Office of Research on Women's Health

National Institutes of Health

Advisory Committee on Research on Women's Health

41st Meeting, April 19, 2016

Meeting Minutes

Call to Order

Janine A. Clayton, M.D., NIH Associate Director for Women's Health
Director, Office of Research on Women's Health (ORWH), NIH

Dr. Clayton called the meeting to order at 9:05 a.m., welcoming participants to the 41st meeting of the NIH Advisory Committee on Research on Women's Health. She noted that the proceedings were open to the public and would be videocast on the NIH network. In addition, she explained that committee members could participate via teleconference with prior approval. Members participating by teleconference were Valerie C. Montgomery-Rice, M.D.; and Teresa K. Woodruff, Ph.D. Igho Ofotokun, M.D., also joined the call.

Dr. Clayton reviewed the confidentiality and conflict-of-interest (COI) requirements, noting that the COI recusal list includes universities and organizations in which advisory committee members have financial interests. She reminded participants to sign and return the forms before the meeting ended.

The amended minutes from the last meeting were approved unanimously by voice vote. They will be posted to the NIH website. Upcoming meeting advisory committee meetings are scheduled for September 27, 2016, and April 4 and September 13, 2017.

Introduction of New Members

Dr. Clayton

Three members have been added to the advisory committee: Chloe E. Bird, Ph.D.; Carolyn M. Mazure, Ph.D.; and David C. Page, M.D.

Dr. Bird, senior sociologist at RAND and editor of the journal *Women's Health Issues*, also is professor of policy analysis at Pardee RAND Graduate School. Her work maps and assesses gender differences in the quality of care for cardiovascular disease and diabetes patients. Her

research interests also include gender determinants and racial/ethnic and community-based differences in health care.

Dr. Mazure is the Norma Weinberg Spungen and Joan Lebson Bildner Professor of Psychiatry and Psychology at the Yale School of Medicine. She created and directs Yale's interdisciplinary research center on health and gender. In addition, Dr. Mazure developed new approaches for identifying risk factors for depression and was the first to demonstrate that stress is a more potent pathway to depression among women than men. Her research interests include the interplay of stress, depression and addictive disorders with a focus on gender-based analyses.

Dr. Page directs the Whitehead Institute and is professor of biology at Massachusetts Institute of Technology. He also is a Howard Hughes Medical Institute investigator. He reconstructed the evolution of today's X and Y chromosomes from an ancestral pair of chromosomes that existed 300 million years ago and discovered molecular evolutionary mechanisms by which the Y chromosome became functionally specialized in spermatogenesis. In addition, Dr. Bird discovered and characterized the most common genetic cause of spermatogenic failure in humans: deletion of the AZFc region of the Y chromosome.

ORWH Director's Report

Dr. Clayton

New Sex as a Biological Variable (SABV) Policy Includes Focus on Scientific Rigor, Reproducibility, and Transparency

Dr. Clayton began by noting that the power of science is to inform and improve health care and that this happens best when preclinical and clinical research and practice are focused on rigor, reproducibility, and transparency, as delineated in the Office of Extramural Research (OER) infographic available at http://grants.nih.gov/reproducibility/index.htm#resources.

The guidance noted in this graphic informs the recently released *NOT-OD-16-011: Implementing Rigor and Transparency Sex as a Biological Variable Policy*. Effective January 25, 2016, applicants and reviewers must consider SABV issues. The justification for including SABV and the specific policy language for this mandate were developed as part of a team effort involving collaboration between the Trans-NIH SABV Working Group and NIH's working group on rigor and transparency. The working groups developed a streamlined approach to enhancing rigor and transparency and provided criteria for grant applicants and reviewers to use when justifying the inclusion or exclusion of the SABV variable. ORWH is where "the rubber meets the road," Dr. Clayton continued. The Office is responsible for educating concerned stakeholders, ranging from journals and other media to Congress and the public, about SABV policy and its

implementation. At present, resources to support policy implementation are being developed and disseminated.

The path ahead for implementing SABV includes several near-term milestones. A funding opportunity announcement (FOA) is being published this spring on tools for cell line authentication that will reduce or eliminate misidentification and contamination. SABV is being included as an element of rigor along with other biological variables to be addressed in the research strategy section of project grant applications. Also, this spring, the guidelines for training scientific review officers (SROs) and reviewers about the grant will be released. The first round of scientific review is scheduled for late spring/summer. The first awards will be made in the fall. ORWH has permission to release the FOA in April if it has not already been done. Dr. Clayton asked advisory committee members to publicize the availability of this small business innovation research grant.

Dr. Clayton noted online ORWH SABV resources that can be found at http://www.nih.gov/sexinscience. She also reviewed recent research, first highlighting a 2016 publication reporting on the sex and age in biomedical research on mouse models: "Research: Bias in the Reporting of Sex and Age in Mice," by Oscar Flórez-Vargas et al., which can be found at https://elifesciences.org/content/5/e13615v2. Dr. Clayton then discussed the NIH Knockout Mouse Project (KOMP). KOMP identified rigorous and useful methods for potentially identifying sex differences that can be generalized across research. More information about KOMP is available at http://commonfund.nih.gov/KOMP2/ and https://www.mousephenotype.org/phenoview/.

Dr. Clayton reviewed the keys for studying sex to strengthen any scientific discipline. The keys, called the 4Cs, are (1) ***c***onsider sex by designing studies that take sex into account or that explain why SABV does not apply, (2) ***c***ollect and tabulate sex-based data, (3) ***c***haracterize sex-based data based on analyses, and (4) ***c***ommunicate results by reporting and publishing the data.

Process and Outcome Evaluation of Building Interdisciplinary Research Careers in Women's Health Program (BIRCWH)

After noting that additional career programs would be discussed in the afternoon by Jennifer Plank-Bazinet, Ph.D., Dr. Clayton described the one-year mixed-method evaluation of BIRCWH, a flagship program established to support mentored career development of junior faculty. The program's goal is to increase the number and skills of investigators who transition to independent scientific careers focused on interdisciplinary research relevant to women's health or sex differences research.

The evaluation was undertaken by an independent contractor and involved Principal Investigators (PIs), mentors, and scholars who participated in BIRCWH from 2000 to mid-2015. The purpose of the evaluation was to assess program management and policies and inform internal decision-making for BIRCWH, which has received more than $172 million and has trained more than 600 scholars at 41 institutions since 2000. Findings included the following:

- Among a group of 187 former BIRCWH scholars, 70 percent reported being on tenure-track positions and 62 percent had attained tenure. The largest number of respondents (51 percent) had become associate professors.
- A group of 188 scholars were asked about the importance of interdisciplinary study and research related to women's health in their current professional positions. Ninety-seven percent said that interdisciplinary study was "very important" or "important"; 87 percent said the same thing about women's health research. These findings demonstrate that BIRCWH scholars continue to use BIRCWH training in their work.

