “Big Data,” is a fundamental ethical tenet and crucial for maintaining public trust in the research enterprise.

A number of protections exist to safeguard the privacy of research participants. These include the Health and Human Services (HHS) regulations for the protection of human subjects (the Common Rule) and the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule. NIH requires all NIH-funded research involving human subjects to adhere to these rules and their important privacy and confidentiality protections. These rules are among the public policy mandates listed in the NIH Grants Policy Statement (GPS), and grantees are required to follow them as a term and condition of NIH awards. Violation of the terms and conditions of award can result in compliance actions including termination of funding. Investigators and key institutional personnel involved in human subjects research studies must also be trained in the protection of human subjects, including safeguards that must be in place to protect their privacy and the confidentiality of information obtained from them.

Additional protections are provided by Certificates of Confidentiality (CoC), and NIH encourages grantees who will be obtaining sensitive, identifiable information from research participants to obtain such documents. Certificates authorize investigators to withhold participant names and other identifying information including genetic information, if the information is ever sought through a Federal, State, or local civil, criminal, administrative, legislative proceeding or other authority. In addition to encouraging and facilitating the use of Certificates during the grant application and award process, NIH highlights their importance in the context of data sharing. For example, the NIH Genomic Data Sharing Policy encourages all grantees conducting large-scale genomic research to submit data to NIH-designated repositories. Those grantees as well as the investigators who are approved to use the data for secondary research purposes are expected to obtain Certificates.

NIH is currently exploring whether there are additional data protections that can be instituted. For example, it may make sense to take further steps to encourage more grantees to take advantage of the protections provided by Certificates. In addition, NIH supports efforts to strengthen protection of patient information, particularly individual level genomic data. Since genomic data is unique to an individual, it is possible to determine an individual’s identity if one has access to an identifiable reference sample. Genomic data can also reveal significant and

sensitive personal information, including susceptibility to or predictability of diseases like Huntington's Disease or cancer.

Item

Blue Ribbon Commission on Scientific Standing – The agreement directs the NIH Office of the Director to fund, in consultation with the National Science Foundation and Department of Education, a contract with the National Academy of Sciences to establish a Blue Ribbon Commission charged with discerning American public opinion on, understanding of, and acceptance of scientific research. The Commission shall examine the present state of scientific repute in America and present recommendations for how to improve scientific literacy, education, and enhance scientific regard amongst the American public.

Action taken or to be taken

Public understanding of science, particularly biomedical research and its applications to health, is a crucial step toward a healthy, productive society. Improving scientific literacy and education will help Americans engage more fully in their health care decisions as well as encourage young people to pursue careers in scientific research, cultivating tomorrow's leaders in innovation. The National Institutes of Health (NIH) relies on the National Academy of Sciences (NAS) for its ability to convene a wide array of stakeholders to deliberate the vital scientific issues of our time in an unbiased forum. NIH appreciates the opportunity to engage NAS expertise on this important issue, and will explore how the NAS can develop recommendations for improving scientific literacy, education, and enhance scientific regard amongst the American public.

Item

Cardiovascular Disease – The agreement reflects awareness that in March 2014, Cambridge University researchers reported that current evidence does not clearly support cardiovascular guidelines that encourage high consumption of polyunsaturated fatty acids and low consumption of total saturated fats. The agreement recognizes that these findings create conflicting information being provided to the public. The agreement request NHLBI convene a state of the science meeting within 180 days after enactment with participants from CDC and other appropriate scientists from all sides of this debate to identify the open questions arising from this new study.

Action taken or to be taken

The Dietary Guidelines for Americans (DGA), issued every five years by the Departments of Agriculture (USDA) and Health and Human Services (HHS), form the basis for nutrition policy in Federal food, education, and information programs, and are intended to provide consistent evidence-based dietary advice to the public. The 2010 DGA recommend consuming less than 10 percent of calories from saturated fatty acids by replacing them with monounsaturated and polyunsaturated fatty acids, within a total fat intake of 20-35 percent of calories. These recommendations are based on strong scientific evidence that as saturated fatty acid intake increases, so does serum LDL cholesterol. Increased LDL cholesterol increases risk for coronary heart disease and resulting mortality.

USDA and HHS are in the process of developing the 2015 DGA to reflect the current state of the science on dietary intake to improve health and reduce chronic disease risk. An external scientific Dietary Guidelines Advisory Committee (DGAC) has completed a systematic analysis of existing scientific evidence, and submitted a report to HHS and USDA. The DGAC report will then be reviewed by appropriate agency staff, will be posted for public comment and then undergo scientific peer review and agency clearance before being released later this year.

The DGAC report will include consideration of the March 2014 study published by Cambridge University researchers among many others. In that study, Chowdhury, et al. conducted a meta-analysis of 49 observational studies and 27 randomized clinical trials to find links between dietary intake or circulating levels of different types of fatty acids and coronary heart disease. Several scientific experts in the field pointed out that the analysis contained errors of commission, omission, and interpretation, some of which were acknowledged and corrected by the authors. The DGAC is conducting a complete accounting of the entire evidence base, which will be used to inform the upcoming guidelines.

In addition, the National Institutes of Health (NIH) continues to explore ways to improve its understanding of emerging scientific evidence as it relates to the impact of diet on chronic disease. In March 2015, NIH is convening a workshop of expert nutrition scientists to critically evaluate key scientific issues involved in setting dietary reference intakes. Scientists from the Centers for Disease Control and Prevention and other appropriate organizations are expected to engage in discussions involving several nutrients, including saturated fat. These discussions may inform the development of future dietary guidelines.

Item

Clinical Trials – The agreement requests GAO to conduct a review of how NIH applied the recommendations from the 2010 IOM report on NCI’s clinical trials across all NIH ICs to improve NIH-wide clinical trial activity. Specifically, the review should provide recommendations related to administering, monitoring, managing, and supporting an appropriate NIH-wide portfolio of clinical trials activity. Further, the agreement expects NIH to review its policies and make changes as appropriate to ensure appropriate minority participation in clinical trials across all NIH ICs.

Action taken or to be taken

In 1994, the National Institutes of Health (NIH) established a policy on the Inclusion of Women and Minorities as Subjects in Clinical Research to promote minority participation in NIH-funded clinical research and clinical trials. The policy requires applicants to address plans for the inclusion of women and minorities in clinical research and clinical trials. In addition, applicants proposing larger clinical trials are required to include plans for valid subgroup analyses as appropriate. During peer review, the evaluation of overall approach (one of the five major review criteria) includes consideration of the plans for inclusion. Reviewers also are provided detailed guidelines and instructions for assessing inclusion, including considerations of the proposed plans for addressing valid analysis of the trial design, and analysis of study results by sex/gender, race, and/or ethnicity. Awards may not be made until plans for inclusion is approved, or concerns about inclusion plans have been resolved through negotiations between NIH Institute and Center (IC) program staff and investigators/institutions. Throughout the life of each project, NIH program staff track cumulative enrollment and compare it to proposed enrollment plans. They advise investigators on how to augment inadequate enrollment. ICs may suspend or terminate projects that do not meet their enrollment targets.

The participation of minorities in clinical trials is important for the advancement of the health of the American people and the reduction of health disparities. As such, NIH will continue efforts to ensure appropriate minority participation in clinical trials across all NIH ICs.

Item

Dental Caries – Although dental caries have significantly decreased for most Americans over the past four decades, disparities remain among some population groups. The agreement is concerned with these trends and encourages NIDCR to explore more opportunities related to dental caries research. In addition, NIDCR should coordinate with CDC Division of Oral Health to identify research opportunities.

Action taken or to be taken

The National Institute of Dental and Craniofacial Research (NIDCR) is committed to investing in research that improves the dental, oral, and craniofacial health of all Americans. Significant advances have been made in promoting oral health and treating oral diseases such as dental caries; however, these advances do not always reach the people and communities who need them most. NIDCR leads the effort to discover novel methods to prevent, diagnose, and treat disease and develop effective strategies to translate this knowledge into improved oral health.

NIDCR supports research on Early Childhood Caries, a severe form of dental decay and one that is much more common in minority and low-income infants and toddlers. When left untreated, this decay leads to pain and infection, impairs children's ability to eat and sleep, and may even result in growth delay. NIDCR invests in development of innovative screening tools for use in primary health care settings to identify those at risk for developing caries, as well as strategies to increase parental knowledge about preventing caries by improving feeding practices and preventive oral health behaviors. Two NIDCR-funded grantees performing this research were recognized by the White House for advancing oral health in children. They received the Presidential Early Career Award for Scientists and Engineers, or PECASE, the highest honor bestowed by the Federal Government on outstanding scientists and engineers beginning their independent careers. Building on the momentum of these studies, NIDCR released an initiative in 2014 to encourage multidisciplinary and collaborative research on oral health disparities with a particular focus on vulnerable children.

