

**National Institutes of Health  
Advisory Committee of Research on Women's Health (ACRWH)  
Concept Clearance Meeting Minutes  
February 25, 2019**

**COMMITTEE MEMBERS PRESENT**

Janine Austin Clayton, M.D., ACRWH Chairperson  
Director, Office Of Research On Women's Health  
Wendy Brewster, M.D., Ph.D.  
Geert Devries, Ph.D.  
Kimberly Gregory, M.D., M.P.H.  
Rachel Jones, Ph.D., R.N.  
Ana Maria Lopez, M.D., M.P.H.  
Ana Langer, M.D.  
Carolyn Mazure, Ph.D.  
Peg McCarthy, Ph.D.  
Louise McCullough, M.D., Ph.D.  
Amy Paller, M.D.  
Marcia Stefanick, Ph.D.  
Susan Wood, Ph.D.

**STAFF PRESENT**

Elizabeth Spencer, BSN, ACRWH Executive Secretary and  
ORWH Deputy Director  
Rajeev K. Agarwal, Ph.D.  
Lisa Begg, Dr.P.H., RN  
Margaret Bevans, CAPT., Ph.D., RN, AOCN, FAAN  
Victoria Cargill, M.D., M.S.C.E., AAHIVS  
Rebecca Delcarmen-Wiggins, Ph.D.  
Melissa Ghim, Ph.D.  
Chyren Hunter, Ph.D.  
Jessica Johnson  
Elizabeth Sekine

**Call to Order, Roll Call and Ethics Statement**

*Elizabeth Spencer, ACRWH Executive Secretary*

The meeting of the NIH Advisory Council for Research on Women's Health Concept Clearance was called to order at 4:00 pm on February 25, 2019 by Elizabeth Spencer, who called Roll by IC (see Roster, above).

Ms. Spencer asked members to review the *Standards of Ethical Conduct for Employees of the Executive Branch* pamphlet, which she said each member received after their appointment. A Federal Advisory Committee member is considered a special government employee, or SGE, and subjected to the same ethics rules as a government employee under the Federal Advisory Committee Act (FACA).

At every meeting, Ms. Spencer said the Committee will review the steps and processes needed to determine any actual or potential conflicts between public responsibilities and private interests. The information that members provided about their professional, personal and financial interests will serve as the basis for assessing real, potential or apparent conflicts of interest. Anything that could be seen as compromising the ability to be objective in giving advice during committee meetings will be used to make this determination.

If the need for individual services outweighs a potential conflict of interest, ORWH will either issue a waiver or recuse the member from that portion of the meeting. Conflicts of interest for general matters are usually waived because ORWH believes the ability to be objective is not necessarily affected by financial interests. Members should be attuned to issues that could affect or appear to affect their judgment. If it is defined as problematic, they will be asked to recuse themselves from that portion of the committee meeting.

A quorum was assembled, and the meeting was turned over to Dr. Clayton.

### **Welcome and Opening Comments**

*Janine Clayton, M.D., NIH Associate Director for Research on Women's Health, and Director of the Office of Research on Women's Health*

Dr. Clayton welcomed ACRWH members and guests and thanked participants for their hard work on the Trans-NIH Strategic Plan for Women's Health Research, titled "*Advancing Science for the Health of Women.*" She observed that concept clearance is a critical step in the Strategic Plan's execution and asked the Committee to be sure they are aligned with its goals before moving forward.

The programs to be considered for Concept Clearance at this meeting were:

1. Building Interdisciplinary Research Careers in Women's Health (BIRCWH)
2. Specialized Centers of Research Excellence (SCORE)
3. Research on the Health of Women of Understudied, Underrepresented & Underreported (U3) Populations
4. Sex and Gender in Health and Disease
5. Administrative Supplement Effects on gender and disease and new Funding Opportunities Announcements (FOA).

Dr. Clayton said the Strategic Plan's five strategic goals lay out an ambitious, needed path towards improving women's health. The goals are to:

- Advance rigorous research that is relevant to the health of women,
- Develop methods and leverage data sources,
- Enhance dissemination and implementation,
- Promote training and careers.
- Improve evaluation.

Dr. Clayton identified disparities in life expectancy as an example of the challenges of meeting these goals. Compared to other industrialized nations, she said the average life expectancy of women in the United States is at or near the bottom. In one ranking of a woman's life expectancy among comparable nations, Japan, Germany and Canada were in the top 10 while

the U.S. came in 12th. Racial disparities among African American women, particularly those involving maternal health and maternal fatalities, are also problematic hurdles.