The evaluation also found some outstanding issues. Among scholars, PIs, and mentors, the most consistently reported challenges concerned funding and collaborations. Difficulties for host institutions included subsidizing salaries and career training. Concerns also were raised about reducing the number of scholars per institution from four to two. Mentors stated that time management was an issue for participants. BIRCWH scholars reported difficulties in establishing relationships with mentors and colleagues. Use of carry-over funds was cited as an administrative challenge.

ORWH is currently reviewing the evaluation findings and recommendations. Committee input about moving forward will be sought in the afternoon session.

2015 GAO Report to Congress

The 2015 U.S. Government Accountability Office (GAO) report, *National Institutes of Health: Better Oversight Needed to Help Ensure Continued Progress Including Women in Health Research*, was submitted to Congress. GAO examined (1) women's enrollment in NIH-funded clinical research and NIH's efforts to monitor this enrollment and (2) NIH's efforts to ensure that its funded clinical trials are designed and conducted to analyze potential sex differences as applicable. To do this, GAO reviewed relevant laws and policies (including the NIH inclusion policy and federal standards for internal control), analyzed NIH enrollment data from fiscal years (FYs) 2005–2014, and interviewed NIH and Institute and Center (IC) officials and other experts.

NIH concurs with the five report recommendations developed by GAO and will move forward with its responsibility to ensure the appropriate inclusion of women (and other groups) in

clinical research and clinical trials. NIH has tackled GAO's third recommendation by developing reports that program officers can use to record their monitoring of awardees plans for, and progress in conducting, analyses of potential sex differences. As a result, NIH has requested that GAO close this recommendation. NIH is working on the remaining four recommendations; these concern enhancements to enrollment data and summary data processes and regular reporting of how the recommendations are being addressed. The advisory committee will be updated on future discussions.

Basic Science Is the Bedrock of Progress

A letter co-authored by NIH Director Francis Collins, M.D., Ph.D., and other NIH senior leaders, including Dr. Clayton, confirms the NIH commitment to leading the way toward a healthier future by supporting a broad portfolio of basic, translational, population, and clinical research studies. The letter was in part motivated to respond to PI concerns that research having an immediate public health impact would be favored in funding decisions.

Upcoming Events

- **Tuesday, May 10:** The inaugural Vivian W. Pinn Seminar will be held as part of the 2016 National Women's Health Week. The seminar will be held in the Cloisters, Building 60, on the NIH main campus from 2:00 p.m. to 3:30 p.m.
- **Monday, June 6:** The Conference on Evidence-Based Innovations to Support Women in Biomedical Research Careers runs from 8:00 a.m. to 5:00 p.m. It will be held in the main auditorium of the Natcher Conference Center on the NIH main campus.
- **Tuesday–Wednesday, June 7–8:** The BIRCWH Specialized Centers of Research program meeting "Forging Ahead" meeting runs from 8:00 a.m. to 5:00 p.m. each day. It will be held in the main auditorium of the Natcher Conference Center on the NIH main campus.

Administrative Supplements Program Update

Over time, the administrative supplements program has grown. In FY 2015, supplementary grants totaled $3.9 million; for FY 2016, $5 million is being disbursed. The number of applicants has increased and now includes commonly funded projects and all ICs.

Farewell to Senator Barbara Mikulski

Dr. Clayton reported that Senator Barbara Mikulski, a long-time staunch supporter of biomedical research and federal workers, is retiring at the end of this Senate term. ORWH has very much appreciated her advocacy for women's health and for the inclusion of women in clinical trials.

Discussion

C. Noel Bairey Merz, M.D., asked about training requirements for reviewers regarding SABV. Dr. Clayton replied that the training is not likely to be optional. Training materials have been developed and will be available at the September 2016 Advisory Committee meeting. The SABV requirement is not being applied to reviews in cases where the application process began before the SABV policy went into effect.

Afaf I. Meleis, Ph.D., said that journal editors continue to need SABV training. Dr. Clayton agreed, noting that existing efforts are being ramped up. She added that ORWH would like to partner with advisory committee members with journal connections and approach the respective editorial boards.

Carolyn M. Mazure, Ph.D., noted that SROs and review committee chairs are critically important arbiters and interpreters of rules, regulations, and policies. She asked whether these individuals were being trained. Dr. Clayton responded that ORWH has had multiple meetings with SROs and chairs. SROs must complete training and new chairs must be oriented. The orientation and training will be offered within the context of being value added.

Carmen R. Green, M.D., asked that ORWH take the opportunity to reach out to a wider audience by writing editorials for journals. Dr. Clayton said that Erica Moore, ORWH's new communications director, will address this issue.

Dr. Green suggested that the impact of BIRCWH on women of color be further discussed. Dr. Clayton replied that issues related to women of color are always on the agenda. NIH is committed to diversity as critical to its success.

Dr. Merz asked that SABV progress reports from NIH and the Institute of Medicine (IOM) be developed and publicized in journals. The reports should emphasize the funds available for SABV research. Dr. Merz offered to help draft such a report. Dr. Clayton said this was of interest.

Angela D. Kashuba, Pharm.D., suggested that a SABV checkbox be added to the list of criteria used by journal article reviewers. They would use the box to indicate whether SABV was discussed in the manuscript. Dr. Clayton agreed that this was a good idea and that it would encourage writers to submit articles addressing SABV criteria.

Emeran A. Mayer, M.D., congratulated ORWH for rapidly implementing advisory committee recommendations.

Mid-Course Progress Report on the NIH Strategic Plan for Women's Health, *Moving Into the Future with New Directions and Strategies: A Vision for 2020 for Women's Health Research*

Juliana M. Blome, Ph.D., M.P.H., Associate Director of Science Policy, Planning, and Analysis, ORWH, NIH
Ching-yi Shieh, Ph.D., Statistician, ORWH, NIH

Dr. Blome explained that 2015 was the midpoint for implementing the NIH 2010–2020 strategic plan. Cross-cutting goals that highlight the breadth and scope of ORWH progress include the following:

Goal 1. Increase sex differences research in basic science studies

Goal 2. Incorporate findings of sex/gender differences in the design and application of new technologies, medical devices, and therapeutic drugs

Goal 3. Actualize personalized prevention, diagnostics, and therapeutics for girls and women

Goal 4. Create strategic alliances and partnerships to maximize the domestic and global impact of women's health research

Goal 5. Develop and implement new communication and social networking technologies to increase understanding and appreciation of women's health and wellness research

Goal 6. Employ innovative strategies to build a well-trained, diverse, and vigorous women's health research workforce

Disbursement of Research Funds

ORWH does not have grant-making authority but rather collaborates across NIH with ICs to increase research in the areas of interest to the Office. ORWH works most frequently with the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), because this institute houses the BIRCWH program. ORWH is working to increase outreach and collaborations with multiple ICs.