To help achieve the goal of translating research discoveries into strategies that improve oral health, NIDCR partners with a number of stakeholders, including other Federal agencies. NIDCR continues to collaborate with and support the Centers for Disease Control and Prevention's dental caries surveillance activities through the oral health component of the National Health and Nutrition Examination Survey (NHANES). NHANES studies the epidemiology of dental caries in the United States, including caries prevalence and disparities by age, race, gender, and socioeconomic status. This rich dataset is available for informing dental practitioners and researchers of current oral health issues. Moving forward, NIDCR will continue its strong commitment to develop new productive partnerships to increase knowledge about the causes of oral health disparities and promote the development of innovative approaches to reduce and eliminate these inequalities.

Item

Disease, Condition, or Topic List – In particular, the agreement continues to support NIH biomedical research activities in the following areas and requests an update for each listed disease, condition, or topic in the fiscal year 2016 budget request to describe the latest efforts ongoing and planned for the fiscal year 2016 request:

Amyloidosis; Amyotrophic Lateral Sclerosis; Angelman Syndrome; ARV based microbicides; Autism; autoimmune diseases; behavioral research and cancer; biomarkers; botanical products to treat cancer; Brain Research through Advancing Innovative Neurotechnologies initiative; breast cancer screenings; chemical risk assessments; chromosome abnormalities; chronic constipation; chronic overlapping pain conditions; chronic pelvic pain; chronic obstructive pulmonary disease; congenital heart disease; contraception research and development; cures related to blindness-inducing illnesses; Cystic Fibrosis; diabetes; diabetes-related kidney disease; DPCPSI portfolio analysis NIH-wide policies; drug rescue and repurposing; Duchene muscular dystrophy; The Entrepreneurs-in-Residence initiative; fiscal management; focal gastric cancer; Fragile X research; gastrointestinal cancer; global health technologies; health disparities in children and adolescents; Healthy Homes; Hepatitis B; heterotaxy research; high risk and high reward research; human placenta project; implementation of CTSA IOM recommendations; implementation of the Recalcitrant Cancer Research Act; inflammatory bowel disease; information technology related to behavioral risk factors for cancer; infusion pumps; interstitial cystitis; Jackson Heart Study; Kennedy’s disease; liver cancer; lower life expectancy; Lupus; Lymphangioliomyomatosis; Malaria and neglected tropical diseases; marijuana research; maternal morbidity; medications in pregnancy; metastasis genetics; minority participation in clinical trials; mitochondrial disease; multiple sclerosis; National Pediatric Research Network Act; Nephrotic syndrome; Neurofibromatosis; Network for Excellence in Neuroscience Clinical Trials; non-small lung cancer; opioid drug abuse; ovarian cancer; palliative care; pancreatic cancer; pediatric low grade astrocytoma research; pediatric kidney disease; performance measures for each NCATS program, project, or activity; precision medicine; preterm birth; psychosocial distress complications; psychotropic medications and children; rare bone diseases; research centers in minority institutions; research focused on drug abuse in veterans; segmental glomerulosclerosis; scleroderma; Sickle Cell disease; sleep disorders; Spina Bifida; spinal muscular atrophy; stroke; telemedicine; temporomandibular disorders; training and career development for clinical investigators (“K” and “T” Awards); translational research results and expenditures since FY 2013; trans-NIH basic behavioral and social science opportunity network; type 1 diabetes; universal flu vaccine; Usher syndrome; vision research relating to “Regenerating Neurons and Neural Connections in the Eye and Visual System”; and Wilms tumor.

Action taken or to be taken

There has not been sufficient time since passage of the appropriations act to prepare individual updates for each of the 94 items listed above. However, many are discussed throughout the Congressional Justification in sections such as the Overview of Budget Request, Program Description and Accomplishments, and individual Institute or Center chapters. The National Institutes of Health will provide the Committees with the requested information at a later date.

Item

Enhanced NIH Reporting on Research Spending – The NIH reports and makes available to the public on an annual basis the amount of research spending by disease. This information is helpful and provides insight to the public and the research community about overall NIH research. The agreement request NIH include, no later than 180 days after enactment and thereafter, the number of Americans affected by each category listed in the RCDC database, according to CDC or another federally-sourced data file.

Action taken or to be taken

The National Institutes of Health (NIH) is currently examining the feasibility of providing burden of illness information in relation to the disease categories in NIH's Categorical Spending report. Burden of illness measures are anticipated to be a better measure of the impact of diseases than prevalence statistics, since burden of illness measures could reflect a combination of potential rates of mortality, rates of disability, years of life affected by the illness, or effects on quality of life. For example, equal numbers of Americans might be affected by influenza and cancer, but the rates of mortality and long-term disability, and impact on quality of life are not the same for influenza and cancer.

Our initial assessments of the feasibility of reporting on burden of illness reveal that many of the categories in the Categorical Spending report do not correspond to diseases for which burden of illness information is available.

- Specific disease and condition categories represent only a subset of the 237 Research, Condition, and Disease Categories (RCDC) reported by the NIH on its Categorical Spending website. Of the 237 reported, 83 are areas of research (e.g., Neuroscience) where the number of Americans affected by the categories cannot be defined. An additional 21 categories are broad composites of a large number of specific diseases and/or conditions (e.g., Heart Disease; Women's Health) where the total cases cannot be calculated by adding the individual disease sub-components because the sub-components are not mutually exclusive and/or the health statistics are calculated in different ways.
- The remaining 133 categories report on specific diseases or conditions that may have relevant health statistics. However, additional caveats have been identified that may further limit the number of disease categories to which NIH can match health statistics. Many of NIH's disease and condition categories do not match the categories enumerated in Centers for Disease Control and Prevention (CDC) or other federally sourced data. NIH is currently consulting with the CDC's National Center for Health Statistics to identify additional opportunities to pair burden of illness data with the disease and condition categories.

NIH will continue to examine the issues surrounding reporting on burden of illness in relation to the disease and condition categories.

Item

Extramural and Intramural Research – The agreement requests an update in the fiscal year 2016 budget request on what processes NIH has in place to ensure consistency between the application of scientific policies to both extramural and intramural researchers. The update should also describe how NIH has implemented the request that all peer reviewers for extramural research are provided detail knowledge on the scope of intramural activities that are related to the subjects under consideration within their study sections to prevent unintended support for duplicative research activity.

Action taken or to be taken

The National Institutes of Health (NIH) sets similarly high expectations for its extramural and intramural scientists regarding research quality, impact, and accountability. The extramural program is built upon a combination of investigator-initiated and targeted research topics, and research proposals for discrete projects are prospectively assessed under a competitive peer review process. On the other hand, the structure and resources of the intramural program are designed, in part, to provide support for projects that fall beyond the general scope of the extramural program, such as those requiring long-term support, those necessitating an unusually rapid response to meet an urgent public health need, and those that present unusual scientific opportunities. As a result of its unique mission, intramural programs employ certain specialized oversight and budget review processes. Given the differences between the functions of the intramural versus the extramural program, the review processes for oversight and accountability of intramural scientists differ from those in place for the extramural program. For example, the scientific merit of intramural projects is reviewed retrospectively, rather than prospectively, by outside scientific experts, and the process by which budgets are allocated is based on research teams and not individual projects, as is the case for the majority of extramural research. Central oversight and the coordination of the intra- and extramural research programs are the responsibilities of the NIH Director and the Institute and Center (IC) Directors, in consultation with IC leadership (e.g., Division Directors from extramural programs and the Scientific Directors of intramural programs).

While the structure and complementary missions of NIH's intra- and extramural programs lend themselves to tailored policies and processes, both rely on review by recognized experts in the larger scientific community. For extramural programs, review of scientific merit for research applications is conducted by extramural scientists in peer review study sections, with secondary review conducted by National Advisory Council/Boards. On the intramural side, each IC's laboratories are examined by Boards of Scientific Counselors, composed of external peer review panels. The Boards of Scientific Counselors review the scientific progress and accomplishments of each intramural research program and principal investigator at least every four years and report annually to the National Advisory Council/Boards. IC Directors chair the National Advisory Council for their Institute and receive recommendations from their Board of Scientific Counselors; they carefully weigh each body's advice when making funding decisions and creating and implementing policies.

Scientific Review Officers oversee the extramural peer review process and are charged with recruiting reviewers who are scientific experts for their study sections; peer reviewers are knowledgeable about the current state of the science, and thus are well aware of the ongoing research activity in their fields, including the scope of relevant intramural activities.

Additionally, NIH program officers follow ongoing research activities in their field, including those of intramural investigators, to identify new research opportunities as well as areas of scientific overlap, and advise their ICs about the best ways to invest in their research portfolios. The extramural scientific experts who serve as members of the Boards of Scientific Counselors or National Advisory Council/Boards are selected because they are pre-eminent leaders of their field with broad expertise across many specific areas of science within the purview of the IC, and are therefore highly capable of providing advice regarding the science to be pursued in intramural and extramural research.