Dr. Clayton stated that she is proud of the Strategic Plan as a final work product. She added that she is also very pleased with the priorities and goals that have been set for all of NIH, and the OWHR for responding to women's health research needs. These goals and priorities are driven by ORWH's mission to:

- Carry out the mandates of the 21<sup>st</sup> Century Cares Act
- Reaffirm NIH's commitment to women's health research
- Provide a path to achieving our vision of a world in which biomedical research integrates sex and gender
- Ensure that every woman receives evidence-based needs prevention and treatment that are tailored to her own needs, circumstances and goals
- Enable women in science to reach their full potential

### **Building Interdisciplinary Research Careers in Women's Health (BIRCWH) RFA Presentation**

*Lisa Begg, Dr. P.H., RN, Senior Research Officer, ORWH and Melissa Ghim, Ph.D., Health Scientist Administrator, ORWH*

The Building Interdisciplinary Research Careers in Women's Health (BIRCWH, pronounced "BIRCH"), is the only trans-NIH training/career-development program that exclusively focuses on the development of junior faculty.

Dr. Begg said the purpose of this ORWH Signature program is to expand support for training/career development in basic, translational, behavioral, clinical, and/or health services research relevant to the health of women. The BIRCWH findings will not only fill in critical gaps on women's health but may improve men's health, as well. Where appropriate, both sexes are included in studies to better understand the role of sex as a variable in health and diseases.

Since its creation in 2000, BIRCWH has graduated 700 Scholars from various programs at 20 geographically-representative centers nationwide. From 2010-2015, 70 percent of them submitted at least one subsequent NIH Research Project Grant (RPG) application. Half of these were successful, and 70 percent resulted in 10-year tenure-track appointments of the Scholars at the time of evaluation in 2015.

Although BIRCWH initially focused on reproductive health issues, its broad-based scientific portfolio now includes virtually every condition that affects women. Two RFA's support 20 active BIRCWH programs on aging, autoimmunity, cancer, cardiovascular disease, mental health, musculoskeletal disorders, neurosciences and infectious diseases, such as HIV/AIDS.

The original RFA funded 10 of the 20 active programs from coast to coast. The proposed RFA reissuance funded half of these under RFA-OD-15-001. The K12 Institutional Career Development Award is the mechanism used by several institutes to support clinical research programs, and the ORWH is part of that group. The one-time RFA request for reissuance falls under the new definition of clinical trials and will allow BIRCWH Scholars to lead a clinical research program using the K12 grant mechanism.

The rationale for continuing the RFA is that BIRCWH is the only trans-NIH career development program that focuses broadly on the health of women. Congressionally designated in 1999, the

program remains a priority as defined by the 21st Century Cures Act, while its RFA's support the Strategic Plan for Advancing Research on Women's Health, 2019-2023. Objectives 4.1, 4.2, 4.3 and 4.4 of Goal 4 specify four areas to promote training and careers and develop a well-trained, diverse and robust workforce for advancing the science for the health of women.

### **BIRCWH Discussion and Vote**

Interest was expressed in whether the forecast for the new RFA will come out once it has been approved. Dr. Begg said that BIRCWH was permitted to issue a Notice of Intent to Publish a Funding Opportunity Announcement for Limited Competition. Approval for publication is expected by the last week of March once the RFA is cleared by the internal clearance process.

Several members asked if the current RFA differs from the previous version. Dr. Begg said it will reflect new policies for institutional training and clear development grants that have evolved since FY 2015 and reflect more complexities in the science. She stated that the RFA is still within internal review but once it was published in the NIH Guide in late March, she and Dr. Ghim would be available to answer any specific questions. Dr. Wood asked if the committee's role in this meeting was to provide high-level concept clearance and not dig directly through the RFA. Dr. Begg stated that was correct.

Carolyn Mazure brought a nomination to the floor to move this concept forward. Susan Wood seconded. A vote was taken. The motion carried unanimously.

### **Specialized Centers of Research Excellence (SCORE) on Sex Differences FDA Presentations**

*Chyren Hunter, Ph.D., Associate Director, Basic & Translational Research, ORWH*

Dr. Hunter presented a proposal to expand the Specialized Center on Sex Differences (SCOR) and rename it the Specialized Centers of Research Excellence (SCORE) on sex differences. She said that SCORE is well positioned to study disease and conditions that affect women and enhance the health of both sexes.

SCOR is the only disease-agnostic program on sex differences at NIH, and views sex as a biological variable that affects all stages of a disease. Each of the centers shares interdisciplinary, translational goals to: (1) expedite interdisciplinary development and application of new knowledge to human diseases that affect women; (2) learn more about the etiology of these diseases; (3) foster improved approaches to treatment and prevention of diseases that affect women.