The ORWH research budget was flat from FY 2010 to FY 2015 at about $40 million per year. The Office spent about $32 million per year on grants funded with other ICs. This included research project grants, meetings and conferences, and research and development contracts.

ORWH research dollars are spread across programs and funding mechanisms. Significant funds go to BIRCWH and interdisciplinary specialized centers of research. The sex/gender administrative supplements began in FY 2013, with increasing numbers of applications every

year. The number of cofunded grants in FYs 2014 and 2015 remained fairly stable but represented smaller percentages of the overall budget, because greater percentages of research funds were going to administrative supplements and R56 grants. This year, ORWH funded a record number of administrative supplement programs. Advancing Novel Science in Women's Health Research (R-21) and the Women's Reproductive Health Research program have been discontinued.

Dr. Shieh conducted an analysis of the Office's research program funding portfolio from FY 2010 to FY 2015 by downloading all grants that ORWH cofunded during those years from the NIH database system known as IMPAC II. Data was merged from the FY 2010 to FY 2015 IMPAC II frozen and current/history files. The frozen data was used to identify awarded applications and their costs. The current/history data files were utilized to identify research, condition, and disease categorization (RCDC) terms and variables not available from the frozen files. The methodology was similar to that used by other ICs; the ICD-10 coding system was used.
Dr. Blome discussed funding by RCDC for FYs 2010 through 2015. Various comparisons could be made using the charts she presented.

Dr. Blome also noted that research funding focuses across the lifespan, with slightly less money going to research on aging. ORWH support covers the gamut of study types with increased interest in cutting-edge studies. In general, the Office is doing well in leveraging its investments.

Communications (Goal 5)
The ORWH website is a key resource for information related to women's health research. There is a consistent uptick in the number of unique visits to the ORWH website each month, and the website received more than 6,500 visits during the last two months.

The Office disseminates resources via a number of different channels such as e-newsletters and social media platforms, including Twitter and Facebook. ORWH's Facebook page gained 1,417 new followers in February and reached almost 100,000 users. ORWH's Twitter page has nearly 11,000 followers.

Workforce (Goal 6) and BIRCWH Data
BIRCWH is the primary program source for workforce funding and focuses on creating a well-trained, diverse, and vigorous cadre of women's health researchers. Award sizes have decreased since FY 2013, in part due to grants management efforts to handle carry-over funding.

Data have been collected across 30 BIRCWH institutions and 335 scholars for FYs 2010 through 2015. The largest number of institutions has been involved in the program for 6 to 10 years. Among participating institutions, the number of publications since the program's inception was most often between 61 and 80. The program success rate was 85 percent, and 79 percent of the

scholars had completed their training. Fifty-five percent of the BIRCWH participants had or are in training to receive doctoral-equivalent degrees, including Ph.D., D.Sc., and Sc.D. degrees. Thirty percent have received or are on track for medical doctor degrees or their equivalent, such as M.D., M.B.B.S., and D.O. degrees. The remaining survey participants are pursuing dual or other professional degrees. Specific measures of success include the finding that the level of publications is higher than would be expected among four new programs. Also, BIRCWH scholars continue to apply for NIH grants.

About 44 percent of the scholars did not identify their race/ethnicity. Among those who did, the majority were non-Hispanic Whites. Dr. Blome suggested that the advisory committee discuss ways to increase response rates and better categorize diversity.

Discussion

Teresa K. Woodruff, Ph.D., suggested that ORWH reach out to nonresponders and consider emailing them. Dr. Blome replied that one of the challenges is categorizing diversity in ways that feel appropriate to the individuals involved. Many of them may be reluctant to identify themselves by checking one box on a list with a limited range of options. She also noted that it is labor intensive to reach out to individuals. ORWH plans instead to work with grantee schools.

Jill B. Becker, Ph.D., asked whether scholars on a tenure track were more likely to report. Dr. Blome said that was the case.

Dr. Merz commented on RCDC funding, noting that reproductive medicine has other grant sources. She also asked whether the mental health funding was used for behavioral or Freudian grants. Dr. Clayton replied that ORWH focuses on brain science, not psychoanalysis.

Dr. Becker noted that 90 percent of existing research on depression is conducted with male animals and asked how to change this situation. Dr. Clayton responded that committee comments would help ORWH initiate early discussions of specific research priorities with ICs. Dr. Blome added that ORWH has liaison staff working with all the ICs; this staff encourages the IC researchers to meet ORWH goals. ORWH funds, she explained, are used “to get a seat at the table.” With this access, ORWH can work to get its goals included in ICs’ research.

Dr. Kashuba noted that shorter-term grants are increasingly being provided to investigators. She asked about the impact of these newer grants on the investigators’ ability to obtain other grants. Dr. Clayton said that this question would be a good topic for future discussion.

Raising the Bar: The Health of Women in America

Amy Mistretta, M.P.H., Epidemiologist, ORWH, NIH

Overview

A growing number of studies document the relative and growing health disadvantage of U.S. women when compared with women in other countries. In particular, the 2013 National Research Council and IOM report *U.S. Health in International Perspective: Shorter Lives, Poorer Health* found that across many measures, the health of women in the United States was significantly worse than the health of women in many other high-income countries. That report and subsequent discussions have spurred further analyses of the differences to explore their causes and detail their effects.

Changes in the lives of American women over the past 25 years have been linked to negative impacts on their health. Key changes include reduction in physical activity and increased consumption of unhealthful foods. In addition, increasing numbers of American women are becoming heads of household and bearing children later in life. The growing number of stressors—both mental and physical—and their impact on women's health need deeper examination.

Other findings indicate that Americans have been dying at younger ages than people in almost all other high-income countries. The disadvantage has been getting worse for three decades—particularly among women—regardless of race, economic class, geographical region, or level of education. The pervasive health disadvantage affects all age groups up to age 75 and is observed for multiple diseases, biological and behavioral risk factors, and injuries.