Ultimately, responsibility for the assessment of scientific and budgetary overlap, including overlap with intramural projects, is not the responsibility of outside experts. Rather it is the responsibility of the IC Directors with assistance and counsel from their extramural Program Directors and intramural Scientific Directors. It should be noted that it is common that a given problem may be undertaken by more than one research team; healthy for competition, novel perspectives, and complementary approaches are critical aspects of advancing research.

Item

Funding Decisions – The NIH is expected to base its funding decisions only on scientific opportunity and the peer review process. In accordance with longstanding tradition, funding is not directed to any specific disease research area.

Action taken or to be taken

Peer review, scientific opportunity, and public health needs are key factors in the National Institutes of Health's (NIH's) priority-setting and resource allocation processes. Making funding decisions based on these factors allows the agency the flexibility to make strategic investments to advance its mission. As such, NIH can prioritize promising, innovative research aimed at reducing illness and disability, while maintaining the capacity to respond immediately to urgent public health needs.

NIH's rapid response to the Ebola crisis in West Africa demonstrates the value of this flexibility. Together with its Federal partners, NIH was able to provide substantial support for researchers to study how the virus spread and to test new prevention and treatment strategies to combat the disease. As a result, multiple promising vaccine and therapeutic candidates have been further developed and entered clinical testing, in tandem with the private and non-profit sectors. NIH and other HHS partners will be initiating a large Phase 2/3 vaccine trial in affected West African countries.

At the same time as NIH responds to immediate public health needs, the Agency can also encourage and capitalize on cutting-edge innovations that have the potential to shape the future of biomedical science and medicine. Recent improvements in how researchers measure and interpret the genetic variability between individuals are spurring research on more precise, tailored health care. This growing field, known as precision medicine, may one day develop novel approaches to promoting health, treating disease, and building safe and effective medical devices.

Item

Moderate Drinking – Numerous epidemiological and basic science studies have demonstrated that moderate drinking can be beneficial to health by reducing risk for coronary artery disease, type 2 diabetes, and rheumatoid arthritis, among others. However, these studies used different protocols or questionnaires, and may be difficult to compare. The agreement encourages NIAAA to undertake a multicenter, multiyear clinical study to clarify the health impact of moderate alcohol consumption.

Action taken or to be taken

The National Institute of Alcohol Abuse and Alcoholism (NIAAA) appreciates the Committee's interest in the beneficial health effects of moderate alcohol consumption, which is defined by the U.S. dietary guidelines as up to 1 drink per day for women and up to 2 drinks per day for men. While various studies have demonstrated an association between moderate alcohol consumption and beneficial effects on health, including decreased risk of mortality due to heart disease, decreased risk of ischemic stroke, and decreased risk of Type 2 diabetes, there is concern in the scientific community that these results may be partially explained by factors such as overall health status and health-seeking behavior.

NIAAA encourages research studies on the effects of moderate alcohol consumption on both the decreased and increased risks of chronic diseases through Program Announcements, and has supported cross-sectional work in this domain based largely on secondary analysis of epidemiological studies. At the same time, the Institute recognizes the need for a large, prospective, randomized clinical trial to answer definitively key questions about the relationship between moderate alcohol consumption and risk for chronic diseases. Such a study would be complex and expensive, requiring collaboration and contributions across multiple National Institutes of Health (NIH) Institutes and Centers as well as with other entities. In FY 2014, NIAAA supported a meeting that brought together an international panel of experts with expertise relevant to carrying out a long-term randomized alcohol clinical trial to discuss how such a study might be designed and undertaken. In that same year, NIAAA also funded a one-year cooperative agreement to develop a research plan for a multi-center, international, long-term, randomized clinical trial on the effects of moderate alcohol consumption on key clinical outcomes, including cardiovascular disease, cancer, diabetes, trauma/fracture, accidents, mortality, and progression to heavy or at-risk drinking. NIAAA will continue to explore collaborative opportunities across NIH and externally to determine the feasibility of undertaking a study of this scale and complexity. Information from the clinical trial would better inform individual choices about alcohol consumption as well as the advice health care providers give their patients about alcohol use.

Item

NIH Workforce Study – NIH performed a workforce study in 2008 that examined the state of the biomedical workforce in the United States and provided insight on the future workforce capacity and the need for new investigators to sustain the enterprise. The agreement requests NIH update the NIH New Investigator Projection (PI) report development by the NIH Office of Budget, assuming level funding. It should consider the historical data, success rates of new investigators, the success rates of second (R01 (first renewal) applications for early stage investigators, trends in the workforce, data and actuarially sound assumptions with updates on the number of researchers who received NIH F or K funding who then go on to work in industry. In addition, the report should survey the historical change over time of university policies that feed into the length of time to become a PI and use that data to update the PI projection model to ensure it has the correct mix of new and experience PIS in the work force.

Action taken or to be taken:

In 2008, the National Institutes of Health (NIH) produced a report titled the “NIH New Investigator Projection Report” developed jointly between the NIH Office of Budget (OB) and the Office of Extramural Research (OER). The report was conducted in response to an aging workforce and a desire from NIH leadership to identify ways to maintain a viable and cutting-edge workforce into the future. Since the report, NIH has engaged in multiple activities, studies, and research projects to advance our understanding of workforce dynamics, especially as it relates to new investigators. Examples of these activities include (but are not limited to) various studies and reports from the NIH Advisory Committee to the Director (ACD)¹, the development of a new Division for Biomedical Research Workforce Programs (DBRWP) within OER, and a current undertaking of modeling efforts to expand our ability to understand and, to some extent, predict future workforce dynamics given historical trends.

In 2015, NIH plans to initiate modeling efforts similar to that of the NIH New Investigator Projection (PI) report completed in 2008 that examined the Nation’s biomedical research workforce – focusing on the role of new investigators as a pivotal element of our future capacity to sustain scientific discovery. Efforts will incorporate an assumption of level funding based on the total budget authority received by NIH Institutes and Centers (ICs) via FY 2015 enacted appropriations consistent with Congressional direction. The revision effort will access expertise in workforce analysis and capacity modeling equivalent to that used to prepare the original study supported by OER and OB, tapping experiences of ICs where appropriate. In recognition of Congressional concerns regarding scope and content, the NIH report update will consider specific aspects of workforce evolution, such as success rates of new investigators, the success rates of R01 first renewal applications for early stage investigators, and the number of researchers who received NIH Fellowship Awards (F series) or Career Development Awards (K series) funding that are later employed by industry. In addition, efforts will take into account the historical change over time of policies that impact the length of time needed to achieve Principal Investigator (PI) capability and use that data to adjust the PI projection model assumptions regarding the workforce mix of new and experienced PIs.

¹ Related working groups include: ACD Working Group on Diversity in the Biomedical Research Workforce, ACD Working Group on Biomedical Workforce, and the ACD Working Group on Physician-Scientist Workforce. For more information on the ACD working groups, see: <http://acd.od.nih.gov/working-groups.htm>.

Item

Nurturing Talent and Innovation in Research – The agreement understands that NIDA is considering a new kind of award, which would blend NIH’s Pioneer and New Innovator Award mechanisms. The agreement requests that NIH provide the data used to develop this approach, the expected outcome measures for this mechanism, and annual updates on the progress related to the measures prior to any forward movement on this approach.

Action taken or to be taken

Avenir Award Program for Research on Substance Abuse and HIV/AIDS or Genetics or Epigenetics of Substance Abuse – Avenir means future in French, and this award looks toward the future by supporting early-stage investigators proposing highly innovative studies. The National Institute on Drug Abuse’s (NIDA’s) Avenir Award program is crafted after the National Institutes of Health’s (NIH’s) New Innovator Award and Pioneer Award programs, which have been successfully supporting innovative talent for several years. The Avenir Award Program is different from traditional (NIH) grants in several ways. It utilizes the NIH Director’s New Innovator Award program (DP2) funding mechanism and is designed specifically to support unusually creative new investigators with highly innovative research ideas at an early stage of their career when they may lack the preliminary data required for an NIH Research Project Grant Program (R01) grant. The emphasis is on innovation and creativity; preliminary data are not required, but may be included. No detailed annual budget or extensive background material is requested in the application. The procedure for evaluating applicants’ qualifications is distinct from the traditional NIH peer review “study section” process and involves two phases: 1) initial review by an outside, multidisciplinary expert scientific review group who evaluate the scientific and technical merit of the application; and 2) an editorial-style panel secondary review that considers the applications and comments from the initial review and selects the most meritorious applications for in-person interviews. Final selection of awardees are made by the NIDA Director based on the outcome of the initial peer review, the recommendations of the second level of review, concurrence of the National Advisory Council on Drug Abuse, and programmatic considerations.