SCOR's consideration of both sexes in research design, analyses and reporting on sex and gender factors that affect women's health preceded implementation of the NIH SABV policy (OD-15-002) by more than a decade. Co-sponsored by nine NIH institutes and centers, and the Food and Drug Administration, its initiatives reflect broad scientific and geographic diversity of projects within the specialized centers. The centers work cooperatively and collaboratively together and with NIH to pursue emerging scientific opportunities and advance the study of conditions and diseases that affect both women and men.

Nine NIH institutes and centers and the FDA have co-sponsored SCOR research on sex differences in such areas as: Neurocognition, Addiction, Musculoskeletal and Reproductive Organs/Female Urinary Tract infections.

To build on its successes, SCOR proposes to preserve and expand. Using its new moniker, the expanded SCORE will provide model educational resources for SABV training for every stage of the next generation of biomedical and behavioral researchers' careers. Each center will employ a scientific core for two or more cores that support multiple research projects.

SCORE will address Goals 1-5 of the FY 2019-2023 Trans-NIH Strategic Plan for Women's Health Research and become known as a national resource for research and SABV training on emerging scientific opportunities, as well as its studies on sex and gender factors that affect women's health. Three interrelated interdisciplinary and translational projects will support and work cooperatively with one another and NIH to capitalize on emerging scientific opportunities.

### **SCORE Discussion & Vote**

Dr. Jones wanted to know where the technology piece fits into the plan. She said some SCORE centers should be required to include a core on imaging technology, engineering, and IT professionals to reach populations in isolated communities that lack access to care. Dr. Hunter said it is up to the individual centers to decide what works best for them, but that SCORE's cooperative agreement could open opportunities for developing a technology core.

Dr. DeVries asked what sets SCORE apart from its predecessor. Dr. Hunter pointed to the career education core and cooperative agreement between the NIH and centers. She said there would also be new distinctions in the research/education and cooperative agreement between the NIH and centers and that at least 11 core SCORE programs would again be funded.

A Motion to move this concept forward was made by Amy Paller. The vote to move the concept forward was unanimous.

### **Understudied, Underrepresented, Underreported (U3) Populations FOA Presentation** *Victoria A. Cargill, M.S., MSCE Associate Director, Interdisciplinary Research, ORWH*

The purpose of the ongoing U3 Administrative Support FOA is to support interdisciplinary, transdisciplinary and multidisciplinary research on the effect of sex/gender influences at the intersection of social determinants of health. These determinants apply to: race/ethnicity, socioeconomic status, education, health literacy, common root cause of disparities and pathways for illness/disease manifestations at the individual, community, and national levels.

Research under the Administrative Supplement includes preclinical, clinical, behavioral and transitional studies linked to a one-year parent grant for addressing health disparities among women. The populations to be targeted are women who experience a disproportionate burden of illness but are understudied, underrepresented and underreported in biomedical research.

The U3 supplement reflects two guiding principles of the Strategic Plan for: (1) advancing vigorous research relevant to the health of women, and; (2) developing methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women.

Several U3 accomplishments involve collaborations with most institutes on infectious diseases, brain disorders and mental health conditions, such as post-partum depression. In May 2018, the U3 collaborated on a workshop with the Medical College of Virginia that focused on interdisciplinary, multidisciplinary and trans-disciplinary research and its role in women's health

research. Kathleen T. Brady, M.D., Ph.D., vice president for research at the Medical University of South Carolina. gave a keynote on opioid use in women and intersecting factors.

The FOA also led to the creation of the U3 Webinar series. The first in the series was held in February 2019 and featured Crista Johnson-Agbakwu, an obstetrician and gynecologist and Clinical Research Affiliate of the Southwest Interdisciplinary Center at Arizona State University. Dr. Johnson-Agbakwu has authored several evidence-based publications on genital mutilation and cutting and was a presenter.

U3 hopes to build on its successes by collaborating with a community of scientists that will participate in future webinars and workshops.

### **U3 Discussion & Vote**

Members offered wholehearted support for continuing the U3 program. Carolyn Mazure made a motion and Rachel Jones seconded. The motion to move this concept forward was unanimous.

### **Administrative Supplements For Research On Sex/Gender Differences (Admin Supps) FDA Presentation Rajeew K. Agarwal, PhD, Senior Program Officer, ORWH**

Reissuance of the Sex And Gender Administrative Supplement program was proposed based on the significant impact it has had on NIH institutes, centers and offices. ORWH has provided more than \$33 million in supplements to 343 investigators across 21 NIH institute centers and offices to spur exploratory research on sex and gender differences.

One-year administrative supplements to NIH-funded peer-reviewed grants have supported three types of research approaches on sex gender influences in human health and illness. The purpose of the administrative supplement program is to support research highlighting the impact of sex gender influences in human health and illness, including basic, preclinical, clinical, translational and behavioral histories. These activities meet one or more of the five goals of the 2019-2023 Trans-NIH Strategic Plan for Advancing Women's Health Research.