2015 Workshop Held by the National Academies of Sciences, Engineering, and Medicine

In September 2015, the National Academies of Sciences, Engineering, and Medicine convened a workshop to shed light on important determinants, consequences, effects, and issues attending the relative disadvantage of women in the United States in comparison with women in other economically advanced nations. One key session addressed factors influencing differences in women's health outcomes, especially access to care, bias in medical care delivery, and gender gaps in quality of care for cardiovascular disease and diabetes. Another session discussed research on factors influencing differences in morbidity and mortality. The final session identified future research directions and summarized key issues in women's health care. Participants noted the following:

- Health care system fragmentation has significant consequences for women. For example, pregnancy and its impact on cardiovascular issues need to be integrated.

- An integrated approach to health care over the lifespan would provide important information for researchers.
- The effects of caregiving and the impact of trauma on women's health needs are two topics of particular concern.

The workshop reached across sectors, disciplines, and areas of expertise. It identified key factors at the system, federal, state, patient, and provider levels that might explain the comparative deficiency of the health of women in the United States. The workshop findings included the following:

- A research agenda with a cross-sector, multilevel approach and a life course perspective is needed.
- Health problems early in women's lives can set trajectories that may be difficult for them to change later.
- The move toward precision medicine raises important questions; the key question—how to integrate precision medicine with population health—pertains to both men and women.
- Accessible data on gender differences is needed that compares subgroups of women as well as females to males. In addition, creative ways must be found to expand gender-based analysis and the utility of existing data. Ideally, inexpensive methods can be used to reanalyze existing data and assess sex differences.

The overall challenge is to create cross-sector solutions that build on the factors identified in the workshop. This requires transparency among federal agencies along with participation by multiple stakeholders. The workshop—which included agencies, journals, public health departments, and advocacy groups—could be a starting point for building even greater stakeholder participation. The report from the meeting, *Improving the Health of Women in the United States*, is now available from the National Academies Press at http://www.nap.org.

Discussion

Geert de Vries, Ph.D., asked whether disparities in wealth contribute to health disparities among women. Dr. Blome replied that this variable has yet to be explored.

Heidi Nelson, M.D., observed that rural women have unique issues; she asked that rural diversity be considered in research and that key stakeholders in the biomedical enterprise—especially grant reviewers and journal editors—be made aware of rural issues. Dr. Blome agreed that rural issues should be further acknowledged.

Mary H. Palmer, Ph.D., asked that further attention be given to studying possible bias in the ways health care providers respond to symptoms reported by women. Dr. Blome noted that this was a significant concern.

Evidence-Based Funding: Thoughts About Extramural Research

Michael S. Lauer, M.D., Deputy Director for Extramural Research, OER, NIH

Measuring Accountability

Dr. Lauer asked what the measure of accountability should be for the biomedical enterprise and suggested that the amount of grants or grant money was not the best possible measure. He suggested that measures of accountability should be constructed that are verifiable, quantifiable, and objective. They also should be comparable to other similar metrics. In addition, the measures should be transparent to the public. Furthermore, inputs (e.g., funding, workforce) should be linked as closely as possible to the outputs, which themselves should be clear benefits (e.g., patents, new drugs and medical devices, better health). However, Dr. Lauer noted that input/output metrics for the research ecosystem are complex and encompass multiple issues. For example, clarification is needed on whether trainees are students or part of the workforce.

Medical research is a $120 billion industry in the United States. Until FY 2004, NIH research funding expanded by 6 percent per year. However, between FYs 2004 and 2012, funding was stagnant. At the same time, funding in the biotechnology and medical device sectors expanded. Dr. Lauer suggested that stagnant NIH funding may be related to the problems measuring results.

Dr. Lauer said that maximizing the return on taxpayers' investments in fundamental research should be a critical consideration when developing measures of accountability. To realistically account for taxpayer investment, the number of investigators supported might be a more appropriate accountability measure than the number or dollar amounts of grants. The number of PIs supported by NIH has been relatively constant over time despite the decrease in funding: 25,000 investigators were supported in FY 2003, while 27,500 were supported in FY 2015.

Research Ecosystem: Capacity and Competitiveness Have Increased

A study of awardees, applicants, and funding rates for all research project grants over time found that the capacity of the research ecosystem increased dramatically between FYs 2003 and 2015. During that time, the research environment also became hypercompetitive. In FY 2003, about 61,000 PIs submitted grant applications; by FY 2015, about 90,000 investigators were submitting applications. About 42 percent of five-year funding applications were funded in FY 2003, but only 30 percent were funded in FY 2015. The hypercompetitive environment has been

further fueled by the decrease in the number of “bread-and-butter” R01 grants funded during that period.

Measuring the Impact of Research

Dr. Lauer explained that there is no single measure of the impact of research. Instead, he posited that the PQRST of appraisal and reward should be implemented. In this approach, “P” stands for productivity, as measured by published trial results and field-normalized high rates of citations; “Q” stands for quality; “R” stands for replication; “S” stands for sharing; and “T” stands for translation.

Dr. Lauer recommended funding as many PIs’ projects as possible. Because it is impossible to predict when and where the next big discovery will occur, spreading funding increases the likelihood that this event will be supported.

In addition to assessing productivity (measured by publications and citations) and funding the maximum number of PIs, NIH can measure the impact of research by the stewardship of clinical trials, the use of various grant mechanisms, consideration of “big” and “small” science, support for diversity, and the balance of time and money. As laid out in its strategic plan, NIH seeks to fund great research, be a good steward of funds, respond nimbly to public priorities, and manage by results. The most effective ways of spending funds, Dr. Lauer added, should be determined by evidence-based research.

Discussion

Judith G. Regensteiner, Ph.D., asked about future funding for NIH. Dr. Lauer said that the short-term picture is looking better. The larger issue is moving from erratic to steady increases.

Dr. Green suggested that minority investigators be given greater consideration in the path forward. She noted that the finish line should be getting the results of scientific investigations back to the people and to the communities that provided the data. Dr. Lauer agreed.

Dr. Mayer asked about funding more investigators at lower career levels. Dr. Lauer noted that 10 percent of PIs get 50 percent of the funding, which may not be justifiable. Steps are being taken now to provide funds for PIs who did not previously receive grants.

Dr. Meleis asked about metrics, suggesting that a measure of success should be the global evolution of a scientific idea. Dr. Lauer replied that the globalization of data should lead to objective answers to international questions and issues.

Dr. Kashuba suggested that degree type should be considered when measuring individuals’ productivity. Dr. Lauer agreed.

NIH Legislative Update

Anne Tatem, M.P.A., Senior Legislative Analyst, Office of Legislative Policy and Analysis (OLPA), NIH

Laura Berkson, J.D., Legislative Analyst, OLPA, NIH

In February 2016, the Administration released its budget for FY 2017, which provides $33.136 billion for NIH, 2.5 percent above the FY 2016 level. The budget includes mandatory funding for the Cancer Moonshot Initiative, the Precision Medicine Initiative Cohort Program, and the Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative. Without the mandatory money for these specific initiatives, the President's budget request for NIH would, in effect, result in $1 billion less than the FY 2016 program level of $32.3 billion.