NIDA has developed two Avenir Award Programs with distinct scientific goals within substance abuse research: one for genetics or epigenetics studies posted March 27, 2014 ([RFA-DA-15-006](#)) and another for HIV/AIDS research posted April 4, 2014 ([RFA-DA-15-007](#)). Creation of each of these programs was prompted by the low success rates for creative young investigators to secure adequate funding to support innovative, high-risk, high-reward research, that if successful, could have a significant impact on the substance abuse field. Special awards such as the Avenir help attract budding young researchers to the field of addiction research and advance the science with fresh ideas. In addition, the Avenir award encourages creative and innovative approaches for very complex analyses, incorporating other biologic information such as epigenetics, gene expression and neuroimaging to discover novel pathways that may be more tractable for intervention approaches. Applications for each program were received in August 2014 and completed scientific merit review in November 2014. Funding selections will be made during the NIDA May 2015 council.

NIDA will monitor the success of the Avenir awardees in a similar fashion as our highly successful Avant-Garde program: publication records of Avenir awardees will be compared to young investigators who have received funding through the R01 mechanism. The monitoring

process will consist of evaluating the number of scientific publications, the quality of the publications (e.g., impact factor of journals), the impact of the publications (number of times the publication is cited) as well as the ability of awardees to secure additional funding through the regular R01 mechanisms. Avenir awardees have no additional annual reporting requirements beyond the annual progress report which is required for all other NIH award mechanisms. As with all other NIH award mechanisms, continued annual funding is contingent upon adequate progress toward meeting the scientific goals detailed in the award application.

Item

Pediatric Cancer – The agreement understands NCI reduced support for some pediatric cancer clinical trials. The agreement requests an update in the fiscal year 2016 budget request with a summary of all pediatric cancer activity supported in fiscal years 2013, 2014, and 2015 estimate. Further, the agreement expects NIH to review how it can use the Cures Acceleration Network (CAN) activity and funds to develop regulatory and other tools that can be used to accelerate the development of pediatric drugs.

Action taken or to be taken

The National Cancer Institute (NCI) supports a comprehensive research program for children with cancer, ranging from basic molecular research, through preclinical testing and clinical trials, to epidemiological studies to identify potential factors that contribute to childhood cancers. A goal of this research is to identify more effective and less toxic treatments so that all children diagnosed with cancer will survive their disease and grow to become healthy adults.

NCI supported the following major research initiatives during FYs 2013 and 2014, and will continue to support these research activities during FY 2015:

- The [Children's Oncology Group \(COG\)](#), which is part of the NCI [National Clinical Trials Network \(NCTN\)](#), develops and coordinates pediatric cancer clinical trials that are available at more than 200 member institutions, including cancer centers throughout the United States and Canada. A component of the COG is the [COG Phase 1 Consortium](#), which conducts Phase 1 and pilot studies to support the introduction of new anticancer agents into the pediatric setting.
- The [Pediatric Brain Tumor Consortium \(PBTC\)](#) is a multidisciplinary cooperative research organization devoted to identifying superior treatment strategies for children with primary brain tumors. In April 2014, NCI approved an additional five-year funding period for PBTC. The FY 2014 funding included increased funding to incorporate genomic evaluations into PBTC clinical trials.
- The [Childhood Cancer Survivor Study \(CCSS\)](#) addresses the long-term effects of cancer and cancer therapy in 35,000 survivors of childhood cancer diagnosed between 1970 and 1999 and approximately 8,000 siblings of survivors.
- The [Pediatric Preclinical Testing Program \(PPTP\)](#), which identifies new, more effective agents for treating childhood cancers, has resulted in collaborations with more than 50 companies to evaluate more than 80 therapeutic agents, including several PPTP-tested agents that are moving into clinical testing. NCI approved a competitive renewal of the PPTP during 2014, and new five-year awards will begin in FY 2015 following the peer review of the applications from potential testing laboratories.
- The [Pediatric Oncology Branch \(POB\)](#) in NCI's intramural Center for Cancer Research conducts high-risk high-impact basic, translational and clinical studies.

NCI is supporting many clinical trials of high-priority novel agents through the NCI clinical trials programs. Examples of these important trials include:

- For children with newly diagnosed anaplastic large cell lymphoma, COG is conducting a clinical trial evaluating two targeted agents (crizotinib and brentuximab vedotin) that show evidence of high activity against this lymphoma subtype ([NCT01979536](#)).

- For children with relapsed low-grade glioma, the PBTC is conducting a clinical trial of an agent (selumetinib) that targets the pathway that is activated by the gene mutations that define this disease ([NCT01089101](#)).
- For children with relapsed/refractory solid tumors and lymphomas, the COG Phase 1 Consortium is pursuing immunotherapy strategies with a phase 1-2 clinical trial of the checkpoint inhibitors nivolumab and ipilimumab ([NCT02304458](#)). This clinical trial will initiate accrual in early 2015. In early 2015, PBTC will also open a phase 1 clinical trial of the checkpoint inhibitor pembrolizumab for children with recurrent brain tumors.
- The POB is pursuing immunotherapy approaches with phase 1 trials of chimeric antigen receptor (CAR) T cells targeting specific markers expressed on acute lymphoblastic leukemia (CD19, [NCT01593696](#)) and on selected pediatric solid tumors (GD2, [NCT02107963](#)).
- COG will open enrollment in January 2015 to a phase 3 clinical trial evaluating the CD19 targeted immunotherapy agent blinatumomab for children with acute lymphoblastic leukemia in first relapse ([NCT02101853](#)).
- For children with newly diagnosed high-risk Hodgkin lymphoma, COG will open a phase 3 clinical trial in January 2015 to evaluate brentuximab vedotin (an antibody-drug conjugate targeting a marker present on Hodgkin lymphoma cells) ([NCT02166463](#)).
- For children with relapsed osteosarcoma, phase 2 clinical trials for four novel agents will open by the end of 2015. Two of these agents, eribulin ([NCT02097238](#)) and glembatumumab vedotin, are being clinically evaluated based on their promising activity against osteosarcoma preclinical models in PPTP testing. The other two agents being evaluated are monoclonal antibodies: denosumab (targeting RANK ligand) and ch14.18 (targeting GD2).

Despite fiscal constraints, NCI has maintained consistent levels of support for both adult and pediatric clinical trials for the past several years. NCI's intramural research programs, which include the POB, experienced reductions due to sequestration in 2013. As described above, NCI provides extramural support for pediatric clinical trials through the Children's Oncology Group, which is part of the recently restructured National Clinical Trials Network. The overall NCTN budget was \$151 million in FY 2014, and this amount is the same as the total budget provided to NCTN's predecessor, the Cooperative Groups, for awards in FYs 2012 and 2013. NCI held funding for this program steady during FY 2013 despite the overall reduction in the NCI budget that resulted from sequestration. COG and other components of the NCTN initially expressed concern that, with the new structure, the budget for this program would be insufficient to support all the clinical trials that could be conducted. Senior NCI staff met with representatives of COG to address these concerns, noting that NCI's investment in modernizing its trials infrastructure will support important studies that use new trial designs and comply with recent regulatory requirements. NCI also made a commitment to work with COG to ensure as smooth a transition as possible.

In addition to specific clinical trials, NCI provides critical support and leadership for a number of areas that fall within or complement the research initiatives outlined above. These include pediatric cancer genomics, immunotherapy research, leadership of pediatric oncology scientific meetings, and collaboration with the pediatric oncology research advocacy community. For example, pediatric cancer genomics research is an important component of NCI's Center for Cancer Genomics (CCG), which includes programs such as the pediatric cancer TARGET ([Therapeutically Applicable Research to Generate Effective Treatments](#)) initiative. TARGET is

harnessing genomics technology to identify molecular targets to diagnose and treat childhood cancers more precisely, effectively, and safely than ever before. TARGET research results have led to two clinical trials for new drugs against childhood tumors and identified numerous new mutations and chromosomal abnormalities associated with pediatric tumors. In addition, NCI will convene a meeting of pediatric cancer genomics experts and research advocates in February 2015 to discuss the status of the field, gaps in knowledge, future research needs, and opportunities for harmonization.

NCI is also in the planning phases for a pediatric precision medicine clinical trial known as the Pediatric [MATCH](#) (Molecular Analysis for Therapy Choice) trial. This study will involve children with advanced cancers that have progressed despite treatments with standard therapies. The studies, which NCI plans to launch in 2015, will use DNA sequencing to identify children whose tumors will respond to an approved or investigational therapy based on a genetic abnormality uncovered during the sequencing. NCI will work with pharmaceutical companies to make the same drugs available for pediatric patients as for adult trials. Pediatric MATCH provides a tremendous opportunity to test molecularly targeted therapies in children with advanced cancers who have few other treatment options. The genomic data captured in the trials will also provide an invaluable resource for studying the genetic basis of treatment failure for pediatric cancers.

In addition to numerous projects focused solely or primarily on pediatric cancer, NCI invests a significant portion of its budget in basic research that has the potential to lead to advances across many cancer types or populations of cancer patients. Although these investments are not tracked to a particular disease type or population, the discoveries from NCI basic research will continue to inform and advance other research and benefit patients into the future.