Since launching the Common Fund in 2014, ORWH has invested nearly \$4 million into supporting 18 investigators. In 2017, ORWH co-sponsored a Common Fund SABV workshop that focused on lessons learned from the grantees about innovative and unique sex differences research, challenges encountered, and SABV.

Keynote speaker Dr. Virginia Miller described the "*Sex Specific Risk for Cardiovascular Dysfunction and Cognitive Decline.*" Sessions covered animal research, gene expression and brain functions, and the influence of external effectors. The poster session was live video casted, recorded and archived. The workshop and other materials appear on the website.

### **Administrative Supplement Discussion & Vote**

Dr. Wood questioned building extra dollars into ongoing NIH projects to perform sex/gender analysis that should have been done as part of the process.. She said the NIH's Policy on the Inclusion of Women in Clinical Research requires all NIH-funded clinical research to elicit information about individuals of both sexes/genders as a biological variable and they should not be rewarded for not doing the work. Dr. Agarwal replied that the SABV Notice to include more

women in studies and identify sex and gender differences only took effect in January 2016 and does not cover grants in the process of noncompeting renewal.

Dr. McCarthy asked what metrics were used for determining the number of investigators that received the supplements and impact of expanding the research program for subsequent grant proposals. Dr. Agarwal said a clear-cut metrics for grant proposals, publications and major findings does not exist, so the program relied on submitted applications and their strategic plan goals and objectives instead. An analysis of the portfolio found that sex difference data supported by the supplements helped researchers to secure independent RO1 funding that is being incorporated into new applications.

Asked about messaging, Dr. Agarwal said the portfolio analysis was based on the application's planned goals and objectives. One constraint of this approach was that published manuscripts often disregard ORWH funding. Investigators mentioned that the administrative supplements sex difference data was used in subsequent proposals and helped secure the RO1 funding.

Several members credited the Admin Supps program with helping investigators to increasingly stumble on serendipitous findings and do secondary analyses they would not have been able to do on their own. One member said the ability to explore sex differences means that within five years, additional modular RO1 funding to pursue new leads will no longer be needed.

Another participant questioned the use of this mechanism as a carrot. She said the RFA should specify that unexpected findings on sex differences are a goal. If something exciting comes up and researchers want to pitch it, she would support giving them a little carrot to let them continue, but not just to get with the program to do what they should have done.

Dr. DeVries moved to advance the concept. The motion was seconded by Dr. Jones and the concept was unanimously approved.

### **Understudied, Underrepresented, Underreported (U3) FOA Presentation**

*Rebecca Delcarmen-Wiggins, Ph.D.*

Dr. DelCarmen-Wiggins said the initiative's primary objectives are to stimulate research on the influence of sex and gender and their intersection in health and disease. U3 will encourage investigator-initiated trans-disciplinary research on integrating sex and gender considerations into health and disease by incentivizing trans-disciplinary approaches, accelerating concept uptake and opening avenues to new discoveries for the health of women.

The FOA also promotes research that addresses strategic goal one, objectives 1.1-1.5 of the 2019-2023 Trans NIH Strategic Plan for Women's Health Research. It will also advances work that integrates sex and gender perspectives in emerging health science fields and translational research and technologies and new conceptual empirical research on women's health. It will leverage prior investments and big data to address sex differences; increase collaborative research partnerships on the differential effects of sex and gender; and intersectionality in women's health among the NIH institutes and centers.

### **New FOA Discussion & Vote**

A member asked whether the difference between U3 and the SCORE project is the mechanism itself or eligible populations. Dr. DelCarmen-Wiggins said the two concepts are distinct. The U3 would be the first cross-cutting project to study the intersection between sex and gender on the

health sciences and translational research. It will also increase collaborative partnerships with NIH institutes and offices to develop new studies on the differential effects of intersectionality in women's health. By contrast, SCORE is a cooperative agreement of several high-level, advanced research projects that have moved the field forward.

A motion on the floor to move this concept forward was made by Marcia Stefanick. Dr. DeVries seconded. The motion carried unanimously.

**Closing Remarks**

*Janine A. Clayton, M.D. and Elizabeth Spencer*

Dr. Clayton thanked everyone in attendance, both in person and by phone, for their thoughts and comments. She expressed appreciation to ACRWH participants for helping to move the concepts forward on a short turnaround and applauded the timely efforts of ORWH staff. Elizabeth Spencer announced that the next meeting will be held on April 10, 2019 and the dinner will take place on the evening of April 9, 2019. The meeting was adjourned at 5:12 pm.



Janine A. Clayton, M.D., Chair

4.3.19

Date



Elizabeth G. Spencer, Executive Secretary  
Executive Secretary

4.3.19

Date