This spring, the appropriations labor, health and human services, education, and related agencies (e.g., the U.S. Department of Labor, the U.S. Department of Health and Human Services [HHS]) subcommittees in both the U.S. House of Representatives and Senate held hearings to consider the President's request for NIH. Ms. Tatem reported that it appears that both the House and Senate are interested in increasing funding for NIH through the appropriations process.

The Senate has started considering the 12 appropriations bills both in Committee and on the Senate floor. Ms. Tatem noted that the House probably won't begin to consider bills until mid-May. She stated that, as is customary, there is no current information on when the Labor/HHS bill will be considered.

Discussion

Dr. Green asked for clarification about mandatory versus discretionary funding. Ms. Tatem explained that the House and Senate Committees on Appropriations set discretionary spending, and discretionary funds require an annual appropriations bill. Mandatory spending refers to spending enacted by law and is not dependent on an annual appropriation bill.

Zika Virus: Unraveling the Public Health Emergency

Catherine Spong, M.D., Acting Director, NICHD, NIH

Overview

Dr. Spong explained that the Zika virus is a mosquito-borne flavivirus. The key difference between the Zika virus and other flaviviruses (e.g., dengue) is in surface envelope proteins.

The virus was first discovered in 1947 in Uganda's Zika forest. Other outbreaks were reported in tropical Africa, Southeast Asia, and the Pacific Islands. In May 2015, Brazil reported the first Zika

virus outbreak in the Americas. Since the first infection in Brazil, which was reported in May 2015, about 500,000 people have been infected. The World Health Organization declared Zika virus to be a health emergency in February 2016. Recently, the government of Colombia confirmed the first cases of Zika virus in South America outside the epicenter of Brazil. In the United States, Zika virus is primarily carried by returning travelers.

Eighty percent of Zika virus infections are asymptomatic. The other 20 percent of infected individuals usually experience mild symptoms—commonly including rashes, fever, joint pain and red eyes—lasting less than 7 days.

The virus can also be transmitted by sex, blood donations/transfusions, and organ transplantations. It is found in postmortem brain tissue and in amniotic fluid and placental tissue and is associated with microcephaly, Guillain-Barré syndrome, and other neurological conditions.

Adverse Pregnancy Outcomes From Past and Current Zika Outbreaks

The French Polynesia Zika virus outbreak identified in 2013 was the largest outbreak documented before the Brazil occurrence. About 30,000 people (11 percent of the population) were infected, and two retrospective studies noted increased cases of abnormalities in neonates.

It had been thought that infection in women occurred primarily during the first trimester of pregnancy and was chiefly associated with microcephaly. Since then, researchers have found that infection might cause fetal problems during any trimester, possibly due to persistence of viremia in the pregnant women. Effects of Zika virus appear to include fetal growth restriction and stillbirth as well as microcephaly. One study found that about 30 percent of 29 infants born with microcephaly also had ocular birth defects such as macular lesions or optic nerve abnormalities. Another study of 23 infants with microcephaly found additional brain abnormalities.

Research Gaps

Dr. Spong noted the following research gaps related to pregnancy and its outcomes:

- Diagnostics
- Risk of infection in pregnancy
- Sequelae of Zika virus in exposed and infected infants without microcephaly
- Long-term reservoirs for Zika virus
- Treatment
- Vaccine

Specific questions associated with items in the list include why the virus is potent now in South America when it was less potent earlier in other locations, whether the Zika virus infection mechanism resembles that of other flaviviruses, and how the virus changes during the trimesters of pregnancy.

Dr. Spong noted other neurological sequelae that might be associated with Zika virus based on articles published recently in the scientific literature and focused on single individuals or small samples. The sequelae, found in either young or old people, included acute myelitis, meningoencephalitis, and acute disseminated encephalomyelitis. These studies give rise to questions about the impact of Zika virus on the very old as well as on the very young. In addition, animal studies showing central nervous system damage associated with the virus provide another line of research to pursue.

Zika Virus in the United States and U.S. Territories

Data from the Centers for Disease Control and Prevention (CDC) published on April 13, 2016, noted that 358 travel-associated cases had been found in the United States; the cases included 31 pregnant women. Seven cases were sexually transmitted. Within U.S. Territories, 471 locally acquired and 4 travel-associated cases had been identified. They included 58 pregnant women.

HHS Response to the Zika Virus Outbreak

Dr. Spong noted multiple HHS responses to the Zika outbreak. On January 15, 2016, a level 2 travel advisory was issued. In addition, states are to report infections to the appropriate agencies, and key agencies have started sharing samples. Notices and a rapid FOA also have been promulgated to promote Zika research. This spring, enrollment will begin in a study of Zika-infected women and their children. A volunteer Zika registry has been established and can be accessed at http://www.cdc.gov/zika/hc-providers/registry.html.

HHS also is involved in responses coordinated with international agencies and with professional societies in the United States. High-level meetings have been held in the United States and Brazil to develop countermeasures and a Zika action plan. In addition, a multination cohort study is scheduled to begin in May. CDC and various medical societies have issues guidance documents available on their websites.

Discussion

Dr. Regensteiner asked whether enough information was available to support a travel advisory. Dr. Spong explained that the advisory was based on the best available evidence.

Dr. Meleis recommended that more research be conducted to verify the link between the virus and microcephaly and to identify the long-term effects of the infection. Dr. Spong agreed.

Kimberly D. Gregory, M.D., M.P.H., suggested that more information be gathered about the viremia during pregnancy. Dr. Spong agreed that this was important.

Dr. Becker asked whether there was any data linking an infant's sex and outcomes. Dr. Spong did not know whether this information existed.

Rachel Jones, Ph.D., R.N., FAAN, asked about whether the Zika trajectory was similar to that of cytomegalovirus. Dr. Spong said the infection trajectories did appear similar.

Dr. Mayer asked whether there was any data about male-to-male transmission. Dr. Spong said she knew of one case.

Sex Differences in Addiction—Animal Models and the Human Condition

George Koob, Ph.D., Director, National Institute on Alcohol Abuse and Alcoholism (NIAAA), NIH
Jill Becker, Ph.D., Patricia Y. Gurin Collegiate Professor of Psychology; Research Professor, Molecular & Behavioral Neuroscience Institute, University of Michigan

Complexity of Sex Differences

Dr. Becker began by explaining that sex differences in the brain are linked to sex chromosomes, developmental hormone exposure (fetal/perinatal, depending on the species), prepubertal experiences, puberty, and gender-specific experiences. She then noted that there are different categories of sex differences that may overlap and affect the addiction process. These include qualitative and quantitative differences in male and female behavior and population differences as seen in male and female distributions of behaviors. In addition, underlying mechanisms can differ, because male and female neural mechanisms give rise to male and female behaviors, respectively.