NCI makes a project list available at the close of each fiscal year of research that is specifically relevant to pediatric oncology and other cancer areas. The list includes the programs outlined above, as well as investigator-initiated research and other research. NCI published the FY 2013 project list in its [NCI Funded Research Portfolio](#). In addition, NCI contributes each fiscal year to the NIH Pediatric Research Initiative Report, which NIH transmits to Congress. The FY 2013 report was submitted in August 2014. NIH is currently drafting the FY 2014 report.

The Cures Acceleration Network (CAN) was authorized to advance the development of “high need cures” and reduce significant barriers between research discovery and clinical trials. To achieve these objectives, which are consistent with NCATS’ mission, CAN provides NCATS with new flexibilities in its funding authorities. CAN has been appropriated approximately \$10 million per year since it became part of NCATS in FY 2012. This funding has been used to support the Tissue Chip for Drug Screening program, which is an initiative to revolutionize the process for predicting drug safety and efficacy, and ultimately may accelerate the development of drugs. While there are numerous other worthy ideas which could utilize CAN authority, including supporting the development of regulatory and other tools that would accelerate the development of pediatric drugs, the current CAN levels do not allow for implementation of new programs.

Item

Rehabilitation Research – The agreement expects the NIH Rehabilitation Coordinating Committee (NIH RCC) to host a trans-NIH State of the Science Conference on Medical Rehabilitation Research, develop and regularly update a trans-NIH plan for medical rehabilitation science, and better coordinate the grants to adhere to the definition of rehabilitation research recommended by the Blue Ribbon Panel on Medical Rehabilitation Research. NIH is urged to establish certain benchmarks to assess whether the coordination proposals being implemented are having a positive impact on rehabilitation science at NIH. Finally, the agreement request the NICHD and the NIH Director receive an annual briefing to discuss progress in rehabilitation research and the level of trans-NIH activity in this area of research.

Action taken or to be taken

The Trans-NIH Rehabilitation Coordinating Committee, convened by the National Center for Medical Rehabilitation Research (NCMRR) at the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) has been actively pursuing recommendations made by the Blue Ribbon Panel on Medical Rehabilitation Research. The Committee meets regularly, including an annual meeting that focuses on one area of rehabilitation-related science. The new NCMRR Director is scheduled to join NICHD in early 2015, and among the Center's priorities is a trans-National Institutes of Health (NIH) State of the Science Conference to assess the state of current science in rehabilitation research, identify research gaps, and develop an updated trans-NIH Plan for Medical Rehabilitation Research. The definition of [rehabilitation research](#) as developed by the World Health Organization, and cited in the Blue Ribbon Panel's report, will help guide these efforts.

NCMRR has tangibly increased coordination of rehabilitation research projects. Following a Panel recommendation, in FY 2014 NCMRR was provided with a dedicated percentage of NICHD's annual appropriation, which has allowed the Center more flexibility to co-fund research projects with other NIH Institutes and Centers (ICs), while funding others on its own. Over the last year, NICHD has cosponsored a range of research funding opportunities with other ICs, seeking grant applications on the Design and Development of Novel Technologies for Healthy Independent Living, and on the trans-NIH program, [Big Data to Knowledge](#) (BD2K). In November 2014, NICHD and NINDS co-sponsored a conference on the State of the Science in Cerebral Palsy that included Federal agencies, scientists, and individuals with cerebral palsy and their families, with a primary focus on improving function even beyond traditional development periods. Currently, NIH ICs are working together to develop and test a better methodology to identify physical rehabilitation grants and projects across NIH, and expect to begin using this methodology in 2015. NICHD already tracks grants, projects, and research publications related to physical rehabilitation research, and is developing additional performance tracking and monitoring methods to assess the results of NIH's efforts to enhance coordination of rehabilitation research.

In addition to reinvigorating the Trans-NIH Committee, NCMRR is working with other Federal agencies, such as a new effort to coordinate with the Food and Drug Administration (FDA) on medical devices. In November 2014, scientific program staff from NIH met with FDA personnel to discuss respective organizational goals, regulatory procedures, and collaborative research opportunities. NCMRR staff also provided scientific and clinical input into the FDA's November 2014 workshop on Brain-Computer Interface Devices for Patients with Paralysis and

Amputation, and is engaging in ongoing discussions about novel treatment devices for traumatic brain injury.

These and other activities related to rehabilitation research will be reported at least annually to the Directors of NICHD and NIH.

Item

Reproducibility of Research Results – The agreement expects NIH to stress the importance of experimental rigor and transparency of reporting of research findings in order to enhance the ability of others to replicate them. The agreement concurs in the view that the gold standard of good science is the ability of a lab to reproduce a method and finding and is therefore concerned with reports that so much published biomedical research cannot be easily reproduced. The agreement expects that NIH will develop incentives for scientists to undertake confirmation studies, best practice guidelines that would facilitate the conduct of replicable research and guidelines to encourage research transparency in the reporting of methods and findings. In addition, the agreement expects an NIH-wide policy and trans-NIH oversight to address the replication concerns. The agreement requests an update in the fiscal year 2016 budget request on the activities NIH has on-going toward this effort, the annual measure and amount of resources spent or estimated each year toward this effort.

Action taken or to be taken

The National Institutes of Health (NIH) has several efforts under way – both new and ongoing – to address reproducibility, rigor, and transparency in biomedical research. To raise awareness, Drs. Francis Collins and Larry Tabak published a commentary in [Nature](#) in January 2014 describing concerns surrounding reproducibility and rigor in preclinical research and the potential steps to address the issues. Since then, NIH has engaged various stakeholder communities to prompt a dialogue and solicit feedback. In June 2014, NIH co-sponsored a meeting with [Science](#) and [Nature](#) that challenged editors representing more than 30 major journals to identify opportunities in the scientific publishing arena to enhance rigor and further support research that is reproducible, robust, and transparent. This meeting led to the development of the [Proposed Principles and Guidelines for Reporting Preclinical Research](#), which now have been endorsed by more than 130 journals, publishing groups, and societies. A workshop also was held with the Pharmaceutical Research and Manufacturers of America (PhRMA) to identify areas of common interest with industry, and as a result, PhRMA is working to gather relevant information, such as good research practices, to share with NIH and the broader research community. In 2014, the NIH Office of the Director published a [Request for Information \(RFI\)](#) on reagent-related barriers to reproducible research to better understand the various reagent-related challenges facing the research community.

Within NIH, the Institutes, Centers, and Offices (ICOs) will continue ongoing pilots to address key concerns surrounding reproducibility and rigor – training, publications, applications and review. The Office of Intramural Research hosted a [workshop in November 2014](#) to discuss the potentials and pitfalls of modern cell biology techniques, such as superresolution imaging and immunoblotting. Two additional workshops, focused on structural biology and genomics, are planned for early 2015. The workshops will draw attention to the limitations of these cutting edge technologies, thereby better preparing new users of these approaches to employ them in a manner that ensures more reproducible reporting. Videocasts of all the workshops will be archived and made available publicly on the [NIH website](#). In early 2015, NIH will release a series of training videos with accompanying discussion materials to highlight common issues related to reproducibility and rigor in the research endeavor, such as bias, blinding, and exclusion criteria. These videos will be incorporated into required training within the NIH intramural program and subsequently made publicly available to the extramural community. Intramural participants will be surveyed pre- and post-training to ascertain if there understanding of the

issues surrounding reproducibility and rigor have been improved. Further, in August 2014, NIGMS and several other ICOs across NIH released a [Request for Applications \(RFA\)](#), soliciting applications for creative educational activities to enhance data reproducibility. Awards are expected to be made this summer.

NIH also is piloting modifications to the NIH biosketch, which complement SciENCv and better reflect the researchers' contributions, including the magnitude and significance of the scientific advances associated with a researcher's discoveries and the specific role the researcher played in those findings, rather than just listing their publications. These changes are expected to be implemented for all grant applications received for FY 2016 funding and beyond. Additional pilots on evaluating the scientific premise of applications and incorporating standards with reviewer checklists on scientific rigor also are being conducted. NIH currently is reviewing potential pathways to incorporate two important components of research – sex as a biological variable and validation of key reagents, including cell lines – into the grant application process. Finally, ongoing pilots are supporting confirmation studies to replicate key scientific findings. The information gained through the pilot activities will be used to decide which approaches could be implemented NIH-wide, kept at the ICO-level, or should not be pursued.

Experimental rigor and transparency are integral components of what is expected and undertaken by the NIH ICOs in pursuit of their ICO-specific missions and the broader mission of the NIH.

Item

Research Allocations – Recent GAO reports (GAO-14-490R and GAO-14-246) on NIH research allocations highlight that NIH’s research allocation process does not significantly take into account any method related to burden of disease on the American public, such as death or prevalence rate. Therefore, the agreement urges NIH to ensure research dollars are invested in areas in which American lives may be improved.

Action taken or to be taken

The National Institutes of Health (NIH) carefully considers disease burden as one of several key factors in priority-setting. In fact, recent studies have shown a significant positive correlation between disease burden and NIH funding levels.^{2,3,4} NIH leadership also takes into account peer review, scientific opportunity, and portfolio balance when deciding how to allocate resources.