Sex Differences in Addiction

Sex differences in addiction, Dr. Becker continued, may be explained at least partially by recent research findings in neurobiology. She noted that sex differences in the neural systems important for maternal motivation result in sex differences in motivated behaviors in general. Additionally, there are sex differences in the neural systems that mediate motivation to engage in reproductive behaviors. The hormones engaged in energy intake modulation also play a role in sex differences in motivation. This is illustrated by the findings that (1) estradiol decreases feeding behavior in females but not males and (2) males eat more than females due to sexual differentiation of the hypothalamus.

Species differences also impact addiction patterns. For example, the territorial versus social patterns among rats and mice impact their addictive behavior. Maternal-child bonds and experiences also are significant factors. For instance, stress to female rats increases the

likelihood that their offspring will be addicted, and early childhood trauma increases the likelihood that a human will become an addict.

Developing a Heuristic Framework for the Neurobiological Bases of the Transition to Substance Abuse Disorders

This cursory examination of sex differences hints at the complexity of the subject and the complications inherent in addiction and its study. Based on the complexity of the research evidence, Dr. Koob developed the following definition of addiction:

> "Addiction is a chronically relapsing disorder that is characterized by a compulsion to seek and take drug or stimulus, loss of control in limiting intake, and emergence of a negative emotional state (e.g., dysphoria, anxiety, irritability) when access to the drug or stimulus is prevented. These negative states are collectively defined as the 'dark side' of addiction."

Recent research on aspects of the complexity underlying addiction mechanisms lead to the following "bottom-line" characterization of the problem: It is (1) an incentive salience disorder, (2) a reward deficit disorder/stress surfeit, and (3) an executive function disorder. Researchers have begun studying executive function disorder and recent findings indicates that the human frontal cortex is not fully developed until a person is about 25 years old. This may explain, to some degree, the poor decision-making that is part of the addictive process.

Dr. Koob explained that the definition and characteristics he described represent the first steps towards a larger goal. This is to delineate a heuristic framework for the neurobiological bases of the transition to substance abuse disorders.

Sex Differences in Addiction to Different Classes of Drugs

Drs. Koob and Becker focused on sex differences in cocaine-taking behavior. Among rats, females become addicted more rapidly and at lower doses. In addition, estradiol enhances the motivation to use and become addicted to cocaine among female rats. Furthermore, female rats have more severe withdrawal symptoms and can be more readily induced to restart addiction when stressed. However, Dr. Becker said, although more females than males preferred cocaine, their neural activity was the same. Among humans, females are less likely to take drugs, but those who take drugs are likely to telescope dependence and behavior (e.g., binge drinking). In fact, the intensity of binge drinking is becoming a national problem, Dr. Koob reported.

Dr. Becker said that all addiction activity is modulated by the stress response. This has been borne out in studies of nicotine withdrawal and relapse in rats. Greater stress leads to greater dysphoria ("dark-side" symptoms) and more rapidly leads to relapse among females than males.

Referring to the different categories of sex differences (qualitative, quantitative, population-related, and functions of underlying mechanisms), Dr. Becker stated that the effect of estradiol was an example of qualitative difference and that the impact cocaine was a quantitative difference. Vulnerability to addiction was classified as a population-based difference.

Sex Differences in Vulnerability for Addiction

Looking more closely at population vulnerability, Dr. Becker recapped specific findings and developed a hypothesis to explain vulnerability across both sexes, including quantitative, qualitative, and underlying mechanisms. She posited the following three findings. First, estradiol enhances the acquisition, escalation, and motivation for drug taking in females. Second, sex-differentiated stress responses exacerbate the greater risk for relapse in females. Third, neural activity modulated by estradiol mediates a more rapid transition to addiction; as a result, more females are vulnerable for addiction. Therefore, she hypothesized,

> "Experience interacts with development to enhance or attenuate the risk for addiction in both males and females. All individuals who are vulnerable for addiction (female and male) exhibit a more rapid down-regulation of drug-induced DA release and down-regulation of the same neural pathways."

Discussion

Dr. Nelson noted that the legalization of marijuana appears to be leading to greater experimentation among the young. In addition, young people may be increasing their use of alcohol. Dr. Nelson asked about the impact of this behavior on young brains.

Dr. Koob replied that about 10 percent of experimenters become addicts. Problems identified among heavy marijuana users include some loss of intellectual ability, psychotic episodes, memory deficits, and possible reproductive issues. In addition, the smoke from the drug may be damaging. NIAAA, the National Institute on Drug Abuse (NIDA), and the National Cancer Institute are currently studying the impact of marijuana and alcohol intake on the adolescent brain. One large NIH initiative is the Adolescent Brain Cognitive Development Study; this cross-IC collaboration is the largest long-term study of brain development and child health in the United States. Dr. Koob added that although stronger strains of marijuana are now available, it remains a Schedule I drug. As a result, study options are limited.

Dr. Regensteiner asked about research in binge drinking among young men. Dr. Koob responded that binge drinking has been found to lead to earlier physical problems (e.g., cirrhosis of the liver) and that newer cultural issues are involved in binge drinking. These can include peer pressure to become intoxicated as quickly as possible and to drink until blackout.

Dr. Green recommended that ORWH take a seat at the table with other ICs studying pain (both acute and chronic) and addiction. The Office could have a unique and pivotal role on this topic and how it relates to both the health of women in general and to the health of women of color. Dr. Clayton responded that the Office has resources to share with other ICs.

ORWH Programs to Support Women in Science

Jennifer Plank-Bazinet, Ph.D., Health Scientist Administrator, ORWH, NIH

Introduction

Dr. Plank-Bazinet began her presentation by demonstrating the underrepresentation of women within the academic life sciences. Although there is relative parity between men and women at the instructor and assistant professor stages, data from a 2013 National Science Foundation (NSF) report demonstrate that women are underrepresented at both the associate and full professor stages. She did not have access to data looking at the intersection of gender and race/ethnicity but presented a graph from the NSF report showing that Hispanic/Latino, Black, and Asian scientists are significantly underrepresented when compared to White scientists. Dr. Plank-Bazinet also noted that a 2009 Association of American Medical Colleges (AAMC) benchmarking report on the number of women in medical school leadership positions found that women were significantly underrepresented in the majority of these positions, especially in the leadership roles of department chairs and deans.