- **Peer Review:** NIH only funds research which has undergone a two-stage peer review process and which has been judged highly meritorious.
- **Scientific Opportunities:** NIH constantly assesses its research portfolio in light of the latest scientific developments. Significant research advances often occur when new findings, sometimes completely unexpected, open up new experimental possibilities and pathways.
- **Public Health Needs:** NIH responds to public health needs, ranging from emerging infectious disease crises to the growing burden of chronic disease management, as well as rare disease research.
- **Portfolio Balance:** NIH strives to ensure the diversity of NIH’s research portfolio. Considerations of balance must include the ratio of basic research to applied, clinical, and translational, as well as cellular to behavioral, animal to human.

To ensure that NIH has the most accurate data for disease burden at its disposal and in response to Congressional request, the Agency currently is investigating the most rigorous and appropriate source measurements of disease burden to map to RCDC funding categories. This will help inform NIH decision makers for future resource allocation.

² Gillum LA, et al (2011). NIH disease funding levels and burden of disease. PLOS One 6(2): e16837.

³ Sampat BN, et al (2013). New evidence on the allocation of NIH funds across disease. The Milbank Quarterly 91(1): 163-85.

⁴ Moses H, et al (2015). The anatomy of medical research: US and international comparisons. JAMA.

Item

Ruth L. Kirschstein National Research Service Awards – The agreement notes concern that the number of Ruth L. Kirschstein National Research Service Awards has declined since fiscal year 2007. The agreement expects the NIH to provide no less than last year in stipend levels and training awards.

Action taken or to be taken

Through the Ruth L. Kirschstein National Research Service Award (Kirschstein-NRSA) program, the National Institutes of Health (NIH) ensures that the Nation's needs for a diverse, well-trained research workforce continue to be met, by providing training grants and fellowships to support graduate students and postdoctorates in biomedical and related fields.

On December 30, 2014, NIH announced stipends for Kirschstein-NRSA awards for FY 2015 that provide a two-percent increase over FY 2014 stipend levels (see NOT- OD-15-048 at <http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-15-048.html>). This increase reflects NIH's commitment to providing regular cost-of living-adjustments for trainees and fellows.

Because of the positive influence of Kirschstein-NRSA training grants and fellowships on research training throughout the biomedical sciences, NIH is also committed to maintaining the number of training awards in FY 2015 at least at the FY 2014 levels, and is currently on track to do so. By the end of FY 2014, NIH had awarded 15,316 NRSA training grants, and currently anticipates making 15,531 awards in FY 2015.

Item

Science, Technology, Engineering and Mathematics (STEM) Education – The President’s fiscal year 2015 budget recommends eliminating several STEM programs at the NIH as part of a government-wide consolidation of STEM education activities. The proposed STEM consolidation would affect NIAID Science Education Awards, NIDA Science Education Drug Abuse Partnership Award, NIEHS Short Term Education Experience for Research, and NINDS Diversity Research Education Grants in Neuroscience. NIH is directed to continue funding these programs in fiscal year 2015 and sufficient funding is provided to do so.

Action taken or to be taken

In the normal course of National Institutes of Health (NIH) activities, some of the STEM education programs listed were already phasing out and others have merged into very similar alternative programs instead. Only the NINDS Diversity Research Education Grants in Neuroscience continues as a stand-alone program, and it will be funded in FY 2015 pursuant to the Committee’s direction. However, this program remains subject to the Administration-wide STEM consolidation initiative, and is proposed for elimination and consolidation again in FY 2016.

In FY 2014, the NIH Director charged the Scientific Management Review Board (SMRB) with examining NIH’s pre-college STEM education programs and offering advice on ways to optimize NIH activities designed to engage pre-college students in biomedical science for the purpose of improving the biomedical research workforce. The SMRB report, to be released in early FY 2015, will contain recommendations aimed at maximizing the impact of these programs.

Item

Sports-Related Injuries – The agreement encourages the Department to investigate the development of new and better standards for testing sports equipment that is supported through independent research, governance, and industrial independence. These standards should actually replicate on-field impacts and produce testing data for “worst-practical-impact” conditions. Such standards will lead to research and development of new safety equipment to ensure that athletes have state-of-the-art gear that significantly reduces injuries.

Action taken or to be taken

For many years, the National Institutes of Health (NIH) has supported research to understand the consequences of mild and repeated Traumatic Brain Injury (TBI), including sports concussions. NIH supported researchers, for example, study the physics of brain movement within the skull following impact, study concussion related markers in the blood, develop brain imaging and EEG methods to better detect effects of mild TBI, and monitor cognitive and behavioral changes in college football players equipped with helmet accelerometers that record physical impacts across the playing season. Recently funded research using instrumented helmets in youth football players is designed to develop novel protective strategies, diagnostic tools, and information to guide return to play decisions. Research on sports concussion has been greatly augmented through the NIH Sports and Health Research Program, which was established by a \$30 million donation from the National Football League to the Foundation for NIH. The Sports and Health Research Program funded several pilot projects that are testing diagnostic and concussion management tools that can be used in the context of sports. Two major cooperative projects funded through this program are supporting ten neuropathologists from eight universities who are working to define the scope of the long term changes in the brain years after mild TBI and to develop a signature of Chronic Traumatic Encephalopathy (CTE) on brain scans in living people. CTE, which can now be diagnosed only on autopsy, is a devastating neurodegenerative disorder in later life that was first recognized in boxers a century ago and more recently has been reported in athletes from football and other contact sports.

Despite research efforts to date, several key questions about the consequences of sports TBI remain unanswered. These include, for example, the role of factors such as the frequency, spacing, and type of blows to the head, and individual differences in players’ susceptibility to long term consequences. Apart from CTE, there are also questions about whether repetitive TBI, or even a single TBI, might increase the likelihood of Alzheimer’s disease in later life. NIH research, together with research now underway through the Department of Defense and the National Collegiate Athletic Association, is designed to answer key questions such as these. NIH also continues to support extensive research, from laboratory animal models through human clinical studies, to improve care for all types of TBI and to develop interventions that will minimize damage.

Helmets were developed to prevent skull fractures, but do not reduce the damaging movements of the brain within the skull that result from rapid acceleration or deceleration. NIH research is developing a sound scientific basis for understanding the biological mechanisms through which such accelerations affect the brain, and to develop more sensitive diagnostics and better care. This research will contribute to the development of better standards for helmets. However, HHS and NIH do not have authority or expertise in consumer product testing, or regulating and setting standards for sports helmets or other sports equipment.

Item

Transforming Basic Science to Preventive Medicine through Technology – The agreement request NIH to develop an NIH-wide approach (including all ICs) to rapidly improve the speed and validity of personalized preventative medicine through the convergence of technology and biomedical science. The agreement requests NIH hold a joint forum with these types of industries, academic, academic engineers, and appropriate biomedical research organizations to develop a range of potential scientific questions, capabilities, gaps, and related biomedical scientific constraints.

Action taken or to be taken

Historically, medical practitioners have relied on disease prevention and treatment recommendations that were based largely on the expected response of an average patient. However, recent advances in technology, along with decreasing costs of DNA sequencing, have developed a compelling and innovative approach to medicine by using individual variability. This emerging practice is known as precision medicine.

Precision medicine allows preventative measures and treatments to be tailored to the individual characteristics of each patient. To accomplish this, scientists and physicians must understand human variability and identify individuals who differ in the susceptibility to a particular disease, in the trajectory of a disease, or in response to a specific treatment. In this way, specific preventative or therapeutic interventions can be adapted for each patient—avoiding needless treatment and expense for those who will not benefit.

The National Institutes of Health (NIH) will emphasize and expand its precision medicine efforts for FY 2016 and beyond. In February 2015, the agency will host a workshop with experts in human genetics, ethics, and information technology, from both the public and private sector and including academic and biomedical research organizations, which will explore the concept of building a large trans-NIH U.S. research cohort to advance the validity of precision preventative medicine. The workshop will host discussion on potential capabilities of the cohort study, gaps in current cohorts and information, and propose solutions to barriers for precision medicine. Information gleaned from this cohort, combined with patient-partnered research approaches and cutting-edge technologies, will help develop new disease prevention strategies, and improve how drugs are prescribed on an individual basis.

Item

Undiagnosed Disease Program – The agreement encourages NIH to create a public/private partnership for the Undiagnosed Disease Network (UDN) similar to other partnerships NIH has fostered with other entities. The partnership should include how the UDN can support physicians who are handling cases of undiagnosed diseases with new knowledge, consistent with applicable privacy laws, including HIPAA privacy and security law, through an ability to search for similar cases and to network and collaborate with physicians handling similar cases in order to accelerate the diagnosis, treatment options, and improve patient outcomes across the country. The agreement expects NIH to fully leverage the public/private partnership with other federal research agencies to facilitate even earlier recognition and improved treatment options of undiagnosed symptoms and diseases across the country.