The most recent ORWH strategic plan lays out the Office's mission, which is to (1) improve women's health, (2) promote sex differences research, and (3) support women in biomedical careers. Dr. Plank-Bazinet's primary responsibility is providing oversight for programs that support women in the workforce. She focused her remaining remarks on the NIH Working Group on Women in Biomedical Careers and on the Research Supplements to Promote Re-entry into Biomedical and Behavioral Research Careers.

NIH Working Group on Women in Biomedical Careers

The NIH Working Group on Women in Biomedical Careers was formed in 2007 response to the National Academies report *Beyond Bias and Barriers: Fulfilling the Potential of Women in Academic Science and Engineering*. The working group is co-chaired by Drs. Collins and Clayton. The group, which includes representatives from most ICs, seeks innovative strategies to address concerns of NIH intra- and extramural communities. Participants focus on issues of career barriers, women of color in science, and mentoring.

The group publishes a bimonthly newsletter that contains summaries of recent studies related to women in science and highlights relevant NIH news that might affect them. The newsletter also profiles women in the field and spotlights institutions that are working to recruit, retain,

and support the advancement of women. Interested individuals can subscribe to the free newsletter at https://womeninscience.nih.gov/nih_programs/listserv/.

Dr. Plank-Bazinet highlighted the activities of several of the working group's six committees. The Committee on Extramural Activities and Mentoring Programs has successfully established family-friendly initiatives and developed a central repository for information on them, located at http://grants.nih.gov/grants/family_friendly.htm.

The Committee on Advancing Women in Independent Positions has helped guide NIH in funding grants on causal factors affecting women's biomedical careers. In 2009, NIH funded 14 grants, worth $16.5 million. In 2012, the committee hosted a workshop for grantees to discuss their research. After the workshop, the grantees developed a research partnership for women in biomedical careers. In June 2014, the committee hosted another workshop; participating stakeholders agreed that institutional change was needed to reduce sexual and racial/ethnic barriers and that there is no one-size-fits-all approach for institutions to use in transitioning.

As of May 2015, committee members had authored 62 manuscripts and given 162 presentations. They had also secured 24 additional grants and won 31 awards. They have been invited to attend the June 6, 2016, Conference on Evidence-Based Innovations to Support Women in Biomedical Research Careers. (See page 4.) In addition, members will convene on July 25, 2016, to identify both existing programs to support women and opportunities for future collaborations. Next summer, this group will have eight publications featured in *Academic Medicine.*

The Committee on Women of Color in Biomedical Careers promotes efforts to improve the hiring, retention, advancement, and visibility of women of color in science. To do this, the committee has held workshops on gender and race. Additionally, the committee seeks to improve visibility of women scientists of color through awards and lectureship nominations. This committee formed an award-winning social networking site for those who value diversity in the biomedical workforce. The Women of Color Research Network shares regularly updated networking and mentoring opportunities as well as other information. Four regional groupings have been developed thus far as part of the network. More information about the network is available at http://www.wocrn.nih.gov.

The Committee on the NIH Intramural Research Program has developed findings and programs that could be adapted by other institutions. Recent surveys conducted by NIH have indicated that men and women who are just beginning their postdoctoral training at NIH are equally likely to want to pursue independent research positions. However, after postdoctoral training, women are significantly less likely to want to pursue careers as independent researchers. In

follow-up focus groups with NIH postdoctoral fellows, the committee found that both men and women were concerned about maintaining a career-life balance and the best ways to address the economic environment during their own careers. Relatively few fellows were interested in becoming PIs, and they regarded staff scientists as an essential component of the research enterprise.

The Committee on Communication and Public Outreach oversaw the launch of the working group website, which is: https://womeninscience.nih.gov/about/committees/asp. The site contains information on NIH programs and grants, recent news and events, and the current ORWH newsletter.

Research Supplements to Promote Re-entry into Biomedical and Behavioral Research Careers
The program supports individuals with high potential to re-enter an active research career after an interruption for qualifying circumstances. Candidates participate fully in a research project led by an NIH-funded investigator and have opportunities to update and enhance their research capabilities and to be part of a carefully planned mentoring program. To participate, the candidate must have a doctoral degree, be a citizen or otherwise lawfully admitted to the country, and not be engaged in full-time paid research. In addition, the candidate's hiatus from research should not be less than 1 year or more than 8 years. The candidate's mentor applies for the program. The applicant must be a PI working on an NIH-funded grant, and the proposed research must be directly related to the parent research grant. Dr. Plank-Bazinet also noted an overall challenge reaching potential candidates: the need for program publicity.

In 2006, a telephone survey was conducted to evaluate the program. Ninety-eight of the 126 candidates participated. Eighty-three percent had published in peer-reviewed journals. The same number said the program had helped them advance their careers. In addition, 81 percent had secured positions involving scientific research, and about one-third had received grants. However, 10 percent of the participants were hesitant to recommend the program to a colleague. They noted that it was difficult to overcome the career hiatus, found it difficult to adjust to the lab culture and dynamics, and felt they received insufficient mentoring.

Discussion
Dr. Meleis asked about the evaluation plan for the re-entry program. Dr. Plank-Bazinet said the re-entry program will be evaluated. Dr. Green added that evaluation is critical.

Dr. Mayer commended ORWH for staff's impressive response to the advisory committee's past discussions. He also noted that it is commonly believed in the biomedical research community that if you leave research you will never be back on the cutting edge. Dr. Plank-Bazinet noted that some work has been done to overcome this cultural bias but more is needed, especially as

the funding environment becomes more competitive. Dr. Clayton said that there are multiple significant factors involved in the decision to return, including the amount of time and money the individual has already invested in his or her career and the reasons for the hiatus in work. She added that cultural change can be quantified and measured.

Dr. Woodruff asked whether NIH maintained links with similar programs sponsored by NSF and whether the Office would partner with NSF to sponsor medical school programs. Dr. Plank-Bazinet said that ORWH does work with NSF and hopes to promote a medical school program.

Dr. Bird asked whether the ORWH programs were working well for women in differing circumstances. For example, is data being collected based on the reason for the leave and/or the field of specialization? Dr. Plank-Bazinet responded that these issues merited study.

Dr. de Vries noted that re-entry is difficult and asked whether applicants were encouraged to look at candidate's personal statements. Dr. Plank-Bazinet said that changes were made in the biosketch to enable applicants to get a better sense of the candidate.

Dr. Meleis stated that mentors need training to help create a sustainable community of scholars. Dr. Plank-Bazinet replied that mentor requirements to that end are now part of the program.