Action taken or to be taken

The National Institutes of Health's (NIH's) initiation and continued support of the UDN is aimed at improving the level of diagnosis and care for patients with undiagnosed diseases, facilitating research into the causes of undiagnosed diseases, and creating an integrated and collaborative research community to identify improved options for patient care and treatments. To facilitate access to this research program, the UDN will perform outreach to identify cases of undiagnosed patients and provide a central portal for physicians to submit applications to the UDN on behalf of their patients. To enable physicians to submit these applications to the UDN, Genzyme Corporation and the National Organization for Rare Disorders (rarediseases.org) are partnering to pay for the preliminary diagnostic testing necessary for each patient application.

Important clinical insights learned through UDN cases will be available to physicians and the public via NIH public databases. For example, to provide guidance to healthcare professionals regarding which individual differences in the DNA code have clinical relevance for patient care, links discovered between specific variants and diseases will be made available through the ClinGen database (a growing catalog of variants in the human genome associated with disease: www.clinicalgenome.org). All UDN research data provided through NIH databases will be managed in accord with rigorous data security and privacy practices regarding access and minimization of any identifiable data held, in compliance with relevant Health Insurance Portability and Accountability Act and Federal Information Security Management Act regulations. Patient-participants will be informed during the research consent process that every effort will be made to minimize the risk to their privacy, but that this risk cannot be completely eliminated.

The UDN also disseminates its expertise and resources for researching undiagnosed diseases across the country through its distribution of ten geographically diverse clinical and research centers. Private physicians who have patients that they believe have undiagnosed diseases may collaborate directly with the researchers and physicians at the UDN clinical sites. These activities are encompassed within the UDN mission and supported through the UDN grants and NIH intramural research program, as funds permit.

Item

Valley Fever – The agreement acknowledges the joint NIH and CDC efforts to combat coccidioidomycosis, also known as Valley Fever. Specifically, the agreement supports ongoing efforts by NIH and CDC to develop a Randomized Controlled Trial (RCT) to identify an effective treatment for coccidioidomycosis, develop a vaccine, and increase awareness of this disease among medical professionals and the public, which can help with early diagnosis and treatments to reduce the length and severity of this disease. The agreement encourages NIH and CDC to work with relevant expert in coccidioidomycosis endemic areas to consider RCT activity.

Action taken or to be taken

Coccidioidomycosis (Valley Fever) is an infection that results from inhalation of *Coccidioides* species fungal spores that are present in the environment. Endemic in the southwestern United States, the highest number of Valley Fever cases occur in Arizona and California. *Coccidioides* has been found to be the cause of an estimated 15 to 29 percent of community-acquired pneumonias (CAP) in highly endemic areas. Many people with Valley Fever have mild influenza-like symptoms and recover spontaneously. However, some individuals experience weeks to months of significant, if not life-threatening, illness after *Coccidioides* infection.

The National Institute of Allergy and Infectious Diseases (NIAID) conducts and supports research to understand the pathology of Valley Fever and to develop therapeutics and vaccines to treat and prevent the disease. For example, NIAID intramural researchers initiated a clinical trial at the National Institutes of Health Clinical Center in Bethesda, Maryland, in 2014, to study the natural history of Valley Fever. The trial builds on longstanding research by NIAID scientists aimed at better understanding the mechanisms of Valley Fever disease and the factors that may contribute to the severity of the disease. This knowledge ultimately may help in identifying novel ways to treat and prevent Valley Fever.

As part of its Valley Fever research portfolio, NIAID has coordinated with the Centers for Disease Control and Prevention (CDC) to conduct a large randomized controlled trial (RCT) to study Valley Fever in the context of CAP. The NIAID RCT will study patients with coccidioidal CAP to compare outcomes in patients treated with the standard of care (i.e., the antibiotic azithromycin) with or without treatment with the antifungal drug fluconazole. To develop the clinical trial protocol, NIAID is working with Valley Fever subject matter experts from endemic areas. The NIAID trial will be conducted through NIAID's Vaccine and Treatment Evaluation Units and is expected to begin in late 2015. In collaboration with NIAID, CDC has identified potential sites in California and Arizona for subjects to enroll in the trial.

In addition, NIAID has funded a small, Phase II RCT to evaluate a novel antifungal drug, Nikkomycin Z (NikZ), in patients diagnosed with coccidioidal pneumonia. NIAID supported the preclinical development of NikZ and will support manufacturing of NikZ for this trial. The NikZ clinical trial is expected to begin in early 2016 and will complement NIAID's larger RCT examining fluconazole as a possible treatment for *Coccidioides* CAP.

NIAID will continue to support intramural and extramural research on Valley Fever to develop new and better diagnostics and treatments. In addition, NIAID encourages applications for the development of vaccines to prevent coccidioidomycosis.

Item

Women's Health Research – The agreement notes the recent 25th anniversary of the NIH's Office of Research on Women's Health. This office was authorized by Congress to correct the gender imbalance of research and highlight the importance of women's health issues to the larger scientific community. The agreement congratulates the office on its longevity and success. In the vein, the agreement supports NIH's recent shift toward achieving balance between females and males in pre-clinical research and encourages the NIH to ensure this applies to experimental models used for basic science research and that both males and females are utilized to investigate diseases that affect men and women. It is recommended that the NIH expand its current policies to require NIH funded investigators to prominently indicate the sex of their experimental model in their grant application and progress reports. Further, those investigators study both sexes, should be required to report, and when appropriate, analyze their data by sex as part of grant progress reporting to the Agency. The same should be encouraged in all published results resulting from NIH funding. When it is unknown what proportions of women and men are affected by a specific disease, NIH is encouraged to require investigators to utilize valid experimental design including consideration of sex as a biological variable in relevant research on animals, cells, and human subjects, as scientifically appropriate.

The agreement recognizes NIH's effort to include female participants in all phases of pre-clinical and clinical trials, as scientifically appropriate. The agreement also supports requiring investigators to analyze study results by sex/gender and minority subpopulations as appropriate, based on the scope of the research. Proposals that include adequate numbers of women and men and include a robust plan for analysis, publication, and distribution of findings should be given priority funding decisions, when appropriate.

NIH is directed to include in their biannual report the proportion of women and minorities as subjects in clinical research participant enrollment by trial phase and in all studies of human subjects. The NIH is also directed to report on preclinical research in terms of the proportion of studies that incorporate sex as a biological variable and of those studies which analyze data by sex as part of grant review, award, and oversight processes and this data should be reported by Institute and Center across the Agency.

The National Library of Medicine is urged to implement changes to Clinicaltrials.gov that will require users to input the number of participants that drop out of trials and break those participants out by sex/gender and race.

Action taken or to be taken

The National Institutes of Health (NIH) is honored by Congress's recognition of the 25th anniversary of the Office of Research on Women's Health and the growing body of knowledge about women's health resulting from the office's activities.

Currently, NIH directs applicants to address plans for valid analysis for larger clinical trials where subgroup analyses by sex/gender, race, or ethnicity may be appropriate. The Scientific Review Groups (SRGs) that review grant applications are directed to consider inclusion, and are provided with [review criteria as well as detailed guidelines](#) for assessing an applicant's plans for inclusion on the basis of sex/gender, race, and ethnicity; reviewers are also instructed to consider inclusion plans as part of the overall priority score for the application, which directly affects the

priority given to an application in funding decision-making. In the case of Phase III clinical trials, reviewers are further directed to assess the proposed plans for valid analysis of the trial design, and the analysis of study results by sex/gender, race and ethnicity.

NIH is now moving to stipulate a deliberate approach in considering the influence of sex in preclinical research. This change will expand the understanding of male and female biology – and ultimately advance our goal of improving the health of all women and men in the United States and nations around the world. The NIH Working Group on Rigor and Transparency has worked to develop a coordinated approach to enhance the rigor and transparency of science. NIH has considered placement, criteria, and language of sex as a biological variable in grant applications. NIH leadership has deliberated on the proposed changes throughout fall 2014, and will submit a formal proposal for policy changes to the Office of Management and Budget in the coming months.

Currently, the [*Biennial Report on Inclusion*](#) provides inclusion enrollment data for all NIH-defined clinical research studies, which is essentially all human subjects research, including clinical trials at all phases. NIH does not collect separate information on all trial phases for the purposes of reporting inclusion. However, NIH does have information on whether a given award involves NIH-defined Phase III clinical trials, and NIH does report enrollment by gender, race and ethnicity for Phase III clinical trials in the *Biennial Report on Inclusion*. [ClinicalTrials.gov](#) collects information on the phase of clinical trials and enrollment by sex/gender, race, and ethnicity, but data on the enrolled study population are currently required for only some trials (of FDA-approved products) and not until one to three years after the completion of the study.

The U.S. National Library of Medicine (NLM) is working with other NIH offices to identify improved methods of monitoring and comparing dropout rates by sex/gender and race. ClinicalTrials.gov collects information on the number of participants who started, completed, and dropped out of each clinical trial, by study arm. It also collects the number of enrolled participants in the trial, by sex/gender. Data submitters are encouraged to submit enrollment information by race and ethnicity, using race and ethnicity categories that are suited to the scientific objectives of their study. Requiring dropout data by sex/gender, race, and ethnicity in ClinicalTrials.gov presents several technical and legal challenges. For example, to serve the scientific objectives of some trials it may be necessary to collect detailed information about gender and race near the end of the trial; thus these data may be unavailable for participants who have dropped out. ClinicalTrials.gov does not establish requirements for information collection, only for information submission. Moreover, requirements for data submission to ClinicalTrials.gov must be set via a rulemaking process (a Notice of Proposed Rulemaking is currently under public comment). NIH is discussing alternative means of collecting dropout information by sex/gender, race, and ethnicity.

Item

Young Investigators – The agreement requests NIH review the grant success rates for early stage investigators in their first two grant submission to consider whether the grant applications submitted by all early stage investigators, regardless of whether they successfully achieved their first submission, should compete against other early stage investigators instead of all submission as a whole.

Action taken or to be taken

The National Institutes of Health’s (NIH’s) New Investigator policy, which extends special review consideration to Investigators who are applying for their first major Research Project Grant (R01), was [strengthened in FY 2009](#) to establish comparable success rates for New Investigators and established investigators, and clustering of R01 applications from New Investigators in the peer review order, to ensure that the review criteria for New Investigators is applied consistently to all applications. The [Early Stage Investigator](#) (ESI) was also designated as a New Investigator who is within ten years of completing the terminal research degree, or within ten years of completing their medical residency. ESIs are identified and the career stage of the applicant considered at the time of review and award. The ESI designation is intended to encourage earlier transition to independence.

The ESI policy just completed its fifth year. Former ESIs who received funding, are only beginning to submit second grant applications. NIH conducted a preliminary analysis to examine the funding success of ESIs on their first and second R01 application submissions in the five-year period FYs 2009-2014, compared to those of established investigators (Table 1).

| Table 1. Funding Success for ESI and Experienced Applicants on their First and Second Submissions: FY 2009 - 2014 | | | | | | |
|--|----------------------------------|-------------------------------|---------------------|--|---|---------------------|
| | Total # of ESI Applicants | Total # of Funded ESIs | Funding Rate | Total # of Experienced Applicants | Total # of Funded Experienced Applicants | Funding Rate |
| First Submission (Total) | 9,928 | 1,118 | 11.3% | 24,849 | 3,638 | 14.6% |
| Second Submission (Total) | 6,107 | 1,392 | 22.8% | 20,004 | 4,188 | 20.9% |
| Subset Funded on First Submission | 460 | 46 | 10.0% | 2,839 | 630 | 22.2% |
| Subset Unfunded on First Submission | 5,647 | 1,346 | 23.8% | 17,165 | 3,558 | 20.7% |

ESI’s had a funding success rate on their first R01 submission of 11.3 percent. Established investigators submitting a new R01 application during the same period had a funding success rate of 14.6 percent on their first submission. ESIs and experienced investigators who were awarded a grant on their first attempt and submitted a second grant application during the intervening period had funding success rates of 10.0 percent and 22.2 percent, respectively. The disparity illustrates the challenge faced by former ESI’s on their second grant submission, when

they are reviewed in the same pool with more experienced investigators. However, it also illustrates that former ESI's second grant submission funding rates are similar to their funding rates for the first attempt, even though their second applications are reviewed alongside applications from investigators with many years of grantsmanship experience. ESI's who were not successful in obtaining a grant on their first attempt, and were thus reviewed as ESI's again during their second grant submission, had a funding success rate of 23.8 percent, in comparison to 20.7 percent for comparable established investigators during the same period.

If NIH extended special review considerations for ESIs to applicants on both their first and second submission, the pool of ESI's would be expanded to include former ESI's who were previously funded. The advantage extended to second time applicants might come at the expense of the inexperienced applicants the policy intends to support. Furthermore, it is predicted that, as the cohort of funded ESIs who attempt their second grant application grows, the funding success rate for this group is likely to increase without the benefit of special review considerations. NIH will continue to monitor the impact of the ESI policy on career transitions of New Investigators, and provide a comprehensive analysis of ESI outcomes as requested in the House Appropriations Report.

NATIONAL INSTITUTES OF HEALTH
National Institute of Environmental Health Sciences
FY 2014 Conference
Significant Item

Item

Worker Training Program – The Committees direct NIEHS to explore the feasibility of incorporating a nominal fee to recoup administrative or other costs associated with the Worker Training Program. NIEHS should include a report that summarizes findings and recommendations with the fiscal year 2016 budget request.

Action taken or to be taken

The National Institute of Environmental Health Sciences (NIEHS) Worker Training Program (WTP) is a long-standing initiative that provides job training to a population that includes underserved, low-income, and/or jobless individuals through a diverse set of grantee institutions, and does so efficiently with low overhead. WTP is an umbrella consortium authorized by Section 126(g) of the Superfund Amendments and Reauthorization Act of 1986. The WTP consortium builds upon Federal-level partnerships that have been created over the last 20 years. The overhead costs for administration of the program continue to be at or below the levels of similarly situated federal cooperative agreement programs.

The National Institutes of Health (NIH) and NIEHS have taken a careful look at the program mission and objectives and have reviewed data from the grantees related to how they provide their services, as well as any income generated from their training programs. Given the program objectives, and in light of the characteristics of both the variety of grantee institutions and the trainee population served, NIEHS finds that it would be both administratively difficult and counterproductive to the mission of the program to attempt to impose a fee across the board for trainees to have access to the program offerings.

The diverse family of WTP programs includes the Hazardous Waste Worker (HWW) training program, the Environmental Careers training program, the Hazmat Disaster Preparedness training program, and the Hazmat Training Program for Nuclear Weapons Cleanup, which is administered through an Interagency Agreement with the U.S. Department of Energy (DOE). Also, grantee organizations come from many different places, including academic consortia developed at four-year universities; Historically Black Colleges and Universities; Community Colleges; industry-based colleges; non-profit organizations dealing with occupational health; joint labor management trust funds; labor-based unions; and other groups. Each of these groups of institutions uses different business models to run their programs and deliver training in a cost-effective way for their target populations. Charging training fees has always been an option, but not a program requirement. In FY 2010, for example, 3 out of 20 grantees generated program-related income (specifically, for the Hazardous Waste Worker training program).

A variety of approaches are incorporated into the training process to ensure an equitable public-private partnership in expending appropriated funds. For example, the Steelworkers Union generates program-related income by soliciting funds from employers to enhance the training provided. Some university groups also charge nominal fees depending on the target audience for

the training. Some targeted groups, such as unemployed or disadvantaged persons, are not able to pay for training; thus, no charges are levied.

NIH policy, as stated in the NIH Grants Policy Statement (last revised, 2012), allows for program-generated income to be proposed by the applicant organization. Program income is defined as gross income, earned by a grantee, a consortium participant, or a contractor under a grant, that was generated directly by the grant-supported activity or earned as a result of the award. Program income includes, but is not limited to, income from fees for services performed; charges for the use or rental of real property; equipment or supplies acquired under the grant; the sale of commodities or items fabricated under an award; charges for research resources; registration fees for grant-supported conferences; and license fees and royalties on patents and copyrights. The grantees are permitted to utilize program income using the additive alternative, in which program generated income is added to funds committed to the project or program and used to advance eligible project or program objectives. The amount of program income earned and expended must be reported on the appropriate annual financial report. In the cases where income has been generated by the WTP, the funds generated have been used to buy supplies and equipment for training or for instructor and curricula development.

NIEHS has further reviewed existing Grants Management Policy for the Department of Health and Human Services (HHS) and NIH to inform any changes in our approach toward program income. This review included analysis of administrative costs associated with collecting, distributing, and using optimal processes for retaining fees from trainees, employers, or the organizations that provide the training through the retention of program income or other methods for revenue capture. A variety of challenges would be expected with the incorporation of a fee for recouping costs, which may limit the viability for some, if not all, grantees.

NIEHS considers that, given the wide variety of grantee institutions serving the WTP, the low income of most of the target populations, and the existing low overhead cap of the program, it would not be feasible to mandate a fee collection model across the board. However, that does not preclude individual grantee programs from choosing to take advantage of existing policy to enhance their offerings.

As NIEHS developed the recent Funding Opportunity Announcement (FOA) for soliciting and competing for new cooperative agreements for this program in FY 2015, we clarified the option under current policy for grantees to generate program-related income where appropriate. Specifically, in the Funding Opportunity Announcement (FOA) RFA-ES-14-008 (released on July 28, 2014), NIEHS WTP included language to encourage applicants to develop sources of program income to supplement the federal grant resources provided to support the development of model training programs in hazardous materials response. This is expected to provide enhanced program support for the future.