Dr. Regensteiner suggested that investigators be encouraged to be flexible to reduce the need for leave. That is the purpose of the Keep the Thread program, Dr. Plank-Bazinet explained.

General Discussion

Lisa Begg, Director, Research Programs, Dr.P.H., R.N., ORWH, NIH

Dr. Begg moderated the advisory committee conversation. The discussion was open to committee members and nominees.

Operationalizing the Definition of Interdisciplinary Science BIRCWH

Dr. Begg began the discussion by providing the following definition of interdisciplinary research based on the work of the National Academy of Sciences.

> "Interdisciplinary research is a mode of research that integrates information, data, techniques, tools, perspectives, concepts, and/or themes from two or more disciplines or bodies of specialized knowledge to advance fundamental understanding or to solve problems whose solutions are beyond the scope of a single discipline or area of research practice."

Dr. Begg suggested that the definition could be employed by BIRCWH and asked for comments.

Dr. Bird observed that examples would be needed specific to BIRCWH and that these could be added over time.

Dr. Meleis said the language was generic. Dr. Begg agreed, adding that each set of funding requirements laid out more specific stipulations.

Number of Scholars per BIRCWH Participating Institution

Dr. Begg asked whether two scholars per BIRCWH institution were too few to help ensure the success of the program. The committee's executive secretary, Terri L. Cornelison, M.D., Ph.D., added that all the IC K–12 programs are grappling with this issue in a time of budget constraints.

Dr. Bird noted that the four-person grouping better ensured that the junior researchers would build supportive relationships and succeed in their work. She added that the team suffers when an insufficient number of scholars are funded.

Dr. Regensteiner asked whether the K–12 effort could be reduced from 75 percent. Dr. Begg replied that the 75 percent effort was mandated in K–12 grants.

Dr. Nelson suggested that the number of participants could be scaled to the size of the institution. In response, Dr. Begg noted that until recently, four scholars per institution has been standard.

Dr. Meleis suggested challenging the institutes to contribute. Dr. Begg replied that this would spark policy issues.

Dr. Green said that a bias toward larger institutions is an ongoing program. She asked whether more investigators should be funded. Dr. Begg replied that NIH is looking into this.

Dr. Meleis suggested that philanthropic organizations be approached to finance the scholars, using the existing program for leverage. In response, Dr. Begg observed that possible partnerships need to be identified.

Questions Raised by Dr. Clayton

Dr. Clayton asked the committee members to respond to the following two questions:

1. What particular scientific question, technical issue or clinical opportunity would you like to highlight?
2. How should we inform all our stakeholders about adopting SABV?

In response to the first question, Dr. Merz said that regenerative medicine researchers need to be encouraged to use female as well as male stem cells.

Dr. Meleis complimented Dr. Clayton and ORWH on the breadth of their work. Dr. Clayton replied by thanking the staff for their team effort. Dr. Meleis suggested that ORWH consider the impact of caregiving on outcomes for women in her response to the first question.

Responding to the first question, Dr. Woodruff suggested that ORWH create a consortium including industry representatives to address adverse events in research on women's health. In her comments on the second question, Dr. Woodruff noted that SABV was recently approved and that dissemination is critical. It is not enough to provide information at study sections. She asked that a checkbox be added to the article application form so that journal manuscript reviewers could note whether SABV was considered by authors. Dr. Clayton noted that reviews recently completed or currently underway were for grants announced before the SABV policy came into force on January 25, 2016. SABV will be considered for applications submitted after January 25. Training for peers, SROs, and review leaders is ongoing.

Dr. Nelson suggested developing a priority list in response to the first question. Regarding the second question, she recommended starting with the "low-hanging fruit."

Commenting on the first question, Dr. Becker noted that ORWH is at the table with NIDA and NIAAA but should take a more active role in the discussions of pain and addiction and their impact on females. In her answer to the second question, Dr. Becker suggested that ORWH create a short video targeting the public; once the public is on board, other stakeholders will follow. Dr. Clayton replied to Dr. Becker's suggestion about pain and addiction. She noted that ORWH is working with other ICs on the NIH national pain strategy. The Office is part of an NIH consortium developing common definitions and research questions to shape the study of pain and addiction. In addition, ORWH is leading the way in pain education. Current challenges include addressing coexisting pain conditions; these are more common in females than males.

Dr. Mazure noted that a finish line is needed to respond to the first question. She raised the following issues: How do we embed sex and gender information into practice guidelines and other professional guidance? How can we involve practitioners in disseminating the data we have developed?

Dr. Clayton agreed that a finish line was needed and that ORWH data need to be integrated into practice guidelines and other guidance. The Office is engaged in conversations with professional organizations and other ICs concerning these topics. ORWH can provide them with free didactic materials, but it is more appropriate for the other groups to move the guidelines and guidance forward. She also noted that professional guidelines and guidance might be a topic for the September advisory committee meeting.

Dr. Mazure noted that translation ends with the patient. Implementation science is part of our mission. Dr. Clayton agreed.

Dr. Bird commended ORWH for progress raising the bar on sex differences. She asked that, as part of the answer to the first question, additional consideration be given to social and biological factors in sex difference research. Commenting on the second question, she suggested that research on sex differences should be more highly scored by grant reviewers, because it is innovative.

Responding to the first question, Dr. Page recommended that ORWH continue and expand its work advancing careers for women in science and promoting the consideration of sex differences in basic and translational research. Regarding implementation of SABV, Dr. Page said that the proposed actions went only part of the way. More conversations with stakeholders are needed, and these should allow for frank sharing of concerns. Dr. Clayton replied that when people hear about the SABV policy, they come to ORWH events to learn more. She agreed that the policy needs to be made part of more ongoing conversations with stakeholders. In addition, individual investigators need to think through the implications of SABV policy for their research and create appropriate study designs.

Dr. de Vries spoke about the need for practical examples in his response to the first question. For example, investigators need ideas about how to address sampling issues, and they need guidance about the consequences of changing study designs to meet SABV requirements.

Ana Maria Lopez, M.D., M.P.H., FACP, lauded the meeting and suggested that "making information available" should be an answer to the first question.

Dr. Gregory recommended that addiction prevention and cultural issues be added to the topics suggested in responses to the first question.

In her comments about the first question, Dr. Green suggested that leadership, sustaining women in the career pipeline, the role of social determinants, and the impact of sex difference research on transgender people should be included in the topics to be highlighted. She also noted that factors related to race/ethnicity should be considered in responding to both questions.

Adjournment

Dr. Clayton

Dr. Clayton thanked the participants for their ideas and comments throughout the advisory committee meeting. She adjourned the meeting at 4:10 p.m.